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Abstracts accepted for presentation at ESMO 2017 as *Proffered Paper* (oral presentation), *Poster Discussion* and *Poster* will be published online on the ESMO website at 00:05 CEST on Thursday, 31 August 2017.

Late-breaking abstracts and abstracts selected for the *Programme* will be made public at 00:05 CEST (Local Swiss time) on the day of the official Congress session during which they are presented.

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19th National Congress of Medical Oncology
Rome, Italy

27–29 October 2017

Guest Editor:

Carmine Pinto
Director, Medical Oncology, IRCCS - S.Maria Nuova Hospital, Reggio Emilia, Italy
President, Italian Association of Medical Oncology (AIOM)
### guest editor letter

### board of directors

### abstracts

<table>
<thead>
<tr>
<th>Session</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plenary Session</td>
<td>vi1-vi2</td>
</tr>
<tr>
<td>Session A - Gastrointestinal (Colorectal) Cancers</td>
<td>vi3-vi16</td>
</tr>
<tr>
<td>Session B - Genitourinary Tumours</td>
<td>vi17-vi24</td>
</tr>
<tr>
<td>Session C - Breast Cancer</td>
<td>vi25-vi43</td>
</tr>
<tr>
<td>Session D - Gastrointestinal (non-Colorectal) Cancers</td>
<td>vi44-vi53</td>
</tr>
<tr>
<td>Session E - Thoracic Cancers</td>
<td>vi54-vi65</td>
</tr>
<tr>
<td>Session F - Sarcomas</td>
<td>vi66-vi67</td>
</tr>
<tr>
<td>Session G - Melanoma and Skin Cancers</td>
<td>vi68-vi69</td>
</tr>
<tr>
<td>Session H - Gynaecological Tumours</td>
<td>vi70-vi72</td>
</tr>
<tr>
<td>Session L - Head and Neck Tumours</td>
<td>vi73-vi74</td>
</tr>
<tr>
<td>Session M - Brain Tumours</td>
<td>vi75-vi77</td>
</tr>
<tr>
<td>Session N - Neuroendocrine Tumours</td>
<td>vi78</td>
</tr>
<tr>
<td>Session P - Prevention, screening and follow-up</td>
<td>vi79-vi81</td>
</tr>
<tr>
<td>Session R - Psychological and Psychosocial Aspects</td>
<td>vi82-vi88</td>
</tr>
<tr>
<td>Session S - Simultaneous Care</td>
<td>vi89-vi92</td>
</tr>
<tr>
<td>Session T - Miscellanea</td>
<td>vi93-vi101</td>
</tr>
<tr>
<td>Session U - Management of Cancer Pain</td>
<td>vi102-vi104</td>
</tr>
<tr>
<td>Session V - Oncology Nursing</td>
<td>vi105-vi112</td>
</tr>
<tr>
<td>Author index</td>
<td>vi113-vi125</td>
</tr>
</tbody>
</table>
Dear Colleagues,

On behalf of the Board of Directors and of the Scientific Committee, it is a great pleasure for me to introduce the proceedings of the XIX National Congress of our Association.

As usual, the abstracts have been published in a special issue of “Annals of Oncology”, the official Journal of ESMO. We continue to observe an increasing number of abstracts suggesting, once again, the presence of a widespread research activity in spite of the shortage of public funds and lack of interest of public authorities. We are pleased with the role of young oncologists. Many young oncologists are co-authors of the abstracts and several are first authors. This should be an encouragement for all of us: there is a present and also a future for AIOM.

As you can realize by reading this issue, all topics of medical oncology have been covered, including prevention, screening, translational research, simultaneous care, ethics and multidisciplinary approaches. They will be debated in several educational and scientific sessions co-organized with several other scientific societies. We would like to highlight that the multidisciplinary approach, including supportive and simultaneous care, is a relevant part of the program of the meeting. As medical oncologists, clinicians involved in the care of the patients, we have to keep in mind that “research” does not mean to forget the daily activity in the ward as well as the ability to answer the patients’ daily needs. Nevertheless, at the same time, we must remember that a research activity improves the care of cancer patients in our Units. The ability to conjugate these two aspects is the only way to improve the chance of cure for our patients.

Finally, I’d like to thank the Scientific Committee and all the reviewers for the invaluable work of the last months and I hope that all of you can enjoy the meeting and that it could be the occasion of sharing knowledge and experiences by providing an enrichment in our skills.
The Board of Directors for the years 2015-2017 includes:

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We are looking forward to seeing you in Rome.

Dott. Carmine Pinto
(President of the Congress)

This abstracts book will be available on-line and will also be freely available to subscribers to the following website from 6 November, 2017 (http://annonc.oupjournals.org)
FOLFOX4/XELOX in stage II–III colon cancer: early survival data of the Italian Three Or Six Colon Adjuvant (TOSCA) trial

A. Zanobetti,1 S. Lorandi,1 R. Labianca,1 M. Di Bartolomeo,2 G. Rosso,1 M. Ronzon,1 N. Pelle,1 M. Banzo,3 M.G. Zampino,4 F. Pasini,10 P. Marchetich11; L. Rimassa,2 E. Matelli1; P. Bidoli1,6; S. Cenini1; S. Barni2; L. Cuffreda2; G. Beretta,1 L. Frontini,6 E. Ruli,1 A. Sabatini1

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Background: Six months of oxaliplatin-based treatment has been the standard of care as adjuvant therapy for stage III colon cancer and an accepted option for high-risk stage II. Given the cumulative neurotoxicity associated to oxaliplatin, a shorter duration of therapy, if equally efficacious, would be advantageous for patients and Health Care Systems.

Methods: TOSCA was an open-label, phase III, multicenter, non-inferiority trial randomizing patients with high-risk stage II or stage III radically resected colon cancer to receive 3 months or 6 months of FOLFOX4/XELOX. Primary end-point was relapse-free survival.

Results: From June 2007 to March 2013, 3375 patients were accrued from 130 Italian sites, 64% receiving FOLFOX4 and 36% XELOX in either arm. Two thirds were stage III. At cut-off time for analysis the median time of follow-up was 62 months and 772 relapses or deaths and 466 deaths have been observed. At 8 years the RFS rate was 75% and the OS rate 80%. This analysis was done when 82% of the planned number of events was reached, with a power of 72% instead of 80%. The decision to anticipate the analysis was based on the participation to the IDEA joint collaborative analysis of studies sharing this clinical question. The Hazard ratio of the 3months vs 6 months for relapse/death was 1.14 (95%CI 0.99-1.31, p for non inferiority=0.056) and the confidence interval crossed the non inferiority limit of 1.20. The HR for survival was 1.07 (95% CI 0.89-1.29, p for non inferiority=0.23). 5yrs DFS was 90.0 with A, 88.0 with E and 89.4 with L (P=0.19). There were no unexpected findings on side-effects in schedule comparison. Few and small significant differences were observed comparing the AE more frequent gastrointestinal side-effects and less frequent hypercholesterolemia with E.

Conclusions: In the TOSCA trial there is no non-statistically significant DFS advantage for UP vs SEQ. No significant difference is evident among the three treatment groups. Supported by the FARM5K3MEE AIFA grant from the Italian Drug Agency.

Patients and methods: FATA-GIM3 is a multicenter, open label, 2x3 factorial phase 3 randomized study of adjuvant A, E and L upfront (UP - for years) or sequentially (SEQ - for 3 years after 2 years of T) in postmenopausal HR breast cancer pts. Two comparisons were planned: UP vs SE and A vs L. DFS (including local or distant relapse, second breast or non-breast cancer, DCIS and death, whichever came first) was the primary end-point; 2% at 3 yrs (corresponding to a HR of 0.79) was defined as the minimum difference required to declare superiority of UP vs SEQ. With two-tailed alpha 0.05, power 80%, 669 events and the enrolment of 3600 patients were planned. Following Data Monitoring Committee advice, final analysis was performed after 5yr median follow-up. For each comparison a Cox regression model was applied adjusted by stratification factors and stratified by the other treatment factor. Analyses were based on intention-to-treat.

Results: From 3/2007 to 7/2012, 3697 patients were enrolled at 76 centres. Median age 64, pT10 69.9%, pN0 64.3%, ER and PGR positive 88.9%, HER2 positive 8.9%, previous chemotherapy 38.3%. At 60 months median follow-up, 401 events were reported. 5yrs DFS was 89.8 with UP and 88.5 with SEQ (delta 1.32%, 95% CI 0.91-3.54; HR 0.89, 95% CI 0.75-1.08; P = 0.23). 5yrs DFS was 90.0 with A, 88.0 with L and 89.4 with L. (P = 0.19)

There were no unexpected findings on side-effects in schedule comparison. Few and small significant differences were observed comparing the AE more frequent gastrointestinal side-effects and less frequent hypercholesterolemia with E.

Conclusions: In the FATA-GIM3 trial there is no non-statistically significant DFS advantage for UP vs SEQ. No significant difference is evident among the three treatment groups. Supported by the FARM5K3MEE AIFA grant from the Italian Drug Agency.
Cisplatin in addition to single-agent first-line chemotherapy in elderly patients with advanced non-small-cell lung cancer (NSCLC): efficacy results of a joint analysis of the multicentre, randomized phase 3 MILES-3 and MILES-4 studies

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Background: The role of platinum in first line treatment of elderly patients with advanced NSCLC is still debated. We tested its efficacy in two parallel phase 3 trials.

Patients and methods: Advanced NSCLC patients, >70 years, ECOG performance status 0-1, were eligible. In MILES-3 patients with any tumor histology were randomly assigned 1:1 to cisplatin/gemcitabine (Cis 60 mg/m² d1, Gem 1000 mg/m² dd1,8) or gemcitabine (Gem 1200 mg/m² dd1,8). In MILES-4 patients with non-squamous histology were randomly assigned 1:1:1:1 to Cis, Gem, cisplatin/pemetrexed (Cis 60 mg/m² d1, Pem 500 mg/m² d1) or pemetrexed (Pem 500 mg/m² d1). Six cycles were planned. In each trial, to have 80% power in detecting a HR of death 0.75 (corresponding to 3-month prolongation of median survival), with 0.05 two-tailed α, 382 events were required. The trials were closed prematurely because of slow accrual, but a joint analysis allowed to properly perform the final analysis, according to IDMC advice. Analysis was based on intention-to-treat and adjusted by trial, histotype, companion drug, stage, PS, gender, age and size of centre.

Results: From Mar 2011 to Aug 2016, 531 patients (MILES-3: 299, MILES-4: 232) were assigned to Cis-doublet (n = 263) or single-agent chemotherapy (n = 268). Median age was 75, 79% were male, 70% had non-squamous histology. Median number of cycles was 4 and 3 with and without Cis, respectively. With a median follow-up of 2 years, 384 deaths and 448 progression-free survival (PFS) events were reported. With and without Cis, median OS was 9.6 vs 7.5 months (HR 0.86, 95% CI: 0.70-1.04, p = 0.14); median PFS was 4.6 vs 3.0 months (HR 0.76, 95% CI: 0.63-0.92, p = 0.005); objective response rate was 15.5% vs 8.5% (p = 0.02). Significantly more severe hematologic toxicity, fatigue and anorexia, were found with Cis. Toxic deaths were 3 (1.1%) and 2 (0.7%), with and without Cis. QoL was not improved with Cis in the joint analysis at the common time-points (cycles 1 and 2), but in MILES-4, with a longer time of observation (cycles 1 to 6), a significant prolongation of the time to global QOL deterioration (items 29/30) was found with Cis (HR 0.53, 95% CI: 0.29-0.97).

Conclusion: Addition of cisplatin to single-agent chemotherapy does not significantly prolong overall survival of elderly patients with advanced NSCLC. However, there is significant improvement in PFS, response rate and time to global QoL deterioration. Partially supported by AIFA (grant FARM8KAJZK) and Eli Lilly.

addenda
Annals of Oncology

2 Plenary session | Volume 28 | Supplement 6 | October 2017

4 Cisplatin in addition to single-agent first-line chemotherapy in elderly patients with advanced non-small-cell lung cancer (NSCLC): efficacy results of a joint analysis of the multicentre, randomized phase 3 MILES-3 and MILES-4 studies

A. Morabito1, L. Cavanna2, A. Lucioni3, P. Maione4, L. Bonanno5, E. Piazza6, S. Leo7, S. Cinieri8, F. Morgillo9, M.A. Burgio10, A. Giudice11, M. D’Alessandro12, M. Costanzo1, C. Sandomenico1, G. Daniele13, S. Signoriello14, C. Gallo15, F. Perrone14, C. Gridelli14

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Conclusion: Addition of cisplatin to single-agent chemotherapy does not significantly prolong overall survival of elderly patients with advanced NSCLC. However, there is significant improvement in PFS, response rate and time to global QoL deterioration. Partially supported by AIFA (grant FARM8KAJZK) and Eli Lilly.
A1** Does bevacizumab plus chemotherapy matter in metastatic colorectal cancer patients with mucinous histology? A multicenter, retrospective analysis on 685 patients

V. Catalano1, F. Bergamo2, C. Cremolini3, B. Vincenzo2, F. Negri2, F. Gazzano2, P. Giordani2, A. Alessandroni2, R. Intini2, L. Rumian2, D. Bosini2, D. Santini2, D. Sarti2, M.B. Rocchi2, S. Lornard3, A. Falcone2, V. Zagone3, R. Matullo1
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Background: In metastatic colorectal cancer (MCRC), mucinous histology has been associated with poor response rate and prognosis (Catalano et al, BJC 2009). We investigated whether bevacizumab (B) combined with different chemotherapy regimens may impact on clinical outcomes of MCRC patients (pts) with mucinous histology.

Patients and methods: The study population included 685 MCRC pts (accrual from 10/07 to 2/16) who were treated with B plus chemotherapy (FP-based: capecitabine/ docetaxel; OXA-based: FOLFOXELX; IRX-based: FOLFIriXE; FOLFOXI). Pts were classified according to the histology in mucinous adenocarcinoma (MC) and non-mucinous adenocarcinomas (AC). Prognostic factors associated with overall survival (OS) were identified using univariate and multivariate Cox proportional hazards analyses.

Results: Ninety-four (13.7%) pts had MC, male/female 401/284, median age 64 years (range, 25-86). Pts received the following regimens: B + IRX-based (MCAC=43/262), B + OXA-based (MCAC=18/159), B + FOLFOXI (MCAC=29/119), or B + FP-based (MCAC 4/39) regimens. More pts in the MC group had at least one metastatic site of disease (60.6% vs 52.3%; p = 0.001), whereas pts in the AC group had at least three metastatic sites (70.1% versus 55.3%; p = 0.02). The overall response rates for MC and AC were 41.5% (95% CI, 31.5-51.4) and 62.4% (95% CI, 58.4-66.6), respectively (chi-test, p = 0.003). With a median follow-up of 50 months, median OS for the MC pts was 28.2 months compared with 27.7 months in the AC group (HR = 0.92, CI 95%, 0.70-1.18; p = 0.50). According to the first-line regimens, pts with MC treated with first-line B+OXA-based regimens had lower OS than AC pts (15.9 vs 26.1 months; HR = 0.51, 95% CI, 0.19-0.84; p = 0.015). No significant differences in OS were found with B+IRX-based (median OS, MC 32.7 vs AC 29.9; months, p = 0.73) and B+FOLFOXI (median OS, MC 32.7 vs AC 28.4; months, p = 0.54). After correcting for significant prognostic factors by multivariate Cox regression analysis, age (HR = 1.02, 95% CI, 1.01-1.03; p < 0.0001), resection of the primary tumor (HR = 1.15, 95% CI, 1.23-1.95; p < 0.0001), and number of metastatic sites (HR = 1.41; 95% CI, 1.15-1.73; p = 0.001) were found to be associated with poorer OS.

Conclusions: Pts with mucinous histology may benefit from the addition of bevacizumab to chemotherapy. FOLFOX and XELOX regimens may not represent the optimal first-line regimens, pts with MC treated with first-line B+OXA-based regimens had lower OS than AC pts (15.9 vs 26.1 months; HR = 0.51, 95% CI, 0.19-0.84; p = 0.015).

A2 Combination of nivolumab (nivo) + ipilimumab (ipi) in the treatment of patients (pts) with deficient mismatch repair (dMMR)/microsatellite instability (MSI-H) metastatic colorectal cancer (mCRC): CheckMate 142 Study

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Background: In metastatic colorectal cancer patients who progressed on or were intolerant of first-line therapy, nivolumab (nivo) and ipilimumab (ipi) showed manageable safety and activity characterized by a high DCR and encouraging survival benefit.

Patients and methods: CheckMate 142 was a non-inferiority phase III study conducted in high-risk stage II and stage III colorectal cancer patients treated with 6 or 3 months of FOLFOX-4 or XELOX adjuvant chemotherapy. We investigated 17 high-risk colorectal cancer patients treated with 6 or 3 months of FOLFOX-4 or XELOX adjuvant chemotherapy.

Results: All 17 pts were evaluable. The primary tumor (HR = 1.02, 95% CI, 1.01-1.03; p < 0.0001), resection of the primary tumor (HR = 1.15, 95% CI, 1.23-1.95; p < 0.0001), and number of metastatic sites (HR = 1.41; 95% CI, 1.15-1.73; p = 0.001) were found to be associated with poorer OS.

Conclusions: Pts with mucinous histology may benefit from the addition of bevacizumab to chemotherapy. FOLFOX and XELOX regimens may not represent the optimal first-line regimens, pts with MC treated with first-line B+OXA-based regimens had lower OS than AC pts (15.9 vs 26.1 months; HR = 0.51, 95% CI, 0.19-0.84; p = 0.015).

A3 Germline variants and clinical outcomes of high-risk stage II and stage III colon cancer patients treated with oxaliplatin and fluorpyrimidines adjuvant chemotherapy: a pharmacogenetic ancillary study to TOSCA trial

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Background: Functional germline variants (SNPs) may characterize sub-populations of cancer patients who gain different benefits from chemotherapy. We investigated 17 SNPs in 11 genes with putative impact on sensitivity to fluoropyrimidines and oxapilatin (TS, MTHFR, ERCC1, XPC, XRCC1, XRCC6, GSTP, GSTT1, ABCC1, ABCG2). Material and methods: TOSCA was a non-profit, Italian, multicentre, randomized, non-inferiority phase III study conducted in high-risk stage II and stage III colorectal cancer patients treated with 6 or 3 months of FOLFOX-4 or XELOX adjuvant chemotherapy. Patients who signed the informed consent were prospectively accrued in this ancillary study.

Results: From July 2007 to October 2011, 524 patients were enrolled in this study. Eight patients were excluded from analysis due to major violation and 4 never started treatment. 185 and 188 patients were treated with FOLFOX-4, 68 and 71 with XELOX in 6-month and in 3-month arm, respectively. Allele frequencies of all SNPs were
consistent with Hardy-Weinberg equilibrium. 82(16%) progression and 71(14%) deaths were observed. Progression or deaths occurred in 106(21%) patients. The XRCII rs25487 G>A shortened significantly RFS (adjusted HR [AA vs GG] 2.02; 95%CI 1.15–3.56; p = 0.015) and OS (adjusted HR [AA vs GG] 3.07; 95%CI 1.57–5.99; p = 0.001). Interactions between SNPs and treatment duration were detected. In detail, 3-month treatment was correlated with a shorter RFS for patients with G allele in XRCC1 rs13181 T>G and for patients with CC genotype (vs TC+TT) in ERCII rs16175 T>C. A better RFS and OS were identified in patients treated for 3 months with GG genotype for ABC2 rs4183586 A>G. Finally, the GG genotype in ABC2C rs1885304G>A increased OS in patients treated with 3 months treatment.

Conclusions: XRCC1 rs25487 G>A produced remarkable differences in RFS and OS in the studied population. Additional functional germline variants involved in the DNA repair pathways may engage a clinical impact according to the duration of the adjuvant chemotherapy program. These findings may impact on the overall chemotherapy treatment strategy of colon cancer patients. Additional prospective studies are warranted for confirming this associations and after adjustment for tumor-related prognostic factors.

A4 Dissecting primary resistance to anti-EGFRs in RAS and BRAF wt metastatic colorectal cancer (mCRC): A case-control study

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Background: Almost half of RAS and BRAF wt mCRC patients do not respond to anti-EGFRs. Different molecular alterations suggested as predictors of primary resistance have not been validated.

Material and methods: We conducted a case-control study to prospectively demonstrate the negative predictive impact of HER-2 amplification or mutations, MET amplification, NTRK/RAS/ROS1/ALK/RET rearrangements, and mutations activating MAPKs or PI3K/Akt axis. Patients with RAS and BRAF wt mCRC clearly resistant (cases) vs. clearly sensitive (controls) to anti-EGFRs were selected. Hypothesizing a prevalence of candidate alterations of 0% and 15% among controls and cases, respectively, 47 cases and 47 controls were needed to be able to reject the null hypothesis of equally prevalent candidate alterations of 0% and 15% among controls and cases, respectively. 47 cases and 47 controls were included. Primary endpoint was met: mentioned alterations were reported in 20 (42.6%) cases and 1 (2.1%) control (p < 0.001).

Results: Fourty seven cases and 47 controls were included. Primary endpoint was met: mentioned alterations were reported in 20 (42.6%) cases and 1 (2.1%) control (p < 0.001). Additionally, 5% of controls presented at low allelic frequency, MSI-high was significantly more frequent among resistant than sensitive patients (17% vs 0%, p < 0.001).

Conclusions: This is the first prospective demonstration that the combined assessment of these rare alterations allows to better select patients for anti-EGFRs, while opening the way to other tailored therapies.

A5 Circulating angiogenesis-related markers as predictors of benefit from regorafenib in metastatic colorectal cancer (mCRC) patients (pts)

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Background: Regorafenib is a treatment option for refractory mCRC pts. Considering its limited clinical benefit and the extremely palliative setting, patients’ selection is essential to optimize the cost-effectiveness balance. The aims of this study were to describe the modulation of selected circulating angiogenic factors by the treatment with regorafenib and to investigate their correlation with clinical outcome.

Methods: IL-8, Ang-2, PDGF, IGF2, Tie-2, vEGFRII, vEGFRII, PIGF, VEGF-A, VEGF-B were assessed by ELISA on plasma samples collected at baseline (d1), after 15 days of treatment (d15), at the best RECIST response (resp), and at the time disease progression (PD) in a cohort of mCRC pts treated with regorafenib, as per indication. Comparisons among concentrations of each marker at different time points were performed by using the Wilcoxon test. Markers showing significant changes were analyzed to identify correlations with outcome.

Results: One hundred and five pts were included. Median PFS and OS were 2.1 and 7.0 months (mos), respectively. As compared to d1, IL-8 and Ang-2 levels increased at PD. An early decrease at d15 was observed for PDGF, Tie-2, vEGFRII and VEGFRII levels, followed by an increase at PD. Conversely, PIGF levels increased at d15 and then decreased at PD. Baseline levels of Ang-2 and Tie-2 below the median value were associated with longer PFS (HR 0.61 [95%CI 0.37-0.81]; p = 0.006, HR 0.69 [95%CI 0.43-0.95], p = 0.04, respectively) and OS (HR 0.45 [95%CI 0.26-0.76]; p < 0.0001, HR 0.68 [95%CI 0.44-0.98]; p = 0.04, respectively). With regard to Ang-2, 40 (45%) out of 89 pts with available plasma samples at d15 showed increased levels at d15 as compared to d1. Among them, 21 (53%) achieved disease control, as compared to 14 out of 49 (29%) pts with Ang-2 decreased levels (p = 0.03). Median PFS of pts with increased and decreased Ang-2 levels were 3.1 and 1.8 mos, respectively (HR 0.57 [95%CI 0.33-0.78], p = 0.004).

Conclusions: A dynamic modulation of plasma angiogenic factors occurs during the treatment with regorafenib. Low baseline Ang-2 and Tie-2 levels seem to be associated with good prognosis. The early modulation of Ang-2 levels may predict benefit from regorafenib. Since Ang-2, as an inhibitory ligand of Tie-2 receptor, promotes tumor angiogenesis, it is conceivable that the successful Tie-2 inhibition by regorafenib might lead to a compensatory increase in Ang-2 and correlate with anti-tumor activity. These results need validation in independent series.

Table: A4

<table>
<thead>
<tr>
<th>Molecular alteration</th>
<th>Cases (Resistant patients) N = 47</th>
<th>Controls (Sensitive patients) N = 47</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER-2 amplification</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>HER-2 mutations</td>
<td>1 (G776V, exon 20)</td>
<td>0</td>
</tr>
<tr>
<td>MET amplification</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>NTRK rearrangements</td>
<td>2 (SCYL3-NTRK1 and TPM3-NTRK1)</td>
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<tr>
<td>ALK rearrangements</td>
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<td>0</td>
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<tr>
<td>ROS1 rearrangements</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>RET rearrangements</td>
<td>1 (CCDC66-RET)</td>
<td>0</td>
</tr>
<tr>
<td>PIK3CA mutations in exon 20</td>
<td>1 (A1035V, exon 20)</td>
<td>1 (H1047R, exon 20)</td>
</tr>
<tr>
<td>AKT1 mut</td>
<td>1 (R25C)</td>
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</tr>
<tr>
<td>PTEN mutations</td>
<td>3 (L247S, R23stop and del P248, exon 7)</td>
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</tr>
<tr>
<td><strong>Total n. of patients with candidate alterations</strong></td>
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<td>1</td>
</tr>
<tr>
<td>Microsatellite instability (MSI-high)</td>
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<td>0</td>
</tr>
<tr>
<td>RAS mutations at low allele fraction*</td>
<td>3 (KRAS G12V, exon 2, 6%, NRAS Q61R, exon 3, 10%, KRAS Q61H)</td>
<td>0</td>
</tr>
</tbody>
</table>

*by Hotspot Cancer Panel v2, (Life Technologies®), previously found wt by pyrosequencing

Annals of Oncology
Background: While in the advanced setting right colon cancer is associated with a worse outcome, this negative prognostic effect has not been definitively demonstrated in the adjuvant setting. We have analyzed the outcome data from 3 large randomized trials (SITAC-1; SMAC and TOSCA) assessing adjuvant therapy in colon cancer patients with stage II and III.

Methods: In order to define the prognostic effect of sidedness we assessed three randomized trials of adjuvant therapy (SITAC-SFUFA vs control, 821 patients; SMAC, intraportal FU vs SFUFA, 990 patients; TOSCA, FOLFOX vs XELOX three vs six months 3531 patients) carried out in Italy from 1987 to 2013 and including 5324 patients. Survival and disease-free survival, overall and in each trial, were analyzed according to right, transversal and left colon location. Right-sided was considered cancer to hepatic flexure, left-sided splenic flexure to rectum and transversal hepatic to splenic flexure. Statistical analysis considered all randomized patients according to allocation arm, with available data on putative prognostic factors. Analysis was planned in order to provide overall and by stage results.

Results: 5324 patients were included in this analysis, 2490 patients were males and 2834 females. Median age was 64 years. 2240 patients had a stage II colon cancer and 3084 a stage III. Right tumors were 1573 (30%), transversal 822 (15%) and left 2929 (55%). Patients characteristics were well balanced among the three trials. In all the 5324 patients DFS was not affected by tumor location (right colon versus left, HR = 1.01; 95% CI = 0.89-1.15) while right tumor was associated to a worse OS compared to left tumor (HR = 1.21; 95% CI = 1.05-1.40).

In stage II patients there was no difference in terms of DFS and OS among the three different tumor location while in stage III patients, right colon cancer had a worse outcome compared to middle and left colon location (HR = 1.37 95% CI = 1.16-1.64, p < 0.001).

Conclusions: This is the largest analysis demonstrating the prognostic effect of tumor location in colon cancer patients receiving adjuvant chemotherapy. The effect however is present only in stage III but not in stage II colon cancer.

A8 Optimization of the combination of bevacizumab with FOLFOX/XELOX in patients with metastatic colorectal cancer (mCRC): the multicentre, randomized phase 3 study OBELOS

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Background: Bevacizumab is a humanized anti-vascular endothelial growth factor (VEGF) monoclonal antibody, approved in combination with chemotherapy in the treatment of mCRC. It is proposed that the schedule of administration might be critical and that anticipating bevacizumab to chemotherapy, might improve treatment efficacy.

Methods: mCRC patients, ≥ 75 years old, ECOG PS ≤ 1, having received no more than one previous treatment, with at least one measurable lesion according to RECIST, were randomized (1:1) to receive standard administration of bevacizumab (5mg/kg d1 Q14) with chemotherapy (mFOLFOX6 regimen for 12 cycles) vs experimental bevacizumab given 4 days before chemotherapy (same dose), at each cycle. Patients could receive maintenance bevacizumab (7.5 mg/kg d1 Q21) until disease progression or unacceptable toxicity in both arms. Primary end point was the objective response rate (ORR). With 80% power and 2-tailed alpha 0.05, an expected 20% increase in response rate, 230 patients were planned. With 163 events, the study also had 80% power to detect a hazard ratio (HR) 0.64 of progression-free survival (PFS). Analyses were based on intention to treat.

Results: From May 2012 to Dec 2015, 230 patients were randomised to experimental (n = 115) and standard (n = 115) arm. Median age was 62 (IQR range 53–68), 79% were PS 0/1, 93% were pretreated, 53% had a single metastatic site, 54% were RAS-mutant (47% and 62% in the standard and experimental arm, respectively). ORR was 54% in both arms (p = 0.89). With a median follow-up of 32.4 months, 204 PFS events and 131 deaths were reported. Median PFS was 11.7 and 10.5 months (HR 0.79; 95% CI: 0.60–1.05; multivariate adjusted p = 0.10) and median OS was 32.7 and 29.9 months (HR 0.73; 95% CI: 0.52–1.04; multivariate adjusted p = 0.08), in the standard and experimental arm, respectively. 37.4% and 59.1% of the patient received at least one following treatment in the standard and experimental arm, respectively.

Conclusion: Anticipating bevacizumab to chemotherapy produced a not statistically significant prolongation of PFS and OS. Objective response rate was not improved. Supported by the Italian Ministry of Health. CT.gov NCT01718873.
A9 Histopathological response and growth patterns of colorectal cancer liver metastases (CRCLM) in patients treated with triplets plus bevacizumab (bev) or anti-EGFRs

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Abstract: The histopathological response to pre-operative chemotherapy is associated with clinical characteristics and to investigate the prognostic role of HGPs and their potential sensitivity to targeted agents.

Methods: Histopathological parameters of response were evaluated in specimens from 159 pts who underwent a de novo resection of CRCLM, after resection by neoadjuvant (FOLFOXIRI or COI) or bev (N = 103) or anti-EGFR (N = 56) in 5 first-line clinical studies (TRIBE, MUMA, MACBETH, COI-B and COI-E). The aims of this analysis were to evaluate the prognostic role of histopathologic response and to explore its association with clinical characteristics, and to investigate the prognostic role of HGPs and their potential sensitivity to targeted agents.

Results: When compared with partial (TRG 3) and no (TRG 4-5) pathologic response (57% vs 17% in pushing and 22% in replacement HGPs, p < 0.01), significant differences were found in both major response and DFS between group A vs B (4 yrs DFS rate: 73.2% vs 72.2%, p = 0.920).

Conclusion: This study suggests delaying surgery beyond 13th week after the end of CRT seemed to result in the highest chance of a pCR and probably in downstaging, in fact to recent published data. The delayed surgery would seem to select a greater number of good responders. Obviously prospective randomized studies of appropriate statistical power comparing various time intervals are needed to examine the optimal timing for surgery and to plan the better management of these setting of patients.

A10 Longer intervals after neoadjuvant therapy in locally advanced rectal cancer: a monocentric experience

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Abstract: No data are available in the literature on the timing of surgery after neoadjuvant CRT for LARC. In the present study we retrospectively evaluated the intervals between the end of CRT and surgery in order to identify the influence of delayed surgery on local control and survival rates.

Results: Out of 159 patients who underwent surgery after neoadjuvant CRT for LARC, 159 pts were enrolled in the present study. The median time from end of CRT to surgery was 13 weeks (range 5–18). Patients were divided in 2 groups based on time to surgery: <13 weeks (group A = 52 pts) and ≥13 weeks (group B = 58 pts). Statistical analysis for DFS and OS rates were calculated with Kaplan Meier nonparametric estimation from date of surgery.

Conclusion: The mean age of patients was 64 years (range: 36–84). pCR was observed in 22.7% (n = 25/110 pts). pCR in group A was 19.2% (n = 10/52 pts) and 25.8% (15/58) in group B with statistically significant difference (p < 0.001). Good responders (Dworak TRG (3)) in group A were 59.6% vs 43.7% in group B. Bad responders (Dworak TRG > 3) in group A were 60.4% vs 54.3% in group B. At this time disease-free survival rates in overall population was 90.3%, 85.2% respectively at 3 and 5 years and overall survival was 77.6%, 72.9% at 3 and 5 years. There was no statistically significant difference in DFS between group A vs group B (4 yrs DFS rate: 73.2% vs 72.2%, p = 0.920).

A11 Cost-effectiveness of anti-angiogenic agents in second-line treatment of metastatic colorectal cancer. Integrating the EUROPEAN Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) with the costs of drugs

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1U.O.C. di Oncologia Medica - Dipartimento di Oncologia - Ospedale Mater Salutis - Az. ULS S. Scaligera, Legnago (VR)

Abstract: In western Countries, colorectal cancer (CRC) is the second most common cause of death from cancer. In particular, the introduction of active new anti-angiogenic agents for the second-line treatment of metastatic CRC (mCRC) is associated with a relevant increase of costs and it is therefore important to make a balance between the costs of treatment and the added value represented by the improvement of the clinical parameters of interest such as progression free survival (PFS).

Materials and methods: The analysis was conducted to assess the effect of second-line therapy with anti-angiogenic agents on the PFS and was restricted to pivotal phase III randomized controlled trials (RCTs). We calculated the pharmacological costs necessary to get the benefit in PFS, for each trial. Calculations were based on an “ideal patient” (RBA 1.8 sqm, weight 70 Kg). The costs of drugs are at the Pharmacy of our Hospital and are expressed in €/month, average price in Italy. The use of the ESMO-MCBS was calculated using the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) to the above pivotal phase III RCTs.

Results: The present study evaluated 4 phase III RCTs, including 3938 patients. PFS ranged from 2.7 months of bevacuzumab alone in the E3200 trial to 7.3 months of the combination of FOLFOLX and bevacuzumab in the same trial. ESMO-MCBS reached medium score for VELOUR trial and low grade scores (grade 1 and 2) for RAISE, TML and E3200 trials, respectively. Dividing the costs of therapy by the measure of efficacy represented by PFS we found out that the lowest cost per month of PFS gained (4581 €) was associated with the use of FOLFOX plus bevacuzumab; the highest cost per month of PFS gained (23827 €) was associated with the use of FOLFOLX plus ramucuzumab.

Conclusions: Combining pharmacological costs of drugs with the measure of efficacy represented by the PFS, aflibercept in combination with FOLFOX is a cost-effective second-line treatment for patients with mCRC. The lack of correlation between PFS and OS is a well known phenomenon with the clinical use of anti-angiogenic treatment and reinforces the importance of the evaluation of PFS as a strong endpoint, even on a pharmaco-economic perspective.

A12 RET rearrangements define an uncommon molecular subtype of metastatic colorectal cancer (mCRC)

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Abstract: RET fusions occur in <1% of CRCs and represent new therapeutic targets, as indicated by earlier promising case reports of patients (pts) treated with tyrosine kinase inhibitors. Although the features of mCRCs harboring ALK, ROS1 and NTRK fusions were recently elucidated, the clinical and molecular landscape of RET rear- ranged mCRC is still largely unknown.

Methods: pts with mCRC harboring RET fusions were identified worldwide taking advantage of 1) previously published molecular case reports; 2) Italian and Korean screening collaborations; 3) Ignyta’s phase 1 trial of RXDX-105 (NCT01877811); 4) Foundation Medicine Database. Clinical and molecular characteristics of RET...
rearranged cases were compared with non-rearranged ones screened at 3 referral Centers in Milan, Paris, and Seoul.

Results: 22 RET rearranged (12 NCOA4-RET, 7 CCDC6-RET, 2 TRIM24-RET and 1 TNNIP1-RET) and 236 not rearranged mCRC pts were included. Rearrangements were more frequent in older pts (p = 0.027), with right sided primary tumors (p < 0.028), RET wild-type (p = 0.001), BRAF wild-type (p = 0.001) and MSI-high (p < 0.001). RET fusions were found in RET and BRAF wild-type tumors and, in 43% of cases, in MSI-high ones. At a median follow-up of 31.5 months, pts bearing RET rearranged tumors had a shorter overall survival (OS) when compared to non-rearranged (HR: 4.81, 95% CI 3.56-6.47; p < 0.001). In the multivariable model including other significant variables (primary tumor resection and location, RET, BRAF and MMNR status), RET rearrangements remained significant associated with shorter OS (HR: 2.82, 95% CI 1.98-3.94; p < 0.001). A RET fusion positive PDx will be presented.

Conclusions: RET rearrangements define a new and rare molecular subtype of mCRCs associated with unfavorable prognosis, and specific clinicopathological and molecular features. The present results in RET rearranged mCRC resemble those previously reported for ALK, ROS1 and NTRK positive ones. Since sensitivity to available treatment options including anti-EGFRs may be very limited, RET specific inhibitors including RET fusion positive PDx will be presented.

A13 Affibber efficacy according to sidedness, RAS and BRAF mutations.

Findings from the VELOUR trial in second line therapy of advanced colorectal cancer patients

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Background: Addition of (ziv)-aflibercept (A) to FOLFIRI in second-line therapy for mCRC patients (pts) is chemotherapy (CT) combined with anti-EGFR or anti-VEGF drugs. Several studies have been conducted to evaluate which is the best choice, without conclusive results. In this retrospective analysis we assessed whether the size of metastatic involvement (evaluated by the diameter of the greatest metastasis), could be related to different activity between the two drugs.

Patients and methods: We included RET rearranged tumors had a shorter overall survival (OS) when compared to non-rearranged (HR: 4.81, 95% CI 3.56-6.47; p < 0.001). A RET fusion positive PDx will be presented.

Table: A13

<table>
<thead>
<tr>
<th>Mutation Status</th>
<th>Med OS</th>
<th>FOLFIRI</th>
<th>HR (95% CI)</th>
<th>Interaction (ratio of HR, 95% CI, p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>KRAS wt</td>
<td>281 116 149</td>
<td>0.074 (0.56-0.99)</td>
<td>1.21 (0.79-1.86)</td>
<td>0.091</td>
</tr>
<tr>
<td>KRAS mut</td>
<td>201 106 126</td>
<td>0.090 (0.65-1.24)</td>
<td>0.38</td>
<td></td>
</tr>
<tr>
<td>EXT-RAS wt</td>
<td>218 117 160</td>
<td>0.139 (0.90-2.13)</td>
<td>0.80</td>
<td></td>
</tr>
<tr>
<td>EXT-RAS mut</td>
<td>264 112 126</td>
<td>0.93 (0.70-1.23)</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td>BRAF wt</td>
<td>446 124 130</td>
<td>0.49 (0.22-1.09)</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>BRAF mut</td>
<td>36 5.5 10.3</td>
<td>0.042 (0.16-1.09)</td>
<td>0.08</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: This is the only study that evaluated the impact of RAS, BRAF and sidedness of an anti-angiogenic drug in the second line of mCRC. Lack of significant interaction between mutation status and sidedness suggests that Affibber seems to have a specific effect on BRAF mutated tumors. Soafib supported this ISS. Clinical trial information: NCT01754272.
Eph A2 levels were significantly associated with a worse PFS and an overall good correlation in PD-L1 staining between tumor cells from the different regions of interest was demonstrated. Between April 2007 and April 2015, 87 patients with biopsy-proven metastatic colorectal cancer (mCRC) were enrolled. The median age at the time of diagnosis of metastatic disease was 64 years. Up to now, published studies have failed to demonstrate a predictive role of PD-L1 in clinical trials. Between TM and IM was 72% (2 out of 6 TM positive were also IM positive). The rate of concordance between TP and IP was 76% (all TP positive were IP negative), and between IP and IM was 74% (4/9 IP were also IM positive; 3 liver and 1 lung). Conclusions: An overall good correlation in PD-L1 staining between tumor cells from primitive tumor samples and therapy activity is tested on dimensional variation of met, we thought it of interest to study the correspondence of PD-L1 expression in a matched series of primitive and surgically resected met tumors.

Patients and methods: PD-L1 immunostaining of matched primary tumor (TP) and metastatic (TM) samples from 30 mCRC pts retrospectively selected were obtained. Positivity was defined as moderate/intense membrane staining in at least 1% of tumor cells. Tumor infiltrate of primitive (IP) and TM was also evaluated and graded according to the number of positive lymphocytes surrounding tumors (0: < 1%, 1: 1-4%, 2: 5-9%, 3: > 10%). Positivity was defined as 2. Results: Tumor sites were (right/left/rectum): 17/20/3, Met were (liver/lung, other abdominal): 26/15/9, 3/50 TP (all right-sided) and 6/50 TM (3 liver and 3 lung) were positive. PD-L1 was more frequently positive in IM of lung than liver (47% vs 19%, p = 0.06). The rate of concordance between TP and IP was 76% (all TP positive were IP negative), and between TM and IM was 72% (2 out of 6 TM positive were also IM positive). The rate of concordance between TP and TM was 86% (23/25 positive were also TM positive), and between IP and IM was 74% (4/9 IP were also IM positive;3 lung, 1 liver).

Conclusions: Overall there are some predictive biomarkers of the development of metastatic colorectal cancer. However, the low number of positive samples prevents any definitive conclusion. For this reason a confirmatory analysis in a second cohort of patients from another institution is ongoing and data from the two cohorts will be presented.

Efficacy of anti-EGFR antibodies combined with chemotherapy for elderly patients with RAS wild-type metastatic colorectal cancer: a systematic review and meta-analysis


Background: The incidence of Colorectal Cancer (CRC) increases with age, reaching a peak around 70-75 years. The anti-EGFR monoclonal antibodies combined with chemotherapy represent a valid option in patients with RAS wild-type (wt) metastatic CRC (mCRC), allowing for a significant improvement in survival. However, few data are available in literature regarding the clinical value of these drugs in the elderly population. The aim of the study is to evaluate the efficacy of adding anti-EGFR monoclonal antibodies (Cetuximab or Panitumumab) to chemotherapy in the treatment of RAS wt mCRC older patients.

A systematic review of the published data using PubMed and EMBASE databases and the congress documents of the main national and international symposia was performed. The random effect model was used to combine the effect estimates, the F and Cochran’s Q index to quantify the between-study heterogeneity unexplained by sampling error.

Four randomized trials (two for Cetuximab and two for Panitumumab) have been selected among the 2765 initially identified studies. None of the studies had been specifically designed for the elderly population, so DFS and OS HR values were extracted from pre-specified subgroup analyses. In our meta-analysis, 605 elderly patients have been included, 289 patients treated with chemotherapy only and 316 patients with chemotherapy in combination with an anti-EGFR antibody. The meta-analysis showed a statistically significant benefit of the combination of chemotherapy and anti-EGFR against chemotherapy alone both in terms of DFS (HR 0.79, IC 95%: 0.64-0.98, p = 0.038, OR = 2.3, 95% IC 1.1-4.7, p = 0.019) and OS (HR 0.82, IC 95%: 0.68-0.98, p = 0.032, Q = 0.57, df = 3, I² = 0%). The meta-analysis of the Panitumumab studies reached statistical significance for OS and not for DFS, while none of the two for Cetuximab was significant. Sensitivity analysis confirmed the results obtained.

The addition of Cetuximab or Panitumumab to chemotherapy in elderly patients with RASwt mCRC could represent a therapeutic option in terms of efficacy. However, the available data in this subset of patients are limited. Dedicated studies are needed in order to determine the best therapeutic strategy.

Conclusions: Image-guided IMRT with a SIB approach concomitant to 5-FU/MMC based chemotherapy is a safe and well tolerated treatment strategy in an unselected anal cancer patient population.

A18

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The addition of Cetuximab or Panitumumab to chemotherapy in elderly patients with RASwt mCRC could represent a therapeutic option in terms of efficacy. However, the available data in this subset of patients are limited. Dedicated studies are needed in order to determine the best therapeutic strategy.
isolated lung metastases predicted for significant better S. At multivariate analysis, only peritoneal carcinomatosis (HR = 1.98; p < 0.0001) and surgery of metastases (HR = 0.276; p < 0.0005) independently affect S.

Conclusions: The proportion of treated patients significantly drops from first-line to forth-line. Inoperable site of metastasis and surgery of metastases are the most important prognostic factors in mCRC pts.

A20 Rechallenge with cetuximab (cet) + irinotecan (iri) in 3rd-line in RAS and BRAF wt metastatic colorectal cancer (mCRC) patients (pts) with acquired resistance to 1st-line cet + iri: the phase II CRICKET study by GONO

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1Università Campus Bio-Medico, Rome; 2 Polo Oncologico, Azienda Ospedaliero Universitaria Pisana, Istituto Toscana Tumori, Università di Pisa, Pisa; 3I.D.C. di Oncologia, Edificio Sud di Pisa, Policlinico G.BRossi, A.U.U. di Verona, Verona; 4Unità di Oncologia Medica I, Dipartimento di Oncologia Clinica e Sperimentale, Istituto Oncologico Veneto, IRCCS, Padua; 5Azienda Ospedaliero-Universitaria Santa Maria della Misericordia, Udine; 6Unità di Oncologia Medica I, Dipartimento di Oncologia Clinica e Sperimentale, Istituto Oncologico Veneto, IRCCS, Udine; 7Dipartimento di Oncologia, AUSL Romagna, Rimini; 8Ospedale San Giovanni Calibita Fatebenefratelli, Rome; 9Unità di Farmacologia Clinica e Farmacogenetica, Dipartimento di Medicina Clinica e Sperimentale, Università di Pisa, Pisa

Background: Clinical benefit from rechallenge with cet-based therapy in KRAS wt mCRC pts previously treated with the same anti-EGFR-based regimen was suggested in a retrospective study. Molecular data highlighting the dynamism of intratumoral heterogeneity under the pressure of systemic treatments may explain this finding.

Patients and methods: CRICKET (NCT02296203) is a multicenter phase II single-arm study in mCRC pts who became resistant to 1st-line cet + iri. Main eligibility criteria are: measurable, unenrollable mCRC; RAS/BRAF wt status; prior 1st-line cet-based, cet-containing regimen with at least RECIST partial response (PR), 18 mos median PFS; 5 pts due to the lack of available data on metformin exposure. Among 135 evaluable pts, 5 pts were excluded because of unconfirmed PR (28%), 2 pts due to progression (PD) after 6 weeks of the last administration of cet; prior 2nd-line oxaliplatin-based and bevacizumab-containing treatment. Pts receive 3rd-line cet + iri until PD. The primary endpoint is response rate (RR) according to RECIST v1.1. Based on the Fleming single-stage design, setting p0 = 5%, and p1 = 20%, with 1-sided -α and β errors of 0.05 and 0.20, 27 pts were required. The null hypothesis P ≤ p0 would have been rejected if RECIST response had been observed in ≥ 4 pts.

Results: Between Jan 2015 and Jan 2017, 22 pts were enrolled in six centers. Pts’ characteristics are: median age 70 yrs, ECOG PS 0/1-2 59%/41%, primary location right/left 36%/64%, time from diagnosis of metastases >18 mos 77%. At the time of data cut-off (Jan 15, 2017), 20 pts were evaluable for response. The primary endpoint was met. Five PRs (one unconfirmed) were reported (RR: 25%). 4 SD (disease control rate: 45%) and eight PD were observed. Three pts experienced clinical PD before disease assessment. No unexpected adverse events were evident.

Conclusions: Rechallenge with cet + iri is active in some pts with RAS and BRAF wt mCRC, initially sensitive and then resistant to first-line cet + iri-based chemotherapy + cet. Analyses on cDNA collected at study entry are ongoing in order to verify whether the detection of markers of acquired resistance to cet may help to identify patients more likely to benefit from this strategy. Partially funded by Merck Serono SpA.
Eighty-eight patients were included in the study, 27.3% had right sided CRC, In accordance to literature, our registry data confirm the prognostic role. In our study an accurate molecular selection based on an all RAS and BRAF analysis along with EGFR GCN and EGFR promoter methylation status seems to (respectively K. Andrikou G. Luppi Median follow up duration was 14.3 months. ciated with reduced ORR (9.1% for methylated vs. 45.5% for unmethylated, p<0.0001). At multivariate analysis EGFR GCN and EGFR promoter methylation main- tained their independent role for ORR (respectively p = 0.0082 and 0.0025). PSF (respectively p = 0.0048 and < 0.0001) and OS (respectively p = 0.0001 and <0.0001).

**Conclusions:** In our study an accurate molecular selection based on all RAS and BRAF analysis in conjunction with EGFR promoter methylation status seems to be more relevant than primary tumour sidedness in the prediction of clinical outcome during cetuximab/irinotecan therapy. However, these data need to be validated with future prospective and translational studies.

**A25**

**Management of folinic acid administration in patients with metastatic colorectal cancer**

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1UOC Oncologia AV3, University and General Hospital of Macerata, Macerata; 2UOC Oncologia AV3, Civilizzano Marche (MC); 3U.O. Farmacia, Civilizzano Marche (MC); 4UOC Oncologia AV3, Civilizzano Marche (MC); 5UOC Oncologia AV3, Macerata

Since the development of 5-fluorouracil (FU) in 1957 this drug remains the agent of choice for the treatment of colorectal cancer both in metastatic and adjuvant treatment. There is no clear consensus about the optimal FU-folinic acid schedule and dose. Sodium folinate acid (NALF) is a new formulation with the same pharmacological parameters as calcium folinic acid. It can be infused in one pump with 5FU without the safety of regimens. It can be infused in one pump with 5FU without the

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**A24**

**Mutational status and metastatic pattern in a cohort of Advanced colorectal cancer patients: the ROAD study**

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1Oncology Department University and General Hospital of Udine, Udine; 2Pathology Department University and General Hospital of Udine, Udine; 3Department of Oncology, San Bortolo General Hospital of Vicenza, Vicenza

Background: Somatic mutation status in advanced colorectal cancer (aCRC) has an increasing role in predicting efficacy of biological therapies and outcome and could correlate with site specific pattern of metastases. Patients and methods: We retrospectively analysed a cohort of 640 consecutive aCRC patients (pts) diagnosed at University Hospital of Udine, Italy, from January 2000 to March 2017. KRAS, NRAS, BRAF and PIK3CA status was locally determined by pyrosequencing and/or mass-Spectrometry Assay, with commercially available kits (Myriapod® colon cancer status kit, diatech pharmacogenetics, Italy). All the patients with complete molecular assessment were classified as all wild type, BRAF, RAS or PIK3CA mutated. Pearson’s χ2 test was performed with uni- and multivariate models to test association of mutational status and site-specific metastatic spread.

Results: Overall, we detected 283 (43%) KRAS mutations, 21 (4%) NRAS mutations, 40 (7%) BRAF mutations, and 61 (14%) PIK3CA mutations. Most common mutations in KRAS gene were located in exon 2 (86%), while about 3% of mutations involved exon 3 and 5% exon 4. NRAS mutations involved equally exons 2 and 3. All BRAF mutated tumours except for one, exhibited exon 15 V600E mutations. Pts with KRAS mutations had an increased risk to develop lung metastases (odds ratio, OR 2.58, 95% CI 1.15-5.76: p = 0.021, in univariate model). Instead, pts harbouring BRAF mutations had higher risk of peritoneal (OR 3.05, 95% CI 1.56-5.96, p = 0.001), and nodal (OR 2.20, 95% CI 1.21-4.66, p = 0.012) spread, in uni- and multivariate models, respectively. Liver metastases were not associated with a specific mutational status. Moreover, no associations between NRAS or PIK3CA status and metastatic sites were found. Globally pts classified as all wild type did not show a specific metastatic pat- tern, instead, RAS mutated had higher risk than all wild type ones to develop lung meta- stases (OR 2.81, 95% CI 1.75-4.56, p < 0.001).

**Conclusions:** Our findings suggest that molecular biology may help predicting the metastatic spread in aCRC pts. If confirmed by further studies, these observations could translate into tailored surveillance and follow-up protocols.
The prognostic differences between left-sided (LCC) and right-sided
In the whole group of patients, no statistically significant difference was
We retrospectively collected data from 899 mCRC pts treated at Candiolo
788 pts with mCRC were analysed; 365 were in the Cohort A and 423 in the
Cum, ascendant, transverse colon and hepatic flexure whereas LSCC were from splenic
RSCC were those arising from ceca-
M. Di Pietro Paolo
Patients and methods:
Conclusions:
Parme
tatectomy and adjuvant treatment, stratified by pTS, were enrolled. RSCC, patients received FOLFOX and 42(34%) XELOX,
With the aim of studying the prognosis of sidedness in radically operated stage III colorectal cancer (CRC) patients treated with adjuvant chemotherapy.
Patien
ts and methods: 110 patients with radically resected stage III CRC were enrolled in our retrospective study. The tumor location was as follows: LCC: 67 patients and RCC: 43 patients. All patients were treated with FU-based adjuvant chemotherapy.

Results:
The p value was bilaterally tested, and values less than 0.05 were regarded as statistically significant.

Conclusions:
In our retrospective study, we did not observe any difference in prognosis for stage III radically operated CRC treated with adjuvant therapy according to tumor sidedness.

Primary tumor site (pTS) as a key factor in adjuvant treatment decision in resected N+ colorectal cancer patients

Primary tumor site (pTS) has been identified as prognostic factor, with a worse outcome for right-sided (RCC) compared to left-sided tumors (LCC) and, in RAS wild type tumors, different activity of anti-EGFR drugs. Aim of this retrospective study is to assess different outcomes for resected stage III colon cancer patients, stratified by pTS and adjuvant treatment.

Patients and methods: pN+ colon cancer patients who received XELOX or FOLFOX adjuvant treatment, stratified by pTS, were enrolled. RSCC were those arising from caecum, ascending, transverse colon and hepatic flexure whereas LSCC were from splenic flexure, descending and sigmoid colon. Patients who had withdrawn from treatment within 3 month time or with rectal cancer were excluded. Relapse free survival (RFS) and overall survival (OS) were calculated accordingly to Kaplan-Meier method and the association with stratification factors was assessed by log-rank test.

Results: 167 patients were enrolled, 89(54%) with LSCC and 78(46%) with RSCC. 39(4%) LSCC patients relapsed with a mRFS of 37 months, whereas 28(36%) RSCC patients had mRFS that was not reached (NR) (p = 0.53, HR 0.85, 95%CI:0.52 to 1.38). Stratifying by chemotherapy regimen, 83(50%) patients received XELOX and 84(50%) FOLFOX, mRFS were respectively NR vs 29 months (p = 0.047, HR:0.49,95%CI:0.30 to 0.79).

According to pTS, 36(46%) RSCC, patients received FOLFOX and 42(34%) XELOX, with a mRFS of 19.8 months and NR respectively (p = 0.017, HR 0.41,95%CI:0.19 to 0.88). No statistically significant differences were seen in LSCC patients receiving XELOX or FOLFOX (mRFS:NR vs 34.78 months respectively, p = 0.12).

Conclusions: Our analysis shows that RSCC patients had lower recurrence rate and better RFS compared with LSCC, although not in a statistically significant fashion. However, this is the first time that a significantly better RFS was observed by using XELOX rather than FOLFOX as adjuvant treatment in pN+ CRC patients. This difference was only observed in RSCC, but not in LSCC. Our hypothesis is that the increased activity of XELOX vs FOLFOX in RSCC might be due to higher expression in RSCC of mechanisms of resistance to treatment with XELOX or FOLFOX (namely higher ERCC1 expression and more frequent MSI-H status).

Survival of metastatic colorectal cancer patients at Candiiiolo Cancer Institute

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Background: Over the last 15 years, survival of patients (pts) with metastatic colorectal cancer (mCRC) has significantly improved. Both surgical indication and a more aggressive systemic approach may have contributed to this result.

Methods: We retrospectively collected data from 899 mCRC pts treated at Candiiiolo Cancer Institute from 2001 through 2016, with at least one course of chemotherapy (CT) for metastatic disease and a minimum follow-up period of two years. Since in 2007 the new molecular targeted agents were introduced in the clinical practice, pts were divided into two groups based on the year of diagnosis of mCRC, Cohort A (2001-2006) and Cohort B (2007-2014). The Cox proportional hazards regression model was used and median overall survival (mOS) was calculated using Kaplan-Meier estimate and compared by log-rank test.

Results: 788 pts with mCRC were analysed; 365 were in the Cohort A and 423 in the Cohort B. The mOS of entire population was 32.0 months (mo), with a significant difference between the two cohorts: 29.2 mo in Cohort A vs 33.5 mo in Cohort B (HR 0.832, p = 0.041).

Surgical indication increased across the years (43.0% Cohort A vs 55.6% Cohort B, p < 0.0001), particularly for extra-hepatic surgery (21.1% Cohort A vs 33.3% Cohort B p < 0.0001). As expected, surgery in addition to CT bestowed a significantly longer mOS when compared to CT alone: 38.5 versus 20.1 mo (HR 0.262, p < 0.0001). However, no significant changes in mOS were observed between cohorts in pts undergoing surgery (38.9 mo Cohort A vs 38.2 mo Cohort B, p = 0.822).

At multivariate analysis, right-sided primary tumor and synchronous metastatic disease were found independent, unfavorable prognostic factors. In these subgroups mOS has improved in Cohort B as compared to Cohort A. In particular, in pts with right-sided primary tumor mOS was 15.8 mo in Cohort A and 25.5 mo in Cohort B (p = 0.041).

Considering only pts treated with CT alone in this subgroup, mOS was 15.1 mo in Cohort A and 22.1 mo in Cohort B (p = 0.046).

Conclusions: The OS improvement in mCRC pts might be correlated to a more aggressive integrated approach with a higher number of pts undergoing extra-hepatic surgery. The medical approach seems to have a more favorable impact in recent years on subgroups characterized by a worse prognosis.

Colorectal cancer (CRC) progression and angiogenesis: tumor infiltrating natural killer cells as novel inflammatory orchestrators

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Background: Epidemiological studies revealed that chronic inflammation predisposes to different types of cancers, including colorectal cancer (CRC). Natural Killer (NK) cells, effector lymphocytes of innate immunity primarily involved in immunosurveillance against tumors, have been recently reported to act as mediators of cancer progression. We previously reported that in Non-Small Cell Lung Cancer patients NK cells can acquire the decidual-like CD56+CD16-VEGF+FGF2+HL-8+IFNγ+ phenotype...
and promote angiogenesis in vitro. Here we extend our NK studies to CRC patients and analyze the molecular mechanisms involved.

Materials and methods: Multicolor flow cytometry was performed using NK cells derived from peripheral blood and tissue samples of CRC patients, compared with those derived from peripheral blood of healthy control and patients with inflammatory bowel disease. Conditioned media (CM) from FACs-sorted NK were used either for secretomic analysis, or for induction of HUVECs, or for angiogenesis functional assays on human umbilical endothelial vein cells (HUEVCs).

Results: We found that CD56+ CD16+ NK cells predominate in CRC adjacent and tumor tissues. flow cytometry analysis showed an increased expression of surface activation and degranulation abilities. NK cells from CRC patients express the decidual NK markers CD99 and CD49a, supporting the hypothesis of a pro-angiogenic-decidual-like polarization. Both secretomic and flow cytometry analysis on CRC peripheral blood NK cells (TANKs) revealed statistically significant up-regulation of several angiogenesis-related factors which was specific for CRC patients. CM by FACs sorted CRC NK cells from peripheral blood and tumor tissue of CRC patients could induce HUVEC proliferation, migration, adhesion and the formation of capillary-like network structures. These functional evidences are related with molecular changes in HUEVCs induced by NK CM, that include the phosphorylation AMPKα, GSKb, P70 S6 Kinase and S6 ribosomal protein.

Discussion: STAT-3 and STAT-5 pathway activation was observed in TANKs, suggesting the potential involvement of these signals in the induction of the CRC-TANK angiogenic switch. Inhibition of STAT-3 in TANKs resulted in the downregulation of many pro-angiogenic factors and inhibited the formation of endothelial network structures by NK CM.

Conclusions: Our data demonstrate that TANKs from CRC patients are switched toward a pro-angiogenic/pro-tumor phenotype and function that could be specific for CRC.

A30 Arteriovenous directed embolization therapy (ADET) with polyethylene glycol microspheres loaded with irinotecan for refractory liver metasteses from colorectal cancer

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Background: Patients with liver metastases from colorectal cancer are in 80% of cases non indicated for resection. The standard first line treatment of unresectable liver metastases is systemic chemotherapy, however this method results in progressions in 70% of patients. The indicated therapy for refractory patients is the arteriovenous directed embolotherapy (ADET). In this study we monitored tumor response, and adverse events after ADET of colorectal cancer liver metastases with polyethylene glycol microspheres loaded with irinotecan. Secondary objectives were to monitor quality of life, time to progression and survival of patients.

Materials and methods: Patients were included in the study if affected by CRC-LM, who were refractory to systemic chemotherapy, treated with ADET using polyethylene glycyl microspheres, and liver involvement >30%. Tumor response, performance status (PS), tumor marker antigens, and quality of life (QoL) were monitored at 1, 3 and 6 months after ADET. QoL was assessed with patient’s scale (PSI).

Results: We treated 50 consecutive CRC-LM patients with ADET using polyethylene glycol microspheres, their tumor response one month after ADET was 43% of complete response (CR), and 52% of partial response (PR), and 4% stable disease (SD). Tumor response 3 months after ADET was CR 15%, PR 60%, SD 10% and progression disease (PD) 15%. Tumor response 6 months after ADET was PR 64%, SD 22% and progression disease (PD) 14%. QoL was >80% PSI at each time point. Median time to progression was 3 months (2.3–4.3 months). Median follow-up was 11 months (1.3–19.2 range).

ADETs were performed with no complications. Observed side effects (mild or moderate intensity) were: pain in 22% of patients and fever in 13%, whereas 30% of patients did not complain any adverse event.

Conclusions: ADET of CRC-LM with polyethylene glycol microspheres loaded with irinotecan was effective in tumor response and resulted in mild toxicity, and good QoL.

A33 Dihydropyrimidinase dehydrogenase (DPD) deficiency: how to translate it in clinical practice?

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Background: The DPD enzymatic activity is the rate limiting of 5FU fluoropyrimidines’ metabolism. DPD gene mutations modify its catalytic activity, but to date the impact of mutation on effective dose reduction is not known.

Materials and method: A total of 615 patients (pts) affected by GI cancer started 5 FU/ Capecitabine containing regimens from December 2012 to April 2017. A total of 68 pts...
with grade (G) 3-4 toxicities (34 pts), rare and persistent G2 toxicities (23 pts) and low risk adjuvant setting with consensus (11 pts) were planned for DPD pharmacogenetic testing on peripheral blood by Sanger sequencing. In the cohort of pts which had toxicity during treatment (57 pts), 496A>G 1610G>A, 1627A>G, 18967G>C, IVS14-1>G, 2194G>A, 2846A>T polymorphisms were analyzed, while in preventive cases IVS14-1>G and 18464T>G were tested.

Results: 34 pts developed G3-G4 toxicities during cycles 1-2, including leuco-neutropenia (44%), diarrhea (32%), piastrinopenia (15%), mucositis (12%), alopecia (3%), dermatitis (3%), 24 pts (70%) were DPD deficient: 496AG (3 pts), 1627AG (8 pts), IVS14 > 1G (1 pt), 1627AG (2 pts), 2194GA (1 pt), 496AG and 1627AG (2 pts), 496AG and 2194GA (1 pt), 1627AG and 2194AT (1 pt), IVS14 > 1G and 1610GA (1 pt). Only the pt with IVS14 > 1G and 1610GA polymorphisms presented life threatening complications, resolved successfully. 23 pts showed poor and persistent G2 toxicities within the first three cycles, including diarrhea (57%), leucopenia (39%), alopecia (30%), piastrinopenia (13%), hyperbilirubinemia (13%), dermatitis (9%). 9 pts (39%) were DPD deficient: 46AA (3pts), 1627AA (1pt), 2194GAT (1pt), 496GA and 18969AA (1pt), 496AA and 1601GA (1pt). About pts analyzed presently, only one was DPD deficient (1627AG) and performed therapy with dose reduction of 50%.

Conclusion: 34 on 68 pts were found to be DPD deficient and nobody died for toxic death. More than one heterozygous mutation was observed in 14 pts. Chemotherapy was discontinued in 12 adjuvant setting pts, 5 metastatic pts suspended fluoropyrimidine, while in 17 pts toxicity improvement was seen after a dose reduction of 50% and pre-planned cycles were performed without delay. To standardize clinical practice we need extensive studies to correlate the heterozygous alleles mutation with type and grade of toxicity, the effective dose reduction or stop therapy.

A34 EPHA2 receptor is involved in vivo acquired resistance to anti-epidermal growth factor receptor (EGFR) treatment in metastatic colorectal cancer

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Background: EPHA2 tyrosine kinase receptor is implicated in cell growth, migration, and invasion in a wide range of cancers. We studied its role as a potential marker of resistance to anti-EGFR drugs in colorectal cancer (CRC).

We previously demonstrated that EPHA2 was differently activated among a panel of CRC cell lines with primary and acquired resistance to cetuximab and the use of ALW- II-41-27 (EPHA2 selective inhibitor) in combination with cetuximab was able to revert this resistance in in vitro experiments (abstract presented at 2016 ESMO Congress in Copenhagen). Here we present the study on in vivo models.

Methods: EGFR-dependent SW48 and LIM1215 cell lines were engrafted into nude mice and treated with cetuximab until disease progression. Once tumors became resistant (SW48-CR and LIM1215-CR) mice were randomized in groups of 10 mice each and assigned to receive ALW- II-41-27 as single agent or in combination with cetuximab, no treatment and cetuximab alone group served as control. ALW- II-41-27 was administered daily at 30 mg/kg by oral gavage and cetuximab intraperitoneally at 1 mg/kg, 10 pts presented double DYPD A and 2846A T polymorphisms were analyzed, while in preventive cases IVS14 > 1G and 1610GA polymorphisms were analyzed by Western Blot.

Results: The combination of the two drugs induced a significant reduction of tumor volume since the first administration. A reduction of 50% of tumor volume was found at baseline, patients with low ALRI levels (HR 1.17-1.96, p<0.001) had a worse survival than those with high baseline ALRI (HR 1.17-1.96, p<0.001). Interaction test involving ALRI levels and treatment efficacy in the chemotherapy plus bevacizumab arm showed a significant interaction for DFS (p = 0.0003) and not for OS (p = 0.228).

Conclusion: Our results indicate that ALRI is good prognostic and predictive markers for mCRC patients who are candidates for chemotherapy plus bevacizumab.

A37 Outcome and prognostic factors after resection of liver metastases in patients with colorectal cancer


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Background: During the last 30 years, liver surgery for metastases from colorectal cancer (CRC) has become the standard of care and an opportunity of cure in selected patients, with reported 5-year survival rates approaching 50%. However, more than 50% of patients will develop early recurrence without any long-term survival benefit. Therefore, the attention has been focused on finding prognostic factors and scores able to select patients who will benefit from surgery.

Material and methods: Medical records from 99 patients with metastatic CRC who underwent potentially curative liver resection from January 2008 to December 2014 at University Hospital of Modena were retrospectively reviewed. Aim of the study was to assess the impact of clinical and biological prognostic factors on relapse-free survival (RFS), 3-year survival and overall survival (OS). Primary or metastatic tumour samples were analyzed for K-RAS (exon 2) mutations using sequencing analysis. Univariate and multivariate Cox regression analysis was performed for K-RAS mutation status, tumor site, resection margin, grading and time to metastases, peritoneal/adjunctive chemo- therapy) were performed.
Results: After a median follow up of 30 months (range 1-98), the median RFS was 10.0 months and the 3-year survival rate was 45%. In multivariate analysis, OS differed significantly according to resection margin (HR 2.40, 95% C.I. 1.29 – 4.45, p = 0.006) and to time to metastases (HR 1.81, 95% C.I. 1.01 – 3.23, p = 0.045). In the univariate analysis, significantly longer RFS can be predicted by FONG score (HR 1.92, 95% C.I. 1.15 – 3.20, p = 0.013). KRAS exon 2 gene mutations, detected in 52/99 patients (52%), had no statistically significant interaction neither in RFS nor in OS.

Conclusions: In our single institution experience, the median overall survival following liver resection was 21 months. Only radical surgical resection (R0) can have an impact on survival. FONG liver score, which includes criteria critical in all patients eligible to surgery, should guide patients’ selection. Overall survival was not significantly shorter for KRAS exon 2 mutated patients.

A38 Focus on metastatic right-sided colon cancer: the best overall response to the first-line non-EGFR treatment correlates with better overall survival


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Conclusions: These preliminary results suggest that PI3K activation plays a central role in the acquired resistance to the combination of anti-EGFR and MEK-i. PI3K activation depends at least in part by the activation of the HER family of RTK, but it can also be activated by other receptors. In vivo experiments on mice are currently ongoing.

A40 Prevalence of KRAS, NRAS and BRAF mutations detected by massive parallel sequencing and differential clinical outcome in metastatic colorectal cancer (MCRC) patients: first line Fir-Bev combination


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Background: KRAS/NRAS/BRAF genotypes guide tailoring of first and subsequent lines of MCRC treatment strategy. First line triplet chemotherapy/BEV regimens significantly improved progression-free survival (PFS) and overall survival (OS) in MCRC patients. OS may be significantly worse in MCRC patients treated with Fir-Bev intensive regimen. Methods: Tumoral sample sizes of 67 MCRC pts treated with Fir-Bev (77% overall) were analyzed through a 50 genes panel (POM/Colon Lung Cancer) by Ion Torrent. KRAS exons 1-2 (KRAS1, KRAS2, NRAS2-4), exons 1-3 (NRAS1, NRAS2, NRAS3) and BRAF were analyzed. Results: KRAS, NRAS, BRAF mutations were found in 43, 26 and 41% of MCRC pts respectively. KRAS mut allele frequencies were 64%, 57% and 56%. In multivariate analysis, OS differed significantly between KRAS mut and wild type pts.

Conclusions: KRAS mut type may be used as a simple predictive marker of response to Fir-Bev regimen in MCRC patients and guide first-line treatment choice. This information can be directly obtained using NGS approach in a single analysis. Further investigations on larger patient populations are needed to confirm these findings.

A39 The acquired resistance to the combination of the anti-EGFR cetuximab and the MEK-inhibitor refametisib in KRAS mutated colorectal cancer cell lines depends on PI3K-signalling

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Background: Previous studies showed that the combination of an anti-epidermal growth factor (EGFR) and a selective MEK-inhibitor displays a significant anti-tumour activity in RAS-wild type colorectal cancers (CRC), while the same combination partially reverts anti-EGFR primary resistance in KRAS mutated colorectal cancer lines. However, mechanisms of resistance to this combination are still unexplored.

Methods: We generated KRAS mutated CRC cell lines, cell lines (HTCT15 and HCT116) resistant to, combination cetuximab (an anti-EGFR antibody) and BAY94-8566 (refametisib, a selective MEK1/2-inhibitor) after continuous exposure to increasing concentrations of the drugs for 8 months. Resistant clones had an IC50 20-100-fold higher than their parental cell lines. Western Blot analysis and quantitative Reverse Transcriptase Polymerase Chain Reaction (qRT-PCR) were used to evaluate potential changes in the expression of genes involved in the PI3K-AKT pathway. The p-AKT (serine 473) and p-GSK3-beta (serine 9) levels were assessed by Western Blot analysis. qRT-PCR data were analyzed using the 2-(-Delta Delta Crt) method.

Results: We found consistent hyperactivation of the PI3K-AKT pathway and concurrent inactivation of the MAPK pathway, coupled to the activation of multiple RTKs of the HER family such as HER2 and HER3 in resistant cells when compared to parental cells. Treatment with GDC-0941 was able to partially restore the sensitivity to the drug combination, suggesting a central role for this pathway in mediating resistance in this setting, while afatinib was not capable of reverting the resistant phenotype when used alone but showed synergistic activity when combined to GDC-0941.

Conclusions: These preliminary results suggest that PI3K activation plays a central role in the acquired resistance to the combination of anti-EGFR and MEK-i. PI3K activation depends at least in part by the activation of the HER family of RTK, but it can also be activated by other receptors. In vivo experiments on mice are currently ongoing.

A41 MTHFR, TSER and PDYPD gene mutation is associated with toxicity and response in pre-operative chemoradiotherapy for local advanced rectal cancer

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Background: Radiation therapy and 5FU based chemotherapy is the most common pre-operative regimen used for CT3-T4, N1 rectal cancer (RC). Evaluation of predictive markers of response and toxicity to radio-chemotherapy is a challenging approach for patients (pts) and drug selection, in the present experience we have analyzed the predictive role of the genetic polymorphisms of MTHFR, TSER and PDYPD on toxicity and response to pre-operative radio-chemotherapy.

Materials and methods: We have enrolled sixteen patients with locally advanced RC treated with pre-operative radiotherapy and fluoropyrimidines base chemotherapy. Genotypic polymorphisms of MTHFR C677T, TSER G1120A, PDYPD IVS15 G>T, PDYP D1284T, PDYD T1679 G>T, TSER 289 bp VNTR were analyzed by PCR and pyrosequencing of genomic DNA extracted from peripheral blood samples. Genetic markers were correlated with toxicity to treatment (chemotherapy and radio-chemotherapy) and clinical response.

Results: Patients characteristics were: male 13 pts, female 3 pts, median age 66 years, ECOG PS 0-1 all pts. We found PDYPD IVS15 G>T 1 G>A; GAG homozygous wild type, PDYD D1284T G>A; PDYPD T1679 G>T, TSER 289 bp VNTR were analyzed by PCR and pyrosequencing of genomic DNA extracted from peripheral blood samples. Genetic markers were correlated with toxicity to treatment (chemotherapy and radio-chemotherapy) and clinical response.
60% of pts and homzygous wild type MTHFR A1298C in 40% of pts. G3-G4 adverse events (diarrhea, neutropenia, anemia, mucositis) were observed in 60% of pts with heterozygous MTHFR A1298C and in 10% of pts with homzygous mutated MTHFR C677t. treated with chemotheriotherapy combined. DPYD homzygous wild type was not associated with severe toxicity. Rectal surgery with TME will be performed 8 weeks after the end of pre-operative chemotheriotherapy. We obtained 7 pathological complete response and nine partial pathological response. Adjuvant chemotherapy was not better tolerated without G3-G4 adverse events. Three pts with pathological complete response were treated with Transanal Endoscopic Microsurgery (TERM) and they are alive without recurrence to twelve months after surgery.

**Conclusion:** Concomitant assessment of genetic polymorphisms of MTHFR and DPYD is promising to predict severe toxicity during preoperative chemotheriotherapy approach for pts with locally advanced rectal cancer. This result does not exclude the need to consider other non-genetic factors that might influence the individual enzyme activities.

**Results:**

- In our clinical practice, afl + FOLFIRI was well tolerated, with a manageable toxicity profile. The safety results confirm the findings from the confirmatory VELOUR trial.
- **Background:** Malignant bowel obstruction (MBO) is common in advanced cancer patients. It develops more likely in gastrointestinal or genitourinary tumors with abdominal burden, but it can arise in other cancers too. It's significant symptoms, nausea, vomiting, abdominal pain, impact negatively on patients' daily life, making MBO a very disabling condition. Surgery is a treatment option only for selected patients who meet surgical criteria. Other patients are usually treated with nasogastric tube to decompress bowel distension, fasting and supportive care. Studies showed that medical treatment with metoclopramide, oxtremo and dexamethasone can significantly improve symptoms and quality of life. Oxtremo has both antiemetic effects which reduce intestinal fluids improving nausea and vomiting and the power of reducing bowel motility, that can weaken abdominal cramps. Here, we report our center experience of MBO medical treatment.

**Material (patients) and methods:** From September 2015 to April 2017, we collected data of 20 patients hospitalized for MBO. Most patients had a gastrointestinal neoplasia (7 colorectal, 2 pancreatic, 2 gastric, 1 esophagus), 3 had ovarian cancer, 4 NSCLC and 1 head and neck tumor. 35% had vomiting episodes at presentation and no one had passage of gas/stool (G3-G4 constipation and bowel obstruction according to CTCAE v.4). We administered intravenous injection of Dexamethasone 8 mg twice a day, metoclopramide 10-20 mg three times a day and subcutaneous Oxtremo 0.1 mg every 8 hour. Evaluation measures were nausea/vomiting and abdominal pain episodes and regain of intestinal transit (according to CTCAE score v.4) during treatment with following hospital discharge.

**Results:** 80% of patients had a significative reduction of nausea and vomiting the same day treatment was started. Abdominal cramps disappeared within 2 days in 19 out of 20 patients. Furthermore, 13 out of 20 patients showed a recovery of intestinal transit within 3-4 days (reaching G1-G2 score of constipation-bowel obstruction) and were able to discharge from medical care unit within 7 days. All patients reported subjective improvement of their clinical condition.

**Conclusions:** Despite the small number of patients treated in our center, medical treatment with intravenous metoclopramide, dexamethasone and subcutaneous oxtremo show to improve clinical status and to reduce symptoms in patients with MBO, giving a quick relief from nausea, vomiting and abdominal pain.

**Background:** In the USA and in Europe, intravenously administered albirecept (af) in combination with FOLFIRI (irinotecan, 5-FU, leucovorin) is approved for the treatment of patients (pts) with metastatic colorectal cancer (mCRC) that’s resistant to or has progressed after treatment with an oxaliplatin-containing regimen, with or without Bevacizumab (Avastin). The efficacy of all in this indication was assessed in a multinational, pivotal phase 3 trial (VELOUR), in which af + FOLFIRI significantly prolonged mOS, PFS and RR, compared with FOLFIRI alone.

**Patients and methods:** Between June 2015 and April 2017, 18 consecutive pts with mCRC were treated with FOLFIRI based chemotherapy. The median age was 57 yrs (78% under 65 yrs and 22% ≥ 65 yrs), 11 pts male (61%), 7 female (39%), 14 (78%) resected and 4 (22%) unrected primary tumor; 13 pts (72%) with left primary tumor location, 5 (28%) with right side; 4 (22%) showed only one metastatic site (liver), 14 (78%) more sites (> 2) of which 5 with peritoneal carcinosis. Most pts had previously received bev (55.5%) or anti-EGFR (22.2%) therapy. Pts received all af + FOLFIRI every 2 weeks as second line treatment. They were evaluated for adverse event (AEs) and serious adverse events (SAEs), graded according to National Cancer Institute Common Terminology Criteria for AEs (version 4.0). A descriptive safety analysis was conducted.

**Conclusion:** Our findings underline that PSE is safe and effective to achieve short-

**Results:** Pts received a median of 6.5 cycles of FOLFIRI + afl and 3 pts continued afl alone as maintenance for a median of 9 weeks. Main reported toxicities G1-G2 were diarrhea (10 pts, 55.5%), nausea (6 pts, 33.3%), arterial hypertension (5 pts, 27.7%), mucositis (4 pts, 22.2%), nausea (3 pts, 16.6%), neutropenia (3 pts, 16.6%) and proteinuria (3 pts, 16.6%). Common grade ≥3 treatment-related AEs were neutropenia (2 pts, 11.1%), diarrhea (1 pts, 5.5%) and asthenia (1 pts, 5.5%). No reported cases of gastrointestinal perforation, thromboembolism and hemorrhage. No fatal events were reported. A retrospective analysis of GI cancer patients with splenomegaly undergoing PSE was performed. Mean platelet count was collected at the following time points: before CT start; at the nadir after CT (post-PSE); five weeks after PSE (post-PPSE); and at the nadir after CT reintroduction post PSE. Time to CT re-start after PSE and the time to recurrent CT, periprocedural laboratory values and adverse events were recorded. Wilcoxon test was adopted to exploratorically compare platelet count before and after PSE.

**Results:** Eleven patients underwent PSE, 5 with colorectal, 3 with pancreatic and 3 with biliary cancer, 73% had metastatic disease. Baseline platelet count before initiation of CT was 146 ± 109/L. Post-PSE platelet count improved significantly (132 x 109/L; range, 67-172 x 109/L) and occurred at a mean of 169 days after PSE (range, 37-664 d). No differences were observed when comparing CT at nadir pre and post PSE (p = 0.003). The mean hospital stay was 1 day. Procedural abdominal pain occurred in 3 patients. All patients resumed CT and mean time to CT re-start after PSE was 43 days (range, 4-193 d). All patients exhibited recurrent thrombocytopenia. Platelet count at nadir after PSE was 54 ± 109/L (range, 28-78 x 109/L) and occurred at a mean of 169 days after PSE (range, 37-664 d). No differences were observed when comparing CT at nadir pre and post PSE (p = 0.447). All patients experienced CT dose delay and 82% of them experienced dose reduction after PSE.

**Conclusion:** Our findings underline that PSE is safe and effective to achieve short-term improvement of CT and resumption of CT in GI patients. However, PSE does not sustain long-term adequate platelet count. Further studies may help guide patient selection by identifying characteristics that allow a sustained improvement in CT.
Pts had the following baseline characteristics: median age 62 yo; ECOG PS 0/1 9/7; tumor location right-sided/left-sided/rectum 5/7/4; KRAS wild-type/mutated 8/8. 37% of pts received 3 or more prior chemotherapy regimens for mCRC and 88% were treated with bevacizumab. At the time of our analysis all pts had progressed and 11 pts had died. No patient achieved partial response and only 2 pts had stable disease, with a disease control rate of 12%. The median progression free survival was 3.7 months and the median overall survival (mOS) was 7.4 months. The most frequent reported adverse events (AEs) were fatigue (31%), hand-foot syndrome (38%), hyperbilirubinemia (50%) and thrombocytopenia (25%). Drug-related AEs grade <= 3 occurred in 38% of pts; discontinuation and dose-reduction due to AEs occurred in 2 and 4 pts respectively. Pts were divided in 3 risk groups according to the prognostic score proposed in REBECCA study, based on ECOG PS, KRAS mutational status, time since diagnosis of metastatic disease, number of metastatic sites, presence of liver metastases, initial dose of regorafenib: mOS was 9.2 months in low-risk group pts, 5.6 months in intermediate-risk group and 3.9 months in high-risk group.

Conclusions: Our results on efficacy and safety of regorafenib in refractory mCRC are consistent with published data, even if we observed a lower disease control rate. The REBECCA prognostic model could be a useful tool for clinicians to better select pts who may most benefit of regorafenib, thus avoiding useless and potentially toxic end-of-life treatment and reducing costs.
CORE-URO-01 study: comparison of safety and efficacy of pazopanib in first-line metastatic renal cell carcinoma (mRCC) with or without renal failure

Background: Pazopanib has been approved for first-line treatment of patients (pts) with metastatic renal cell carcinoma (mRCC) based on the prospective randomized trial that enrolled only pts with adequate renal function. There are no data on the efficacy and toxicity of pazopanib in pts with renal insufficiency (RI). The aim of this study is to investigate the effect of kidney function on treatment outcomes in pts treated with pazopanib for mRCC.

Patients and methods: We retrospectively analyzed the data of the mRCC pts treated with pazopanib with respect to renal function in fourteen Italian institutions from January 2010 to June 2016. Baseline glomerular filtration rate (GFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formula at the time of therapy start. Pts with MDRD <60 mL/min/1.73 m2 (group A) were compared with pts with MDRD >60 mL/min/1.73 m2 (group B) in terms of response rates, progression free survival (PFS), overall survival (OS) and toxicities.

Results: Two hundred and twenty-nine pts were included in this study: 128 pts in group A and 101 pts in group B. 68% of pts were male, median age was 67 years (range 34-80) and median CrCl was 84.2 mL/min in group A. In group B, 64% were male, median age was 64 years (38-85) and median CrCl was 74 mL/min. Pts with MDRD <60 were more likely to have had a previous nephrectomy (87% vs 79%). Median PFS was 3.7 (95% CI 3.5-4.1) and 5.0 months for MS+ (HR 2.77, 95% CI 2.12-3.61 p < 0.0001) and without (MS-) MS, respectively (HR 4.87, 95% CI 2.36-9.58, p < 0.0001). Multivariate analysis confirmed that MS was an independent predictor of OS and PFS.

Conclusions: Although in this study it is necessary to reduce the dose of pazopanib more frequent in pts with RI, kidney function at therapy initiation does not adversely affect the efficacy and safety of pazopanib.

Impact of metabolic syndrome on clinical outcome of castration resistant prostate cancer (CRPC) patients treated with abiraterone and enzalutamide

Background: Metabolic syndrome (MS) is a set of risk factors, including obesity, dyslipidemia, hypertension, and insulin resistance, that has been implicated in the development and progression of CRPC. The study aimed to firstly assess the incidence and impact of MS on progression-free/overall survival (PFS/OS) in CRPC patients (pts) treated with abiraterone (abi) or enzalutamide (enza).

Methods: We retrospectively evaluated CRPC pts in seven Italian Institutes between March 2011 and October 2016. MS, defined by modified Adult Treatment Panel III criteria, was assessed before starting abi or enza, during treatment and follow-up. In addition, we extracted cell free DNA from pretreatment plasma samples and performed copy number of androgen receptor (AR) by duplex TaqMan quantitative real-time PCR assay, digital PCR and targeted next generation sequencing (Comenda et al. Ann Oncol 2017).

Results: We included 551 metastatic CRPC pts treated with abi (N = 317, 57.5%) and enza (N = 234, 42.5%). Most pts (N = 442, 80.5%) previously received a docetaxel-based regimen, and 39 (7.1%) pts also received more than two previous therapeutic lines. Eighty-three of 551 pts evaluated (15%) met MS criteria at baseline without any significant difference between abi and enza groups, whereas for 40 (8.5%) this occurred during treatment. There was no statistically significant difference for age at diagnosis, performance status, Gleason score, type of treatment and number of previous therapeutic lines between pts with (MS+) and without (MS-) MS. Baseline metabolic profile and visceral involvement were significantly associated with MS+. Moreover, we observed no correlation between MS and amplification of cell-free AR gene copy number. Median PFS was 3.7 (95% CI 3.5-4.1) for MS+ vs 8.3 (95% CI 7.4-9.2) months for MS-. HR was 2.77, 95% CI 2.12-3.61 p < 0.0001. Median OS was 6.9 (95% CI 5.4-8.9) and 19 (95% CI 17.4-21.6) months for MS+ and MS-, respectively (HR = 3.43, 95% CI 2.16-5.48, p = 0.0001). No association was reported between the presence of MS and PSA response rate. Multivariate analysis confirmed that MS was an independent predictor of PFS (HR = 2.07, 95% CI 1.03-4.18 p = 0.041) and OS (HR = 4.87, 95% CI 2.36-10.03 p < 0.0001).

Conclusions: The presence of baseline MS is a significant risk factor for worse survival and so to be considered for a better prognostication of CRPC pts treated with abi or enza. A prospective evaluation is warranted.
Safety and efficacy of cabozantinib for metastatic renal cell carcinoma (mRCC): real world data from an Italian Expanded Access Program (EAP)

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1Azienda Ospedaliero-Universitaria di Modena, Modena, Italy; 2Azienda Ospedaliero-Universitaria di Reggio Emilia, Reggio Emilia, Italy

Background: Results from the randomised phase III METEOR trial confirmed a survival benefit of cabozantinib over everolimus in patients (pts) with advanced clear cell renal cell carcinoma (ccRCC) who progressed after at least one prior antiangiogenic inhibitor. The EAP provided the opportunity to treat pts in real world clinical practice.

Methods: Data were collected from 92 pts treated with Cabozantinib across 23 Italian hospitals. Cabozantinib was available, upon physician request, from September to December 2014 to pt age ≥18 years and with mRCC and measurable disease, with Performance Status (ECOG) 0 to 2, who had relapsed after one or more prior systemic treatment. 74 pts had clear-cell RCC, while the other 18 had non-clear-cell histologies (type II papillary and chromophobe). The most frequent site of disease were: lung 54 (69%), brain 43 (54%), bone 28 (31%), liver 15 (19%) and brain 5 (6%). 43 (46%) of pts had two or more sites of disease. Cabozantinib was administered orally at 60 mg once a day in 28 days cycles. Dose reductions to 40 or 20 mg were allowed if toxicity was encountered for adverse events (AEs) using CTCAE v.4.0. The aim of this analysis was to evaluate the safety and activity of Cabozantinib in a large unselected population.

Results: Cabozantinib was administered as second line therapy in 28 (30%) pts, as third line in 18 (19%) pts and as further lines in the remaining 46 (51%) pts. At the time of our analysis, grade 3 and 4 AEs were observed in 21% of pts. Among 91 pts, only 5 (5%) pts discontinued treatment due to AEs. The best overall response was partial in 28 cases (31%), whereas 23 (25%) pts had stable disease and 23 (25%) had progressive disease. 18 pts (18%) are not available for first response assessment. With a median follow-up of 4 months, the median progression-free survival observed was 3.5 months irrespective of the line of treatment.

Conclusions: Our data suggest that Cabozantinib is safe and active in a large unselected population treated according to everyday clinical practice.

Addressing the best treatment for non-clear cell renal cell carcinoma (nccRCC): a meta-analysis of randomised clinical trials comparing VEGFR-TKIs versus mTORI targeted therapies

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1AOU Veneto, Dipartimento di Oncologia Medica, Verona; 2Pollicino S. Orsola-Malpighi, Bologna, Dipartimento di Oncologia Medica, Bologna; 3AOU Veneto, Dipartimento di Patologia e Diagnostica, Bologna, AOU Verona, Clinica Urologica, Verona; 4AOU Veneto, Dipartimento di Patologia e Diagnostica, Verona

Aim: Non-clear cell renal cell carcinoma (nccRCC) is a heterogeneous group of tumors profoundly different in terms of morphology, genetic profile, clinical behavior and prognosis. The optimal treatment algorithm for nccRCC is still unknown and derived from limited phase II studies or retrospective analyses in clinical trials. The aim of our meta-analysis is to compare the efficacy of VEGFR-TKIs and mTORI inhibitors in the treatment of nccRCC patients.

Methods: Searching the MEDLINE/PubMed, Cochrane Library abstracts prospective studies were identified. Data extraction was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The measured outcomes were progression free survival (PFS), overall survival (OS), and the disease control rate (DCR). Results: Four randomized controlled trials were selected for final analysis, with a total of 332 patients evaluable for PFS. Treatment with TKI significantly reduced the risk of progression compared to mTORI (HR = 0.71; 95%CI 0.60 – 0.84; p < 0.0001). This difference remained statistically significant when sumitumib was compared to everolimus in a recent third-line setting (HR = 0.67; 95%CI 0.56 – 0.80; p < 0.0001). In 332 patients evaluable for OS, no significant difference was found between TKI and mTORI (HR = 0.86; 95%CI 0.58 – 1.28; p = 0.49). Furthermore, the OS advantage of TKI over mTORI was not evident when PFS was included in the analysis (HR = 0.71; 95%CI 0.58 – 0.87; p < 0.0001). Conclusions: Compared to mTORI, treatment with TKIs significantly improves PFS better than mTORI. The use of TKIs as first line treatment could offer a benefit in terms of progression compared to everolimus, therefore supporting the standard treatment paradigm broadly used for ccRCC. The relatively modest efficacy of available targeted therapies reinforces the need of future histological-based, molecular-driven therapeutic paradigm.

Prospective translational study investigating circulating predictors of outcome to first-line pazopanib in patients with metastatic renal cell carcinoma (mRCC)

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1Fondazione IRCCS Istituto Nazionale Tumori, Milan

Background: We investigated plasma levels of circulating angiogenic factors (CAFs) involved in angiogenesis in patients (pts) with mRCC treated with first-line pazopanib to assess potential biomarkers of clinical outcome.

Methods: Plasma samples were obtained at different timepoints before treatment and every 4 weeks until radiographic disease progression (PD) as per RECIST 1.1. assessed by CT scan every 12 weeks. Levels of 7 CAFs of interest including: IL-6, IL-8, SDF-1, VEGF-A, HGF, Osteopentin and E-selectin were quantified by Luminex® technology. Baseline levels and changes during treatment were analyzed for association with efficacy [progression-free survival (PFS) and objective response].

Results: 219 of 25 pts were evaluable for OS and 214 pts for PFS. Among 219 pts, only 5 (2%) pts discontinued treatment due to AEs and 43 (19%) pts had grade 3 or 4 AEs. The median follow up was 8 months (IQR 5.1 months). Overall plasma levels of SDF-1 (p < 0.0001), VEGF-A (p = 0.0052) and IL-8 (p = 0.0275) showed the highest modulation during treatment. At the end of first pazopanib cycle (week 4) plasma VEGF-A levels were significantly higher in pts with partial response (PR) (54%) than in pts with PD. IL-8 levels were significantly higher in pts with PD vs pts with PR at the time of response (p = 0.041). Moreover baseline IL-8 levels were significantly higher in pts with PD vs pts with stable disease (SD) (p = 0.0181), while serum levels of SDF-1 (p = 0.012), VEGF (p = 0.002), osteopontin (p = 0.001) and E-selectin (p = 0.001) were significantly associated with best response (PR vs SD vs PD) while IL-6 levels were significantly associated with PFS (p = 0.0082). The 6 months and 1 year estimated PFS rate was 73% and 63% respectively.

Conclusions: Treatment with first-line pazopanib is associated with variation of CAFs levels. Week 4 levels of VEGF-A as well as pretreatment levels of IL-8 showed the strongest correlation with PD suggesting that monitoring these CAFs during treatment may be useful for identifying patients likely to respond. These findings warrant further investigation in larger trials.

Radium-223 with concomitant bone-targeting agents in metastatic castration-resistant prostate cancer (CRPC) patients treated in an international early access program (EAP)

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Background: The bone-targeting agents (BTA) denosumab and bisphosphonates (BPs) are widely used in the supportive care of patients (pts) with CRPC and bone metastases. We present data on pts treated with radium-223 dichloride (Ra-223) with or without a concomitant BTA in an international EAP Methods: This was a prospective single-arm phase IIIB study of CRPC pts with symptomatic or asymptomatic bone metastases (no visceral disease) recruited from 14 countries. Pts received Ra-223 55 kBq/kg (iv injection) every 4 weeks for 6 cycles. Co-primary endpoints were safety and overall survival (OS). Exploratory endpoints included the effects of concomitant denosumab (no BPs) or BPs (no denosumab) on OS and symptomatic skeletal events (SSE). Results: 696 pts received at least one Ra-223 cycle. Of those, 127 (18%) pts were treated with concomitant denosumab (no BPs) and 435 (63%) without any concomitant BTA. Baseline characteristics in pts treated with Ra-223 and BPs were similar to pts treated with Ra-223 without BPs. While key baseline characteristics in pts treated with Ra-223 and BPs versus pts who received Ra-223 without a concomitant BTA (Table). Median OS of (mOS) and median time to first SSE (mSSE) were longer in pts treated with Ra-223 and denosumab versus pts without a concomitant BTA (Table). While key baseline characteristics in pts treated with Ra-223 and denosumab were similar to pts treated with Ra-223 and BPs, adding BPs to Ra-223 did not appear to improve mOS. However, mSSE was prolonged in pts receiving Ra-223 and BPs versus pts who received Ra-223 without a concomitant BTA. Conclusions: In this EAP, pts treated with Ra-223 and a concomitant BTA appeared to have longer time to first SSE than those treated without a concomitant BTA. However, improvement in OS was observed with denosumab but not with BPs. Prospective
randomized controlled studies are required to confirm the benefit of this specific treat-
ment combination in metastatic CRPC.

<table>
<thead>
<tr>
<th>Denosumab</th>
<th>BPs</th>
<th>No denosumab/</th>
<th>No BPs</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 127</td>
<td>N = 125</td>
<td>N = 435</td>
<td></td>
</tr>
</tbody>
</table>

**Baseline characteristics**

<table>
<thead>
<tr>
<th>ECOG PS, n (%)</th>
<th>0</th>
<th>58 (46%)</th>
<th>55 (44%)</th>
<th>144 (33%)</th>
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<tbody>
<tr>
<td>1</td>
<td>55 (43%)</td>
<td>53 (43%)</td>
<td>224 (34%)</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>14 (11%)</td>
<td>16 (13%)</td>
<td>57 (13%)</td>
<td></td>
</tr>
<tr>
<td>Pain, n (%)</td>
<td>123</td>
<td>122</td>
<td>413</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>75 (61%)</td>
<td>72 (59%)</td>
<td>218 (53%)</td>
<td></td>
</tr>
<tr>
<td>Moderate-severe</td>
<td>19 (15%)</td>
<td>24 (20%)</td>
<td>113 (27%)</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>29 (24%)</td>
<td>26 (21%)</td>
<td>82 (20%)</td>
<td></td>
</tr>
<tr>
<td>ALP (U/L), n</td>
<td>127</td>
<td>125</td>
<td>433</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>121.0</td>
<td>137.0</td>
<td>168.0</td>
<td></td>
</tr>
<tr>
<td>PSA (μg/L), n</td>
<td>127</td>
<td>124</td>
<td>433</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>91.2</td>
<td>118.5</td>
<td>174.6</td>
<td></td>
</tr>
</tbody>
</table>

**Efficacy outcome**

<table>
<thead>
<tr>
<th>Overall survival</th>
<th>Median, months</th>
<th>95% CI</th>
<th>Hazard ratio (95% CI)</th>
<th>Time to first SSE</th>
<th>Median, months</th>
<th>95% CI</th>
<th>Hazard ratio (95% CI)</th>
<th>Efficacy outcome</th>
<th>Median, months</th>
<th>95% CI</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NR</td>
<td>NA</td>
<td>0.630 (0.431 - 0.922)</td>
<td>0.846 (0.534 - 1.226)</td>
<td>0.761 (0.493 - 1.173)</td>
<td>0.498 (0.294 - 0.845)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NR/A</td>
<td>not reached/available</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Eight weeks after completing the concurrent radio-chemotherapy regimen, all patients were re-evaluated with cystoscopy and thoracic-abdominopelvic CT. A complete response (CR) was observed in 2 patients (10%) and a partial response (PR) in 7 patients (35%) with a 71% overall response rate (ORR). Median time to progression (TTP) was 38 months (95% CI 29.4–46.7) and the median progression-free survival (PFS) was 13 months (95% CI 8.8–17.3). In the analysis of OS, median OS was 38 months (95% CI 18.9–57.1). Median duration of follow-up was 30 months (95% CI 24.9–35.1). The 5-year overall survival rate was 61.6% (95% CI 47.2–75.9).

Conclusions: The outcomes of this study suggest that the use of a 2-week interval between chemotherapy and radiotherapy is feasible and safe for patients undergoing treatment for BCG-recurrent NMIBC. The patients were re-evaluated with cystoscopy and thoracic-abdominopelvic CT. A complete response (CR) was observed in 2 patients (10%) and a partial response (PR) in 7 patients (35%) with a 71% overall response rate (ORR). Median time to progression (TTP) was 38 months (95% CI 29.4–46.7) and the median progression-free survival (PFS) was 13 months (95% CI 8.8–17.3). In the analysis of OS, median OS was 38 months (95% CI 18.9–57.1). Median duration of follow-up was 30 months (95% CI 24.9–35.1). The 5-year overall survival rate was 61.6% (95% CI 47.2–75.9).

Conclusions: The outcomes of this study suggest that the use of a 2-week interval between chemotherapy and radiotherapy is feasible and safe for patients undergoing treatment for BCG-recurrent NMIBC. The patients were re-evaluated with cystoscopy and thoracic-abdominopelvic CT. A complete response (CR) was observed in 2 patients (10%) and a partial response (PR) in 7 patients (35%) with a 71% overall response rate (ORR). Median time to progression (TTP) was 38 months (95% CI 29.4–46.7) and the median progression-free survival (PFS) was 13 months (95% CI 8.8–17.3). In the analysis of OS, median OS was 38 months (95% CI 18.9–57.1). Median duration of follow-up was 30 months (95% CI 24.9–35.1). The 5-year overall survival rate was 61.6% (95% CI 47.2–75.9).
to compare, at a population level, the clinical outcomes, quality of life and costs associated to different treatment choices.

**Results:** The START protocol has been designed by a multidisciplinary panel of specialists of the Oncology Network and patients' representatives. All the regional Hospital units of Urology and Radiotherapy have been involved (34 centers participate). The project started on May 2015. 274 patients have been already enrolled: 206 chose AS, 66 radical treatments (14 radiotherapy and 52 prostatectomy) and 2 other treatments. A web-site has been implemented with both a public and a reserved area for data collection (www.start.epiclin.it).

**Conclusions:** A population based research framework could represent a powerful and safe strategy to effectively implement AS in the NHS. The project could have a large positive impact on the Regional Health Service to improve long term quality of life of low risk PC patients.

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**B14** Cardiovascular disease (CVD) markers in patients (pts) with prostate cancer (PCa) treated with Gn-RH agonists (AG) or antagonist (AN): a prospective cohort study

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1Policlinico Hospital San Martino—IRCNS for Oncology, Genoa; 2Policlinico Hospital San Martino—IRCNS for Oncology, Genoa

**Background:** An increased risk of CVD in men with PCa on androgen deprivation therapy (ADT) has been described and one proposed explanation is the loss of the cardio-protective property of testosterone. AG and AN are equally recommended in pts with PCa. From retrospective data, pts with preexisting CVD treated with AN have an apparent lower risk of CVD when compared to pts receiving AG. One possible explanation could be the destabilization of vascular lesions. In this observational trial we defined the behaviour of some early CVD risk markers in pts treated with AG or AN.

**Patients and methods:** We prospectively monitored PCa pts on ADT during the first year of treatment. We evaluated changes in aortic stiffness trough pulse wave velocity (PWV), Fibrinogen (FB), ICAM, Selectin, RANKL, Endothelin, proBNP and metabolic parameters changes were also measured.

**Results:** From June 2015 to November 2016 41 evaluable pts (22AG,19AN), were included. Most pts (36/20AG,16AN) received ADT as adjuvant treatment after surgery or concomitantly to radiotherapy. Median (m) age was 70 yrs(AG) and 71yrs(AN); m PSA was 10 ng/mL and 10.9 ng/mL; 10 pts in AG and 11 in AN had baseline hyperlipidemia; 6 AG and 9 AN had previous CVD. All pts had NYHA I class. Results are summarized in the table below:

<table>
<thead>
<tr>
<th>Table: B14</th>
<th>mPWV(m/s)</th>
<th>mproBNP(pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>month</td>
<td>AG</td>
<td>AN</td>
</tr>
<tr>
<td>0</td>
<td>7.60 ± 0.51</td>
<td>7.49 ± 0.49</td>
</tr>
<tr>
<td>1</td>
<td>8.15 ± 0.29</td>
<td>6.94 ± 0.41</td>
</tr>
<tr>
<td>3</td>
<td>6.98 ± 0.29</td>
<td>6.98 ± 0.36</td>
</tr>
<tr>
<td>6</td>
<td>9.66 ± 0.32</td>
<td>8.01 ± 0.75</td>
</tr>
<tr>
<td>9</td>
<td>6.96 ± 0.35</td>
<td>6.41 ± 0.41</td>
</tr>
<tr>
<td>12</td>
<td>7.00 ± 0.44</td>
<td>6.87 ± 0.57</td>
</tr>
</tbody>
</table>

Preliminary results show a moderate and transient increase in the mean values of PWV at month 1 in AG and at month 6 in AN. The behavior of proBNP was comparable, while no major changes in FB levels and in the levels of the other markers on study have occurred so far (but analysis is still ongoing). No CV events were observed in either group.

**Conclusions:** Both AG and AN induce a moderate transient arterial and endothelial damage. Whether and how these changes can play a role in the higher incidence of CVD events reported during ADT with these compounds is not clear yet and under evaluation.

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**B15** A circulating miRNA signature to better stratify prostate cancer patients at diagnosis

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1Imperial College London, London; 2Imperial College, London

**Background:** Prostate cancer (PCa) is the most common cancer in men. Around 80% of PCas are diagnosed at an early local stage but only a subset of these will prove to be fatal. Circulating microRNAs (miRNA) may be an easily usable biomarker target to distinguish true indolent from clinically significant early PCa thus reducing overtreatments.

**Methods:** Blood samples from 24 men with benign prostatic hypertrophy (BPH, n = 8), localised PCa (n = 8) or metastatic PCa (n = 8) were collected at time of diagnosis. All men had intact prostates and were naïve to any endocrine and cancer related therapy. A platform of circulating miRNAs were analysed in serum using the Agilent Human One-color microarray. Data collected were independently verified using Taqman. The miRNAs identified as being significant in each group were then analysed in a published dataset.

**Results:** Serum levels of seven of the miRNAs examined were significantly different in patients with prostate cancer compared to control. A further four miRNAs could distinguish samples from the benign cohort from the metastatic cohort (miRNA-126 P = 0.008, miRNA-150 P = 0.05, miRNA-375 P = 0.007). Kaplan-Meier analysis further identified that the serum levels of four miRNAs could associate with survival rates (miRNA-21 P = 0.032, miRNA-126 P = 0.032, miRNA-150 P = 0.032, miRNA-93 P = 0.019). Examination of these miRNAs in a cohort of 280 men from The Cancer Genome Atlas (TCGA) showed that these four miRNAs had significantly different expression in patients who eventually relapsed (miRNA-21 P = 0.048, miRNA-375 P = 0.021, miRNA-210 P = 0.0003, miRNA-93 P = 0.008).

**Conclusions:** Our circulating miRNAs based signature could be used to stratify men at prostate cancer diagnosis and help identify those who would benefit more from an early radical treatment. These data should be validated in a larger number of patients.

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**B16** Cabacay—evaluating Cabazitaxel efficacy by patterns of treatment and disease in metastatic castration resistant prostate cancer (mCRPC) patients: a 5 years, “Real Life”, mono-institutional experience

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1Division of Medical Oncology, Department of Uro-Gynaecological Oncology, Istituto Nazionale Tumori — IRCCS - Fondazione Pascale, Naples, IT, Naples; 2Unità di Oncologia Medica, ASL, NA 3, SUD, Ospedale Riuniti Area Nolano, Naples; 3Progetto OCNETET2.0 — Linea progettuale 14 per l’implementazione della prevenzione e diagnosi precoce del tumore alla prostata e testicolo — Regione Campania, Italy; 4Istituto Nazionale Tumori — IRCCS - Fondazione Pascale, Naples, IT, Naples

**Background:** Since 2004, Docetaxel represents the standard 1st-line chemotherapy for mCRPC patients. Cabazitaxel shows an OS benefit in patients progressing during and after Docetaxel, including those refractory to Docetaxel. It also retains activity in patients progressing with new androgen receptor-targeted agents (ART) such as abiraterone or enzalutamide. A large early access program showed that Cabazitaxel has a manageable safety profile, without evidence of cumulative toxicity. We aimed at evaluating the activity of Cabazitaxel according to therapy line and disease burden.

**Methods:** 46 patients treated with Cabazitaxel in our National Cancer Institute were retrospectively reviewed. OS, PFS (PCWG2) and PSA response (PSA decrease ≥ 50%) were analyzed by therapy line and disease burden (bone only vs bone plus visceral disease).

**Results:** 10.9% of pts received Cabazitaxel in 2nd line (Doc: >Cab -> ART), 67.4% in 3rd line (Doc: >ART -> Caba) and 21.7% in 4th line or more. At Cabazitaxel initiation, median age was 70.5 years, median PSA was 104 ng/mL and 20% of pts had visceral disease. Median time to castration resistance was 18 mo. Patients were treated with Cabazitaxel (25mg/m2 q21) for a median of 6 cycles and received a median of 4 life extending therapy lines. Overall, median OS from first Docetaxel cycle was 42.3 Mo, median PFS with Cabazitaxel was 6.2 Mo and 47.8% of pts had a PSA response with Cabazitaxel. Results by therapy line and disease characteristics are presented in the table below.

<table>
<thead>
<tr>
<th>Table: B15</th>
<th>miRNA</th>
<th>Mean (log2)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Cancer (n = 16, 8 localised and 8 metastatic)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10b</td>
<td>0.59</td>
<td>0.05</td>
<td>0.02</td>
</tr>
<tr>
<td>125b</td>
<td>0.25</td>
<td>0.56</td>
<td>0.013</td>
</tr>
<tr>
<td>201</td>
<td>1.05</td>
<td>1.35</td>
<td>0.044</td>
</tr>
<tr>
<td>301</td>
<td>1.17</td>
<td>2.97</td>
<td>0.012</td>
</tr>
<tr>
<td>378a</td>
<td>1.19</td>
<td>1.39</td>
<td>0.04</td>
</tr>
<tr>
<td>483</td>
<td>0.56</td>
<td>0.90</td>
<td>0.03</td>
</tr>
<tr>
<td>93</td>
<td>2.72</td>
<td>2.65</td>
<td>0.033</td>
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</tbody>
</table>

**Conclusions:** Evaluating Cabazitaxel efficacy by patterns of treatment and disease in metastatic castration resistant prostate cancer (mCRPC) patients: a 5 years, “Real Life”, mono-institutional experience.
**Table 816**

<table>
<thead>
<tr>
<th>Setting of Disease</th>
<th>Outcome</th>
<th>Units</th>
<th>2 Line</th>
<th>3 Line</th>
<th>4 Line +</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone only</td>
<td>PFS *</td>
<td>Mo</td>
<td>7,1</td>
<td>6,0</td>
<td>5,7</td>
</tr>
<tr>
<td>Bone + Visceral</td>
<td>PSA Response</td>
<td>% Pts</td>
<td>75</td>
<td>48</td>
<td>37,5</td>
</tr>
<tr>
<td>Overall</td>
<td>PSA Response</td>
<td>% Pts</td>
<td>100</td>
<td>50</td>
<td>0,0</td>
</tr>
</tbody>
</table>

*Kaplan-Meier Survival Estimation*

**Conclusions:** These results suggest, despite biases of a retrospective analysis, that treatment pattern could affect patients outcomes, with early use of Cabazitaxel in therapeutic algorithm being associated with higher clinical benefit compared to its administration in subsequent lines of treatment. Additional data will be presented at AIOIM meeting.

**817 Abiraterone acetate (AA) in pre- and post-docetaxel (DX) setting for metastatic castration resistant prostate cancer (mCRPC): a monoinstitutional experience focused on cardiovascular events and on their impact on clinical outcomes**

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**Background:** AA is a therapeutic option for mCRPC patients (pts). Treatment is effective in pre- and post-DX setting and it is commonly well tolerated. However it requires the concurrent administration of corticosteroids and it can induce relevant adverse events (AEs) including: fluid retention (FR), hypertension (HT), cardiac disorders (CD) and hypokalemia (HK).

**Methods:** We retrospectively analyzed mCRPC pts treated with AA and prednisone in pre- and post-docetaxel (DX) setting. We evaluate the incidence of AEs and the putative impact of baseline characteristics and AEs on common outcomes.

**Results:** We analyzed 105 pts (30 DX-naive). Median age was 74 yrs, 19% of pts had ECOG 1-2 and 21.9% were symptomatic. Median PSA was 37.8 ng/ml and 52.4% of pts had a Gleason Score (GS) >7. Pre-existing CD and HT were in 37.1% and 62.9% of patients, respectively. BMI was >25 among 47.6% of pts. In the whole cohort, median OS and median PFS was 24.6 months and 14.9 months, respectively. In pre- or post-DX setting OS was 24.8 and 19.9 months while PFS 20.9 and 13.8 months, respectively. After multivariable analysis, PSA >10 ng/ml (p = 0.007), GS >7 (p = 0.008), ECOG 1-2 (p = 0.0002), prior androgen-deprivation therapy (ADT) <43.2 months (p = 0.01), and BMI >25 (p = 0.03) were associated with worse PFS; pain presence (p = 0.01), ECOG 1-2 (p = 0.004), prior ADT <43.2 months (p = 0.05), and BMI >25 (p = 0.042) led worse OS. Incidence of AEs was HT 17.1%, fluid retention (FR) 4.8%, CD 8.6%, and hypokalemia (HK) 16.2%. Age ≥75 years predicted for the occurrence of CD (p = 0.01) and FR (p = 0.03). Pts who developed one or more AEs had not worse outcomes, in fact HK was associated with better median OS even after multivariable analysis (unadjusted p = 0.01; adjusted p = 0.03).

**Conclusions:** Outcomes in our series are consistent with those from pivotal trials, confirming that this treatment proves effective in “real world”. This regimen was safe and well tolerated, even though pts aged 75 and over seemed to be at higher risk for cardiovascular AEs, therefore pointing at a population in need of more rigorous cardiovasculal monitoring. The occurrence of cardiovascular AEs did not imply worse outcomes.

**B18 Safety and Efficacy of Abiraterone Acetate in Patients (pts) aged 75 or more with Metastatic Castration Resistant Prostate Cancer (mCRPC) in Both Pre-chemotherapy and Post-chemotherapy Settings: Real Life Experience of Our Institution**

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**Background:** Prostate cancer affects mainly elderly patients (pts) that are usually frail and subject to comorbidities. Abiraterone acetate is a selective androgen synthesis inhibitor that showed its efficacy in either CT-naive pts or those pretreated with docetaxel. Its oral administration and excellent safety profile make it a manageable treatment for elderly mCRPC patients.

**B19 Patient (pt) characteristics and treatment patterns in the radium (Ra)-233 REASURE observational study**


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**Background:** Since April 2013 we treated 43 mCRPC elderly pts (>75 years) with abiraterone acetate. 22 pts (51%) were pre-treated with docetaxel and 21 (49%) pts were chemotherapy-naive. The median age was 79 yrs (r. 75-86). Post-CT pts had more extensive disease with multiple mts sites, higher baseline PSA and ECOG Performance status. 18 pts (40%) had PS ECOG 2. All pts had comorbidities: 22 pts (60%) had hypertension and also diabetes was a frequent comorbidity with eight patients (19%). At baseline all pts underwent cardiac echography, octagenerians 17/43 pts (40%) received also geriatric assessment.

**Results:** Median duration of hormonal therapy before castration resistance was 34 months (r.3-132), 14 pts (30%) received ≥ 5 hormonal manipulations. In post-CT group the median number of docetaxel cycles was 9 (r.2-10). Median duration of treatment with abiraterone was 11.9 months (r.3-29.8). ORR was 44% with 9% of complete responses. 12% of pts did not respond. 30 pts (70%) obtained >50% PSA reduction in 3 months (r.1-10). Median PFS was 11.9 months, 10.9 in post-docetaxel and 13.7 in CT-naive pts. We observed mOS 26.9 months (r.3,7-45,2) in post-CT group while for CT-naive pts OS data were not mature. The treatment was well tolerated with no WHO grade 4 toxicity reported, while only 6 pts (13%) reported WHO grade 3 toxicity that led to dose reduction. In all these pts the full dosage was restored after a maximum of 2 months. In one pt the treatment was interrupted after 4 months because of accidental death. After progressing on abiraterone, 17 pts (40%) received at least one subsequent treatment.

**Conclusions:** We reported outcome of abiraterone in 43 elderly patients with mCRPC treated in our hospital. Even if almost all the pts reported numerous comorbidities and nearly a half of them had PS ECOG 2, we were able to complete the treatment with abiraterone without its premature withdrawal due to toxicity. Only a few pts required dose reduction. According to our experience abiraterone was well tolerated and it has shown to be an effective treatment option also for elderly patients.
Recent data have shown that the TRITON programme will assess the efficacy and safety of rucaparib.

TRITON2 (EudraCT 2016-003162-13, NCT02952534) is a phase 2 study that, between August 2013 and August 2016, enrolled 83 patients (pts) with metastatic CRPC (mCRPC).

Radium-223 (223Ra)-chloride was well-tolerated and showed survival benefit and high symptom control in 130 pts with bone metastases.

Background: Radium-223 (223Ra)-chloride, a novel alpha emitter, has been shown to improve overall survival (OS), to delay skeletal-related events and to reduce pain in patients (pts) with castration-resistant prostate cancer (CRPC) and bone metastases. Our retrospective observational study is the first multinational and multicenter Italian experience in evaluating the efficacy and safety of 223Ra therapy in daily medical practice.

Methods: Between August 2013 and August 2016, 83 pts with metastatic CRPC (mCRPC) received 223Ra therapy at three Italian Centers. 223Ra-chloride (50 kBq/kg or 55 kBq/kg according to NIST2015) was administered every four weeks up to the programmed six cycles of therapy. Study’s endpoints were OS, progression-free survival (PFS), pain according to a numeric rating scale (NRS), biomarker response, numbers of symptomatic skeletal-related events (SSEs) and toxicity.

Results: Median age was 75 years (range 53–89 years). The majority of pts had a Gleason score of 7 (n = 25), 8 (n = 16), or 9 (n = 21). Forty-one pts completed 6 cycles of treatment; 33 discontinued treatment after 1 (n = 7), 2 (n = 5), 3 (n = 7), 4 (n = 5) or 5 (n = 9) cycles. 9 pts were under treatment during data collection. NRS pain scores significantly improved during 6 cycles of therapy (p < 0.00001). OS was 10 months; median OS had not been reached at time of reporting. Kaplan-Meier estimates for OS and PFS were 17.3 and 7.7 months, respectively. OS and PFS were significantly associated with number of 223Ra cycles; most benefit occurred in pts who received all 6 cycles. Stratifying pts according to ALP’s levels (> 220 and ≤ 220), a significant difference was found in two groups in terms of expected OS and PFS according to Kaplan-Meier estimation. 223Ra was well tolerated, no serious adverse events occurred during treatments.

Conclusions: 223Ra represents an important treatment option for pts with CRPC and symptomatic bone metastases and it seems to be useful in improving OS, PFS and level of pain; especially OS, PFS and ALP’s level.

The TRITON clinical trial programme: evaluation of the PARP inhibitor rucaparib in patients with metastatic castration-resistant prostate cancer (mCRPC) associated with homologous recombination deficiency (HRD)

Background: Recent data have shown that ≥20% of patients (pts) with mCRPC have a germline or somatic alteration in either BRCA1, BRCA2 or ATM (homologous recombination [HR] genes) (Robinson et al. Cell 2015;161:1215-28), suggesting these molecular markers may be used to select pts with mCRPC for targeted treatment with a poly(ADP-ribose) polymerase inhibitor (PARPi). PARPis have demonstrated preliminary evidence of antitumour activity in pts with sporadic mCRPC and an HR gene mutation (Mateo et al. N Engl J Med 2015;373:1697-708). These results provide a strong rationale for investigating rucaparib in pts with mCRPC associated with HRD.

Methods: TRITON2 (EudraCT 2016-003162-13, NCT02952534) is a phase 2 study evaluating rucaparib 600 mg BID in pts (n = 160) with mCRPC who have a deleterious germline or somatic BRCA1, BRCA2 or ATM mutation (per local and/or central testing). Pts with tumours harbouring an alteration in any of 12 other specified HR genes (eg, RAD51C, RAD51D or PALB2) will also be enrolled in an exploratory cohort.

Pts must have progressed on androgen receptor (AR) signalling-directed therapy (eg, abiraterone or enzalutamide) and 1 prior taxane-based chemotherapy for mCRPC. The primary endpoint of TRITON2 is response rate (modified RECIST v1.1/PCWG3) in pts with soft-tissue disease and prostate-specific antigen response in pts with nonmeasurable disease. TRITON3 (NCT02975934) is a randomised phase 3 study evaluating rucaparib 600 mg BID vs physician’s choice of treatment (abiraterone, enzalutamide or docetaxel) in pts (n = 400) with mCRPC and a deleterious germline or somatic BRCA1, BRCA2 or ATM mutation (per local and/or central testing). Pts must have progressed on AR-signalling-directed therapy for mCRPC; prior chemotherapy for mCRPC and prior PARPi are exclusions. Pts will be randomised 2:1 to rucaparib or physician’s choice; the latter group may cross over to rucaparib after radiographic progression confirmed by independent radiology review (IRR). The primary endpoint of TRITON3 in IRR-confirmed radiographic progression-free survival (modified RECIST v1.1/PCWG3 criteria).

Results: Both TRITON2 and TRITON3 are currently enrolling pts.

Conclusions: The TRITON programme will assess the efficacy and safety of rucaparib treatment in pts with mCRPC associated with HRD.

### Table B19

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Total pts</th>
<th>1L</th>
<th>2L</th>
<th>≥3L</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ECOG 0–1, n (%)</strong></td>
<td>451 (77)</td>
<td>0</td>
<td>232 (82)</td>
<td>118 (73)</td>
</tr>
<tr>
<td><strong>No. of mets, n (%)</strong></td>
<td>302 (64)</td>
<td>0</td>
<td>156 (46)</td>
<td>90 (56)</td>
</tr>
<tr>
<td><strong>&lt;6</strong></td>
<td>160 (30)</td>
<td>0</td>
<td>92 (36)</td>
<td>37 (24)</td>
</tr>
<tr>
<td><strong>6–20</strong></td>
<td>102 (20)</td>
<td>0</td>
<td>55 (18)</td>
<td>29 (19)</td>
</tr>
<tr>
<td><strong>&gt;20</strong></td>
<td>83 (15)</td>
<td>0</td>
<td>44 (14)</td>
<td>19 (13)</td>
</tr>
<tr>
<td><strong>Superscan</strong></td>
<td>40 (7)</td>
<td>0</td>
<td>16 (5)</td>
<td>10 (7)</td>
</tr>
<tr>
<td><strong>ALP (U/L), median</strong></td>
<td>134</td>
<td>0</td>
<td>112</td>
<td>145</td>
</tr>
<tr>
<td><strong>&lt;140 U/L, n (%)</strong></td>
<td>211 (36)</td>
<td>0</td>
<td>105 (37)</td>
<td>59 (36)</td>
</tr>
<tr>
<td><strong>&gt;140 U/L, n (%)</strong></td>
<td>189 (34)</td>
<td>0</td>
<td>74 (26)</td>
<td>64 (40)</td>
</tr>
<tr>
<td><strong>PSA (ng/mL), median</strong></td>
<td>61</td>
<td>0</td>
<td>28</td>
<td>74</td>
</tr>
<tr>
<td><strong>LDH (U/L), median</strong></td>
<td>273</td>
<td>0</td>
<td>260</td>
<td>272</td>
</tr>
<tr>
<td><strong>Concomitant use, n (%)</strong></td>
<td>153 (26)</td>
<td>0</td>
<td>86 (31)</td>
<td>47 (29)</td>
</tr>
<tr>
<td><strong>Docetaxel or cabazitaxel</strong></td>
<td>19 (3)</td>
<td>0</td>
<td>10 (4)</td>
<td>5 (3)</td>
</tr>
</tbody>
</table>
Table: B22 Subgroup analysis

<table>
<thead>
<tr>
<th>ALP ±220 UI/L</th>
<th>Median PFS</th>
<th>Mean OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 220</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>≥ 220</td>
<td>9</td>
<td>10.3</td>
</tr>
<tr>
<td>ALP response</td>
<td>p = 0.45</td>
<td></td>
</tr>
<tr>
<td>PR</td>
<td>12</td>
<td>13.4</td>
</tr>
<tr>
<td>SD</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>PD</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>PSA response</td>
<td>p = 0.23</td>
<td></td>
</tr>
<tr>
<td>PR</td>
<td>11.1</td>
<td>13</td>
</tr>
<tr>
<td>SD</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>PD</td>
<td>9.7</td>
<td>12</td>
</tr>
<tr>
<td>Scintigraphic response</td>
<td>p = 0.0001</td>
<td>16.2</td>
</tr>
<tr>
<td>PR</td>
<td>13</td>
<td>16.2</td>
</tr>
<tr>
<td>SD</td>
<td>12</td>
<td>11.3</td>
</tr>
<tr>
<td>PD</td>
<td>6</td>
<td>6.3</td>
</tr>
<tr>
<td>Pain response</td>
<td>p = 0.3</td>
<td></td>
</tr>
<tr>
<td>PR</td>
<td>13</td>
<td>13.4</td>
</tr>
<tr>
<td>SD</td>
<td>12</td>
<td>12.1</td>
</tr>
<tr>
<td>PD</td>
<td>8</td>
<td>10.6</td>
</tr>
</tbody>
</table>

Background: Bone metastases (mts) represent a substantial cause of morbidity in pts with CRPC, with a high rate of related skeletal events (SREs). Ra223 dichloride is a targeted a-emitter that selectively binds to areas of increased bone turnover in bone mts and emits high-energy a-particles of short range. The ALSYMPCA study assessed the efficacy of Ra223 compared to placebo in terms of OS, time to first SRE and QoL in men with CRPC and symptomatic bone mts and unknown visceral mts. The aim of our analysis is to evaluate the efficacy of Ra223 in terms of bone pain control.

Patients and methods: We retrospectively collected clinical data of 12 pts affected by CRPC treated with Ra223 for symptomatic bone mts at the Department of Nuclear Medicine of our Institute from July-15 to April-17.

Serum PSA, ALP and blood count were assessed every cycle at day 1 and day 14. To evaluate the efficacy of treatment, at every visit we asked pts to report changes in bone pain compared to baseline and it was classified as ‘increase’, ‘no change’, ‘decrease’ or ‘complete cessation’.

Results: From July-15 to April-17, 12 pts underwent treatment with Ra223 at 50kBq/kg i.v. every 4 weeks; 7 of 12 pts (58%) received all 6 expected infusions, 2 pts (17%) are still under treatment, 3 (25%) died during the treatment. 2 pts were pre-treated with less than 3 lines therapy (28%), 5 pts with 3 or more lines.

The most common side effects were anemia (57% G1-2, 28% G3), thrombocytopenia (42% G1, 14% G2), neutropenia (14% G2). An increase of PSA value from 1st to 6th cycle was found in 6 of 7 pts (85%) with a median of 173ng/ml. ALP value decreased in 6 of 7 pts (85%), with a median of 63 U/L. At the 1st Ra223 infusion, 5 pts (72%) were receiving nonsteroidal anti-inflammatory drugs (NSAIDs) + opioid drugs for pain relief. 1 pt (14%) only NSAIDs, 1 pt (14%) only opioid analgesic. 6 pts (86%) reported a decrease pain intensity since the 3rd cycle, also confirmed after the last dose; 1 pt (14%) reported no change.

Antalgic drug dose was reduced in 3 of them. Choline PET or bone scan performed 1 month after the end of treatment showed 2 PD (28%) and 3 SD (42%). 2 pts didn’t undergo restaging because of rapid PD and death. In 4 of the 5 living pts the first SRE was observed after 2 months, in 1 of them after 1 month.

Conclusions: In our analysis, Ra223 proved to be well tolerated and effective in terms of pain control. No PSA response was detected while ALP levels significantly decreased.
C  - BREAST CANCER

C1  Trends in the choice of first line treatment for hormone -responsive (HR+), human epidermal growth factor receptor - 2 negative (HER2-) metastatic breast cancer (MBC) patients (pts): results of a multicentric Italian observational study


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Background: Most of HR+ MBC pts are treated with both hormonal therapy (HT) and chemotherapy (CT) during the course of their disease. International guidelines indicate that HT is the preferred first-line treatment option for these pts restricting the use of CT only to pts not responsive to HT or at risk of visceral crisis. Data from observational studies indicate that nearly 50% of this pts to receive CT as first-line treatment. The present study aimed to evaluate if this behaviour changes in recent years.

Methods: All consecutive MBC pts treated at 13 centers of GIM (Gruppo Italiano Mammologia) with a first-line therapy (CT or HT) were included. The baseline characteristics were: age, histology, primary tumor characteristics (ER and/or PgR, HER2; and Ki67 < 20%). Treatment was classified as: monotherapy (n = 161/223 treated patients were evaluable for the primary endpoint. Abemaciclib is a potent oral CDK4- and 6-inhibitor. NeoMONARCH was a randomized, multicenter, open-label phase 2 neoadjuvant study in postmenopausal women with early-stage HR+/HER2- breast cancer (BC). Materials and methods: 224 patients stratified by progesterone receptor status and tumor size were randomized 1:1:1 to receive abemaciclib (150mg Q12h) plus anastrozole (1mg OD), abemaciclib monotherapy (n = 24), or anastrozole monotherapy for 2 years, then all patients received abemaciclib plus anastrozole for 14 weeks. Abemaciclib-treated patients received prophylactic loperamide during the first 28 days of therapy, then at the discretion of the investigator. The primary objective was to assess the change from baseline Ki-67 expression after 2 weeks of therapy with abemaciclib plus anastrozole versus abemaciclib monotherapy and anastrozole monotherapy. Clinical activity and safety were evaluated as secondary objectives. The statistical design provided 80% power to detect superiority of the combination vs anastrozole, at a 1-sided alpha level of 0.1.

Results: 161/223 treated patients were evaluable for the primary endpoint. Abemaciclib plus anastrozole (n = 56) as well as monotherapy (n = 31) significantly reduced Ki-67 expression vs anastrozole monotherapy (n = 54) at week 2 based on geometric mean change and complete cell cycle arrest (Ki-67<2.7%). Change in proliferation gene mRNAs at 2 weeks (Modaplex) correlated with the change in Ki-67 expression. Objective response rate was 54.7% (n = 106) for patients who completed the treatment with abemaciclib plus anastrozole. Most common adverse events were diarrhea, constipation, nausea and fatigue.

Conclusion: Monotherapy with abemaciclib as well as abemaciclib plus anastrozole showed significantly higher biological activity compared with anastrozole alone and the study’s primary endpoint was met. The majority of patients experienced an objective response. No new safety signals for abemaciclib when combined with anastrozole were detected. These data support continued evaluation of abemaciclib in early-stage BC.

C4  Bone health management in early breast cancer patients: an Italian Osteoncology Center experience


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Background: Bone health evaluation is important for the optimal management of early stage breast cancer (BC) both in post and pre-menopausal setting. Adjuvant endocrine

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A total of 1,165 women with early pre and post-menopausal BC were evaluated. Our analysis confirms, in real world HER2 MBC pts, the efficacy of P, T and D in association with ET.

Materials and methods: Data on patients (pts) with early BC were collected from 2011 to 2016 in a single Institution. We investigated the prevalence of vertebral fractures in pre and post pts treated with ET and other potential independent risk factors associated to bone fractures. To evaluate association with bone fractures and clinical factors, uni-variable logistic models were carried out. P-value of less than 0.05 was considered significant.

Results: A total of 1,165 women with early pre and post-menopausal BC were evaluated; for 702 (66.2%) pts treated with ET was available a X-Ray of the spine and chest were included in the analysis. The median age was 61 year-old (31.86-84). A total of 124 were pre-menopausal and 578 were post-menopausal. Frequency of bone fractures was 17.6% in post-menopausal and, among them, the majority of bone fractures was associated with AI treatment (ORR 4.7, p<0.005); in pre-menopausal pts bone fractures incidence was 6.4% and the major risk was associated to LHRH+AI treatment (ORR 2.18, p<0.007). Higher risk of bone fractures was associated with presence of back pain (OR 6.8, p<0.006), a lower BMD (ORR 2.9, p<0.001) for pts with BMI DBD 25) and lower level of Vitamin D (ORR 2.0, p<0.030 for pts with > 10 in univariate analysis. Further analysis are ongoing.

Conclusions: This Italian experience confirms the importance of bone health evaluation prior to pre-menopausal women in the management of pre and post-menopausal early BC treated with ET.

Efficacy of pertuzumab in combination with trastuzumab and a taxane in first line treatment for metastatic breast cancer (MBC): a multicenter retrospective observational study

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1Medical Oncology Unit ASL Frosinone, Frosinone; 2Oncologia Medica Ospedale San Filippo Neri, Rome; 3Unit Catholic University of Sacred Heart, Rome; 4Medical Oncology Unit Policlinico di Tor Vergata, Rome; 5Oncologia Medica Ospedale C.Urbani, Jesi, Jesi; 6Oncologia Medica Ospedale S. Filippo Neri, Rome

Background: Pertuzumab (P), Trastuzumab (T) and Docetaxel (T) is standard first-line treatment in patients (pts) with HER2 + metastatic breast cancer (MBC). This multicenter retrospective observational study was performed to evaluate the activity of P and T in combination with D or Paclitaxel (T) in real world HER2 + MBC pts.

Methods: We identified HER2 + MBC pts treated with P, T and D or T optionally followed by P. T and endocrine therapy maintenance (ETm) in hormone positive (HR+) MBC, in 17 Italian cancer centres between 09/2012 and 04/2017. Overall Survival (OS) and Progression Free Survival (PFS) were calculated. Kaplan-Meier product-limit method and Log-rank test were used to assess difference between subgroups.

Results: 239 pts were included in our analysis. Pts characteristics: median age 55 years (range 29-88); OS in 161 (67%) pts and OS in 61 (28%); 138 (58%) had visceral metastases (mst), 32 (13%) only bone mts and 47 (20%) brain mts, 165 (69%) were pretreated with T. ET maintenance in association with P and T in HR+ pts was premenopausal, < 45 years PFS 77.8 vs 58, p=0.007. 702 (60.2%) pts treated with ET was available a X-Ray of the spine and chest were included in the analysis. The median age was 61 year-old (31.86-84). A total of 124 were pre-menopausal and 578 were post-menopausal. Frequency of bone fractures was 17.6% in post-menopausal and, among them, the majority of bone fractures was associated with AI treatment (ORR 4.7, p<0.005); in pre-menopausal pts bone fractures incidence was 6.4% and the major risk was associated to LHRH+AI treatment (ORR 2.18, p<0.007). Higher risk of bone fractures was associated with presence of back pain (OR 6.8, p<0.006), a lower BMD (ORR 2.9, p<0.001) for pts with BMI DBD 25) and lower level of Vitamin D (ORR 2.0, p<0.030 for pts with > 10 in univariate analysis. Further analysis are ongoing.

Conclusions: This Italian experience confirms the importance of bone health evaluation prior to pre-menopausal women in the management of pre and post-menopausal early BC treated with ET.

Introduction: Dynamic contrast – enhanced magnetic resonance (DCE-MR) imaging of breast cancer (BC) is a powerful tool for non-invasive analysis of tumor microvasculature and stroma, and has been used in radiotherapy and as a potential predictive biomarker.

Results: A total of 131 EBC pts were enrolled; median age was 38.9 years (24.8-45.34). Nine pts (6.7%) had pre-received all FP. Reasons for refusal were no interest in fertility preservation (5 pts), previous pregnancy (3 pts), no interest in having children (1 pts). LHRHA was accepted by 120 pts (91.6%) and 27 pts (20.6%) accepted gynecologic OC. Main reason for refusal of cryopreservation procedures was fear of delaying cancer treatment (3 pts). No complications were observed among women who underwent OC or OTC. Median number of mature oocytes yielded and cryopreserved was 8.5 (4-13). A patient had a spontaneous pregnancy following adjuvant treatment.

Conclusions: Despite the great importance of fertility issues in young EBC pts, a minority of them (7.6%) require to access cryopreservation procedures. This is crucial information from a public health perspective and for resource allocation.

Evaluation of stromal tumour-infiltrating lymphocytes (TILs) in breast cancer by Dynamic contrast – enhanced magnetic resonance (DCE-MR) imaging

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Introduction: Dynamic contrast – enhanced magnetic resonance (DCE-MR) imaging of the breast is increasingly used as an adjunct to mammography and ultrasonography (US) to improve the detection and characterization of primary and recurrent breast cancers. Correlation between morphological features, DCE-MRI and prognostic factors of breast cancer (BC), including tumor size, axillary lymph node status, histological grade, presence of vascular invasion and necrosis, ER, PR, c-erbB-2 status and Ki-67, has been previously analyzed. The aim of this study was to analyze the relation between DCE-MRI parameters of BC and the presence of stromal tumour-infiltrating lymphocytes (TILs).

Patients and methods: Patients with newly diagnosed breast cancer who underwent DCE-MRI examination within two weeks prior to surgery from January 2013 to January 2017 were selected. Patients who underwent MR imaging beyond two weeks prior to surgery or previous neoadjuvant chemotherapy (NAC), with BC histotype different from Invasive Ductal or Lobular Cx, were excluded. The dataset was evaluated according to the International TILs Working Group 2014 recommendation. TILs was reported as a continuous variable. Based on the TILs Score proposed by Adam et al., patients were classified into four subgroups based on the range of TILs percentage. MR imaging was performed with a 1.5 T magnet (Philips Achieva, software v 2.6) and the post-contrast kinetic sequences were analyzed.

Results: 109 patients have been analysed. 53% tumors were poorly differentiated (G3). 25 (23%) Luminal A, 46 (42%) Luminal B/HER2 negative, 20 (18%) Luminal B/HER2 positive, 7 (6%) HER2 and 11(10%) TN subtype. Luminal tumors were associated with high values of Wash-in rate and Absolute Maximum Enhancement. On the other hand, HER2 + and TNBC tumors are characterized by slower or reduced Wash-in rate and lower values of Absolute Maximum Enhancement. Time-to-peak in TNBC and HER2 + have significantly higher values than Luminals. Reversity of Enhancement, analysed in type III curve, related to cluttered vasculatization, was statistically correlated to high percentage of TILs (p<0.02). Presence of TILs correlates with Area under curve higher than 500.000 and values of Absolute Max Enhancement.
Conclusion: At the best of our knowledge, this is the first study investigating whether MRI kinetic imaging can predict the presence and the percentage of TILs in BC tissue.

Results: Data from 739 pts were gathered (median age 57 years; yrs); Luminal/Triple-Negative/HER2 positive: 98%/16%/4%, respectively. At a median follow-up of 78 months, 5-10 yrs DFS and OS were 79.4%/66.0% and 91.4%/75.6%, respectively. At the multivariate analysis, tumor-size according to TNM (HR 1.34, 95% CI 1.04-1.72, p = 0.025) and lymph-node status (HR 2.39, 95% CI 1.47-3.89, p < 0.0001) were independent predictors for DFS. Tumor-size (HR 1.87, 95% CI 1.09-3.54, p = 0.05), lymph-node status (HR 3.24, 95% CI 1.69-6.22, p < 0.0001), Ki67 (HR 2.48, 95% CI 0.95-6.42, p = 0.06), and age (HR 2.23, 95% CI 1.16-4.30, p = 0.016) were independent predictors for OS. A significant prognostic effect of aCT upon OS was found after adjusting for independent factors with the propensity score analysis, as shown.

C6 Brain metastases and ado-trastuzumab emtansine (T-DM1) treatment in HER2 positive metastatic patients: an Italian multicenter analysis

Background: Ado-trastuzumab emtansine (T-DM1) is a drug-antibody conjugate whose activity has been confirmed in HER2+ advanced breast cancer (BC) patients by the phase 3 EMILIA trial. Within the 991 patients enrolled in this trial, about 10% were affected with brain metastases (BM); in this subgroup, safety and efficacy of T-DM1 were confirmed although without any PFS improvement.

Patients and methods: In an Italian, multicenter, retrospective analysis involving 303 BC patients: 148 pts with BM, 283 pts without BM (BM-group). The study wanted to evaluate the efficacy of T-DM1 on BM; furthermore we compared BM-group with the remaining 216 patients without BM (nBM-group) in terms of outcome. MRI was used as assessment imaging. The number of extracranial metastatic sites was 1 for 10 patients (11.5%) in the BM-group and 74 (34.3%) in the nBM-group, 2 for 23 and 93; for 25 and 38; or for more for 29 and 11 respectively. In the BM-group, 5 patients (5.7%) had received surgery alone as local treatment for brain metastases. 13 surgery plus stereotactic radio-surgery (SRS), 4 surgery plus whole-brain radiotherapy (WBRT), 23 SRS alone, 40 WBRT alone and 2 WBRT followed by SRS. Twenty-eight patients (32.9%) and 89 (42.4%) in the BM-group and nBM-group, respectively, received T-DM1 as second line, 24 and 49 as third line and 33 and 72 as fourth line. Mean number of cycles was 6 in both groups.

Results: Among BM-group, 53 patients (60.9%) were evaluable for response. Two (3.8%) obtained brain complete response (CR), 14 (26.4%) partial response (PR) and 13 (24.5%) stable disease (SD) [brain disease control rate: 54.7%]; 24 progressed (PD) (50%) while the other 29 patients (55%) remained stable. In the nBM-group, 145 patients (67.3%) were evaluable for response. Four (2.8%) obtained brain CR, 21 (15.3%) PR and 104 (76.9%) SD [brain disease control rate: 86.8%]; 21 progressed (PD). The overall response rate during T-DM1. Regarding extracranial metastases, overall response rate was 35.1% in BM-group and 11 months in nBM-group (p = 0.674). When T-DM1 was given as second line, median PFS was 5 months in the BM-group and 11 months in nBM-group (p = 0.01) while as third line, in which 60% of patients received lapatinib/capcitabine before TDM1, median PFS was 12 and 13 months (p = NS), respectively.

Conclusions: T-DM1 showed a good activity on BM in BC patients. A better outcome was shown in patients previously treated with lapatinib. The identification of clinical and biological prognostic factors could be needed to better select more responder patients with BM to T-DM1.

C9 A propensity score analysis exploring the impact of adjuvant chemotherapy (aCT) in 739 patients (pts) affected by early stage pure Invasive Lobular breast Carcinoma (ILC)

Background: In the lack of prospective data for the restricted context of ILC, the magnitude of the benefit of aCT for this histotype is still not sizable. Thus, the aim of this analysis was to explore the effect of aCT in a multi-center series of early stage pure ILC.

Methods: Clinical-pathological data of consecutive pts affected by resected pure ILC, diagnosed at 3 Italian Institutes, were correlated with disease-free and overall survival (DFS/OS) using a Cox model. Two different survival analyses were performed. The first, following the Cox model. Results: The hazard ratio (HR) and the 95% Confidence interval (95% CI) were estimated according to the Cox model. The propensity score analysis was performed to investigate the prognostic impact of aCT. Kaplan-Meier curves were compared with Log-Rank analysis.

Results: Data from 739 pts were gathered (median age 57 years; yrs); Luminal/Triple-Negative/HER2 positive: 98%/16%/4%, respectively. At a median follow-up of 78 months, 5-10 yrs DFS and OS were 79.4%/66.0% and 91.4%/75.6%, respectively. At the multivariate analysis, tumor-size according to TNM (HR 1.34, 95% CI 1.04-1.72, p = 0.025) and lymph-node status (HR 2.39, 95% CI 1.47-3.89, p < 0.0001) were independent predictors for DFS. Tumor-size (HR 1.87, 95% CI 1.09-3.54, p = 0.05), lymph-node status (HR 3.24, 95% CI 1.69-6.22, p < 0.0001), Ki67 (HR 2.48, 95% CI 0.95-6.42, p = 0.06), and age (HR 2.23, 95% CI 1.16-4.30, p = 0.016) were independent predictors for OS. A significant prognostic effect of aCT upon OS was found after adjusting for independent factors with the propensity score analysis, as shown.

C10 Neutrophil-to-lymphocyte and lymphocyte-to-monocyte ratios in breast cancer

Background: Immunity plays a central role in cancer progression and prognosis.

Methods: This retrospective study analyzed a consecutive cohort of 657 patients (pts) with a diagnosis of pT1 BC (N =), without restrictions regarding lymph node status (T1BC), or metastatic BC (MBC) (N =) treated between 2004 and 2017 at the Department of Oncology of Udine (Italy). Differences in terms of NLR and LMR among the two cohorts and between clinico-pathological characteristics in the T1BC subgroup were explored through the Kruskal-Wallis test. The prognostic impact in terms of OS in the T1BC population was investigated using uni- and multivariate Cox regression.

Results: Both NLR and LMR distributions were significantly different among the T1BC and MBC cohorts. In particular, pts with T1BC had a higher median LMR (3.8 vs 2.9, P = 0.0001) and lower NLR (2 vs 2.7, P = 0.0001). When stratifying T1BC and MBC cohorts according to molecular profile, pts with luminal B-like subtype showed significantly different differences in terms of both LMR (4.2 vs 5, P = 0.0001) and NLR (2 vs 2.5, P = 0.0001). In triple negative subtype, the difference between T1BC and MBC was observed for NLR (1.9 vs 3.2, P = 0.0272). No differences between T1BC and MBC were highlighted for the other subtypes. When focusing on the clinico-pathological characteristics of the T1BC cohort, LMR was associated with progesterone receptor (PR) expression (P = 0.0261) and marginally with the estrogen receptor (ER) expression, while NLR with tumor diameter (P = 0.044) and marginally with grading. Furthermore, among T1BC pts, NLR had no prognostic impact in terms of OS, while LMR was associated with a better outcome also when a correction for ER, PR and HER2 status was applied (HR 0.44, 95%CI 0.28-0.71, P = 0.001).
**C13** Relevance of immunohistochimical (IHC) surrogates classification of pT1 breast cancer in luminal-like subtypes: a 15-years long-term observational retrospective study


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**Background:** Molecular BC subtypes may improve risk assessment in order to individualize therapeutic strategies. However, gene expression tests are too often expensive and not available in real-life clinical practice. The aim of study was to discover whether IHC surrogates reclassification on luminal subtypes could be a precision metric information regarding outcome compared to conventional prognostic factors.

**Methods:** We reviewed the records of 511 patients with pT1 BC treated at single Oncology Unit between 1995 to 2010. We reclassified tumors of patients into five IHC surrogates intrinsic tumor subtypes: Luminal A-like, Luminal B-like HER2+, Luminal B-like HER2+, HER2-enriched, TN. Primary end-points was to evaluate at 15-years of follow-up (FU) distant metastases free survival (DMFS), disease free survival (DFS) for each subgroup of Luminal-like tumors.

**Results:** On overall population, the 15-years DMFS rate was 99% for Luminal A-like, 65% for Luminal B-like HER2-, and 41% for Luminal B-like HER2+ tumors (p = 0.036); DFS was 78% for Luminal A-like, 57% for Luminal B-like HER2+, and 18% for Luminal B-like HER2+ (p = 0.006). In the cohort of 440 Luminal-like tumors, the Kaplan-Meyer curves showed faster disease recurrence in luminal B-like HER2+ tumors patients after 5 years of FU. At a long-term FU, low expression of PR (< 20%) was associated with recurrence events both in terms of DMFS (88% vs 87%; p = 0.018) and DFS (50% vs 73%; p = 0.02). HER2 expression was significantly associated with DFS (p = 0.014) and a DFS of 14% vs 60% (p = 0.002). In BC tumors with Ki-67 rate = 20%, the analysis showed a significant difference only for DMFS rate at 15-years (63% vs 86%, p = 0.042). Multivariate analysis confirmed that the main independent prognostic factors involved for delayed distant recurrences were low expression of PR (HR = 2.27; p = 0.04) and HER2 overexpressed (HR = 2.46; p = 0.03). Only HER2 overexpression was the independent prognostic factor (HR = 2.53; p = 0.005) for DFS.

**Conclusion:** Despite the notable limitation of retrospective analysis, our results confirmed the utility in the clinical practice of IHC-surrogate reclassification of BC. In patients with pT1 Luminal-like tumors, low PR expression, HER2 overexpression and high Ki67 rate are the main prognostic factors for long-term outcomes. Finally, our long-term results seem to the appropriate way to establish an extended follow-up for women with Luminal B-like breast cancer subtype.

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**C12** BRCA related breast cancer and sporadic tumors: some prognosis or survivorship bias?

Z. Ballatore, B. Dal Cin, F. Giannani, E. Maccarone, L. Belvederisci, C. Brugnati, A. Mummer, S. Pagliarotta, M. Pistelli, R. Berardi


Germline BRCA mutations are found in about 5% of all breast cancers (BCs). They are inherited in autosomal-dominant fashion conferring BC increased risk up to 80% by age 70. Literature data are controversial about BC prognosis in BRCA carriers respect sporadic tumors patients. Aims of study were to compare outcome among BC BRCAdom (BCB) and BCBRCan (BBC) and to investigate the relationship between BCRA mutations and main standardized prognostic factors.

Pathologic and clinical features were recorded in all consecutive women with BC referred to perform genetic counseling, which resulted eligible for BRCA genetic testing. A total of 485 patients were included, 160 (32.9%) hosted BRCA pathogenic mutation: 84 (52.5%) BRCA1, 76 (47.5%) BRCA2. At diagnosis, median age was 45.9 years (range18-84.4) and 254 patients (52.3%) developed BC earlier. BRCA related tumors had higher Ki67 and grading than set one (p = 0.011), BRCA1 had a significantly strong association with triple negative phenotype (p = 0.001) and stage II-III (p = 0.03). No variable showed prognostic impact on RFS and OS in BBC1A1 tumors. In BBC2A2 group, small tumor size and negative node status were confirmed as prognostic factor of RFS (p = 0.037, p = 0.021 respectively) and OS (p = 0.001, p = 0.006, respectively). There were no differences in RFS between wt patients and BBC1A1 and BBC2A2 carriers (p = 0.96 and p = 0.91, respectively) and OS between BBC1A1 carriers and wt at 10 years (p = 0.44 from diagnosis or later (p = 0.38). Differently, in the first 10 years BBC2A2 tumors reported worse prognostic trend (p = 0.044), which was later (p = 0.10). BBC2A2 tumors had more frequent node involvement and higher stage than others maybe because younger age at diagnosis, outside current mammographic screening range. Common prognostic factors do not have significant impact in BBC1A1 patients. Comparing BBC1A2 and wt patients prognosis no significant differences emerged because some kind of compensation between the high mortality in the first years in TNBC and the decreased mortality after the first 10 years post diagnosis in luminal. It is like each prognostic factor would be “mitigated” by extended follow-up, survivorship bias and received specific treatments for subtype.
Conclusions: Our preliminary results highlight the activity and safety of the combination of CT plus P and T in unselected HER2+ MBC patients. The study is ongoing and updated results will be presented.

C15 Time to surgery after neoadjuvant chemotherapy for early breast cancer
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Background: In early breast cancer (BC) patients, a delay between surgery and adjuvant chemotherapy (CT) has been associated with worse outcome, but little is known about timing-related consequences in the neoadjuvant setting. The aim of this study was to evaluate the impact of the interval between the end of neoadjuvant CT and surgery (CTTS) on relapse free survival (RFS) and overall survival (OS).

Patients and methods: This study retrospectively analyzed a series of 469 consecutive BC patients receiving neoadjuvant chemotherapy (CT) at the Department of Oncology of Udine University Hospital. Patients were classified as follows: period A (between 2005 and 2009) and period B (between 2010 and 2014). CTTS was defined as the time between the last CT administration and surgery. The impact on survival-related outcomes was investigated through Cox regression.

Results: The study population consisted of the following subtypes: Laminar-like (53.66%), HER2-positive (29.26%) and triple negative (17.05%). Median age at CT start was 67 years. 80% were HR negative and HER2 positive (95% CI 65.9-96.2; p = 0.02). Multivariate analysis showed similar results: HR = 0.81 (95% CI 0.63-1.03; p = 0.09).

Conclusion: The use of mCHT in the treatment of HER2+ BC pts has deeply changed across the last 5 years, new metronomic regimens have demonstrated an ORR comparable to that produced by standard regimens with a low incidence of severe side effects.

Table C16

<table>
<thead>
<tr>
<th></th>
<th>ORR, n/N (%)</th>
<th>DCR, n/N (%)</th>
<th>TTF (range)</th>
<th>OS (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CM</td>
<td>16/113</td>
<td>76/113</td>
<td>4.8</td>
<td>18.9</td>
</tr>
<tr>
<td>(14.2%)</td>
<td>(67.2%)</td>
<td>(4.1-5.8)</td>
<td>(14.1-26.6)</td>
<td></td>
</tr>
<tr>
<td>CAPE-based</td>
<td>32/111</td>
<td>74/111</td>
<td>5.8</td>
<td>21.8</td>
</tr>
<tr>
<td>(28.8%)</td>
<td>(66.6%)</td>
<td>(4.8-7.0)</td>
<td>(16.6-29.4)</td>
<td></td>
</tr>
<tr>
<td>VRL-based</td>
<td>60/182</td>
<td>149/182</td>
<td>6.2</td>
<td>22.5</td>
</tr>
<tr>
<td>(33.0%)</td>
<td>(81.9%)</td>
<td>(5.5-7.1)</td>
<td>(17.4-27.8)</td>
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leads to anti-tumor activity. Old regimens included Cyclophosphamide-Methotrexate (CM), whereas in the last years new regimens, such as Vinorelbine (VRL) and Cepaedite (CAPE)-based have been developed. Aim of this observational retrospective ongoing study is to describe the use of mCHT in ABC pts across 5 years and the clinical characteristics of the pts together with efficacy of old (CM-like) vs new (VRL/CAPE-based) metronomic regimens.

Methods: We retrospectively identified from clinical records those HER2+ve ABC pts who have received any kind of mCHT in the years 2011-2015, alone, or in combination with a non-metronomic drug. Standard statistical approaches were used for describing the sample characteristics. Logistic and non proportional hazard analysis were used to identify factors associated with response, and time to treatment failure and survival, respectively. This preliminary analysis focuses on Response Rate (RR) and Disease Control Rate (DCR).

Results: From June 2011 to December 2015, 431 pts have been identified till now and 404 are fully evaluable. Median age at mCHT start was 67 years. 80% were HR+ and 68.2% had visceral disease. 113 pts (27.9%) received CM, 182 (43%) VRL-based and 111 (27.4%) mCAPE-based regimens. mCHT use increased over the time from 17% (2011) to 24.6% (2015). Overall Response Rate (ORR) was 26.6%, 14.2% in the CM group and 31.4% in the VRL/CAPE group and 33.3% in the VRL. One median time to mCHT failure was 5.6 months (5.2-6.2). Median OS was 21.8 months (18.1-24.6). TTF and OS according to the type of mCHT is detailed in Table 1.
The development of BMs negatively affects the prognosis of pts with MBC. Median follow-up was 44 months (mo). Median Progression Free Survival (PFS) was 10 mo at 1st line (L), 5 mo at 2nd L, and 4 mo at 3rd L. Near 92% of cases were observed according to institution type, title, age or geographical location. The most relevant factors influencing the M-MBC strategy were the presence of TN disease (73%), the con- tradiccion for exam (69), the presence of clinically measurable disease (68), and treatment safety profile (67), while patients’ socio-economic status (61) or logistics (26) were less relevant. M-MBC was considered to influence quality of life with a score of 69/100 and survival with a score of 39/100. Only 16% thought that strategies of M-MBC were defined by guidelines and 70% called for literature data. Negligible differences were observed according to institution type, title, age or geographical location.

Conclusion: The study describes the attitude of Italian oncologists on M-MBC. The potential consequences for breast cancer patients need prospective studies on M-MBC, also in order to support guidelines implementation.

### Table C18

<table>
<thead>
<tr>
<th></th>
<th>1st L OR [95%CI]</th>
<th>2nd L OR [95%CI]</th>
<th>3rd L OR [95%CI]</th>
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<tr>
<td><strong>TM use</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Frequent oncology office visit*</td>
<td>1.60 [1.26-2.02]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High educational level</td>
<td></td>
<td>5.29 [1.47-19.1]</td>
<td></td>
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<tr>
<td>Senior prescriptor</td>
<td></td>
<td>9.7 [2.31-40.9]</td>
<td></td>
</tr>
<tr>
<td><strong>CT/RM use</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequent oncology office visit*</td>
<td>3.07 [2-4.72]</td>
<td>2.28 [1.32-3.95]</td>
<td></td>
</tr>
<tr>
<td>Presence of cutaneous/subcutaneous metastases</td>
<td></td>
<td>0.34 [0.12-0.98]</td>
<td></td>
</tr>
<tr>
<td>Luminal A type</td>
<td></td>
<td>0.22 [0.06-0.78]</td>
<td></td>
</tr>
<tr>
<td>Age &gt;65 years</td>
<td></td>
<td>0.33 [0.10-0.82]</td>
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*Volume in any 1 month.
The Breast-DX Italy prospective study evaluated the impact of the 21-
gene RS on adjuvant treatment decisions for early BC patients. Methods: The study was conducted in 9 centers of the Veneto Region (2 hub and 7 spoke). All consecutive patients with ER+/HER2-, T1 to T3, N0 to N1 early BC who met protocol-defined clin-
ical-pathological criteria for “intermediate risk” were included. Pre-RS and post-RS physicians’ treatment recommendations.

Results: From November 2014 to August 2016, n = 124 N0 and n = 126 N1 patients were enrolled (65% at hub and 35% at spoke centers). The majority had PgR+ (86%), G2 (71%) and pT1c (63%) BC. Median age was 55 years, median Ki67 was 20% (range 2-
70%). The distribution of RS was: ≤18 (61%), 18-30 (32%) and >30 (7%). Main factors associated with higher RS were G3, low PgR expression and high Ki67. The addition of chemotherapy (CT) to hormonal therapy (HT) was initially recommended for 48% of the patients (38% of N0 and 57% of N1 patients; 54% and 37% of patients enrolled at hub and spoke centers, respectively). The post-RS recommendation changed from the pre-RS recommendation for 40 patients, mostly from CT-HT to HT (n = 30; n = 22 with low and intermediate RS). Change was more frequent for N1 patients (Table). Of the 72 N1 patients initially recommended to CT-HT, 28% had a post-RS indication to HT alone. From pre-RS to post-RS, the recommendation to CT-HT was reduced from 48% (120/250) to 40% (100/250), McNemar’s p < 0.0016, more evidently for N1 patients and at Hub centers.

Conclusions: Pre-RS indication to HT alone was frequent, in particular for N0 patients. The use of the 21-gene RS further contributed in sparing CT administration, more so for N1 patients and at hub centers. The impact of the RS when used at discretion of the clinicians is currently under investigation in the prospective ROXANE study.

Table: C20

Change in Pre-RS to Post-RS

<table>
<thead>
<tr>
<th>Comparison</th>
<th>N0 (n = 124)</th>
<th>N1 (n = 126)</th>
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<tbody>
<tr>
<td>Any change, n(%)</td>
<td>15 (12%)</td>
<td>25 (20%)</td>
</tr>
<tr>
<td>HT to CT+HT</td>
<td>5 (33%)</td>
<td>5 (20%)</td>
</tr>
<tr>
<td>CT+HT to HT</td>
<td>10 (67%)</td>
<td>20 (80%)</td>
</tr>
</tbody>
</table>

C21 Expression and clinical-pathological correlations of the androgen receptor (AR) in a series of ER and PgR negative breast cancers undergoing surgery: our center experience

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Background: Many evidences have shown that the direct action of AR-mediated androgens is the main mechanism used to influence tumor growth. Unlike ER and PgR, AR is commonly expressed in high invasive breast cancers (BC), high-grade ductal BCs, in mutated BRCA BCs, in breast Paget’s disease and also in apocrine differentiated BCs, where it is greater the hyper-expression of c-erbB-2. In the basal subset of invasive BC, AR expression is commonly lost. From a prognostic point of view, in a cohort of negative ER BC patients, the majority younger than 50 years old, AR’s positivity is associated with a significantly longer disease-free survival, with a recurrence risk of only the 33% when compared with negative AR cases.

Materials and methods: We consecutively analyzed 220 ER and PgR negative BC cases undergoing surgery between 1 January 2009 and 31 December 2015, with the aim of investigating the expression of AR and its correlation with relevant clinical and patho-
logical parameters. Median follow-up time is 36 months.

Results: We had 159 triple negative and 61 HER2 positive BC. In 20 pts we found apoc-
rine-like histology. Positivity for AR was found in 39.1% of cases. 40 pts had recurrence and 36 pts died due to BC disease. In the univariate analysis, we did not find any statisti-
cally significant correlation between AR expression and monophasal status, disease stage, p53 expression, BRCA mutational status, disease-free survival, and mortality. There is, however, a close correlation between AR and apocrine-like histology (p < 0.001) and HER2 positivity (p < 0.0001). From the multivariate analysis emerges that only the stage of BC disease influences relapse (p = 0.0021) and mortality (p = 0.045).

Conclusions: According to current literature data, AR expression is a relatively com-
ommon feature of ER and PgR negative invasive BC. Our investigations confirm the correlation between AR expression, HER2 status, and apocrine-like histology. However, differently from what has been shown in the recent meta-analysis, in our study, no prognostic differences emerge between positive and negative AR cases.

C22 Assessment of critical factors related to return to work in women after breast cancer

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Background: New diagnostic, surgical and therapeutic techniques allow an increasing number of women to preserve their status and psychosocial vulnerability.

Materials (patients) and methods: This descriptive observational study uses an ad hoc questionnaire to explore the variables detected in scientific literature as negative factors for job reintegartion after the therapeutic pathway. The main risk factors were verified by multivariate statistical analysis. Study cohort: 1578 women with breast cancer resident in the area of AUSL Bologna. They have had cancer surgery in a public or private structure. Average age: 55 years (July 2014).

Results: 47% of women came back to work presenting problems of varying nature and severity. It was possible to identify the four homogeneous groups of problematic factors that are predictive for a problematic return to work: 1. live alone; 2. needs for non-
ocnological post-surgery treatments; 3. physical and psychological problems related to the return to work; 4. long duration of absence from work after surgery. It is also proved that even receiving maximally invasive treatments (mastectomy, DA chemotherapy) represent a negative predictive factor.

Conclusions: Returning to work is problematic for about 50% of women. This suggests the importance to set up personalized rehabilitation programs in order to counteract the chronicity of physical and psychological diseases and the consequent disability. Probably, information on pre-intervention status should be evaluated within breast units as well as clinical and biological parameters, affecting the result of the treatments. Collaboration between territorial oncology and associations of oncological patients could be an important contribution in this direction.

C23 Stromal periluminal and intratumoral infiltrating lymphocytes: how immunity influences prognosis in triple negative breast cancer

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Background: Triple negative breast cancer (TNBC) is an aggressive subgroup of breast cancer (BC) with poor clinical outcome. The lack of target therapies switches attention on the role of immune interaction between host and tumor. Tumor-infiltrating lymphocytes (TILs) is a biomarker of immunogenity that in TNBC can correlate with DFS and OS. The aim of our study was to evaluate the prognostic role of TILs and its associa-
tion with clinicopathological parameters in TNBC.

Materials and methods: Nine-three consecutive patients with primary diagnosis of TNBC referred to our institution between January 2009 and December 2015 were enrolled. We collected their clinico pathological data. In each tumor sample the pathol-
ologist evaluated stromal intratumoral TIL percentage (area of stroma occupied by infiltr-
ating lymphocytes) and stromal periluminal TIL percentage (percentage of stroma lymphocytes encountered in entire circumferential invasive tumor front). Lymphocytes predominant breast cancer (LCBC) were the most TILs of all BCs (54.2% vs 40% of TILs). The most TILs were correlated with clinico pathological data, OS (time between diagnosis and death or last follow up) and DFS (time between diagnosis and relapse either as local recurrence or distant metastasis). All data were analysed by Chi square test. Kaplan-Meier curves for OS and DFS were applied. Univariate and multivariate Cox propor-
tional hazard models were conducted to correlate between TIL, OS and DFS. Level of significance p value was set at 0.05.

Results: We found a significant association between stromal intratumoral TIL and stro-
mal periluminal TIL (p = 0.0008). A significant difference was also seen in LPBC subgroup (p = 0.0001) and HER2 positive (p = 0.001). From the multivariate analysis emerges that only the stage of BC disease influences relapse (p = 0.0021) and mortality (p = 0.045).

Conclusions: According to current literature data, AR expression is a relatively com-
ommon feature of ER and PgR negative invasive BC. Our investigations confirm the correlation between AR expression, HER2 status, and apocrine-like histology. However, differently from what has been shown in the recent meta-analysis, in our study, no prognostic differences emerge between positive and negative AR cases.
TIL percentage of expression. Intratumoral TIL did not demonstrate significant correlation with DFS, unless a TIL percentage ≥ 1% (p = 0.029 95% CI 1.286-10.329), nor with OS. At the multivariate analysis TIL did not show a significant correlation with DFS and DFS.

Conclusions: Peritumoral TIL correlates with DFS and OS in TNBC. This is an intriguing data not enough considered in literature yet which suggest that the location of TIL may help to stratify prognostic BC subgroups to guide future therapeutic decisions.

C24 Prognostic value of tumor-infiltrating lymphocytes in small HER2- positive breast cancer

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Background: Standard treatment for patients with small, node-negative, human epidermal growth factor receptor 2 (HER2)-positive breast cancer (BC) is still controversial. No data are available on the prognostic role of tumor-infiltrating lymphocytes (TILs) in this subset of patients.

Methods: Pathological material has been selected. Hematoxylin and eosin (H&E) slides from node-negative, pT1a-b HER2-positive BC surgical specimens were retrieved from pathology archives to assess TILs and their association with outcome.

Results: TILs were evaluated in 205 patients with HER2 positive, pT1a-b tumors who underwent breast surgery between 1997 and 2009. At a median follow-up of 11 years, we did not observe any association between the presence of TILs, either assessed as a continuous variable or dichotomously (< 50 vs ≥ 50%) and outcome.

Conclusions: TILs cannot be used as a prognostic biomarker in pT1a-b HER2-positive BC. Additional biomarkers are needed for selecting patients with stage I HER2-positive BC candidate to adjuvant therapy de-escalation.

C25 Fulvestrant (FUL) as first-line therapy in HR-ve, HER2-ve advanced breast cancer (ABC) patients (pts): when clinical practice comes earlier than clinical trials. Results from the Gim-13 AMBRA study

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Introduction: Hormone receptor positive tumors represent the most common form of breast cancer. Endocrine therapy (ET) represents the main initial therapeutic strategy for these patients and has been associated with significant clinical benefits. One of the available therapeutic strategy is FUL; in a Phase II study, FUL demonstrated improvements in time to progression (TTP) and overall survival (OS) in comparison to anastrozole (ANA). In a recent Phase II trial, comparing FUL vs ANA as 1st-line therapy, FUL was significantly longer in the FUL group than in the ANA group (16 vs 6 vs 13-8 months). The benefit in FUL seems to be limited to patients without visceral sites of disease. Aim of the present study is to describe pts’ characteristics and outcome treated with FUL in a real-life setting.

Patients and methods: We used data of the HR-ve pts of the AMBRA study, a longitudinal cohort study, describing the choice of first and subsequent lines of treatment in HER2-ve MBC pts, treated between 1997 and 2009. In our population, our data confirm that ESR1 mutations are frequent in patients who are resistant to aromatase inhibitor (Ai) therapy in hormone-refractory metastatic breast cancer (MBC). Endocrine therapy (ET) is a cornerstone in the treatment of both early and metastatic disease, but its effectiveness is limited by the developing of acquired resistance and more rarely by de novo resistance. Understanding the mechanisms of resistance to ET represents a challenge. Recently acquired mutations in ESR1, has been associated with resistance to aromatase inhibitor (Ai) therapy in hormone-refractory metastatic breast cancer (MBC).

Materials and methods: We retrospectively collected data of 85 patients (pts), treated at our Institution between 2007 and 2015, diagnosed with ER+ HER2- MBC, previously exposed to ET both in adjuvant or metastatic setting, whose tissue samples were available from primary (N = 40) and metastatic tumor (N = 45). We performed sequencing of DNA tissue to detect hotspot ESR1 mutations at codons 536-538 using Sanger sequencing and next-generation sequencing (NGS). Moreover, we collected blood samples from 7 pts to detect ESR1 mutational status in circulating cell free DNA (cfDNA) using E-Ice-COLD for the amplification of ESR1 region and droplet digital PCR (ddPCR) or NGS to analyze the amplicons.

Results: We detected no mutations in primary tumor and 6 somatic mutations in 45 of metastatic specimens (overall 13.3% frequency). In our population, the most frequent mutation was Y537S (3 pts) and in 2 pts D538G: all data were confirmed at NGS analyses. In one case a Y537C mutation was detected using only Sanger method. Blood samples from 7 patients were collected a long time away from the biopsy of metastatic lesions, after exposition at further lines of therapy. In 2 pts respectively Y537S and Y537L mutation has been detected in plasma and none mutation in metastasis, in 1 pts a Y537C was found in metastasis but not in cfDNA, 1 pts presented Y537S both in plasma and metastatic tissue and 3 pts either in plasma or in tissue were ESR1 wild-type. We observed an increase incidence of ESR1 mutations according to the number of endocrine lines administrated: 8,8% in pts with one line, vs 33% in pts with more than 3 lines of ET.

Conclusions: With the limitation of the retrospective nature of the study and the small population, our data confirm that ESR1 mutations are frequent in patients who...
progress after ET with AIs. Their early detection and monitoring in plasma across meta-
static disease might help in the choice of best treatment.

C28 Role of DCE-MR imaging of the breast in predicting breast cancer subtypes: where are we going?

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Background: Dynamic contrast–enhanced magnetic resonance (DCE-MR) imaging of the breast is increasingly used as an adjunct to mammography and ultrasonography (US) to improve the detection and characterization of primary and recurrent breast cancers. Correlation between morphological features, kinetic parameters of DCE-MR and prognostic factors of BC has been previously analyzed, providing conflicting results. Aim of the study is to expand the evaluation of the dynamic characteristics of MMM, analyzing potential correlation with the histopathologic and immunohisto-
chemical characteristics of breast cancer to orient the subsequent clinical and therapeut-
ical management.

Patients and methods: Between January 2012 and June 2016, 95 consecutive patients with histopathologically confirmed invasive breast cancer underwent MR imaging were eligible. Patients with rare forms of breast cancer (different from invasive ductal/ lobular carcinoma) were excluded. In patients with multifocal, multicentric or bilateral carcinoma, the largest lesion was analyzed.

Results: The immunohistochemistry was shown to be significantly related with Maximum Enhancement (p = 0.05), Time to peak (p = 0.04) and Wash-in rate (p = 0.01). Furthermore, a significant association between Maximum and Relative Enhancement (p = 0.004 and p = 0.02, respectively), Wash-in rate (p = 0.0018) and Area under curve (p = 0.006). In addition, PR status and vascular invasion were significantly related to Time to peak (p = 0.048 and p = 0.02, respectively). Type of RMN curve doesn’t show any significant association in relation to the histological, immunohisto-
chemical and locoregional features of BCs.

Conclusion: Our analysis demonstrated that Max Enhancement Absolute and Relative,
Some tumors characteristics have been statistically significant associated with

C29 Small luminal-like breast cancer: determinants of adjuvant chemotherapy use

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Background: The use of adjuvant chemotherapy (CT) in small luminal-like breast can-
cer (BC) is still heavily debated. International guidelines identify endocrine therapy
in 80% of cases as the first line of treatment, despite the presence of validated prognostic significance. We aimed at evaluating the impact of TS on the use of CT.

Methods: This retrospective study analyzed 601 consecutive pts with pT1 (≤ 2 cm)
luminal-BC treated between 2004 and 2015 at the Department of Oncology of Udine (Italy). No restrictions were applied regarding lymph node status. The cut-off point of 1% was used to define ER and/or PR positivity. Factors influencing the pre-
scription of CT were investigated through uni- and multivariate logistic regression with

C30 Neutrophil-to-lymphocyte ratio in metastatic breast cancer patients: relationship with tumor characteristics and survival

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Introduction: The neutrophil-to-lymphocyte ratio (NLR) is a good reflection of inflammation, which plays an important role in tumor progression and metastasis. The presence of an elevated NLR has been recognized as a poor prognostic factor in various tumors, including breast cancer (BC); however, its prognostic role was still little explored in patients (pts) with metastatic breast cancer (mBC).

Patients and methods: Clinicopathological features and treatment outcome of 595 consecutive mBC pts treated at the Department of Oncology of Udine, Italy, between 2004 and 2014, were retrospectively analyzed. NLR was calculated from the blood count performed before first line therapy starts. Differences in NLR according to clinicopathological characteristics were investigated through chi-square test. Cox regression was used to determine the prognostic impact of NLR.

Results: Some tumors characteristics have been statistically significant associated with higher NLR in mBC pts: high histologic grade (p = 0.009), ductal histotype (p = 0.02), ER negativity (p = 0.003), PgR negativity (p = 0.0001), high Ki-67 (p = 0.03). No statistical differences in NLR were found between HER2-positive and HER2-negative disease (p = 0.33). Among subtypes, luminal HER2+ BC were associated with lower NLR, while triple-negative BC with higher NLR (p = 0.004). No statistical differences in NLR were observed according to visceral disease (p = 0.13) nor according to bone-only disease (p = 0.24). At univariate analysis, a NLR > 2.64 (medium value of the whole popu-
lation) was associated with worse progression-free survival after first line therapy (HR 1.41, 95%CI 1.11-1.79, p = 0.005) and with worse overall survival (HR 1.76, 95%CI 1.32-2.36, P < 0.0001); however, the statistical significance was lost at multivariate analysis (P = 0.08 and P = 0.13, respectively). Interestingly, a subgroup analysis revealed a significant prognostic value of NLR in HER2-positive subtype (HR 4.89, 95%CI 1.13-21.23).

Conclusions: In our cohort study, although a high NLR did not represent an independ-
ent prognostic factor at multivariate analysis, it turned out to be associated with pecu-
liar pathological features of BC. Further efforts are needed to establish the appropriate cut-off value of NLR, as well as to identify the BC subtypes in which the prognostic role of this easy to collect parameter could be more useful.

C31 Insights from a long-term follow-up evaluation of early breast cancer (BC) outcomes by tumor subtype (TS)

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Background: Immunohistochemistry (IHC)-based classification of BC is mostly used in common practice and provides surrogate definitions of intrinsic molecular subtypes with validated prognostic significance. We aimed at evaluating the impact of TS on long-term BC mortality.

Material and methods: We used a retrospective cohort of women diagnosed with early BC between 1985 and 1990. Surgical samples underwent centralized pathology review and IHC re-assessment for ER, PgR, HER-2 and Ki67 expression. Multivariate Cox and Fine-Gray’s proportional hazard regression models assessed associations of TS with overall survival (OS) and breast cancer-related survival (BCRS), adjusting for menopausal status, tumor (T) size, nodal status and receipt of adjuvant treatment.

Results: Of 208 patients, 42.0% had Luminal A-like, 33.5% had Luminal B-like. Human epidermal growth factor (HER2)-negative, 8.5% had HER2-positive and 17.0% had triple negative BC. At the time of diagnosis, 68.5% of patients were post-
menopausal, 53.8% had T > 2 cm, and 47.5% had node-positive disease. Over a median follow-up of 18.7 years (range 3.9-32.0), we recorded 140 death events, of which 73 were BC-related. Median OS was 18.5 years (95% confidence interval [CI] 15.8-21.2), Luminal A-like tumors experienced the longest absolute median OS (21.2 years [95%CI 17.4-24.9]), although no statistically significant differences in the hazards of death for all causes were observed across subtypes. Luminal B-likeHER2-negative subtype was significantly associated with worse BCRS vs Luminal A-like (adjusted hazard ratio [HR] = 1.86 [95% CI 1.09-3.16]). After multivariate analysis, T size > 2 cm (HR [95% CI 1.09-3.16]).
A literature-based meta-analysis of randomized trials

So far, 791/1500 pts have been registered into the study, 107 (13.5%) received 330 pts were enrolled, with a median age of 51 years (range 23-72). 78% of the patients had DFS, the secondary was the overall survival (OS); moreover, a subgroup analysis of Trieste, Piazza Ospitale 1, 34129 Trieste, Italy, Trieste; 6University of Medical Oncology, Viale Bracci 11, 53100 Siena, Siena, Italy

Background: Endocrine treatment, in particular with aromatase inhibitors (AIs) for 5 years is nowadays the preferred adjuvant treatment for hormone receptor–positive breast cancer. However, very few data are available on efficacy of the extended approaching with AIs up to 10 years as adjuvant treatment. We performed a meta-analysis to assess the real impact on the disease-free survival (DFS) of extended adjuvant therapy with AIs.

Methods: A literature-based meta-analysis of randomized controlled trials (RCTs) in accordance with the preferred reports for items in systematic reviews and meta-analyses guidelines was undertaken. Relevant publications from PubMed, the Cochrane Library, and abstracts from meetings were searched. The primary endpoint was DFS, the secondary was the overall survival (OS); moreover, a subgroup analysis was performed to elucidate the role of nodal involvement on the primary endpoint.

Results: The pooled analysis from the RCTs of AIs revealed a significantly increased DFS (hazard ratio (HR) for DFS: 0.72, 95%CI: 0.61-0.84; P < 0.0001, 12–50%)

Conclusions: This analysis confirmed the efficacy of extended treatment with AIs in the adjuvant setting on DFS for hormone receptor–positive early breast cancer and no impact on OS. A greater DFS efficacy was observed in women with positive nodal status.
About 10-16% of TNBCs harbor a Breast Related Cancer Antigens (BRCA) germline mutation and 70% of breast cancers developed in BRCA1 germline mutation carriers are TNBCs, resulting in a “haplosufficiency of homologous recombination”. We present detected BRCA mutations in patients with TNBCs at our Institution.

**Patients and methods:** A total of 147 women affected by TNBCs were selected for genetic counseling and underwent BRCA genetic testing between 2002 and 2016 to our Institution. Risk assessment was performed according to the clinical criteria of Modena and using BRCApro tool (total score ≥10). However, women under the age of 50 have also been tested, taking into account that triple-negative phenotype is now considered a sufficient requirement. BRCA genes were evaluated using Multiplex Ligation Probe Amplification (MLPA). We referred mainly to the Breast Related Cancer Antigens (BRCA) LOVD and to the ClinVar archive. The identification of three of the most common BRCA1 mutations worldwide (185delAG; 5382insC; 300T>G) and 1 large deletion of several exons. According to the literature, most of the TNBCs (n = 35, 80%) was associated with BRCA1 mutations, mainly involving exons 5 (300T>G) and 11 (962delA, 390delT). Three founder mutations were detected: two commonly encountered in Askenazi Jews (185delAG; 5382insC) and one in Poland (300T>G); this was also, the most frequent pathogenetic mutation in our BRCA1 carriers. Among BRCA2 mutations, 9106C>T is one of the most commonly in Italy, frequently reported in early-onset male breast cancer as well as ovarian cancer.

**Conclusions:** Our study describes a consecutive series of TNBCs referred for genetic counseling and testing for BRCA germline mutations, with a high detection rate (55%). The identified BRCA mutations have also been tested, taking into account that triple-negative phenotype is now considered a sufficient requirement. BRCA genes were investigated by sequencing and multiplex ligation probe amplification. The most effective regimens for breast cancer are often complicated by alopecia. The chemotherapy-induced hair loss (HL) is one of the main reasons for patients (pts) to refuse chemotherapy. The scalp-cooling device (SCD), causing cutaneous vasodilatation, may be able to improve the following side effects. We report our preliminary experience with SCD in reducing chemotherapy-hair loss (CT-HL) and related distress in breast cancer pts undergoing adjuvant (adj) CT.

**Materials and patients (and methods):** From March 2016 to March 2017 we prospectively selected pts with for stage I-II breast cancer and eligible for HL inducing 46 failures. The regimen used were: paclitaxel (P) for 12 weeks plus trastuzumab (T) for 1 year, docetaxel-cyclophosphamide (TC) and doxorubicin-cyclophosphamide (AC) both for 4 cycles. The HL grading and the treatment adherence have been evaluated during CT every 21 days through the DEAN’s scale by pts and operators (op) and the administration of a comfort analogic scale. We administered Hospitality Anxiety depression scale questionnaire at the baseline and at the end of treatment to assess CT-HL related distress.

**Results:** Among the 46 patients identified, 27 accepted SCD. The median age was 56 (36-76), 22 (81.4%) pts received TC, 3 (11.1%) AC, 2 (7%) P weekly plus T 24 (89%) completed the treatment whereas the 3 pts (11%) treated with AC interrupted prematurely the SCD use for inefficacy: grade (G) 3 HL after 2 cycles. At last cycle of CT, of 24 pts, 3 pts (12.5%) reported a G 4 HL, no pts reported a G 0, 11 (45.8%) a G 2, 5 (20.8%) a G 1 and 5 a G 3. Concurrently, the op described a G 4 in no pt, G 0 in 1 patient (3.7%), G 2 in 16 (53.9%), G 1 in 4 (14.8%) and G 3 in 1 (11.1%). The evaluation of the concordance between the HL G reported by pts and op was not statistically significant with the Cohen test. On the contrary a statistically significant reduction in anxiety and an increasing in depression was described with the Wilcoxon test. The treatment was quite well tolerated in the majority of pts (81%), with a better tolerability during the cycles succession. There was no serious adverse device related events.

**Conclusions:** In our study the SCD results in a reduced CT-HL in taxane-based CT and is associated with a better QoL. Furthermore it suggests a discordance in HL perception between pts and op.
Of BC are hereditary, and are characterized by aggressive/bilateral disease and early age of onset. The aim of our observational study was to describe the percentage of BRCA mutations in patients (pts) with BC treated in Medical Oncology Department (MDO) of Brindisi, Italian Salento.

Materials (patients) and methods: A total of 317 consecutive pts (312 women and 5 men) were tested for analysis, according to national AIO3 guidelines 2016. All pts had BC diagnosis and 4 pts (1.3%) had both BC and ovarian cancer (OC). Data about base-line characteristics, treatment, BRCA1/2 status and family history of cancer were collected according to the local Ethical Committee guidelines. We used multiplex ligation-dependent probe amplification (MLPA) to screen mutations in BRCA1 and BRCA2 in serum DNA samples.

Results: Of the 317 pts analyzed, 55 (17.3%) were BRCA1/BRCA2 mutated, 31 (9.8%) had 1 allele altered, 22 (7.0%) had 2 altered and 3 (1%) had 3 altered. BRCA1 gene mutations were identified in 22 pts (7.0%), BRCA2 in 17 pts (5.4%) and 3 (1%) had both BRCA1 and BRCA2 mutations present. A total of 23 BRCA1 gene mutations and 27 BRCA2 gene mutations were identified in these 55 pts with BC and OC (a total of 50 mutations). In BRCA1 gene, c.5266dupC (71%) was the most frequent mutation. In BRCA2 gene, c.11008dupC (41%) was the most frequent mutation.

Conclusions: Few data have been published regarding on anthropological and geographical distribution in families with BRCA1/BRCA2 mutations in Italy, and particularly in Mediterranean population. The BRCA1 c.5266dupC mutation was first described in the Ashkenazi Jewish (AJ) population; however, this alteration is also present in Europe, Brazil and North America. The high incidence of c.5266dupC mutations in our pts may be linked to the presence in Salento of Jewish communities in the Middle Age. Actually there is no knowledge of organized Jewish settlements in this Area. Different ethnic and geographical regions have different BRCA1/2 mutation prevalence: understanding genetic predisposition to BC may contribute to definition of more cost-effective screening measures in populations.

C40 PerTe: efficacy and safety of pertuzumab in “real life setting” for the neoadjuvant treatment of HER2-positive breast cancer patients


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The standard preoperative systemic therapy for HER2+ breast cancer (BC) patients includes chemotherapy (CT) and trastuzumab (T), improving pathological complete response rate (pCR). In June 2015 the EMA approved Pertuzumab (P) in neoadjuvant regimens for HER2+ BC. Two phase II trials have evaluated pertuzumab plus-trastuzumab—based therapy in the neoadjuvant setting. In NeOpHera trial, the use of dual HER2-targeted therapy combination with docetaxel was associated with a significantly improved pCR. In TRYPhAENA study low rates of symptomatic systolic dysfunction were noted and there was no evidence that P increased the rate of cardiac dysfunction.

PerTe is an observational pilot study, aimed to evaluate efficacy and safety of P for the Neoadjuvant Treatment of HER2+ BC pts. The medical records of 2 different Italian Institutions were reviewed to identify pts treated with P + T + CT as neoadjuvant therapy from Jul 2015 to day. Twenty patients were treated according 2 different CT regimens, based on the clinical practice of belonging institution. The 70% of pts received T+P followed by T+weekly Paclitaxel for 12, and the remaining 30% received T+P+Docetaxel (6 cycles). Our primary objective is to evaluate the safety profile of dual HER2 blockade. Up to now 20 pts treated with dual HER2 blockade completed the study treatment. 60% of pts had a ductal infiltrating carcinoma (CDI). Luminal B HER2+, while the remaining 40% had a CDI HR negative and HER 2+.

The 70% of pts received radical mastectomy. The pCR was achieved in 85% of pts. The remaining 25% achieved a partial response (PR), all these pts had high level of ER/PgR and low ki-67 and 2 of them did not receive TCH; one of them experienced a disease recurrence. No cardiac toxicity was detected.

Addition of P to T+CT in neoadjuvant setting seems to be beneficial and not to increase the rate of cardiac dysfunction, regardless of CT regimen used. Levels of ER/PgR and different CT regimens seems to produce different pathological response. Up to now other pts are on treatment and we are going to involve more institutions in order to collect a larger sample.

C41 The APE1/NPM1 axis in triple negative breast cancer: prognostic and therapeutic implications

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Background: Heterogeneity and absence of a molecular target are a challenge in triple negative breast cancer (TNBC). Apurinic/apyrimidinic endonuclease 1 (APE1) is a pivotal enzyme of the Base Excision Repair (BER) pathway, while Nucleophosmin (NPM1) is involved in ribosome biogenesis and cell proliferation. We previously demonstrated that NPM1 stimulates BER activity in cells through direct protein interaction with the N-domain of APE1. Aim of the study was to explore the utility of APE1, NPM1 and their interaction as a prognostic factor and a novel therapeutic target.

Methods: Cell line models used were based on the HCC70 and HCC1937 TNBC cells. Cell viability after platinum-based treatment, protein levels and their localization were analyzed through IHC assay, Western Blotting and immunofluorescence analysis (IF), respectively. A retrospective analysis of 129 consecutive TNBC patients was conducted. Correlations between cyttoplasmic APE1 (cAPE1), nuclear APE1 (nAPE1) and NPM1 were evaluated through Spearman’s test. Associations with clinico-pathological features were investigated and the prognostic impact of APE1 and NPM1 was explored in an early TNBC subset.

Results: HCC70 and HCC1937 cell lines were differentially responsive to platinum-based treatment. An up-regulation of NPM1 was observed in HCC70 cells only, while APE1 levels were unaffected in both TNBC cell lines. IF data showed a relocalization of APE1 and NPM1 to the nucleoplasm after treatment with cisplatin and carboplatin, independently from the cell line used. APE1 inhibition caused a significant sensitization to cisplatin in HCC70 cells, but not in HCC1937 cells. When analyzing the retrospective cohort, higher levels of NPM1 significantly correlated with higher levels of nAPE1 (P < 0.0001), but not with cAPE1. Counterparty, higher levels of cAPE1 significantly correlated with lower levels of nAPE1 (P < 0.0001). No associations were observed between both nAPE1 or cAPE1 and baseline clinical characteristics, while significantly lower levels of NPM1 were found in stage pT3 or pT4 (P = 0.047) tumors and among patients who developed distant localization in the whole clinical history (P = 0.011).

Levels of nAPE1 higher than 89% predicted a favorable prognosis in terms of event free survival (HR 0.42, 95%CI 0.42-0.16, P = 0.026).

Conclusions: APE1 and NPM1 are promising prognostic factors and therapeutic targets in TNBC. Inhibitors of APE1, NPM1 and their interaction are currently under further investigation.

C42 The ENDOPREDICT® molecular test for breast cancer prognostic: clinical-pathological correlations and therapeutic implications on a selected cohort of patients

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Background: Gene signatures of prognosis are emerging for treatment strategies in breast cancer (BC), based on individual risk profile. These molecular tests are useful for patients who are affected by estrogen receptor (ER) positive/HER2 negative BC of indefinite prognosis. We focused on ENDOPREDICT® (Myriad Genetics), a multi-gene test, which gives both a molecular fingerprint of the tumors (the “EP score”) and a score obtained by combining the EP score with the tumor size and number of metastatic lymph nodes (LN) (the “EPclin score”), EPclin score discriminates between patients having “low risk” or “high risk” of relapse within 5 years. To verify the utility of this test in clinical practice, we decided to: (i) correlate EP score and EPclin score with clinical pathological features; (ii) test the ability of the EPclin score to influence therapeutic choices.

Materials and methods: From July 2014 to December 2016, we selected in Piedmont Region a cohort of 56 ER+ HER2- BC patients at intermediate risk of recurrence (tumor size < 3 cm; LN involvement from 0 to 3; Ki67 15-30%), for which the eligibility to endocrine therapy (ET) was not universal. For each case, clinical and pathological data were recorded. ENDOPREDICT® was performed on each case and EP score and EPclin score were noted. We correlated both scores with clinical and pathological data. The data base was then submitted to 26 oncologists, who indicated the therapeutic option (hormonothalamic treatment (HT) versus ET) after the ENDOPREDICT® results.

Results: EP score was related with LN status (p = 0.008), tumor grade (p < 0.001) and progesterone receptor (PgR) expression (p = 0.007) ; EPclin score was related with tumor grade (p < 0.001), PgR (p = 0.033) and Ki67 (p = 0.009). In 11 cases the risk was assessed as “high” according with EP score and “low” in 3 cases. The risk was “low” by EP score and “high” by EPclin score. Treatment agreement was low when
oncologists were blind to Endopredict® results (Cohen’s K: 26%; Z: 26.47) and improved following the results of the molecular test (Cohen’s K: 58%; Z: 24.32). The therapeutic indication changed from HT to HT + CT for 9 patients and from HT + CT to HT alone for 6 patients.

**Conclusions:** Both EP score and EPclin score correlate with grade and PgR expression.

We obtained a median LNR of 0.18 (range 0-1). We compared pts with a Neoadjuvant chemotherapy (NCT) is the standard treatment strategy for advanced BC patients treated with NCT.

An indirect comparison with a network meta-analysis comparing EE with PL for advanced BC patients treated with NCT.

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**Background:** To compare the efficacy of EE to PF or PL in the treatment of metastatic HR+, HER2- breast cancer. Indirect comparisons with network meta-analysis for early BC, while their use in metastatic BC is still open to debate. The research for reliable inflammatory biomarkers will be a major focus in future years.

**Results:**
- All the data of the BOLERO-2 trial, the Bachelot et al network meta-analysis (Breast Cancer Treat Rep 2014), the PALOMA-2 and the Paloma-3 trial were analyzed and indirectly compared in a network meta-analysis. 2 orders of comparison were performed: EE vs PL for patients treated with AI for advanced disease and EE vs PF for patients pre-treated with AI for advanced disease. The pooled HR and 95%CI were respectively 0.89 (0.59-1.35) (p = 0.89) and 1.0 (0.76-1.31) (p = 0.87) for EE vs PL (never treated with AI) and EE vs PF (pre-treated with AI). No major reasons of clinical and methodological heterogeneity were detected in an independent qualitative analysis, while a moderate quantitative heterogeneity was detected using the I² test.

**Conclusions:** Txl: today EE and PL or PF represent active treatments for patients with metastatic HR-, HER2 breast cancer treated or untreated with AI, and no direct comparisons between EE and PL or PF exist in literature. Although our data have not the power to detect any definitive difference in PFS between EE and PL or PF (probably with the exception of EE vs PL, where a trend in favor of EE could be hypothesized), EE, PL or PF seem to be comparable in terms of PFS; it follows that the better safety profile or the economic profile could help physicians in daily clinical practice.

**C45 Role of inflammation parameters in locally advanced breast cancer: the debate is still open**

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**Background:** Neoadjuvant chemotherapy (NCT) is the standard treatment strategy for locally advanced breast cancer (BC). Data about clinical utility of blood-derived inflammation parameters as prognostic factors are robust in early BC, while their use in metastatic BC is still open to debate. The research for reliable inflammatory biomarkers will be a major focus in future years.

**Methods:** An indirect comparison with a network meta-analysis comparing EE with PL for patients never treated with AI for advanced disease and EE vs PF (pre-treated with AI). No major reasons of clinical and methodological heterogeneity were detected in an independent qualitative analysis, while a moderate quantitative heterogeneity was detected using the I² test.

**Conclusions:** Txl: today EE and PL or PF represent active treatments for patients with metastatic HR-, HER2 breast cancer treated or untreated with AI, and no direct comparisons between EE and PL or PF exist in literature. Although our data have not the power to detect any definitive difference in PFS between EE and PL or PF (probably with the exception of EE vs PL, where a trend in favor of EE could be hypothesized), EE, PL or PF seem to be comparable in terms of PFS; it follows that the better safety profile or the economic profile could help physicians in daily clinical practice.

**C44 The role of ribociclib in hormone receptor-positive (HR+)- human epidermal growth factor receptor 2-negative (HER2-) early breast cancer: the EarLEE adjuvant clinical trials program**

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**Background:** In the phase 3 clinical trial MONALEESA-2, the CDK4/6 inhibitor ribociclib in combination with letrozole extended PFS versus placebo in post-menopausal women with HR+, HER2- advanced breast cancer (BC) and no prior therapy for advanced disease (HR = 0.56, 95%CI: 0.43-0.72; P = 3.29 x 10⁻⁸; Hortobagyi et al. N Engl J Med 2016). Although adjuvant endocrine therapy (ET) reduces the risk of recurrence of early BC (EC), it is not yet known if the addition of ribociclib to ET would provide a benefit in this setting, where disease recurrence is common in patients with adverse clinical and pathological features. EarLEE-1 (NCT03087751) and EarLEE-2 (NCT03081234) will examine the efficacy and safety of ribociclib plus ET versus placebo plus ET as adjuvant therapy in patients with high- and intermediate-risk EBC, respectively.

**Trial design:** In these double-blind, placebo-controlled, phase 3 trials, women and men with fully resected, HR+ tumors – EBC are being randomized 1:1 to ribociclib (600 mg/day, 3 weeks on/1 week off for ~24 months) plus ET or placebo plus ET. Adjuvant ET may include tamoxifen, letrozole, anastrozole, or exemestane for ≥ 60 months with ovarian suppression for premenopausal women (in EarLEE-2, ovarian suppression is per investigator discretion). High-risk EBC is defined as AJCC 8th ed Prognostic Stage Group III, or > 2 mm residual disease in axillary lymph nodes and > 10 mm in breast after neoadjuvant chemotherapy. Intermediate-risk EBC is defined as AJCC 8th ed Prognostic Stage Group II. Randomization is stratified by menopausal status, geographical region, and risk factor. Prior adjuvant chemotherapy is optional in EarLEE-2 and is an additional stratification factor; patients eligible for EarLEE-1 must have completed (neo)adjuvant chemotherapy. Eligible patients must have tumor tissue from the surgical specimen, adequate bone marrow and organ functions, normal serum electrolytes, QTc interval < 450 msec, and must have completed and recovered from acute toxicities of adjuvant radiotherapy (if indicated) and adjuvant chemotherapy (for patients in EarLEE-1) or investigator discretion in EarLEE-2). The primary endpoint for both studies is invasive disease-free survival. Secondary endpoints include recurrence-free survival, distant disease-free survival, overall survival, quality of life, and safety. Global recruitment of ~2,900 patients (EarLEE-1) and ~4,400 patients (EarLEE-2) is ongoing.

**C46 Prognostic value of lymph node ratio in early breast cancer: a retrospective single institution analysis of clinical-pathological characteristics and outcomes**

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**Background:** Nodal involvement is recognized as negative prognostic factor in early breast cancer (BC), but the role of the lymph node ratio (LNR) is less defined.

**Methods:** In our retrospective single institution study we analyzed the association between LNR and risk of recurrence in 96 BC patients (pts) who underwent to surgery as first disease treatment and reported local or distant recurrence. We collected patient demographics, tumour characteristics, initial clinical stage and treatment received.

LNR was defined as the number of positive lymph nodes divided by the number of dis-
In recent years, increasing evidences showed that several types of dietary intervention could be effective in breast cancer, although its value seems to be restricted to specific subtypes. The aims of this study was to investigate the effects of short term starvation in breast cancer cells treated with doxorubicin under STS conditions for 48h. In addition, the expression of mRNAs and miRNAs specifically induced by STS was analyzed in MCF-7, MDA-MB-231 and SkBr3 cells using Real-time PCR analyses.

Materials and methods: Vitality assays were used to assess the effects of STS on cell proliferation. Using a TaqMan Low Density Array Human microRNA microarray analysis, the expression profile of 577 miRNAs was analyzed in healthy and malignant breast cells, MCF10A and MDA-MB-231 respectively, treated for 24h with 1μM doxorubicin under STS conditions for 48h. In addition, the expression of miRNAs and mRNAs specifically induced by STS was analyzed in MCF-7, MDA-MB-231 and SkBr3 cells using Real-time PCR analyses.

Results: In vitro cell vitality assays showed that STS, in association with doxorubicin treatment, significantly reduces breast cancer cell proliferation and viability, whereas it appears to protect healthy breast cells from chemotherapeutic treatment. Microarray analysis showed that a subset of miRNAs involved in molecular pathways related to drug sensitivity/resistance was found to be differentially expressed in breast cancer cells following the doxorubicin treatment and STS. Finally, expression analysis of hypothetical miRNA/gene targets involved in therapy response have confirmed the coherence of our results.

Conclusions: This work establishes, for the first time, an interesting link between anti-cancer effects of STS and miRNA expression changes in doxorubicin-treated breast cancer cells, suggesting the potential involvement of some miRNAs in molecular pathways mediating the effects of STS in breast cancer.

C47 Potential miRNAs involved in molecular pathways mediating the anti-cancer effects of short term starvation in breast cancer cells treated with doxorubicin

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Background: In recent years, increasing evidences showed that several types of dietary approaches restricting food intake, including Short Term Starvation (STS), may exert a protective role against aging and other age-related pathologies as well as cancer. Interestingly, the dietary restriction showed significant anti-cancer effects able to prevent cancer onset, slow its progression and improve therapy response. Since recent studies showed that miRNAs may modulate sensibility/resistance to antiblastic therapy, the aim of our study was to investigate the STS-induced molecular changes in breast cancer cells treated with doxorubicin, focusing our attention on miRNA expression profile.

Materials and Methods: Vitality assays were used to assess the effects of STS on cell proliferation. Using a Taqman Low Density Array Human microRNA microarray analysis, the expression profile of 577 miRNAs was analyzed in healthy and malignant breast cells, MCF10A and MDA-MB-231, respectively, treated for 24h with 1μM doxorubicin under STS conditions for 48h. In addition, the expression of miRNAs and mRNAs specifically induced by STS was analyzed in MCF7, MDA-MB-231 and SKBr3 cells using Real-Time PCR analyses.

Results: In vitro cell vitality assays showed that STS, in association with doxorubicin treatment, significantly reduces breast cancer cell proliferation and viability, whereas it appears to protect healthy breast cells from chemotherapeutic treatment. Microarray analysis showed that a subset of miRNAs involved in molecular pathways related to drug sensitivity/resistance was found to be differentially expressed in breast cancer cells following the doxorubicin treatment and STS. Finally, expression analysis of hypothetical miRNA/gene targets involved in therapy response have confirmed the coherence of our results.

Conclusions: This work establishes, for the first time, an interesting link between anti-cancer effects of STS and miRNA expression changes in doxorubicin-treated breast cancer cells, suggesting the potential involvement of some miRNAs in molecular pathways mediating the effects of STS in breast cancer.
Materials and methods: 34 HER2+ metastatic BC patients were included: 18 patients with HR+/HER2+ and 14 with HR-/HER2+. Data regarding tumor characteristics, treatment information and clinical outcomes were collected. The expression of 770 genes and 13 molecular pathways were evaluated by means of Nanostring PanCancer pathway panel performed on BC formalin-fixed paraffin-embedded tissues from diagnostic core biopsy or surgical resection specimen.

Results: Gene expression analysis identified 118 genes with significantly different expression in the two cohorts. All but one of these genes were over-expressed; only the gene CACNG6 was down-regulated in HR+/HER2+ group. In particular, 93 genes were over-expressed in HR-/HER2+ while 24 were over-expressed in HR+/HER2+. Most of these genes encoded growth factors, pro- or anti-inflammatory interleukins and DNA repair factors. 62% of these genes were involved in PI3K, MAPK and RAS pathways (32, 22 and 18, respectively). PI3K, MAPK and NOTCH pathways were differentially expressed between HR+/HER2+ and HR-/HER2+ (p = 0.003, p = 0.0018, p = 0.02, respectively). All these three pathways were over-expressed in HR+/HER2+ group. In particular, all the significantly different expression genes in NOTCH pathways were up-regulated in HR+/HER2+ group.

Conclusions: This genome expression analysis identified a gene expression profile able to differentiate HR+ versus HR-/HER2+ metastatic BC. The overexpression of PI3K, MAPK and NOTCH pathways in HR-/HER2+ BC could justify its more aggressive behaviour. The validation of this HER2+ BC profile needs further investigation.

Correlation between categorical variables was assessed using chi-square test and Fisher’s exact test.

Results: From March 2015 to April 2017, 48 women with a median age of 53 underwent scalp-cooling during chemotherapy for breast cancer. 5 patients (pts) were treated in neoadjuvant setting, 29 in adjuvant setting and 1 in advanced setting; 27 pts received anthracycline-based chemotherapy, 13 taxane-based chemotherapy, 5 both anthracyclines and taxanes and 3 other regimens. Median scalp-cooling phase 3 (range 1-14). Hair preservation was reported in 17 women (37%). According to literature data, women treated with taxane-based chemotherapy had higher rate of hair preservation than women treated with anthracycline-based chemotherapy (54% vs 31%), even if no correlation between chemotherapy regimen and hair loss wasn’t statistically significant in our analysis. Different variables (such as age, BMI, smoking status, comorbidities, previous chemotherapy, neutropenia) were tested, but only neutropenia G3-G4 during treatment resulted significantly related to hair loss (chi-square 4.9, p = 0.049). Early interruption of scalp-cooling occurred in 26 pts, due to hair loss < grade 3 (21 pts) or intolerance (5 pts). 15 pts reported adverse events, all graded < 2, the most common being headache, cost sensation and mild cranial pressure. 1 had to use a wig, even if 5 of them experienced alopecia G1-2. No scalp metastases were reported, but follow-up data are still immature.

Conclusions: Our analysis suggests that scalp-cooling has a moderate efficacy in reduc- ing CIA and is well tolerated. Further clinical trials are needed to determine exact indi- cations for scalp-cooling and to improve the efficacy and adherence, to reduce side- effects and to define the best cooling procedure.

C51 Use of scalp-cooling device to prevent alopecia for breast cancer patients receiving chemotherapy: a single-institution prospective study
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Background: Previous studies have suggested that scalp cooling may prevent chemothera- py-induced alopecia, a common adverse event with a relevant impact on quality of life.

Patients and methods: Two DigniCap scalp cooling system devices are available at the Istituto Oncologico Veneto. The PROTECT prospective observational study evaluated the performance of scalp cooling for patients with breast cancer receiving different adjuvant/neoadjuvant chemotherapy schedules. Scalp cooling was initiated 30 minutes prior to each cycle, with a scalp temperature maintained at 3-5 °C, throughout chemotherapy and for 90 to 120 minutes afterwards. Patients’ questionnaires were adminis- tered every 3 weeks during treatment and at 3 weeks from the last cycle. Success of scalp cooling was defined as self-reported hair loss ≤50% according to Dean scale.

Results: From May to December 2016, 40 patients were included in these treatment cohorts: n = 10, Doctracet-Cyclophosphamide q2w x4 (TC); n = 10, Paclitaxel q2w x12 (TDx); n = 10 Epirubicin-Cyclophosphamide q4w x4 followed by Tdx q2w x12 (EC-Tdx); n = 10, Tdx q2w x12 followed by EC q4w x4 (TDx-EC). HER2+ (n = 11) patients received trastuzumab. Success rate at 3 weeks from the start of treatment was 85% (34/40). Three patients in the TC and 3 in the EC-Tx cohort reported a hair loss >50%. Full assessments have been completed so far in the TC, Td and EC-Tx cohorts (3 patients in the Td-EC cohort are still undergoing chemotherapy). Rate of final scalp cooling success was 18/30 (60%). No failure was reported in the Td cohort. Failure was reported by 6 patients in the TC and 6 patients in the EC-Tx cohort and led to prema- ture scalp cooling discontinuation in 1 and 3 patients, respectively. Two more patients discontinued scalp cooling in these cohorts: 1 patient due to chemotherapy toxicity and 1 patient in the EC-Tx cohort due to low scalp cooling tolerability. Most frequent cool- ing-related symptoms were: chill (26/30), heavy head (18/30), scalp pain (14/30), headache (3/40); respectively mean highest scores (in a self-reported scale of 1 to 4 with 4 as extreme) were: a single

Conclusions: Use of scalp-cooling system for chemotherapy-induced alopecia preven- tion was successful in the majority of patients, but relevant difference was observed across treatment groups.

C52 Scalp cooling: a real opportunity to prevent alopecia in breast cancer patients undergoing chemotherapy
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Background: Hair loss is one of the most distressing side effects of chemotherapy. Recent clinical trials demonstrated the efficacy of scalp-cooling in preventing and reducing the risk of chemotherapy-induced alopecia (CIA), but factors predicting out- come are still unknown. The aim of this study was to evaluate efficacy of scalp-cooling in preventing CIA and its predictive factors. Alopecia was graded according to the Dean’s Scale: a score of 0-2 (hairs lost < 50%) was considered successful.

Patients and methods: Data on women with breast cancer stage I-IV who used the Paxman scalp-cooler during chemotherapy at Ferrara Oncology Unit were prospectively collected. Efficacy and safety of scalp-cooling device were assessed using clinici- ans-reported data and patients direct interviews. Alopecia was graded according to the Dean’s Scale: a score of 0 to 2 (hairs lost < 50%) was considered successful.

Results: Of 144 patients, 92 (64%) patients received scalp-cooling with complete follow-up. 50/92 (54%) patients showed CIA prevention. Univariate analysis identified previous chemotherapy and greater CIA with severe alopecia, CIA > grade 3 (p < 0.001), baseline CIA > grade 2 (p = 0.011), longer treatment duration (p = 0.049), and presence of comorbidities (p = 0.049) as predictors of CIA prevention. Conversely, scalp-cooling was not associated with a higher rate of scalp-cooling discontinuation (p = 0.831) or with a lower rate of adverse events (p = 0.261). Multivariate analysis identified the presence of comorbidities (p = 0.038) and baseline CIA > grade 2 (p = 0.049) as independent predictors of CIA prevention.

Conclusions: Use of scalp-cooling is an effective way to prevent CIA in breast cancer patients undergoing chemotherapy. However, the presence of comorbidities and the severity of CIA before treatment are associated with CIA prevention, despite being not independently associated with CIA prevention. Further studies are needed to better define the role of scalp-cooling in preventing CIA.
C56  Electrochemotherapy in the treatment of cutaneous metastases from breast cancer: a multicenter cohort analysis


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Background: The management of breast cancer (BC) skin metastases represents a therapeutic challenge. Electrochemotherapy (ECT) combines the administration of bleomycin with temporary permeabilization induced by locally administered electric pulses. Preliminary experience with ECT in BC patients is encouraging.

Methods: A total of 125 patients with BC skin metastases who underwent ECT between 2010 and 2013 were enrolled onto a multicenter retrospective cohort study of the GISEL group (Gruppo Italiano Senologia ed Elettrochimioterapia). The treatment was administered following the European Standard Operative Procedures of Electrochemotherapy. Tumor response was clinically assessed adapting the Response Evaluation Criteria in Solid Tumors, and toxicity was evaluated according to Common Terminology Criteria for Adverse Events 4.0. Cox regression analysis was used to identify predictive factors.

Results: Response was evaluable in 113 patients for 214 tumors (median 1 per patient, range 1–3). The overall response rate after 2 months was 90.2%, while the complete response (CR) rate was 58.4%. In multivariate analysis, small tumor size (P = 0.001), absence of visceral metastases (P = 0.001), estrogen receptor positivity (P = 0.016), and low Ki-67 index (P = 0.024) were significantly associated with CR. In the first 48 h, 10.4% of patients reported severe skin pain. Dermatologic toxicity included grade 3 skin ulceration (8.0%) and grade 2 skin hyperpigmentation (8.8%). Tumor 1-year progression-free survival was 86.2% (95% confidence interval 79.3–93.8) and 96.4% (95% confidence interval 91.6–100) in the subgroup of those with CR.

Conclusions: In this study, small tumor size, absence of visceral metastases, estrogen receptor positivity, and low Ki-67 index were predictors of CR after ECT. Patients who experienced CR had durable local control. ECT represents a valuable skin-directed therapy for selected patients with BC. A new prospective protocol has been recently approved by the coordinator centre of Padova for an observational multicentre study on BC patients treated with ECT. GISEL group is open to new centres interested in giving their contribution to the study.

C57  Bald is beautiful: no more. The stigma of alopecia during chemotherapy: Brindisi Oncology Department experience


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Background: The cancer treatments often bring with it body image challenges, causing low self-esteem and contributing to worsen the quality of life (QoL). Chemotherapy (CT)-induced hair loss (HL) is one of the most emotionally disturbing side effects of several breast cancer (BC) treatments. The DigsCaps system, using the scalp cooling system, has been shown to reduce CT-induced alopecia (A) in a multicenter prospective trial. The purpose of this prospective observational study was to describe our experience.

Materials (patients) and methods: From February 2016 and April 2017, 40 consecutive early stage BC pts who received anthracycline and/or taxane-based treatment were enrolled, post local Ethics Committees approval. A nurse and a psychologist were dedicated for these pts. A/HL has been graduated according to the Dean’s scale: G0 < 25% HL; G1 < 50% HL; G2 = 50%–75% HL; G3 = 75%–100% HL: G4 > 75% HL.

Results: A total of 40 women were enrolled; median age was 49 years (range 31–64). Seventeen pts (42.5%) received 4 courses of EC (etoposide at 90 mg/m2 and cyclophosphamide at 600 mg/m2 intravenously on day 1, with 21 days between cycles) followed by 12 courses of Paclitaxel 100 mg/m2 intravenously once a week; 21 (52.5%) received 4 courses of EC and 2 pts (5%) Paclitaxel (P 80 mg/m2 intravenously once a week) and concurrent Trastuzumab (2 mg/kg intravenously; loading dose 4 mg/kg) for 12 consecutive doses. Full preservation of hair (G0) was observed in 6 pts (15%), G1 in 15 pts (37.5%) and G2 in 7 pts (17.5%) (Table 1). Twenty-eight pts (G0–2 = 70%) did not need a wig or other hair piece to mask their hair loss during the chemotherapy period; only 6 pts (15%) used wig or head cover. The majority of pts tolerated DCS very well. Among G3 DCS-related side effects, coldness (n = 11, 27.5%), neck pain (n = 4, 10%), and headache (n = 3, 7.5%) were the main toxicity. Overall, 4 (n = 4) of pts discontinued DCS because of unsatisfactory hair preservation (n = 3, 7.5%) and cold discomfort (n = 2, 5%).

letrozole (2.5 mg/day); men and premenopausal women will receive concomitant goserelin (3.6 mg subcutaneous implant every 28 days). Treatment will continue until disease progression or unacceptable toxicity. Patients are limited to − 1 line of chemotherapy and no prior ET for advanced disease; patients receiving (neo)adjuvant ET with a nonsteroidal aromatase inhibitor must have a disease-free interval of ≥ 12 months. Exclusion criteria include Eastern Cooperative Oncology Group performance status ≥ 2, or prior CJKD/46 inhibitor treatment. Planned hematologic and chemistry laboratory assessments will be completed every 2 weeks for the first 2 months, then monthly to Cycle 6, and as clinically indicated to Cycle 36. Tumor assessments are recommended every 12 weeks or at intervals per local standard of care during the treatment phase. The primary outcome is safety and tolerability. Secondary outcomes include time to progression, clinical benefit rate, overall response rate, safety, and patient-reported outcomes (PROs). Adverse events and drug-drug interactions will be monitored using CT Scholar; PROs will be collected for female patients using the FACT-B questionnaire to better understand health-related quality of life and treatment side effects. Global recruitment of the planned 3,000 patients is ongoing, with the majority occurring in Europe. Clinical trial NCT02941926.
Our results confirm previous evidences, showing that DCS is a good chance to keep hair during CT. Further trials are needed to refine pts selection and to improve the effect and tolerance.

Materials and methods: This was a single institution retrospective analysis of MBC patients treated with eribulin from August 2012 to May 2016. These patients had received at least 2 lines of prior therapy for metastatic disease. Patients received standard doses of eribulin and were monitored for responses.

Results: Forty-four patients were included in this analysis who received at least one cycle of eribulin. Median patient age was 58 years (range 43-76). All 44 pts were pretreated with antracyclines and taxanes and 72% with capetcitabine. Brain metastases were present in 29 (65%) patients of the initial time of initial eribulin administration. Most patients were heavily pretreated with a median of 3 (range 2-7) previous chemotherapy lines prior to eribulin and had significant visceral involvement (median 3 organs). A median of 5 cycles of eribulin was delivered. There were no complete responses; partial responses were 20% (9/44) with a 54.3% of disease control rate (25/44). Forty-four patients were included in this analysis who received at least one cycle of eribulin. Median patient age was 58 years (range 43-76). All 44 pts were pretreated with antracyclines and taxanes and 72% with capetcitabine. Brain metastases were present in 29 (65%) patients of the initial time of initial eribulin administration. Most patients were heavily pretreated with a median of 3 (range 2-7) previous chemotherapy lines prior to eribulin and had significant visceral involvement (median 3 organs). A median of 5 cycles of eribulin was delivered. There were no complete responses; partial responses were 20% (9/44) with a 54.3% of disease control rate (25/44). Progression-free survival was 4.5 months (95% CI: 2.8-6.2) and median overall survival was 12 months (95% CI: 7.8-16.4). Only one patient experienced grade 3 neurotoxicity. Three patients (6.8%) stopped eribulin due to fatigue grade 3. No hypersensitivity reactions; partial responses were 20% (9/44) with a 54.3% of disease control rate (25/44). Progression-free survival was 4.5 months (95% CI: 2.8-6.2) and median overall survival was 12 months (95% CI: 7.8-16.4). Only one patient experienced grade 3 neurotoxicity. Three patients (6.8%) stopped eribulin due to fatigue grade 3. No hypersensitivity reactions. 

Conclusion: Eribulin monotherapy is an effective and safe regimen for MBC patients. We reviewed data regarding patients (pts) with early MBC diagnosed in our Medical Oncology Unit from January 1991 to March 2016. The aim of this study was to assess in real-life the efficacy and expected toxicities. In our experience, eribulin maintains its activity out of clinical trials, without unexpected toxicities.

Background: The discovery of new anti-HER2 targeted therapies has significantly improved the outcomes in the metastatic setting. However, the population enrolled in clinical trials is not always representative of the clinical practice. Moreover, only 7% of breast cancers (BCs) present as metastatic disease at the first clinical observation. In most cases, metastatic BCs develop in pts with a history of BC already treated in the neo/adjuvant setting. This latter subgroup is largely under-represented in clinical trials.

Methods: This is a multicenter, observational, retrospective study conducted in 6 Oncology Italian Centers. The aim of this study was to assess in real-life the efficacy and safety of dual HER2 blockade as 3rd line in Trastuzumab-pretreated pts in the neo/adjuvant setting. Primary end-points: progression free survival (PFS) and overall survival (OS). Secondary end-points: response rate and cardiac safety. PFS and OS curves were estimated using the Kaplan-Meier method. Tumor response was assessed according to RECIST 1.1 and safety with CTCAE v4.0.

Results: We evaluated 35 HER2-positive MBC from November 2013 to December 2016, 60% with tumors Luminal B, 40% HER2-enriched. The most common metastatic sites were: lung (20%), lymph nodes (14.3%) and liver (11.4%). Median (m) age: 50 (range 20-71), mECOG PS 0 (range 0-1). At a m follow-up of 55.6 months (mos) (range 6-170), all pts were evaluable for efficacy and safety. The m number of cycles administered was 6 (range 2-10). The mPFS was 12 mos (95% CI 2-3.8). The mOS was 15.2 mos (95% CI 2.3-36). 14.3% of pts had a complete response, 60% a partial response and 25.7% a stable disease. m baseline LVEF was 65%, m final LVEF 61%.

Conclusions: Our preliminary data confirmed the efficacy and no increase in cardiac toxicity of the combination Pertuzumab, Trastuzumab and Docetaxel in Trastuzumab-pretreated pts, mirroring the PFS data but not the OS reported in the CLEOPATRA study. A longer follow-up for OS is needed for a comprehensive evaluation of the antitumor activity of dual-HER2 blockade in Trastuzumab-pretreated pts.

Background: To investigate the cardiac safety of adjuvant Non-Pegylated Liposomal Doxorubicin (NPL-DOX) combined to Cyclophosphamide (CTX) and followed by weekly Paclitaxel, in older patients (> 65 years) with diagnosis of high risk breast cancer. The main end point of this prospective study was the detection of early episodes of symptomatic congestive heart failure (CHF).

Methods: The cardiac function was evaluated by left ventricular ejection fraction (LVEF) measurements with repeated echocardiograms, performed 2 weeks before the beginning of chemotherapy and every 6 months, until 30 months after the study entry; then yearly for at least 5 years.

Results: Median cardiac follow up period was 405 months (range, 18-66-66 months). Forty-seven patients were enrolled from two Italian Divisions of Medical Oncology. Final results revealed no early episodes of symptomatic CHF within the first 12 months from the enrolment. Only two cardiac events were observed: an episode of atrial flutter after the first cycle of NPL-DOX and CTX, with a quick return to normal rhythm, and a grade 3 (scored to NCI-CTCAE, version 3.0) CHF episode, 18 months later chemotherapy start. No other relevant toxicities were reported. Median LVEF values remained the same for all the period of time (60%), with minimal changes within the 10th and 90th percentiles, when compared to baseline. For the survival assessment, after a median follow-up of 40-55 months (range, 18-66-66 months), eight patients (17%) experienced disease relapse. Five patients with stable relapse, died for progression of disease.

Conclusions: This adjuvant combination including NPL-DOX in elderly patients, resulted in a low rate of cardiac toxic effects. Comparative trials should be encouraged to confirm these findings.
recurrence. Seven pts of 47 pts (15%) who hadn’t received RT in adjuvant setting had local recurrence; 4 of them underwent surgery and RT and also with systemic therapy (HT or CHT or both). 3 pts were treated only with chemotherapy+2 pts had central recurrence, that was surgically removed, followed by RT. Nine pts had distant recurrence and were treated with CT. At a median follow-up of 10 years (1-25 years) 23 patients (43%) are alive; the median DFS and OS are 78 months and 97 months, respectively.

Conclusions: Our patients presented at an older age, earlier stage and presented an aggressive disease. Prognosis is not well defined but the clinical course seems aggressive. MBC patients with advanced metastatic disease has been extrapolated from experience treating breast cancer. Further prospective multicenter studies are needed to determine the best treatment and it is very positive that EORTC in 2014 started a prospective international registry.

**C62 Safety and efficacy of non-pyelated liposomal doxorubicin (NPLD) in HER2 negative metastatic breast cancer (mBC) patients (PTS) as second-line (2L) and beyond: a retrospective single institution analysis**

**Background:** NPLD has shown comparable efficacy but lower risk of cardiotoxicity, compared to conventional anthracyclines, in mBC pts. Up today, its label indication is limited to the first-line treatment, however, in daily clinical practice, it is widely used in pretreated pts, where limited data exist.

**Materials and methods:** We retrospectively collected all consecutive, HER2 negative, mBC pts treated at our institution with NPLD 60 mg/m² iv every 21 days in 2L or beyond. We reported pcts characteristics, outcomes and adverse events (AEs).

**Results:** Between Nov 2010 to date, we identified 42 pts. Median age: 52 years (range 34-73). Molecular subtype: luminal A (17%), luminal B (19%), HER2 (48%); triple negative 5 (12%). 18 pts (43%) were previous exposed to anthracyclines (antra) and 24 pts (57%) in metastatic setting. 10 pts (24%) received adjuvant radiotherapy on the left breast and among them 6 pts (14%) were treated with antra. NPLD was administered as: 2L in 14 pts (33%); third-line (3L) in 12 pts (29%) while 16 pts (38%) received it after three or more lines. 36 pts (86%) had visceral disease. Median number of cycles was 5 (range 1-11). Overall 40 pts were evaluable. Partial response was reported in 7 pts (17%) and 13 pts (32%) had stable disease with a clinical benefit of 50%. 20 pts (50%) showed a progressive disease (PD) as best response. Median PFS was 5.3 months (mos) (range 0.7-18.3) in 2L, 3.9 mos (range 0.7-14.3) in 3L and 4.4 mos (range 0.7-18.7) in fourth-line and beyond. There was no difference in mPFS between patients previously exposed or not to antra: 5.1 mos (range 0.7-18.7) vs 5.6 mos (range 0.69-12.93) respectively (p > 0.05). AEs were mild: nausea G1-2 in 19 pts (45%), fatigue G1-2 in 18 pts (43%), vomiting G1-2 in 7 pts (20%), skin toxicity G1-2 in 7 pts (20%), mucositis G1 in 12 pts (29%) and anemia G1 in 11 pts (26%). The most common G3-4 AEs were neutropenia observed in 12 pts (28%). An asymptomatic reduction in the left ventricular ejection fraction (LVEF) of ≥ 50% was shown only in 2 pts (5%). One of them received previous anthra.

**Conclusions:** With the limitation of the retrospective nature of the analysis, our single institution, real life experience demonstrate that NPLD is effective and safe in mBC pts, also as 2L or beyond, irrespective of previous exposure to anthracyclines.

**C63 Efficacy and safety of everolimus and exemestane for metastatic breast cancer patients: a real-life experience of three Oncology Departments**

**Background:** Everolimus and exemestane regimen for metastatic breast cancer (mBC) is an effective and widely adopted treatment in hormonal receptor positive (HR+) and human epidermal growth receptor 2 negative (HER2-) patients. The pivotal phase 3 BOLERO-2 trial showed a significant progression-free survival (PFS) improvement in patients previously treated with nonsteroidal aromatase inhibitors (NSAI) and tamoxifen. Patients with previous or current use of medium PFS (median PFS 6 months) or low PFS (median PFS 3 months) did not confer a significant improvement in the secondary endpoint overall survival (OS). Many other experiences reported results in patients mostly endocrine-treatment naïve or treated with tamoxifen only. Therefore, the real-life experience of these evidences is still debated.

**Patients and methods:** We evaluated the efficacy rates obtained from a cohort of consecutive treated patients at three different Oncology Departments. We compared our PFS and OS outcomes to the results showed in the BOLERO-2 trial (published as a pre-planned interim analysis after 359 observed PFS events), in order to evaluate if applicable also in out-of-trial real-life series. Adverse events were graded according to the NCI CTCAE, version 4.0.

**Results:** We overall analysed 95 patients. The median age of patients was 51 years (range 30-86). 70 patients (73.7%) received previous adjuvant endocrine treatment; 35/70 patients were treated with adjuvant aromatase inhibitors. Median PFS was 6 months (BOLERO-2 trial showed a local-assessed PFS of 6.9 months). Visceral disease (62.9%); 65% showed a significant worse outcome compared to bone metastases group of patients (p = 0.043). Concerning age, median PFS was 7 months (< 65 years) versus 6 months (>65 years), no significant (p = 0.61). If used in 1-11 line of chemotherapy the median PFS showed a significant improved outcome (8 months versus 5 months in case of G1-2; Δloc = p = 0.05). The OS of our series was 20 months; patients affected by visceral disease at time of treatment had a comparable median OS compared to the bone metastases group of patients (17 versus 15 months; p = 0.64).

**Conclusions:** Real-life use of everolimus plus exemestane regimen in our clinical routine practice supported the BOLERO-2 trial outcomes, confirming the expected efficacy in several subgroups of patients affected by HR+/HER2- MBC patients.

**C64 Alopecia/hair loss in all patients treated with trastuzumab and paclitaxel: myth or reality?**

**Background:** The treatment for patients (pts) with small, node-negative, human epidermal growth factor receptor type 2 (HER2)-positive breast cancer (BC) is controversial. In January 2015, Tolanyak et al. published on the NEJM data about pts undergoing chemotherapy schedule for node-negative, HER2-Positive BC with adjuvant (P) and Trastuzumab (T) without anthracyclines. The authors observed the most common side effects and described that Alopecia (A)/Hair Loss (HL) was expected in the vast majority of pts. However, data regarding its real incidence were not collected.

Based on this lack, in our center we gathered data about A/HL in pts treated with adjuvant P and T.

**Materials (patients) and methods:** From December 2015 to April 2017, 28 consecutive early stage HER2 positive BC pts were treated with adjuvant P and T schedule in our center. The treatment consisted of intravenous administration of 80 mg of P per square meter of body-surface area weekly for 12 weeks and a loading dose of 4 mg of intravenous T per kilogram of body weight on day one, followed by 2 mg per kg weekly, for a total of 12 doses. The main goal was to analyse the HL/A grading in pts treated with this schedule using the Dean’s scale: G0 = no HL; G1 < 25% HL; G2 = 25–50% HL; G3 = 50–75% HL; G4 > 75% HL. This scale is the most common way to measure the degree of chemotherapy-induced A/HL.

**Results:** A total of 28 pts were treated with this schedule; median age was 59 years (range 36-76). All grades of A were observed in 93% (n = 25): G1 in 5 pts (18%), G2 in 12 pts (43%), G3 in 9 pts (33%). No pts had G4 HL. Full preservation of the hair (G0) was observed only in 2 pts (7%).

**Table: C64. HL according with Dean’s scale**

<table>
<thead>
<tr>
<th>HL</th>
<th>n (%)</th>
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<tbody>
<tr>
<td>G0</td>
<td>2 (7.4)</td>
</tr>
<tr>
<td>G1</td>
<td>5 (18.5)</td>
</tr>
<tr>
<td>G2</td>
<td>12 (43)</td>
</tr>
<tr>
<td>G3</td>
<td>9 (33)</td>
</tr>
</tbody>
</table>

**Conclusions:** Data collected in our experience confirm that this schedule causes a gentle-to-average A/HL in the vast majority of pts (93%, n = 25). Nevertheless 19 pts (68%) experienced a non-severe A/HL, which does not require the use of wigs, scarfs or head-pieces. In the light of these data, it would be useful to deepen this topic for improving the selection of which pts can better benefit from the Scalp Cooling device in order to prevent A/HL.

**C65 Are anti-HER2 agents the best choice in metastatic breast cancer with an HER2 positive switch from primary tumour? A retrospective multi-institution analysis of clinical-pathological characteristics and outcomes**

**Background:** Our patients presented at an older age, earlier stage and presented an aggressive disease. Prognosis is not well defined but the clinical course seems aggressive. MBC patients with advanced metastatic disease has been extrapolated from experience treating breast cancer. Further prospective multicenter studies are needed to determine the best treatment and it is very positive that EORTC in 2014 started a prospective international registry.

**Results:** We overall analysed 95 patients. The median age of patients was 51 years (range 30-86). 70 patients (73.7%) received previous adjuvant endocrine treatment; 35/70 patients were treated with adjuvant aromatase inhibitors. Median PFS was 6 months (BOLERO-2 trial showed a local-assessed PFS of 6.9 months). Visceral disease (62.9%); 65% showed a significant worse outcome compared to bone metastases group of patients (p = 0.043). Concerning age, median PFS was 7 months (< 65 years) versus 6 months (>65 years), no significant (p = 0.61). If used in 1-11 line of chemotherapy the median PFS showed a significant improved outcome (8 months versus 5 months in case of G1-2; Δloc = p = 0.05). The OS of our series was 20 months; patients affected by visceral disease at time of treatment had a comparable median OS compared to the bone metastases group of patients (17 versus 15 months; p = 0.64).

**Conclusions:** Real-life use of everolimus plus exemestane regimen in our clinical routine practice supported the BOLERO-2 trial outcomes, confirming the expected efficacy in several subgroups of patients affected by HR+/HER2- MBC patients.
Between 1991 to date we retrospectively identified all consecutive patients (pts) with HER2 positive metastatic breast cancer, proved by a biopsy on a secondary lesion, who had a primary tumour without HER2 expression.

**Results:** We obtained clinical and pathological data from 22 BC pts. 21 pts (95%) underwent surgery for primary tumor; histology: ductal carcinoma 19 (90%) pts, medullar carcinoma 5 (1%) pts, unknown 1 (5%). Stage at first diagnosis: stage I 1 (5%), stage II 5 (23%), stage III 5 (23%), stage IIIA 3 (14%), stage IIIB 1 (5%), stage IV 1 (4%), while in 4 pts (18%) no data were available. 14 pts (64%) received adjuvant chemotherapy (12 anthracycline-based; 2 CMF) and 16 (73%) adjuvant hormonal therapy (1 Tamoxifen; 4 Aromatase Inhibitor). 4 pts (18%) received neoadjuvant treatment and among them no pCR was observed. No pts was treated with anti-HER2 agents in adjuvant/neoadjuvant setting. We observed a mDFS of 25.95 months (mos); range: 0-285. All pts received a first line treatment for the metastatic disease: 2 chemotherapy alone, 2 trastuzumab (T) + hormonal therapy, 6 chemotherapy + T (3 vinorelbine + T, 3 paclitaxel + T), 12 pertuzumab (P) + T + taxanes. We noticed a mPFS of 17.2 mos, range 2.9 – 77.7 mos; but a mPFS of 10.89 mos for pts treated with P + T + taxanes. 15 to 22 received T-DM1 as a subsequent therapy; 9 of them as second line therapy, mPFS was 3.88 mos (range 2.0 – 12.2 mos); and was consistently lower for pts (n = 9) previously treated with P + H + taxanes: 2.81 mos (range 2.0 – 12.2 mos). Most of pts (n = 10) showed a progressive disease as best response.

**Conclusions:** Our real-world study showed a lower efficacy of anti-HER2 agents for treatment of metastatic HER2 positive breast cancers that changed HER2 status at the time of recurrence. Particularly most of pts did not benefit from a treatment based on T, DM1, suggesting that the use of the antibody-drug conjugate may not be an adequate therapeutic option in this specific subgroup.

**Methods:** Between 1991 to date we retrospectively identified all consecutive patients (pts) with HER2 positive metastatic breast cancer, proved by a biopsy on a secondary lesion, who had a primary tumour without HER2 expression.

**Results:** We obtained clinical and pathological data from 22 BC pts. 21 pts (95%) underwent surgery for primary tumor; histology: ductal carcinoma 19 (90%) pts, medullar carcinoma 5 (1%) pts, unknown 1 (5%). Stage at first diagnosis: stage I 1 (5%), stage II 5 (23%), stage III 5 (23%), stage IIIA 3 (14%), stage IIIB 1 (5%), stage IV 1 (4%), while in 4 pts (18%) no data were available. 14 pts (64%) received adjuvant chemotherapy (12 anthracycline-based; 2 CMF) and 16 (73%) adjuvant hormonal therapy (1 Tamoxifen; 4 Aromatase Inhibitor). 4 pts (18%) received neoadjuvant treatment and among them no pCR was observed. No pts was treated with anti-HER2 agents in adjuvant/neoadjuvant setting. We observed a mDFS of 25.95 months (mos); range: 0-285. All pts received a first line treatment for the metastatic disease: 2 chemotherapy alone, 2 trastuzumab (T) + hormonal therapy, 6 chemotherapy + T (3 vinorelbine + T, 3 paclitaxel + T), 12 pertuzumab (P) + T + taxanes. We noticed a mPFS of 17.2 mos, range 2.9 – 77.7 mos; but a mPFS of 10.89 mos for pts treated with P + T + taxanes. 15 to 22 received T-DM1 as a subsequent therapy; 9 of them as second line therapy, mPFS was 3.88 mos (range 2.0 – 12.2 mos); and was consistently lower for pts (n = 9) previously treated with P + H + taxanes: 2.81 mos (range 2.0 – 12.2 mos). Most of pts (n = 10) showed a progressive disease as best response.

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**Methods:** Between 1991 to date we retrospectively identified all consecutive patients (pts) with HER2 positive metastatic breast cancer, proved by a biopsy on a secondary lesion, who had a primary tumour without HER2 expression.

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**Conclusions:** Our real-world study showed a lower efficacy of anti-HER2 agents for treatment of metastatic HER2 positive breast cancers that changed HER2 status at the time of recurrence. Particularly most of pts did not benefit from a treatment based on T, DM1, suggesting that the use of the antibody-drug conjugate may not be an adequate therapeutic option in this specific subgroup.
Show a better PFS or OS in patients that receiving only sorafenib. The aim of this study was to validate the prognostic significance of M in patients with HCC treated with S.

Methods: 280 patients with HCC consecutively treated with S twice daily between March 2005 and August 2016 were included in the study. Patients who had been taking insulin (I) for at least 5 years at the time of the HCC diagnosis were considered “patients with diabetes treated with I” whereas those who had been on M at for at least 5 years when HCC was diagnosed were considered “patients with diabetes treated with M”.

Results: The median PFS of all patients was 2.6 months (95%CI 1.4-4.3) and median OS was 10.7 months (95%CI 9.1-12.8). In patients treated chronically with M the treatment with S was associated with a median PFS of 1.9 months (95%CI 1.8-2.3) compared to 3.7 months (95%CI 3.1-4.6) for patients without DM2 and compared to 6.4 months (95%CI 5.3-11.4) for patients treated chronically with I (P < 0.0001). In patients treated chronically with M the treatment with S was associated with a median OS of 6 months (95%CI 4.6-8.7) compared to 10.8 months (95%CI 9.0-13.5) for patients without DM2 and compared to 16.6 months (95%CI 14.3-25.5) for patients treated chronically with I (P = 0.0081). M effects on clinical outcome were also investigated in relation to ORR. Patients treated chronically with M showed a higher percentage of progression at the first CT re-evaluation than those patients treated with I and patients without DM2 (89% vs 70% respectively). Considering the overall population, the risk of progression was higher in DM2 patients taking M compared with patients without DM2 (HR = 1.91, 95% CI 1.28-2.8). Regarding the risk of survival, similar results were observed (HR = 1.70, 95% CI 1.42-2.05). Considering the overall population, the risk of progression was lower in DM2 patients taking I compared with patients without DM2 (HR = 0.65, 95% CI 0.48-0.89), similar results for survival (HR = 0.62, 95% CI 0.44-0.87). Considering diabetic patients only, the risk of progression was higher in patients taking metformin than in those taking insulin (HR: 2.91; 95% CI: 1.84–4.6), similar results for survival (HR: 2.74; 95% CI: 1.69–4.3).

Conclusions: These findings could be explained by an increased tumor aggressiveness and resistance to S in patients treated with M.
The results show that addition of cisplatin and capecitabine to the AG Akt inhibitors synergistically enhanced the antiproliferative activity of gemcitabine.

Pancreatic ductal adenocarcinoma (PDAC) is among the most lethal solid tumors. Despite extensive predclinical and clinical research, the prognosis of this disease has not significantly improved, with a 5-year survival rate around 7%. There is an urgent need to better understand the molecular pathology of PDAC in order to improve patient selection for current treatment options and to develop novel therapeutic strategies. The PI3K/AKT/mTOR pathway plays a crucial role in PDAC: activation of Akt is a frequent event and has been correlated to poor prognosis and resistance to chemotherapy. Against this background, effective blockage of Akt signaling can lead to adverse effects, especially related to apoptosis.

Materials and methods: Immunohistochemistry of tissue microarrays with specimens from radically-resected patients (n = 100) revealed a correlation between high phospho-Akt expression and worse outcome. Patients with low expression had a median overall survival (OS) of 16.2 months (95% CI, 14.8-20.1), while patients with high expression had a median OS of 12.0 months (95% CI, 9.0-14.9, P = 0.03).

Results: Akt inhibitors synergistically enhanced the antiproliferative activity of gemcitabine in the LPO28 primary cells, characterized by high expression levels, while this combination was antagonistic in LPC006 cells, characterized by low expression levels. Inhibition of Akt decreased cell migration and invasion, which was additionally reduced by the combination with gemcitabine. However, the combination of Akt inhibitors with gemcitabine significantly increased apoptosis, associated with induction of caspase-3/9/9, PARP and BAD, and inhibition of Bcl-2 and NF-kB in LPO28, but not in LPC006 cells.

Conclusions: Our results support the analysis of phospho-Akt as a new biomarker both for PDAC prognosis and for the development of new therapeutic approaches. In particular, perifosine interact synergistically with gemcitabine in cells with phospho-Akt overexpression.

**Table D3**

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>PAXG</th>
<th>AG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>42</td>
<td>41</td>
</tr>
<tr>
<td>Male/female</td>
<td>20/22</td>
<td>23/18</td>
</tr>
<tr>
<td>KPS</td>
<td>90-100</td>
<td>34 (81%)</td>
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<tr>
<td>70-80</td>
<td>8 (19%)</td>
<td>15 (37%)</td>
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<tr>
<td>Age</td>
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<td>Biliary stent</td>
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</tr>
<tr>
<td>Ca19.9</td>
<td>&gt;ULN</td>
<td>32 (76%)</td>
</tr>
<tr>
<td>Neutrophil/Lymphocyte &gt;5</td>
<td>median</td>
<td>1413</td>
</tr>
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</table>

**Conclusions:** The results show that addition of cisplatin and capecitabine to the AG backbone is feasible and linked with improved disease control. The PAXG regimen warrants further exploration in this setting of patients.

**Table D5. Multivariate analysis (elderly pts)**

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>2L PFS</th>
<th>2L OS</th>
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<tr>
<td></td>
<td>HR</td>
<td>95%CI</td>
</tr>
<tr>
<td>ECOG PS 1 vs 0</td>
<td>1.25</td>
<td>0.93-1.67</td>
</tr>
<tr>
<td>ECOG PS 2 vs 0</td>
<td>2.62</td>
<td>1.79-3.84</td>
</tr>
<tr>
<td>1st-line PFS &gt;6.2</td>
<td>0.79</td>
<td>0.61-1.02</td>
</tr>
<tr>
<td>2L start ≥11.5 vs &lt;11.5 g/dL</td>
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<tr>
<th></th>
<th>HR</th>
<th>95%CI</th>
<th>P</th>
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<tbody>
<tr>
<td>ECOG PS 1 vs 0</td>
<td>1.35</td>
<td>1.00-1.81</td>
<td>0.051</td>
</tr>
<tr>
<td>ECOG PS 2 vs 0</td>
<td>2.57</td>
<td>1.74-3.80</td>
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<tr>
<td>1st-line PFS &gt;6.2</td>
<td>0.69</td>
<td>0.53-0.90</td>
<td>0.006</td>
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<tr>
<td>2L start ≥11.5 vs &lt;11.5 g/dL</td>
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**Conclusions:** The second-line treatment efficacy in elderly vs. non-elderly advanced gastric cancer patients: an Italian multicentre real-world study.

Background: Gastric cancer incidence rises with age, but elderly patients (pts) are scarcely represented in clinical studies. Therefore, the treatment of elderly population with advanced gastric cancer (AGC) remains a challenge, being difficult to translate trials’ results into standard management.

Patients and methods: Baseline parameters, tumour features, and treatment data of 868 AGC pts treated with at least 2 lines of therapy at 19 Italian institutions were retrospectively analysed. Characteristics of elderly (>70 years at second-line (2L) start) and non-elderly pts were compared using 2-tailed Fisher exact test or chi-square test. The Cox proportional hazard regression model was used to identify prognostic factors. Progression-free survival (PFS) and overall survival (OS) were calculated using Kaplan-Meier estimation and examined by log-rank test.

Results: Overall, median OS was 13.6 months, median 2L OS 5.8 months and median 2L PFS 2.8 months. The elderly accounted for 31.8% of the population. No statistical difference in gender prevalence between age groups was found (P = 0.38) and TNM stage at diagnosis (P = 0.38) between age groups. At stage IV diagnosis, liver metastases were more frequent in elderly (P = 0.02), while the rate of peritoneal and ovarian metastases was higher in non-elderly pts (P = 0.002). In both groups, median number of cycles received in 2L was 4 and a similar percentage of pts received further therapy lines (P = 0.17). Elderly had similar 2L PFS (HR 0.86, P = 0.13) compared to non-elderly pts. In the elderly, 1st-line PFS 6.2 months was associated with longer survival, while ECOG PS 2 negatively impacted on prognosis (Table 1).

Conclusions: Our large cohort study, while highlighting some differences in tumour features, did not show any statistical survival difference between age groups, indicating that age per se should not limit the use of 2L therapy in AGC pts. Toxicity analysis is ongoing.

**Table D4**

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>2L PFS</th>
<th>2L OS</th>
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<tr>
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<td>HR</td>
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Conclusions: Our large cohort study, while highlighting some differences in tumour features, did not show any statistical survival difference between age groups, indicating that age per se should not limit the use of 2L therapy in AGC pts. Toxicity analysis is ongoing.
Sorafenib, an oral multikinase inhibitor, represents the standard care for Chronic hepatitis (hep) is an established etiologic factor of biliary tract Cancer (BTC). The estimation of life expectancy of mGC pts in the second-line setting is necessary. The higher prevalence of hep in IHC pts suggests an epidemiological nexus between these two entities. Albeit in hep patients (pts) were older than hep- (median 68.4 vs 64.4 years). At time of start of BTC treatment, hep did not affect either progression-free survival to CT1 (median 4.4 months vs 3.6 months, HR 0.86, IC0.59–1.27) or overall survival (11.2 months vs 11.3 months, HR 0.81, IC0.53–1.24). Concerns: The higher prevalence of hep in IHC pts suggests an epidemiological nexus between these two entities. Although in hep- IHC pts there was an increased pre-treatment NLR, hemocytometric analysis failed to reflect at systemic level a supposedly more pronounced local inflammatory background. Hep- IHC doesn’t show evidence of an accelerated carcinogenic process, such as worse clinical-—radiological presentation or younger age at diagnosis, nor is characterized by worse survival in treated pts.

## Estimation of 12-weeks life expectancy in patients (pts) with metastatic gastric cancer (mGC) candidates for second-line treatment: the “Gastric Life” nomogram


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- **Medical Oncology Unit—Azienda Ospedaliero-Universitaria Careggi, Florence;**
- **Medical Oncology Unit, Fondazione Poliambulanza, Brescia;**
- **Department of Abdominal Oncology, Istituto Nazionale Tumori, Milan;**
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- **Department of Oncology, San Bortolo General Hospital, Vicenza**

**Background:** The estimation of life expectancy of mGC pts in the second-line setting may be biased by the absence of objective prognostic tools to be used for the enrollment in clinical trials and for the decision making in the everyday practice. The availability of evidence-based second-line treatment options highlights the need of a prognostic tools that may assist clinicians in refining pts’ clinical selection in the salvage setting. The aim of this study was to...
build a nomogram for predicting the individual 12-weeks overall survival (OS) of mGC pts starting a second-line treatment.

Materials and methods: At 26 Italian Institutions, 320 mGC pts receiving second-line chemotherapy, ramucirumab or paclitaxel-ramucirumab were used as developed set. Putative prognostic variables (age, gender, ECOG PS, T resection, Lauren’s histotype, primary anatomic site, synchronous presentation, number and location of metastatic sites, PS and response to 1-line, LDH, neutrophil/lymphocytes ratio) were selected using a random forest model and included in a Cox multivariable model from which the nomogram was derived. The nomogram performance was evaluated by means of calibration plots and discrimination ability (Harrington’s C-index).

Results: Three variables were selected and included in the nomogram: ECOG PS, neutrophil/lymphocytes ratio and perinodal involvement. The model discriminative ability index was 0.712. The internal calibration plot did not show any significant difference to the observed and the predicted 12-weeks OS probabilities. External validation analysis is currently ongoing.

Conclusions: Our nomogram may be a useful tool to predict the 12-weeks life expectancy in mGC pts candidates for second-line therapy. Based on 3 easy-to-collect variables, “Gastro life” nomogram may help clinicians to refine pts’ selection for second-line treatments and assist researchers for the enrollment in clinical trials.

D10 Prognostic impact of nutritional support in patients affected by locally advanced or metastatic pancreatic cancer (PC) undergoing chemotherapy

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1Oncologia AOUI Verona, Verona; 2Biastistici Istituto Nazionale Tumori Regina Elena, Verona

Background: Patients affected by PC frequently present nutritional disorders that may influence their quality of life and prognosis. In addition to the disease, the systemic treatment may contribute to the malnutrition status of these pts. Few studies investigated the role of nutritional support during treatment of PC pts. Therefore, the aim of this analysis was to assess the nutritional status and the prognostic value of nutritional interventions in pts affected by advanced PC undergoing chemotherapy.

Materials and methods: Pts affected by locally advanced or metastatic PC, undergoing chemotherapy, receiving nutritional counseling at the AOUI of Verona between July 2013 and October 2016 were included. Nutritional status was assessed by Malnutrition Universal Screening Tool (MUST), Body Mass Index (BMI), weight loss in the past 6 months (WL), presence of symptoms that may affect food intake and energy intake. Descriptive statistics was adopted. Clinical, pathological and nutritional data were properly correlated to Overall Survival (OS) using a Cox model.

Results: Data from 109 pts (47 males [43.1%] and 62 females [56.9%]) were gathered (median age 63 years, median follow-up 8 months). At baseline, in seventy pts (64.2%) the MU2 was >2, significantly correlated with the PS (ECOG) (p < 0.0001), the median WL was 11.5% (range 0–35.4) and most patients suffered from early satiety (78%), loss of appetite (83.3%), dysgeusia (47.2%), dyspepsia (66.1%) and diarrhea or constipation (69.7%). The oncologist initially prescribed the nutritional counseling in only 33% of cases. At multivariate analysis, the time between the diagnosis of PC and the nutritional counseling (HR 2.22, p = 0.017), the Performance Status (HR 1.38 q = 0.075), the surgery of the primary (HR 5.89, p = 0.005) and the response to the first line (HR 5.9, p = 0.03) were significant predictor for OS. Furthermore, a weight gain more than 2% (p = 0.03; OR = 2.66) obtained by the Maximally selected Log-Rank statistics analyses from the baseline weight was correlated with the time between the diagnosis and the nutritional intervention (p = 0.021): in pts receiving nutritional support within 5 months from diagnosis, a 2% weight gain was associated with a 2-year OS benefit (50.3% vs 33.0%; p = 0.04).

Conclusions: These data suggest that the nutritional support may impact on prognosis of pts affected by advanced PC undergoing chemotherapy. External validation is ongoing.

D11 Early changes in plasma levels of mutant KRAS DNA as a sensitive marker of response to chemotherapy in pancreatic cancer

M. Del Re1, C. Vivats,1 E. Rolf,1 E. Vasile1, M. Miccoli1, C. Caparella1, P. d’Arienzo1, L. Formaro1, A. Falcone1, R. Danesi1

1Clinical Pharmacology and Pharmacogenetics Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa; 2Medical Oncology Unit, Department of Translational Research and New Technologies in Medicine, University of Pisa, Pisa; 3Department of Clinical and Experimental Medicine, University of Pisa, Pisa

Background: Pancreatic cancer (PDAC) is still lacking of good markers to monitor tumor response and chemotherapy represents the gold standard to treat advanced disease. Ca19.9 is the only one approved, however, it has several limitations in sensitivity and specificity. Since mutations of KRAS occur in more than 90% of tumors, its detection and variations in circulating free tumor DNA (cfDNA) could represent a biomarker to monitor chemotherapy response.

Material and Methods: Twenty-seven advanced PDAC patients given first-line 5-Fluoro, irinotecan and oxaliplatin or gemcitabine and nab-paclitaxel were enrolled. Three ml of plasma were collected 1) before to start chemotherapy (baseline), 2) at day 15 of treatment and 3) at each clinical follow-up. CFNA was extracted and analysed for KRAS mutations (mutKRAS) by digital droplet PCR to monitor its variation and to compare its predictive role respect to Ca19.9. Results: A total of 27 patients with locally advanced (n = 4) and metastatic (n = 23) PDAC were included in this prospective study. Median FFS and OS were 7.4 and 11.5 months, respectively. Nineteen patients displayed a mutKRAS in baseline plasma, and there were no significant statistically differences in median FFS and OS in patients with baseline positive or negative cfDNA mutKRAS (median FFS: 7.4 months vs. not reached, p = 0.24; median OS: 11.5 months vs. not reached, p = 0.16). Monitoring mutKRAS cfDNA during treatment and correlation with outcome was possible in 25 patients. There was a statistically significant difference in FFS and OS in patients with increase vs. stability/reduction of cfDNA in the sample collected at day 15 (median FFS 2.5 vs 7.5 months, p = 0.03; median OS 6.5 vs 11.5 months, p = 0.009). None of the other parameters (sex, age, stage, PS, primary tumor location, baseline Ca19.9) was significantly correlated with FFS or OS. Moreover, mutKRAS cfDNA variations were deeper than those of Ca19.9, suggesting that mutKRAS cfDNA can be more accurate and sensible biomarker (Table 1).

Conclusions: The results of this study support the hypothesis that mutKRAS in plasma may be used as a new marker for monitoring treatment outcome and disease progression in PDAC, suggesting that cfDNA mutKRAS changes are associated with tumor response to chemotherapy.

Table D11. Comparison of mutKRAS cfDNA and Ca19.9 is a patient undergoing progression of disease (PD).

<table>
<thead>
<tr>
<th>MutKRAS cfDNA (copies/ml)</th>
<th>Baseline</th>
<th>2 weeks</th>
<th>8 weeks - PD</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>200</td>
<td>290</td>
<td>2800</td>
</tr>
<tr>
<td>10</td>
<td>2600</td>
<td>2000</td>
<td>1500</td>
</tr>
</tbody>
</table>

D12 Whole-exome sequencing analysis identifies recurrent mutation rate in BAP1 gene in intrahepatic cholangiocarcinoma patients exposed to asbestos

G. Brandi1, M. Desertì,2 A. Astolfi,3 V. Indirì4, A. Fanò5, S. Mattioli6, A. Palloni6, S. De Lorenzis1, I. Gargiulo1, F. Vasari1, A.D. Penna7, M. Cencio8, 5, Tenza3

1Università di Bologna, Bologna; 2University of Bologna, Bologna

Background: The past three decades have registered a progressive worldwide increase in incidence of extra-hepatic cholangiocarcinoma (ICC), a malignancy arising from the biliary tree within the liver. Recently, in two case-control studies (one retrospective and one prospective), we observed a 4.8- and 7-fold, respectively, increased risk of ICC in workers exposed to asbestos. These findings strongly suggest a putative role of asbestos in ICC carcinogenesis and, possibly, in its increasing incidence. Since the identification of environmental diseases is gaining increasing attention because of their high impact on public health, the present study aimed to identify putative molecular biomarkers of asbestos-driven ICC carcinogenesis.

Material and methods: A total of 22 ICC patients were enrolled. For each patient, data on established or suspected ICC risk factors were collected; asbestos exposure was assessed by modified ReNaM questionnaire. On the basis of modified ReNaM questionnaire, patients were divided in two groups: asbestos-exposed and the control group of not-exposed. Whole exome sequencing (WES) was performed on DNA from 22 tumors and matched blood samples. Somatic single nucleotide variants, insertions and deletions were identified and functionally annotated. Mutated genes of interest were selected according to the frequency of mutations within the asbestos-exposed patients’ subgroup and based on a priori knowledge about cancer-related genes, with particular attention for those ones already reported to be mutated with high recurrence in malignant pleural mesothelioma (MPM), a classic model of asbestos-related cancer.

Results: According to ReNaM questionnaire, 10 (45%) out of 22 ICC patients resulted exposed to asbestos. WES analysis revealed a frequency of 27% (6 over 22) of somatic mutation in BRCA1 associated protein -1 (BAP1), corresponding to 5 over 10 of asbestos-exposed ICC patients (50%) and to 1 over 12 of not exposed (8%). According to chi-square test, BAP1 alterations were significantly associated with asbestos exposure (p-value = 0.0289).

Conclusions: BAP1 mutation occurred with a high recurrence rate in asbestos-exposed ICC patients and, as already reported in MPM, could serve as a putative candidate for genetic alterations associated with asbestos exposure in this malignancy: Further studies based on a larger patients population are needed to confirm this preliminary finding.
Background: Modified FOLFIRINOX (mFOLFIRINOX) is a standard treatment in advanced pancreatic cancer (aPC). Because of the presence of either loss-of-function mutations in DPYD (c.1697T>G, IVS1+1G>A, c.2194G>A, c.2846A>T) or UGT1A1*28 variant associated with reduced UGT1A1 expression, deficiency of DPD and UGT may result in drug accumulation and severe toxicities caused by fluoropyrimidines and irinotecan, respectively.

Material and methods: The present study analyzes the association between DPYD and UGT variants and adverse drug reactions (ADRs) in aPC patients (pts) treated with mFOLFIRINOX. Blood samples were collected from 104 pts, and analyses of DPYD c.1697T>G, IVS1+1G>A, c.2194G>A, c.2846A>T and UGT1A1*28 were performed through sequencing. Statistical analysis was performed by chi-square, Mann–Whitney and Spearman’s rho tests on SPSS v.23.

Results: Non of the pts was carrier of the c.1679G and c.2846T alleles. Only one pts treated since 2001 in 12 Italian centers, and analyzed their impact on overall survival (OS) and progression-free survival (PFS) through Cox proportional hazards model. DPYD IVS14G>T, c.1679T>A, c.2194G>A, c.2846A>T and UGT1A1*28 were per- formed through sequencing. Standard analysis was performed by chi-square, Mann–Whitney and Spearman’s rho tests on SPSS v.23.

Conclusions: Our data confirm that DPYD IVS14G>T, c.1679T>A, c.2194G>A and c.2846A>T alleles are association with a higher risk of G3/4 thrombocytopenia and neutropenia, and should be included in routine practice to personalize treatment in aPC.

D14 Prognostic factors in unresectable biliary tract cancer: a GICO (Gruppo Italiano OLGiangiocarcinoma) retrospective analysis

F. Leone1, R. Filippi1, A. Palloni1, L. Fornaro1, A. Casadei Gardini1, G. Aprile2, N. Silvestris3, M.A. Satolli1, A. Casadei Gardini1, G. Ciccolini3, G.L. Frassati1, S.K. Garattini1, M. Russono1, M. Scartezini1, C. Cagnazzo2, M. Aglietta4, B. Giovannini1

1University of Turin - FPO-IRCSS Candolo, Candolo; 2SamOltohla Miborgo Hospital - University of Bologna, Bologna; 3AAU Pisana, Pisa; 4Istituto Scientifico Ramanaglia per la Studio e la Cura del Tumor (I.R.S.T.), Meldola; 5San Bartolo Hospital ULSS East District, Vicenza; 6National Cancer Institute IRCCS Giovanni Paolo II, Bari; 7University Hospital “Città della Salute e della Scienza”, Turin; 8Udinese University Hospital; 9University of Ferrara; 10University of Pisa; 11FPO-IRCSS Candolo, Candolo

Background: Faced with a general background of a poor prognosis, individual histories of patients (pts) with advanced biliary tract cancer (BTC) may vary to a considerable extent. However, incidence and heterogeneity of this group of neoplasms prevents an unambiguously and consistent identification of clinical and laboratory features, useful to estimate the expected prognosis and to allow the prediction of the benefit of chemotherapeutic treatment (CT).

Methods: The Gruppo Italiano OLGiangiocarcinoma (GICO) conducted a retrospective study of different variables at the time of beginning of 1st line CT in a cohort of BTC pts treated since 2001 in 12 Italian centers, and analyzed their impact on overall survival (OS) and progression-free survival (PFS) through Cox proportional hazards model.

Results: The demographic and clinical characteristics of the 830 collected histories were: median age 65.3 years, 47.6% female, 90.4% ECOG PS 0-1, 8.9% chronic viral hepatitis, and 15.3% high risk of death at diagnosis (defined as Eastern Cooperative Oncology Group (ECOG) 3-4). The impact of: tumor factors (T3 vs T1, T4 vs T1), chemotherapy and laboratory variables (markers, white blood cell count, platelet count) plus histological blood tests carried out at baseline (the day before the start of treatment). Results: 27% patients treated with resection or ablation, who received DAA therapy. The mechanism that could explain the high rate of tumor relapse after DAA treatment is one of the main issues rising from these studies. Microenvironment and viral induced inflammation play a role in chronic liver injury and tumor initiation. In contrast, the immune system has also an anti-tumor function several inflammation and immune-based prognostic scores, such as lymphocyte count, neutrophil-lymphocyte ratio (NLR), and systemic immune-inflammation index (SII), have been developed to predict survival and recurrence in cancers, including HCC. Herein, we evaluated the potential role of SII, NLR and PLR as predictors of relapse or new HCC in patients treated with DAA.

Methods: We analysed 439 consecutive cirrhotic patients without HCC and 92 patients with previous HCC. Information on neutrophil, lymphocyte and platelet counts from hematologic blood tests carried out at baseline (the day before the start of treatment). Results: During 24-week follow-up, HCC was detected in 60 of 92 patients with previous HCC and 29 of 439 patients without previous HCC. In patients with previous HCC the increase of NLR was associated with a early release of HCC (HR 1.104854, 95% CI 1.0117-1.199, p = 0.04). In patients without previous HCC the value of NLR, SII and PLR not was associated with early release of HCC. In this patients the increase of AST (HR 1.007475, 95% CI 1.000872-1.004376 p = 0.019), lymphocyte (HR 0.4732381, 95% CI 0.2611029-0.8577245, p = 0.014) and platelet (HR 0.9854083, 95% CI 0.976986-0.9933357, p = 0.0001) and decrease of albumin (HR 0.2708881, 95% CI 0.1353519-0.542065 p = 0.0001) was associated with early release.

Conclusions: Overall, the high rate of HCC recurrence after DAA treatment in patients with prior HCC suggests that a close follow-up of these patients remains mandatory. The NLR represent potential prognostic indicator in patients with previous HCC.
Annals of Oncology
differently for patients without previous HCC where the risk of relapse is due to the stage of cirrhosis.

D17 Transarterial radioembolization versus chemoembolization for hepatocarcinoma patients: a meta-analysis of randomized trial

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1IRST-IRCCS, Medolla; 1ASL Romagna, Faenza; 1ASL Romagna, Forlì; 1IRST-IRCCS, Forlì; 1ASL Romagna, Rimini

Introduction: A novel technique of loco-regional treatments for HCC is called transarterial radioembolization with yttrium-90 (TARE), which induces tumor necrosis by means of injection of glass or resin microsphere loaded with yttrium-90. TARE, which is in fact a novel form of liver-directed brachytherapy. Although several studies comparing the two locoregional techniques have been recently published, whether there is a clear superiority of one treatment over the other is still debated. In this study, we performed a meta-analysis to compare the efficacy of TARE and TACE in treating patients with unresectable HCC and we considering only the three randomized study.

Materials and methods: Randomized controlled studies that included patients with intermediate hepatocellular carcinoma were included in to the analysis.

Results: A total of 3 studies published from 2014 to 2016 were analyzed, which included 49 HCC patients treated with TARE and 48 who underwent TACE. A significant between-study heterogeneity was found for OS (I² = 78%), while the heterogeneity was detected for the other outcomes. OS at 1 year was similarity between the two treatment groups (OR = 1.21, 95% CI: 0.51-2.83, P = 0.67). Overall survival at 1 year was 63.2% for TARE compared to 66.6% for TACE. For PFS at 1 years the data were not statistical significant between two treatment (OR = 0.25, 95% CI:0.02-3.03, P = 0.28). We also analysed progression disease, disease control rate and transplanted patients. For progression disease and disease control rate not statistical significant was detect. For progression disease rate the OR was 0.61 (95% CI:0.14-2.70, P = 0.51) and for disease control rate the OR was 1.80 (95% CI:0.51-6.30, P = 0.36). For transplanted patients the OR was 0.68 (95% CI:0.23-2.01, P = 0.49). In the group treatment with TARE the transplanted patients were 36% compared to 20.8% of patients treated with TACE.

Conclusion: Our meta-analysis reveals that TARE and TACE show similar effects in unresectable HCC patients in terms of OS, disease control rate, patients transplantate and progression disease. However, important evidence emerging from the various studies and this meta-analysis is that TARE seems to have a more down-staging compared to TACE especially in early-stage patients.

D18 Early loss of skeletal muscle mass (LSMM) as prognostic factor in metastatic pancreatic cancer (PC) patients

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1Department of Oncology, University Hospital of Udine, Italy; 2Department of Medicine, Unità di Malattie Metaboliche, Ospedale Universitario di Udine, Italy; 3Department of Endocrinology, University Hospital of Udine, Italy; 4Department of Oncology, San Bortolo General Hospital, Vicenza, Italy; 5Department of Oncology, University Hospital of Udine, Italy; 6Deparment of University Medicine, San Bortolo Hospital, Vicenza, Italy

Background: PC patients (pts) have multiple risk factors for sarcopenia and LSMM that in turn may cause more intense treatment toxicities, reduced response to cancer therapy, prolonged hospital stay, impaired quality of life, and worse prognosis. Material and methods: we retrospectively analyzed 127 consecutive metastatic PC pts treated at the Department of Oncology of Udine between Jan 2012 and Mar 2017 to evaluate if baseline sarcopenia and/or early LSMM (measured at first radiological evaluation) was an independent significant role as predictor of better OS only for locoregional treatment with TACE.

Results: This study is to assess the role of several factors in MGC such as metastatic site, tumor stage of cirrhosis. Other side the Interdisciplinary Treatment Groups (GIC) that define more appropriate treatment paths for each patient. Early reports of pancreatic cancer patients to the Dietetics and Clinical Nutrition Unit may positively affect medical and surgical treatments such as single site of metastatic involvement, high probability of achieving R0 resection and long disease-free interval.

D20 Multidisciplinary approach and nutritional impact on the patient with pancreatic cancer

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Background: Early nutritional assessment and nutritional status play an important role in patients’ prognosis and quality of life. The A.O.U. City of Health and Science of Turin (Città della Salute and della Scienza di Torino), together with the Oncology Network of Piedmont and Valle d’Aosta (Rete Oncologica Piemont-Valle d’Aosta), established on one side the Reception and Services Center (CAS), that aims at taking care of patients through the involvement of different health professionals and on the other side the Interdisciplinary Treatment Groups (GIC) that define more appropriate treatment pathways for each patient. Early reports of pancreatic cancer patients to the Dietetics and Clinical Nutrition Unit may positively affect medical and surgical treatments.

Materials and methods: 61 patients with pancreatic cancer were investigated for nutritional status, food intake and health status. The aim of this study was to assess the role of several factors in MGC such as single site of metastatic involvement, high probability of achieving R0 resection and long disease-free interval.
Conclusion: The early nutritional assessment and the multidisciplinary approach showed a reduction in the percentage of the weight loss, due to an increase of calories and proteins intake (oral food) together with an increase in oral nutritional supplements. Serum proteins and albumin changed from 6,2 mg/dl (+/- 0.6) and 3.2 mg/dl (+/- 0.6) at T0 to 6.3 mg/dl (+/- 0.5) and 3.4 mg/dl (0.6) at T2.

**D21** Prediction of overall survival after 3 months of treatment using the NLR-over-the-time-curve in pancreatic cancer patients

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1Radioclínico Tor Vergata, Rome; 2DARC, Roma Tre University, Rome; 3Tor Vergata University Hospital, Medical Oncology Unit, Rome

**Background:** High NLR is an established adverse prognostic feature in pancreatic cancer, however his change over the time during the entire course of the disease and its ability to precisely predict survival have never been investigated.

**Methods:** We analysed 2975 blood cell counts from 85 metastatic pancreatic cancer patients to build a NLR-over-the-time-curve from the beginning of the disease history until death. The shape of NLR-over-the-time-curve was evaluated and the minimum timepoints needed to predict the entire curve was assessed using the error-vs-partial measurements function.

**Results:** The NLR-over-the-time-curve was found to have a clear rectilinear shape in all analyzed patients. The best fitting linear curves proved to have a coefficient of determinatiion, namely “R-squared”, about of 24-25% for nearly all patients. In order to investigate how linear extrapolations of initial (partial) data can predict the whole phenomenon, we compared such extrapolations with the final best fitting curve in terms of R-squared and considered the prediction to be adequate when the correspond- ing R-squared attained the same final value of the best fitting curve. Overall, the R-squared of 24-25% could be attained in an early as three months of blood cell count measurements. Since the near-end-of-life NLR was > 4 in 95% of cases, then a precise overall survival prediction was possible using NLR values assessed during the first three months of patient management.

**Conclusion:** Building the NLR-over-the-time-curve is a precise tool to predict overall survival in pancreatic cancer patients. Future studies need to understand how interventions to change the slope of the curve (such as anti-inflammatory therapies) may impact on prognosis.

**D22** Prognostic factors associated with survival and recurrence in resectable gastrointestinal cancer: retrospective analysis of 338 patients operated at the Hospital of Cremona in ten years’ time

M. Ghidini, B.M. Doniglia, D. Lombionto, M. Ratti, C. Pizzolo, L. Toppo, V.Rametti, C. Santi, G. Tanzi, M. Martinotti, R. Pasalacqua, G. Tomasselli, M. Ravalli
1U.O. di Oncologia, Dipartimento Oncologico, ASST di Cremona, Cremona; 2U.O. di Chirurgia, Dipartimento Chirurgico, ASST di Cremona, Cremona; 3U.O. di Anatomia Patologica, Dipartimento Oncologico, ASST di Cremona, Cremona

**Background:** Surgical resection remains the only curative treatment for non-metastatic gastrointestinal (GE) cancer. A large cohort of GE cancers derived from a high-volume Italian center was analyzed to describe clinical outcomes and prognostic factors.

**Methods:** 338 patients (pts) diagnosed with GE cancers who underwent curative resection from 2007 to 2016 were considered. Variables analyzed were: age, sex, tumor location, histology, tumor (T), nodal status (N), resection margin status (R), grade (G), (neo) adjuvant therapy, adjuvant chemo (ne)oadjuvant therapy, UICC and AJCC stage (1-2 vs 3-4), lymph node (LN) and lymphadenectomy status (D2 vs D3). Statistical analysis was performed according to intention to treat principle.

**Results:** Included pts were 131 women (39%) and 207 men (61%), median age 75 years. Adenocarcinomas (Lauren intestinal type) accounted for 69% (232 cases), 76 cases were diffuse carcinomas (22%) and 30 of mixed histology (9%). In 182 cases TNM stage was I or II (54%), 128 pts had stage III (38%) and 28 stage IV (8%).

**Conclusion:** Building the NLR-over-the-time-curve is a precise tool to predict overall survival in pancreatic cancer patients. Future studies need to understand how interventions to change the slope of the curve (such as anti-inflammatory therapies) may impact on prognosis.

**D23** Treatment and outcome for small bowel adenocarcinoma (SBA): a real life experience of two Italian centres

1Medical Oncology Unit, Sant’ Andrea Hospital, “Sapienza” University of Rome, Rome; 2Oncology Unit, ASST of Cremona, Cremona; 3Oncology Unit, Ivrea Hospital, Rome

**Background:** Small bowel adenocarcinomas (SBA) are rare tumours with an increasing incidence. The duodenum is the most common primary location. They are often spora-dic, but Crohn’s disease and genetic syndromes have been indentified as risk factors. Bowel obstruction and bleeding are common at clinical presentation. Surgical resection represents the best option for resectable tumours. The role of adjuvant treatment has not yet been established by randomised trials and in metastatic disease, the best treat- ment is fluoropirimidine and platinum based chemotherapy.

**Patients and methods:** In this retrospective observational study we enrolled patients with histological diagnosis of SBA treated at two Italian Hospitals. Their clinical courses and outcome were evaluated considering tumour location and treatment received.

According to Kimea Classification we divided duodenum-ampullary carcinoma in intestinal and bilo-pancreatic type.

**Results:** 39 patients were evaluated. Median age at diagnosis was 66 years (range 29- 88); male/female 21/18. According to tumour location we identified 3 duodenum adenocarcinomas (8%), 30(77%) duodenum-ampullary adenocarcinomas (23%) intestinal and 7(17%) biliary type), 3(8%) jejunal and 3(8%) ileal adenocarcinomas. At diagnosis the majority of the cases were stage I (16;41%) and G3 (15;23%) adenocarci-nomas, while 8 pts were metastatic/unresectable. 20 of 31 early stage resected patients received adjuvant chemotherapy, mainly fluoropyrimidine based (17,85%). 13 of them showed relapse of the disease. Overall, in the cohort of the resected patients we observed a median DFS of 14 m and a median OS of 33 m, 7 of the 8 unresectable/metastatic pts received a 3FU and oxaliplatin based first line chemotherapy and 1 of the 8 underwent a definitive chemoradiation for unresectable primary tumour. The unresectable/meta- static group showed a median PFS of 9 m and a median OS of 26 m. In the subgroup of resected ampullary adenocarcinoma OS was longer for intestinal type than biliary type with a median value of 40 m and 17 m respectively.

**Conclusions:** According to literature data, our analysis confirm the poor prognosis of SBA at all stages. Ampullary intestinal adenocarcinoma may have a better prognosis than ampullary biliary type. Fluoropyrimidine based chemotherapy could be an option in the adjuvant setting and its combination with oxaliplatin could be a valid treatment for unresectable SBA.

**D24** Small bowel adenocarcinoma (SBA) is a rare and heterogeneous disease: results of a retrospective analysis

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1Oncologia Medica Azienda Ospedaliero-Universitaria di Modena, Modena; 2Oncologia Medica Azienda Ospedaliero Universitaria “Ospedali Riuniti” di Ancona, Ancona

**Background:** Small bowel adenocarcinoma (SBA) is a rare disease representing about 1-3% of all gastrointestinal malignancies. Risk factors for SBA include inflammatory bowel disease and hereditary colorectal cancer syndromes. Moreover, SBA is sometimes associated with colorectal cancer. Because of its rarity, SBA biology and clinical course

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**Table: D22. Multivariate analysis for mDFS and OS**

<table>
<thead>
<tr>
<th>Variable</th>
<th>mDFS (p value)</th>
<th>mOS (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Tumor location (GE-cardia vs others)</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Histology (Lauren)</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>T (1-2 vs 3-4)</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>N (0 vs 1-2)</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>R (0 vs 1-2)</td>
<td>0.033*</td>
<td>0.001*</td>
</tr>
<tr>
<td>G (3-4 vs 1-2)</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Stage (I-II vs III vs IV)</td>
<td>n.s.</td>
<td>0.012*</td>
</tr>
<tr>
<td>NLR (&gt; vs &lt; median value)</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Lymphadenectomy (D1 vs D2-D3)</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Adj CTRT (no vs yes)</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>NecadJ CT (no vs yes)</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Adj CT (no vs yes)</td>
<td>n.s.</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

*: statistically significant; n.s.: not significant
Results: Forty-six patients with a median age of 73 years (range: 70–79) were included in this analysis: males: 19 (41%); PS2: 6 (13%); primary location: head 26 (57%); biliary stent: 14 (30%); previous surgery: 5 (11%); adjuvant chemotherapy 5 (11%). Overall response rate (ORR) was 33.3%; median progression-free survival (PFS) was 7 mo (95% CI 5.899–10) and median overall survival (OS) was 12 mo (95% CI 10.7–16.13). Treatment was well tolerated. No grade 4 toxicity was reported. Grade 3 toxicity included neutropenia in 5 pts (10%), peripheral neuropathy in 2 pts (4%), thromboembolism in 2 pts (4%), diarrhea in 3 pts (6.5%), nausea and vomiting in 1 pt (2%), and fatigue in 2 pts (4.3%). No significant difference in terms of efficacy and safety was recorded with a cohort of 50 pts under 70 years of age: ORR: 36.6%; median PFS 6 mo; 95% CI 5.966–8.034, and median OS 10.5 mo (95% CI 7.864–12.16). Finally, pain control was achieved in 15 of 24 pts (62.5%) with a performance status improvement of 10% according to the Karnofsky scale.

Conclusion: Although pancreatic cancer mostly affects elderly people, clinical trials often include few elderly pts. These data suggest that combination of gemcitabine plus nab-paclitaxel is effective and safe in an unselected population of elderly pts showing no differences in outcome between older patients and younger patients treated with this combination.

Methods: We have retrospectively analyzed 43 patients with histological diagnosis of metastatic pancreatic adenocarcinoma and an Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1. 53 (53.5%) and 20 (46.5%) of 43 patients received Folfirinox and Gemcitabine/Nab-paclitaxel as first line chemotherapy respectively. Only 19 (44.1%) patients, after progression disease, started second line chemo-therapy. 8 patients received Folfirinox, whereas 11 patients were treated with Gemcitabine Nab-paclitaxel as second line regardless of prior chemotherapy. The sequence of chemotherapy Folfirinox/gemcitabine/Nab-paclitaxel versus Gemcitabine/Nab-paclitaxel Folfirinox was administered to 10 patients 5 for both, respectively.

Results: Median Progression-Free Survival was 5 months in the Folfirinox group as compared with 6 months in gemcitabine Nab-paclitaxel group (hazard ratio for disease progression, 0.83; 95% CI 0.34 to 1.32; P Value = 0.59). No difference between the two groups were identified in first line. The median of progression-free survival in second line was 2.5 months in the Folfirinox group and 4 months in the gemcitabine Nab-paclitaxel. Hazard ratio for second disease progression was 0.62; 95% CI 0.24 to 1.00; P value = 0.03. The median overall survival in patients with the sequence of chemotherapy - Folfirinox/gemcitabine/Nab-paclitaxel versus Gemcitabine/Nab-paclitaxel Folfirinox was retrospectively 8 months and 11 months.

Conclusion: In this retrospective study, similar progression-free survival we observed between Folfirinox group and Gemcitabine/Nab-paclitaxel group in first line metastatic pancreatic cancer. These data need to be confirmed in prospective randomized trial.
and their care givers”. It provided a multidisciplinary training course for medical and nursing staff, a cooking class for patients and their families and a database of involved patients.

**Results:** In November 2016, the 1st edition of the course “The nutrition management of the patient with pancreatic cancer” was opened to the oncology, radiotherapy surgery and medical and nursing staff. The course was organized in a 8-hour study day. At the end of each session, an interactive discussion allowed the professionals to debate about the key points of the event. In the same month, the cooking class was organized too, involving for four hours 15 patients and their family members, with dietitians, oncologists and dieticians as well. The practical course was held in an equipped kitchen, after a brief lesson about food, spices, various types of cooking and food preservation. All the participants got a brochure with dietary advice and recipes presented during the course. All participants were asked to write a feedback about the event.

**Conclusion:** In recent times there has been an increase of the attention on the links between food and health from patients and family members. It is necessary to convey to the patient and to the care giver a message that follows validated guidelines, with the aim of improving the quality of life. We believe that some decisions on medical actions affecting patients and their families can be shared with the Patient Associations. The success of this small project (we have told you) convinced us to continue in the patients undergoing high enteric gastrointestinal cancer, with a further study with the involvement of the Oncology Network Piemonte-Valle d’Aosta and other hospital companies.

**Table: D29**

<table>
<thead>
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<th>Age &gt; 70</th>
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<th>%</th>
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<tbody>
<tr>
<td></td>
<td>10</td>
<td>50</td>
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<tr>
<td>KPS &gt; 80</td>
<td>12</td>
<td>60</td>
</tr>
<tr>
<td>Jaundice</td>
<td>6</td>
<td>30</td>
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<tr>
<td>Abdominal pain</td>
<td>5</td>
<td>25</td>
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<tr>
<td>Weight loss</td>
<td>1</td>
<td>5</td>
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<tr>
<td>GG1 increase</td>
<td>3</td>
<td>15</td>
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<tr>
<td>Other</td>
<td>5</td>
<td>25</td>
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<tr>
<td>Biopsy</td>
<td>17</td>
<td>85</td>
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**1**\textsuperscript{-}Line: GP, GemOx

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<tr>
<th>2**\textsuperscript{-}Line</th>
<th>N = 20</th>
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<tbody>
<tr>
<td>GP</td>
<td>7</td>
<td>35</td>
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<tr>
<td>GemOx</td>
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<tr>
<td>XelOx</td>
<td>1</td>
<td>5</td>
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<td>Gem</td>
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</tbody>
</table>

**Conclusions:** Despite the small number of patients and with the limits derived from retrospective analysis, our experience confirms literature data regarding the role of second-line CT in selected patients in good clinical conditions.

**D29 Does second-line therapy affect the outcome of the patients with cholangiocarcinoma? A single institution experience**

I. Gurreri\textsuperscript{1}, F. Giudici\textsuperscript{1}, D. Federle\textsuperscript{1}, A.M. Dicorato\textsuperscript{1}, M. Malagoli\textsuperscript{1}, S. Moroso\textsuperscript{1}, G. Del Conte\textsuperscript{1}, F. Zancanaro\textsuperscript{1}, A. Guglielmi\textsuperscript{1}

\textsuperscript{1}Department of Oncology, Azienda Sanitaria Universitaria Integrata di Trieste, Trieste; \textsuperscript{2}Department of Histopathology, Azienda Sanitaria Universitaria Integrata di Trieste, Trieste

**Introduction:** Metastatic cholangiocarcinoma (MC) remains at poor prognosis with median overall survival lower than 10 months. In these patients, chemotherapy constitutes the only treatment strategy. After progression to a first-line chemotherapy, there is no established second-line therapy for these patients. Indeed, literature data suggest limited activity of most second-line agents without a specific drug. The purpose of this study is to evaluate in our experience the actual role of first and second-line chemotherapies comparing to the literature data.

**Materials and methods:** We retrieved data of 20 consecutive MC patients referred to our Department between January 2012 and December 2016. Follow-up was closed on January 2017. We analyzed clinical data: age, Karnofsky performance status (KPS with cut-off of 80%), diagnosis (radiologic or biopsy), clinical symptoms, first-line chemotherapy with gemcitabine plus cisplatin (GP) or oxalaplatin (GemOx) and second-line when used. Median Overall survival (mos) was calculated using the Kaplan Meyer method.

**Results:** At the diagnosis median age was 70.8 years (range 33 to 84). Jaundice was the main symptom (30%), following abdominal pain and other clinical manifestations (25%). Histological diagnosis was present in 17 pts (85%). Only 17pts (85%) received second-line chemotherapy: GP, GemOx, Gem, XelOx, FOLFIIRI, Capecitabine, FOLFIRI.

**Conclusion:** In recent times there has been an increase of the attention on the links between food and health from patients and family members. It is necessary to convey to the patient and to the care giver a message that follows validated guidelines, with the aim of improving the quality of life. We believe that some decisions on medical actions affecting patients and their families can be shared with the Patient Associations. The success of this small project (we have told you) convinced us to continue in the patients undergoing high enteric gastrointestinal cancer, with a further study with the involvement of the Oncology Network Piemonte-Valle d’Aosta and other hospital companies.

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**Conclusions:** Despite the small number of patients and with the limits derived from retrospective analysis, our experience confirms literature data regarding the role of second-line CT in selected patients in good clinical conditions.

**D30 Nab-paclitaxel plus gemcitabine in the treatment of metastatic pancreatic cancer: our experience**

M. Mare\textsuperscript{1}, S. Muna\textsuperscript{1}, S. German\textsuperscript{1}, C. Colarossi\textsuperscript{1}, D. Sciacca\textsuperscript{1}, D. Guiffrida\textsuperscript{1}, G. Giarronne\textsuperscript{1}

\textsuperscript{1}Division of Medical Oncology, Mediterranean Institute of Oncology, Viagrande (CT), Italy; \textsuperscript{2}Division of Pathology, Mediterranean Institute of Oncology, Viagrande (CT), Italy; \textsuperscript{3}Division of Surgery, Mediterranean Institute of Oncology, Viagrande (CT), Italy

**Background:** Pancreatic cancer (PA) is the fourth most fatal cancer for both man and women. Many of patients(pts) with metastatic disease are often not included in clinical trials due to comorbidity such as diabetes, jaundice, etc. and poor performance status at diagnosis. These patients are the most treat in our clinical practice and they have few opportunities for care. Von Hoff D. et al. (2013) published the data of the phase III MPACT study showing a statistically significant benefit of the nab-paclitaxel gemcitabine vs gemcitabine alone in terms of OS (8.3 vs 6.7 months) and PFS (5.5 vs 3.7 months) as first line treatment for metastatic disease with acceptable toxicity.

**Materials and methods:** From September 2015 to May 2017 we collected the data of 26 unselected metastatic pancreatic cancer pts treated with nab-paclitaxel 125mg/mq and gemcitabine 1g/mq on days 1,8,15 q 28 days cycle, as first line treatment. Median age was 64 year (range 46-78); 9pts (34%) were over 70 years old. 9pts (34%) were male and 17(65%) female. PS 0: 10pts (38%), PS1: 10pts (38%), PS2: 6pts (23%). NLR was > 5 in 6pts (23%). They received a median of 15 drug administrations (range 1-32).

**Results:** The treatment was well tolerated. No toxic death or grade 4-toxicity were recorded: Hematologic G3 toxicity included: Neutropenia 4pts (15%), Thrombocytopenia 4pts (15%). Non Hematologic G3 toxicity included: Neuropathy 1pts (3%), Asthenia 2pts (7%). ORR was 38% (10/26), DCR (PR+SD) was 53% (14/26), median PFS was 6 months (range 1-12), median OS was 9 months (range 2-18).

**Conclusion:** We believe that nab-paclitaxel plus gemcitabine is an active and discreetly tolerated schedule and that the literature data can be reproduced in clinical practice in unselected pts with metastatic disease.
Efficacy and safety of Nab-paclitaxel plus gemcitabine in metastatic pancreatic cancer


Background: Nab-paclitaxel is a solvent-free, taxane-based antitumor drug approved for the treatment of metastatic pancreatic cancer, as first line therapy in association with gemcitabine. This retrospective analysis examined clinical benefit and toxicities in a group of consecutive MPC patients.

Patients and methods: Until Jan. 2017 we analyzed 18 consecutive patients affected by metastatic pancreatic cancer. Nab-paclitaxel was given intravenously at a dose of 125 mg/m² in association with gemcitabine 1000 mg/m² on days 1-8-15 q.28 for 3 cycles, and until progression for responders. Clinical benefit was defined as disease control rate (DCR), classified by radiologic evaluation every 3 months. We also evaluated median time to progression (mTTP) for responders and overall survival. Toxicity was recorded every cycle.

Results: We recorded 18 pts (1 F + 17 M) on average 57 years old (41-76). All patients were caucasian, with adenocarcinoma, a median of 15 stage IV, PS 0-1. Metastatic lesions were 6 in liver, 4 in lung, and 5 in peritoneum. Biliar duct stents were performed in 7 pts. The median number of CT cycles was 5 (range: 1-9). At first clinical/radiologic evaluation after three cycles the DCR was 56% (7 pts RP; 5 pts NC). The responders continued CT until progression disease, with 3 pts that underwent local RT also and five pts underwent to second line treatment with 5FU or Oxaliplatin. Peripheral neuropathy G3 was the major toxicity in 20% of cases. We observed only 4 cases of neutropenia G3, 4 cases of neutropenia G3 with 3 cases of anemia G3 that required blood transfusions. Fatigue G 1-2 was 20% and thrombocytopenia G 2 was 10% The median time to progression in 7 responders pts was 5 months (range 2-8 months), Median OS was 12 months with 50% pts live at 1 year, 25% at 18 months and 11% at 2 y.

Conclusion: This retrospective study shows the efficacy, clinical benefit and tolerability of nab-paclitaxel associated with gemcitabine in MPC with only mild neurological and hematological toxicity.

E1 Crizotinib in ROS1 rearranged or MET deregulated non-small-cell lung cancer (NSCLC): final results of the METROS trial

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1AUSL Romagna, Dipartimento di Oncologia ed Epatologia, Ravenna; 2Ospedale Santa Maria della Misericordia, Perugia; 3Azienda Ospedaliero-Universitaria, Parma; 4Pneumonologia Universitaria, Dipartimento Cardiotoracico Vascicolare, Ospedale Cisanello, Pisa; 5Istituto Scientifico Romagnolo per la Studio e la Cura dei Tumori (IRST), Meldola, Lugo; 6Oncologia Medica 2, Istituto Oncologico Veneto, Padua; 7Azienda ospedaliera San Gerardo, Monza, 8Divisione di Oncologia Medica, Istituto Europeo di Oncologia, Milan; 9Ospedale Maggiore, Novara; 10Istituto Nazionale Fonzalizzazione Pascali, Naples; 11Azienda Ospedaliera S G, Moscati, Avellino; 12Oncologia Medica Toracica, IRCCS Oncologico Giovanni Paolo II, Bari; 13Azienda Ospedaliero-Universitaria Policlinico, Modena, 14UCS Tumori Polmonari, IRCCS AO San Martino IST, Istituto Nazionale per lo Studio e la Ricerca sul Cancro, Genoa; 15Istituto di Oncologia Universitaria di Toppo, Turin, 16Dipartimento di Patologia Chirurgica, Medica, Molecolare e dell’Area Clinica, Università di Pisa, Pisa

Background: Crizotinib is an orally active inhibitor of receptor tyrosine kinases effective in NSCLC with AKL rearrangement. Recent data showed that the drug is dramatically effective in patients with ROS1 rearrangement (ROS1+), with promising activity also in individuals with MET exon 14 mutations (MET14+) or MET amplification (MET14++).

Material and methods: The METROS is an Italian multicenter prospective phase II trial designed to assess the efficacy and safety of crizotinib in ROS1+ or MET14+ advanced NSCLC patients who failed at least one standard chemotherapy regimen. The co-primary end-point was response rate (RR) in cohort A (ROS1+ centrally confirmed ROS1 rearrangement) and cohort B (MET+ centrally confirmed MET amplification) defined as ratio MET/CEP7 > 2.2 or locally confirmed MET14++.

Results: Eligible patients received crizotinib at the standard dose of 250 mg BID orally. At the data cut-off of April 30th, 2017, both cohorts completed accrual. Among 498 screened patients, 51 accounted for the intent-to-treat population (ITT) and received crizotinib. After 1L treatment, 26 resulted ROS1+, 16 MET14+, 8 MET14++ and 1 had MET14++++. Notably, 3 MET14+++ patients had concurrent KRAS mutations. Cohort A included individuals with adenocarcinoma histology, median age of 55 years (range 29-86), predominantly female (61%) and never smokers (54%). Cohort B included older subjects (median age 68, range 39-79), predominantly current/former smokers (68%) and with adenocarcinoma (92%). In both cohorts crizotinib was mainly offered as second line treatment (74%). In ITT population RR, median progression-free survival (PFS) and overall survival (OS) were 69%, 17.2 months (mos) and not reached in cohort A and 20% and 3.1 mos and 5.3 mos in cohort B, respectively. For cohort B, responses were numerically higher in MET14+++ than in MET14++, with evidence of rapid progression in patients carrying MET14+++.

Conclusions: The METROS is the first prospective trial confirming remarkable efficacy of crizotinib in ROS1+ NSCLC. MET14++ advanced lung cancer is a very aggressive disease, requiring additional and innovative therapeutic approaches.

E2 ASTRIS, a real world treatment study of osimertinib in patients (pts) with EGFR T790M positive non-small cell lung cancer (NSCLC): preliminary analysis of the Italian cohort

1Istituto Europeo di Oncologia, Milan; 2Ospedale Santa Maria della Misericordia, Perugia; 3Azienda Ospedaliero-Universitaria, Parma; 4Azienda Ospedaliero-Universitaria, San Camillo-Forlanini, Rome; 5Azienda Ospedaliero-Universita, Verona; 6Policlinico S Onofrio-Malpighi, Bologna; 7Ospedale S G, Moscati, Avellino; 8Azienda Ospedaliero-Universitaria, Pisa, Pisa; 9IRCCS AO San Martino IST - Istituto Nazionale per la Ricerca sul Cancro, Genoa; 10Azienda Ospedaliero-Universitaria Policlinico Vittorio Emanuele, Catania; 11Ospedale Maggiore della Carità, Novara; 12ASST Spedali Civili, Brescia; 13AORN dei Colli, Naples; 14ASST Indisdì Rundì, Livorno; 15IRCCS Istituto Tumori Giovanni Paolo II, Bari; 16Ospedale Burisio, Caggiano, 17Istituto Nazionale Tumori Regina Elena, Rome; 18Azienda Ospedaliero-Universitaria S Maria della Misericordia, Udine; 19Casa di Cura La Maddalena, Palermo; 20Azienda Ospedaliero Italiana, Bologna

Background: Osimertinib is an oral, irreversible, CNS active, EGFR tyrosine kinase inhibitor (TKI) selective for both EGFR-TKI sensitising and T790M resistance.

Mutations. ASTRIS is the international phase IIIb study that followed US FDA and EMA approval in NSCLC T790M pts. We report results from the first predefined interim analysis of the Italian ASTRIS cohort (NCT02474355).

Methods: Pts received osimertinib 80 mg once daily. Eligible pts had Stage IIIb/IV NSCLC harbouing a T790M mutation determined by local validated molecular test, received prior EGFR-TKI therapy, had WHO performance status (PS) 0 – 2, acceptable organ and bone marrow function and no history of interstitial lung disease (ILD) or QTc prolongation. Asymptomatic, stable CNS metastases were permitted. The primary efficacy outcome is overall survival; other outcomes included investigator-assessed response rate (RR), progression-free survival, time to treatment discontinuation and safety events.

Results: From study start (18 Sept 2015) to data cut-off (DCO; 3 Nov 2016), 438 pts received osimertinib from 25 italian sites with a median follow-up of 4.6 mths (<1 – 14 mths) median age 65 yrs (33–92 yrs), 69% female, 85% WHO PS 0/1, 53% had only one prior EGFR TKI. 159 pts of 339 (47%) pts had CNS involvement at enrollment. All pts tested positive for T790M, identified from tissue/cytology in 153 pts (35%), plasma ctDNA in 275 pts (63%) and other specimens in 10 pts (2%). Most frequent concomitant mutations to T790M were Del19 (58%), L858R (21%) and Exon 20 insertions (14%). The molecular testing methods most commonly used were Therascreen (45%) and Roche cobas (17%). In pts evaluable for response, the investigator-assessed RR was 60% (173/288; 95% CI 54.6%). Median duration of exposure was 4.4 mths (<1 – 13 mths). Adverse events (AEs) leading to dose modification and treatment discontinuation were reported in 59 (14%) and 23 (5%) pts, respectively. Serious AEs were reported in 46 pts (11%) and AEs leading to death in 14 pts (3%). ILD/pneumonitis-like events were reported in 5 pts (1%); no QTc prolongation was reported.

Conclusions: ASTRIS, the largest reported clinical study of osimertinib in Italy for T790M-positive NSCLC, demonstrates disease response activity similar to that observed in the AURA program with no new safety signals.
**Table 1: E3**

<table>
<thead>
<tr>
<th>Baseline characteristics, n(%)</th>
<th>RAM+DOC n = 178</th>
<th>PBO+DOC n = 182</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), years</td>
<td>63(23-84)</td>
<td>60(29-87)</td>
</tr>
<tr>
<td>Male</td>
<td>137(77)</td>
<td>127(70)</td>
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<tr>
<td>ECOG PS</td>
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<td></td>
</tr>
<tr>
<td>0</td>
<td>53(30)</td>
<td>50(27)</td>
</tr>
<tr>
<td>1</td>
<td>125(70)</td>
<td>132(73)</td>
</tr>
<tr>
<td>&lt;9 months since prior therapy</td>
<td>156(88)</td>
<td>154(85)</td>
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</tbody>
</table>

**Histology**

<table>
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<tr>
<th></th>
<th>Overall</th>
<th>Adenocarcinoma</th>
<th>Squamous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-squamous</td>
<td>130(73)</td>
<td>130(71)</td>
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<tr>
<td>Adenocarcinoma</td>
<td>111</td>
<td>101</td>
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</tr>
<tr>
<td>Squamous</td>
<td>46(26)</td>
<td>50(27)</td>
<td></td>
</tr>
</tbody>
</table>

**ECOG PS, Eastern Cooperative Oncology Group performance status**

**Table 2: E3**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Overall</th>
<th>Adenocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RAM+DOC</td>
<td>PBO+DOC</td>
</tr>
<tr>
<td></td>
<td>HR (95%) CI</td>
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</tr>
<tr>
<td>n = 178</td>
<td>n = 182</td>
<td>n = 112</td>
</tr>
<tr>
<td>n = 101</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median OS, m</td>
<td>8.3</td>
<td>8.5</td>
</tr>
<tr>
<td></td>
<td>6.3</td>
<td>6.2</td>
</tr>
<tr>
<td></td>
<td>0.86(0.68, 1.08)</td>
<td>0.79(0.57, 1.09)</td>
</tr>
<tr>
<td>Median PFS, m</td>
<td>4.0</td>
<td>4.0</td>
</tr>
<tr>
<td></td>
<td>2.5</td>
<td>2.6</td>
</tr>
<tr>
<td></td>
<td>0.71(0.57, 0.88)</td>
<td>0.630(0.47, 0.85)</td>
</tr>
<tr>
<td>ORR</td>
<td>23%</td>
<td>20%</td>
</tr>
<tr>
<td></td>
<td>13%</td>
<td>15%</td>
</tr>
</tbody>
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**Table: E4**

<table>
<thead>
<tr>
<th>Molecular Portrait</th>
<th>MA-based therapy, N = 105</th>
<th>Non MA-based therapy, N = 47(54%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at inclusion</td>
<td></td>
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<tr>
<td>Median</td>
<td>59</td>
<td>59</td>
</tr>
<tr>
<td>Range</td>
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<td>36-78</td>
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<tr>
<td>Sex</td>
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<td></td>
</tr>
<tr>
<td>Male</td>
<td>50(48%)</td>
<td>15(50%)</td>
</tr>
<tr>
<td>Female</td>
<td>55(52%)</td>
<td>15(50%)</td>
</tr>
<tr>
<td>ECOG Performance Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>26(25%)</td>
<td>9(30%)</td>
</tr>
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<td>1</td>
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<tr>
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<td>7(23%)</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>11(10%)</td>
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<tr>
<td>Smoking</td>
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<tr>
<td>Never smoker</td>
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<tr>
<td>EGFR mutated</td>
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</tr>
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**Conclusions:** The effect of RAM+DOC for treating pts with advanced NSCLC refractory to II therapy appears consistent with that for the intent-to-treat population. The benefit/risk profile for refractory pts, including pts with refractory adenocarcinoma, suggests that RAM+DOC is an appropriate treatment option even in this difficult-to-treat population.

**Background:** The choice of anti-cancer treatments in non-small cell lung cancer (NSCLC) is currently based on both histological and molecular subtype. The goal of our analysis is to describe molecular profiles and clinical outcomes of the metastatic NSCLC patients (pts) cohort enrolled in the MOSCATO 01 trial.

**Methods:** Pts were identified within the MOSCATO 01, a trial that aimed for personalizing the treatment on the basis of the molecular alterations (MA) identified by targeted Next Generation Sequencing (NGS), Whole Exome Sequencing (WES), array Comparative Genomic Hybridization (aCGH) and RNA sequencing [Massard et al Cancer Discovery 2017].

**Results:** 110 NSCLC pts with a representative fresh tumor biopsy were evaluable and for 105 (described in table 1) a molecular portrait was obtained.

Of these pts, 57 (54%) had an actionable MA and 30 pts (29%) received a MA-based therapy, either in a clinical trial (23) or an off-label target therapy (7). Pts received EGFR TKi (7), inhibitors of MET (5), FGFR (4), BRAF (3), MEK (3), HER2 (2), MTOR (1), NOTCH (1), ALK (1), ROS1 (1), RET (1) and MDM2 (1). In the group of pts with MA-based therapy the PFS2/PFS1 > 1.3 ratio was achieved for 23% of pts (7/30), median (m) PFS2 was 2.2 (0.9-26.6), mOS was 13.9 (3.1-58.6) months.

Not oriented pts (47) were treated with chemotherapy (20), target therapy (16) or other (1). The median OS was 11.1 months.

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Integrating programed cell death ligand 1 (PD-L1) and neutrophil to lymphocyte ratio (NLR) as predictive panel of response to nivolumab in non-small cell lung cancer (NSCLC)

K. Nakatani1, E. Giron2, L. Paz-Ares2, S. Ponce², J. Corral-Jarre4, O. Juan-Vidal4, F. Nafaral2, K. Kiura5, S. He6, J. Treanor2, R. Dalal7, P. Lee8, M. Reck9, S. Nevala (non-author presented)2

1Kinki University School of Medicine, Osaka; 2UALC Medical Center, Santa Monica; 3Hospital Doce de Octubre, Madrid; 4Hospital Virgen del Rocío, Seville; 5Hospital Universitario La Fe, Valencia; 6Instituto Católico d’Oncología, Hospitale, Barcelona; 7Okayama University Hospital, Kitakata, Okayama; 8El Lilly Company and Indianapolis, 9Formerly El Lilly and Company, Bridgewater; 10Lungen Clinic Grosshadern, Airway Research Center North (ARCN), German Center for Lung Research (DZL), Grosshadern; 11El Lilly Italia S.p.A, Sexta Fiorenro

Background: Ramucirumab, an antiangiogenic IgG1 VEGFR2-targeted monoclonal antibody, and erlotinib, an EGFR tyrosine kinase inhibitor, are both active in advanced NSCLC. This global phase 1b/3 study (NCT02441448) will assess safety, tolerability and efficacy of the combination of ramucirumab with erlotinib in previously untreated patients with EGFR mutation-positive stage IV NSCLC. Here we report phase 1b safety results.

Methods: Eligible patients with ECOG PS 0-1, an activating EGFR mutation, and previously untreated stage IV NSCLC received ramucirumab 10 mg/kg intravenously on day 1 of repeating 14-day (± 3 days) cycle and erlotinib 150 mg orally daily. Treatment continued until disease progression or unacceptable toxicity. The primary objective of part A was to assess the safety and tolerability, in terms of dose limiting toxicities (DLT), of adding the recommended dose of ramucirumab for phase 3 (part B) to standard dose erlotinib. Data were analyzed in part A (cohorts 1 and 2) and part B (cohorts 1 and 2). The DLT assessment occurred during the first 2 cycles (approximately 28 days).

Results: As of Dec 16th, 2015, 14 patients were treated in the phase 1b part of this trial and 12 were DLT evaluable (6 IP and 6 EU). Overall, 6 grade (Gr) 3 treatment-emergent adverse events (TEAE) were noted, with at least one TEAE in 5 patients: no serious adverse events or Gr 4-5 TEAEs occurred. In the JP cohort the median age was 73 (64-79), 57% had ECOG PS 1 and 29% had a history of smoking. Four patients (57%) experienced a Gr 3 TEAE, of which one was a DLT (elevation of alanine aminotransferase) while the others (hypertension [n = 2], dermatitis acneiform, and diarrhea) were not DLTs. In the US/EU cohort the median age was 71 (31-83), 86% had ECOG PS 1, and 4 patients had a history of smoking. One patient experienced Gr 3 TEAE of rash; no DLTs were observed in this cohort.

Conclusion: Enrollment on the phase 1b portion of this trial is complete and the safety results were consistent with previous combinations of antiangiogenic/erlotinib in this patient population. All treatment-emergent toxicities were identified. Phase 3 enrollment has been initiated maintaining the dose of ramucirumab at 10 mg/kg Q2W.

Efficacy of ceritinib administered to patients with crizotinib-refractory, ALK-positive, advanced NSCLC within the Italian compassionate use program


Background: Ceritinib is an effective treatment for patients (pts) with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) who progress on crizotinib. We assessed the efficacy of ceritinib administered within a compassionate use (CU) program.

Patients and methods: This collaborative study involved pts with crizotinib-refractory, ALK-positive, advanced NSCLC treated at multiple Institutions. The clinical data of pts for whom ceritinib was requested as CU at the recommended dose of 750 mg/d without food were collected and analyzed.

Results: Twenty-five Centers took part to the study, for a total of 70 pts who received at least one dose of ceritinib from July 2014 to March 2017. Pts characteristics were as follows: median age 56 years (22-86), 67/70 (95.5%) adenocarcinomas, 36/70 (51.5%) female, 47/70 (67%) never smokers, 14/70 (20%) ECOG PS 2 ≤, 17/70 (24.3%)...
pretreated with ≥ 2 lines of chemotherapy, 49/70 (70%) metastatic to the brain. Median time on prior crizotinib was 359 days (31-1644). The starting dose of ceritinib was 750 mg/d in 67/70 (96%) pts. The most common any grade treatment-related adverse events (TRAEs) were nausea and/or vomiting (60%, 7% grade 3 or 4), diarrhea (30%, 1.5% grade 3 or 4), ALT and/or AST elevation (47%, 18% grade 3 or 4) and fatigue (57%, 8.5% grade 3 or 4). Unusual TRAEs consisted of an increase in serum creatinine in 2 pts. Dose reduction due to TRAEs occurred in 31/63 (49%) pts who started at 750 mg/d. Of them, 17/63 (27%) pts reduced to 600 mg/d, 6/63 (12.5%) pts to 450 mg/d, and 6/63 (9.5%) pts to 300 mg/d. Permanent dose discontinuation due to toxicity occurred in 4/70 (5.5%) pts. Of the 61 evaluable pts, 27 (44.5%, 95%CI: 31.5-57.6) responded to treatment, the median duration of response being 11.2 months. At a median follow-up of 6.7 months (<1-24), the median progression-free survival (PFS) was 7.2 months, with 6- and 12-month PFS rates being 54.5% and 31.5%, respectively. No statistically significant difference in terms of PPS was observed between pts with (n = 38) or without (n = 32) dose adjustments (8.2 months vs. 4.2 months, respectively, P = 0.20).

Conclusions: Ceritinib CU program in Italy confirms the efficacy of the drug in a “real-world” setting, with a safety profile that is similar to that observed in clinical trials. A high rate of dose adjustments due to TRAEs was observed, which, however, did not appear to affect the activity of the drug.

Compliance to diagnostic and therapeutic pathways and innovative drug recommendations in advanced non-small cell lung cancer: preliminary results from the MOST study

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Background: Evidence-based diagnostic therapeutic pathways (PDTA) and innovative drug recommendations are needed in order to promote high-quality and high-value cancer care, particularly in case of ‘me too’ drugs with the same indication such as gefitinib (G), erlotinib (E) and afatinib(A) in EGFR mutated (EGFRm) Non-Small Cell Lung Cancer (NSCLC).

Patients and methods: The primary aim of the MOST (Multicenter prospective observational study on EGFR TKIs as first-line treatment of EGFRm NSCLC) study was the assessment of Veneto Oncology Network centers compliance to NSCLC PDTA and recommendations on A as first-line treatment of metastatic EGFRm NSCLC. Secondly, we evaluated treatment outcome, safety profile, budget impact of G, E and A in a ‘real world’ practice. Selection criteria for first-line treatment choice were also explored. Data about the diagnostic pathway of non-squamous NSCLC patients and first-line treatment of EGFRm cases were collected in the time-frame of 12 months and followed in the observation period of 18 months. The compliance of the participant centers to PDTA and treatment recommendations was assessed through specific indicators and benchmarks aiming at evaluating their quality and adequacy.

Results: Fourteen centers were recruiting at the time of this preliminary analysis on the first 182 evaluable patients. All non-squamous NSCLC cases underwent EGFR mutational analysis (benchmark 100%). Median time frame between histological sample acceptance and EGFR results was 16 working days (median 10 wd). In 124/188 cases EGFR analysis was performed automatically without physician request. EGFRm (N=47) NSCLC patients who received EGFR as first-line treatment were 45 (96%) (benchmark 96% or more). Among these patients 26/58% received G, 8/18% received E and 11/24% received A (benchmark for A 10%-30%). In the first 26 evaluable patients, response rate was 50% for A and G and 67% for E. We observed definitive treatment interruption for adverse events in 10% patient receiving A (benchmark 8%), 11% patient receiving E (benchmark 6%), and no patient receiving G (benchmark 6%).

Conclusions: Compliance to the diagnostic pathway of NSCLC should be improved in the clinical practice, particularly the timing of molecular tests. So far, treatment recommendations were followed. Primary, secondary and exploratory endpoints results on a wider sample size will be presented at the conference.

Results of an integrated multi-platform analysis in squamous cell lung carcinoma (SqCLC) revealed PI3K/RICTOR-mTORC2 axis as a potential prognostic biomarker and drug target

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Background: We built a risk classification model for resected SqCLC (R-SqCLC) based on clinicopathological predictors to discriminate patients’ (pts) prognosis (Pilotto JTD 2015) and we externally validated this model in a pts’ cohort of > 1,300 R-SqCLC (Bria WCLC 2016). To identify potentially druguable modulators we performed an integrated multi-platform genome analysis of prognostic outliers and we selected PI3K/RICTOR-mTORC2 axis (PI3K/RICTOR-mTORC2 axis) as the main candidate. Here we present the results of transcriptome, we validate our genomic findings in an external cohort and we enhance our rationale with in vitro studies.

Material and methods: Next Generation Sequencing (NGS) analysis of somatic mutations (SM) and copy number alterations (SCNA) was performed on Ion AmpliSeq Lung & Colon Cancer Panel: 2 genes, a SqCLC customized panel: 20 genes, the Ion AmpliSeq Comprehensive Cancer Panel: 409 genes). Transcriptome libraries were prepared using the AmpliSeq Transcriptome kit and sequenced on an Ion Proton. In vitro experiments were performed using the SqCLC cell line H-1703 (Rictor amplified 6 copies). PF-05212384 (PI3K/mTOR), AZD2014 (mTORC1/2), MK-2206 (panAkt), everolimus (mTOR) and chemotherapeutic drugs (Docetaxel, Gemcitabine) were tested. Cell viability was assessed by crystal violet assay and the half maximal inhibitory concentration (IC50) was estimated.

Results: Main results of 97 pts (Training/Validation: 60/37) are presented in the table.

Table: E10

<table>
<thead>
<tr>
<th>Gene</th>
<th>Training Set [%]</th>
<th>Validation Set [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>SM</td>
<td>TE1</td>
<td>4 [6.7]</td>
</tr>
<tr>
<td></td>
<td>PTEN</td>
<td>6 [10]</td>
</tr>
<tr>
<td></td>
<td>PI3KCA</td>
<td>3 [5]</td>
</tr>
<tr>
<td>SCNA Gains</td>
<td>RICTOR</td>
<td>14 [23.3]</td>
</tr>
<tr>
<td></td>
<td>PI3KCA</td>
<td>26 [43.3]</td>
</tr>
<tr>
<td>SCNA Losses</td>
<td>PTEN</td>
<td>19 [31.7]</td>
</tr>
<tr>
<td></td>
<td>TSC2</td>
<td>7 [11.7]</td>
</tr>
</tbody>
</table>

Regarding the transcriptome, poor prognosis pts (n = 17) showed a majority of repressed (n = 63) than overexpressed (n = 27) genes compared to good prognosis (n = 17). Top genes (fold expression change>8) with higher expression in poor prognosis were XAGE1C, SGBB132, PPF1R1B and EREG. The in vitro results supported a significant inhibition of H-1703 cells proliferation by Gemcitabine, Docetaxel, PF-05212384, MK-2206 and AZD2014 with IC50 values of 0.4 nM, 0.45 nM, 10 nM, 66 nM, 110 nM, respectively.

Conclusions: A multi-step genomic analysis of R-SqCLC is technically feasible and it allows investigating the differential profiles of pts stratified according to prognosis. The PI3K/RICTOR-mTORC2 axis emerged as the main candidate and our in vitro results justify pursuing mTOR inhibition, focusing on mTORC2, in RICTOR-aberrant tumors.
The close link between anxiety and cluster symptoms in lung cancer patients during first-line chemotherapy: further data from a dedicated WALCE (Women Against Lung Cancer in Europe) survey

Background: Lung cancer (LC) patients refer a simultaneous incidence of physical and psychosocial symptoms defined cluster symptoms (CS). Preliminary results currently under evaluation for publication showed an association between anxiety and chemotherapy-induced nausea and vomiting (CINV). As among CINV, predictors, anxiety is a modifiable factor, once having identified subjects at higher risk, this toxicity could be prevented. With this additional analysis of the survey we aimed to identify the factors associated with anxiety during chemotherapy in stage IV LC patients undergoing first-line treatment.

Materials and methods: The WALCE survey investigated in 11 Italian centers, at four consecutive evaluations (T0, T1, T2 and T3) and by means of a Numerical Rating Scale, the following items: anxiety, lack of self-confidence, fatigue, lack of appetite, pain, somnolence, dyspnea, lack of appetite, sadness, and lack of treatment) scores. The value assigned to the anxiety item, anxiety was categorized as absent (0), mild (1-3), moderate (4-7), severe (8-10). The evaluated items number was too high to be included in a multivariate model, thus factor analyses were run at each time point. The factor scores obtained were included as covariates (together with sex, age class and chemotherapy scheme) in the multivariate logistic ordinal models, run at T0, T1, T2 and T3 evaluating the risk factors.

Results: 188 patients completed the questionnaire at T0, 164 at T1, 138 at T2 and 101 at T3. The global incidence of anxiety was equal to 90%. The factor analyses showed that behind the considered variables, there were two latent factors composed by the same items at each evaluation: factor 1 (physical CS), composed by fatigue, somnolence, dyspnea and lack of self-confidence, and factor 2 (psychological CS), composed by lack of trust in treatments, general status and lack of appetite. Only physical CS was associated with an increased risk of pre-chemotherapy anxiety, while during chemotherapy, both physical and psychological CS seemed to exert an influence on anxiety development at T1, T2 and T3.

Conclusions: To date, there is no clear cause-effect relationship between CS and anxiety, however, their linkage and simultaneous intensity growth is well demonstrated during chemotherapy. More attention should be paid to the detection of CS and anxiety in LC patients during first-line chemotherapy.

Prospective generation of PDTX (patient derived tumor xenografts) and molecular profiling of NSCLC (non small cell lung cancer) patients with EGFR TKI treatment in advanced NSCLC patients: association with KRAS mutation and thymidine synthase (TS) levels

Background: The generation of “xeno-patients” is a valuable tool to prospectively reproduce in vivo molecular mechanisms underpinning cancer progression, by recapitulating human heterogeneity. Furthermore, this method allows to overcome intrinsic limitations of in vitro models. In NSCLC, xeno-patients have been described from early and late stages, with heterogeneous results. The project aims to confirm the reliability of this model in NSCLC and to prospectively characterize their genetic profile.

Materials and methods: From February 2014 to September 2016, 125 early stage (I-III) NSCLC patients who underwent radical lung resection and 14 metastatic NSCLC patients were enrolled. Written informed consent was required. Fresh intact tissue (from surgery or radio-guided biopsy) was collected and kept in serum free medium, embedded in 20% matrigel and subcutaneously engrafted into NSG and NOD SCID mice, within 24 hours from sample collection. Next Generation Sequencing was conducted on explanted paraffin embedded samples after first passage. Mutigenic mutational analysis of hotspot regions of 52 genes (Oncomine Focus Assay) was conducted on 21 out of 30 engrafted samples.

Results: The engrafted samples were 125 from radical lung resections and 14 from TC- guided biopsies. Histologically, early stage samples were found as adenocarcinoma (65%), squamous carcinoma (28%), sarcomatoid carcinoma (2%). LCNEC (3%) and carcinoid (2%). In late stage samples, the main observed histological subtypes were adenocarcinoma (43%), squamous carcinoma (21%) and SCLC (14%). The engraftment rate was equal to 23.2% in surgical samples and 7.1% in biopsy samples. Engraftment was significantly higher in squamous histology (52.97 vs 71.42 ng/ml, p = 0.004). Any significant difference was not observed for the specific mutation is mandatory to design the proper therapeutic algorithm. Abundant histologic tumour specimens are usually preferred for mutational analyses in regarding small and cytologic specimens. Unfortunately, these ones still represent the only available material for several patients. We aim to compare the DNA amount extracted from cytologic and histologic samples for EGFR tests performed in a single Institution.

Methods: Positive EGFR tests performed at San Luigi Hospital from 2008 to 2015 were included. Information about pts’ characteristics, type of mutation, sample, detection method and DNA amount for EGFR test were collected. The comparison of median DNA amount was performed using the independent T test, while the chi-square test was used for the evaluation of cytological sample ratio over time.

Results: We collected 152 tests performed on 136 EGFR mutated pts. The median age was 66 yrs (range 32 – 86), 80 (58.8%) were females, 135 (99.3%) adenocarcinoma, 120 (82.8%) never or former smokers, 95 (69.8%) presented a metastatic disease at diagnosis while 41 pts presented a localized or locally advanced disease. Eighty-five pts (61.25 ng/ml ± 52.97 vs 71.42 ng/ml ± 75.47, p = 0.348) nor between specimens from bronchoscopic and thoracic biopsy (64.07 ng/ml ± 57.53 vs 52.51 ng/ml ± 42.39, p = 0.233) was detected.

Conclusions: In this retrospective evaluation, no difference in DNA amount availability for EGFR analysis was detectable in cytologic or histologic specimens. This result supports previous data showing a similar sensitivity in EGFR detection in both types of samples, confirming the indication to perform the less invasive procedure in specimen obtaining. Our institution progressively increased the number of cytologic samples over time, showing to get more confident with this analysis over time.

Efficacy of platinum-based chemotherapy in EGFR WT nonsquamous advanced non-small cell lung cancer (NSCLC) patients: association with KRAS mutation and thymidylate synthase (TS) levels

Background: Preclinically, KRAS mutation has been associated with enhanced dependency on the folate metabolism in non-small cell lung cancer (NSCLC). Whether this phenomenon is related to increased sensitivity to anti-metabolites and/or lower thymidylate synthase (TS) levels in KRAS mutant patients (pts) is unknown.

Methods and materials: Pts with EGFR WT nonsquamous advanced NSCLC were retrospectively evaluated at one Center. Only pts with a known KRAS mutation status...
who were treated with platinum-based chemotherapy as first-line were eligible. One-step RT-PCR was used to evaluate the expression of genes potentially associated with treatment outcome (including TS, ERCC1, RRM1 and BRCA1) in pts with available tissue.

**Results:**KRAS-mutant pts who received platinum/pemetrexed (85/136, 62.5%) had a shorter progression-free survival (PFS) (4 vs. 6 months, *P* = 0.05) and overall survival (OS) (8 vs. 20 months, *P* = 0.001) compared to those with wt KRAS/G12 (51/136, 37.5%). Similarly, a significantly lower overall response rate (28.2% vs 47%, *P* = 0.02) and disease control rate (50% vs 72.5%, *P* = 0.01) was observed for platinum/pemetrexed combined with platinum/gemcitabine (51/136, 37.5%). No significant differences in PFS and OS were observed in the KRAS WT group according to the type of plati-
num-doublet received. When focusing only on pts treated with platinum/pemetrexed, a shorter PFS (4 vs. 6 months, *P* = 0.01) and OS (8 vs. 16 months, *P* = 0.0065) were noted for KRAS-mutant pts. On the other hand, among pts treated with platinum/gem- citabine no differences in terms of PFS and OS were observed according to KRAS muta-
tion status. TS, ERCC1, RRM1 and BRCA1 level were assessed in 93 KRAS-mutant and in 103 KRAS-WT pts with PFS. KRAS-mutant pts had a significantly longer mean expression levels of TS (P = 0.036) and higher mean expression levels of ERCC1 (P = 0.05) while no differences in terms of RRM1 and BRCA1 mean expression levels were observed. In unselected pts, KRAS mutation status. TS, ERCC1, RRM1 and BRCA1 levels were assessed by ROC analysis, had a significantly higher probability to bear a KRAS mutation (P = 0.02 and 0.04, respectively).

**Conclusion:** In EGFR WT nonsquamous advanced NSCLCs a poor outcome on plati-
num/pemetrexed was reported for KRAS-mutant pts, which could not be justified based on TS expression levels. Rather, activation of the KRAS pathway may drive resis-
tance to platinum/pemetrexed regardless of TS levels. Whether platinum/gemcitabine represents the best option in KRAS-mutant pts should be assessed prospectively.

**E15 Programmed death ligand 1 (PD-L1) expression status as prognostic factor in early stage non-small cell lung cancer (NSCLC)**


**Background:** Therapeutic strategies against PD-1/PD-L1 may drive resistance to platinum/pemetrexed regardless of TS levels. Whether platinum/gemcitabine represents the best option in KRAS-mutant pts should be assessed prospectively.

**Methods:** PD-L1 expression was evaluated in a cohort of 289 surgically resected IA-
IIIA stage NSCLC samples by immunohistochemistry using the SP263 clone (Ventana). Tumors were considered PD-L1 positive (PD-L1 +) if ≥ 50% of tumor cells expressed the ligand. PD-L1 status correlated to clinical characteristics, progression free survival (PFS) and overall survival (OS) were studied with Chi Square, Fisher Exact Test and Kaplan Meier analysis.

**Results:** Patients were mostly males (79%), former or current smokers (81%), with median age of 69 years, non-squamous histology (68%) and high-grade tumors (55%). PD-L1 positive tumors were 18.7% (54/289). There was no significant correlation with age, sex, smoking status and histology. PD-L1 expression was mostly limited to grade 3 tumors (G1 vs G2 vs G3: 0 vs 13% vs 25%, *P* = 0.005). In the whole cohort no statistical difference was noted both in median PFS (PD-L1 + vs PD-L1 - NR vs 63.2 mo, *P* = 0.152) and OS (PD-L1 + vs PD-L1 - 47.5 mos 32.2 mo, *P* = 0.5). When the survival analysis was restricted to grade 3 tumors, PFS was significantly longer in PD-L1 - patients (PD-L1 + vs PD-L1 - NR vs 61 mo, *P* = 0.046). OS was not affected by PD-L1 status.

**Conclusions:** PD-L1 is mostly expressed in high grade NSCLC. HighPD-L1 expression is a prognostic marker for PFS but not for OS in the subset of G3 tumors. Further stud-
ies are needed to confirm PD-L1 correlation to grading in the metastatic setting and to evaluate whether grading could represent a surrogate biomarker for sensitivity to immunotherapy.

**E16 Prognostic impact of hyponatremia in patients affected by advanced non-small cell lung cancer (NSCLC) with bone metastases (BMs)**


**Background:** In recent years, due to the development of new treatment options, the outcome of patients with metastatic non-small cell lung cancer (NSCLC) has improved. However, hyponatremia and bone metastases still correlate with poor prognosis. Some studies suggest that hyponatremia is associated with higher risk of osteoporosis and bone fracture, but no data are available about the relationship between hyponatremia and bone metastasis. Aim of this study is to investigate the prognostic role of hypona-
tremia in patients with bone metastases (BM) due to NSCLC.

**Material and methods:** NSCLC patients’ data were retrospectively collected. Survival curves were estimated using Kaplan-Meier method, and comparisons were made using chi-square test. Age, gender, tumor stage, histology, Eastern Cooperative Oncology Group–Performance Status (ECOG–PS), smoking history and presence of hypona-
tremia were included in the Cox proportional hazard model to assess their prognostic relevance.

**Results:** 647 patients with advanced NSCLC were enrolled; of them 440 (68%) were male. Median age was 72 years (range 32–93y). A total of 264 patients (41%) presented with BMs, which were synchronous in 170 patients (34%) and metachronous in 94 (15%). At diagnosis, hyponatremia was described in 105 (16%) patients, a total of 237 (37%) patients developed hyponatremia during the first line. Median overall survival was 15.9 months (95% CI 14.1–17.7 months) for patients without BMs, 11.4 (95% CI 9.4–13.4) months for patients with BMs, while mOS was 16.3 (95% CI 14.6–18.0) months for eunatremic patients and 10.3 (95% CI 7.6–12.8) months for patients with hyponatremia. Considering the two variables, mOS was 10.1 (95% CI 4.3–15.9) months for patients with BMs and hyponatremia, 11.9 (95% CI 11.4-12.4) months for patients with hyponatremia without BMs, 13.1 (95% CI 12.0–14.2) months for eunatremic patients with BMs. 17.1 (95% CI 15.2–19.1) months in eunatremic patients without BMs (p = 0.0020). Metachronous BMs appeared earlier in hyponatremic patients (3.73 vs. 3.76 months, *p* = 0.0187). At multivariate analysis in the whole population, ECOG–PS ≥ 2, IV tumor stage, male sex, hyponatremia and BMs were independent prognostic factors for worst OS. In patients with BMs, smoking history, IV tumor stage were independent prognostic factors for worse OS.

**Conclusions:** Our study suggests that hyponatremia represent an important prognostic factor and it should be necessary considered in order to optimize the management of NSCLC patients with BMs.
Squamous cell carcinoma of the lung (LSCC) is the second most common histological subtype of non-small cell lung cancer (NSCLC) having smoking habit as the major risk factor. LSCC in non-smokers is a rare and clinical and biological landscape is largely unexplored.

Methods: This is a retrospective multicenter study investigating clinical features of never-smoker LSCC patients (pts) referred to three Italian Centers between 2010 and 2016. Relapse (RFS) or progression free (PFS) and overall (OS) survival curves were calculated by Kaplan-Meier method. Cox regression proportional hazards model was used to estimate the impact of covariates on OS.

Results: Among 810 LSCC pts, 394 (49%) occurred in never-smokers; our case series included 21 males and 18 females with a median age of 63 years. ECOG PS was 0-1 in 31 (79%) pts. Median Charlson Comorbidity Index (CCI) was 7. Two (5%) pts referred second-hand smoking history and 13 (3.3%) occupational exposure. Additional tumor history was reported in 18 (4.6%) pts; head and neck (N=5), basocellular carcinoma (N=5), breast (N=2), lung (N=2), prostate (N=1) and leukemia (N=1). Molecular characterization was performed in 13 (33%) pts; in two different pts were found a KRAS mutation and an ALK rearrangement, respectively; an EGFR mutation has been identified in 2 pts. Median time from symptoms appearance and diagnosis was 7 weeks. Thirteen (33%) pts showed a limited stage, while the other 26 (67%) showed advanced/disseminated disease at the diagnosis. Nineteen (49%) pts received a first-line palliative chemotherapy (pc), mostly platinum-based doublets plus gemcitabine (N=11) or taxane (N=3), achieving a response rate and disease control rate of 37% and 58% respectively. Three patients harboring a drugable molecular alteration were treated with gefitinib (N=2) and crizotinib (N=1), achieving partial response. Median RFS in resected patients (N=9) was 21 months. Median PFS and OS after first-line pc were 5 months and 8.5 months respectively, without covariates impact.

Conclusions: Never-smoker LSCC pts represent a rare subgroup characterized by more favorable outcomes compared with the known features of smoker LSCC. Molecular assessment should be considered. Treatment outcome after pcr for advanced disease is still dismal as for most LSCC pts.
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Background: Nivolumab (N) is a novel therapeutic option in NSCLC, with a significant survival gain compared with Docetaxel (D). However, predictive biomarkers are lacking and no strategies have been adopted to date for optimal patients (pts) selection. The presence of systemic inflammation has been correlated with poor outcome in many cancer types. We aimed to evaluate whether there is a correlation between some indicators of inflammation and response in pts treated with N or D.

Methods: 28 consecutive pts with NSCLC receiving N were analyzed. Baseline white cell count (WBC) and ANC were collected and correlated with tumor response. 34 NSCLC pts treated with D were used as controls. An ANC ≥ 7500 cell/μL was defined neutrophilia. dNLR was calculated as: ANC/(WBC-ANC). PLR ratio was defined as platelet count (PLT)/ANC.

Results: Baseline characteristics: median age 68 years (range 45-82); sex M 77%; histology: 49% squamous, 44% adenocarcinoma; 8% small cell; 12% mixed histology/NOS. Smoking status: 90% smokers/former smokers. Among non-squamous pts, 16.2% were EGFR mutated and 8.1% were KRAS-mutated, with an equal distribution in both treatment groups. Line of therapy: range 2-8 in N group and 2-4 in D group. Overall response rate (ORR): 12.5% with N vs 9% with D; 8.3% of pts with N experienced unconventional responses. Baseline neutrophilia (18% with N and 26% with D) and thrombocytosis (3.5% and 3%, respectively) were not associated with response (ORR 0%). High dNLR was associated with no response to N, but not with D (ORR 0% and 12.5%, respectively), whereas high PLR correlated with low treatment response in both groups (ORR 8.3% and 0%, respectively). Among refractory pts (i.e. progressive disease as best response), a higher incidence of thrombocytosis (7% and 5%), neutrophilia (28.5% and 40%), high PLR (75% and 50%) and high dNLR levels (28.5% and 55%) were detected compared with the overall population.

Conclusions: The difference was not statistically significant. Patients were 30.3 (95% CI: 7-36.9) and 16.3 (95% CI: 0.2-32.4) months respectively. OS and RFS of non-resected patients were 13.4 (95% CI: 5.3-21.5) and 8.3 (95% CI: 0.2-16.5) months respectively. The difference was not statistically significant.

Overall survival of (OS) of selected patients (Pts) with non-small cell lung cancer (NSCLC) receiving nivolumab beyond progression

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Background: The role of platinum-based chemotherapy (PBC) as first treatment (1T) for elderly patients (Pts) with advanced non-small cell lung cancer (NSCLC) is still debated, mainly due to the lack of data in platinum-based chemotherapy (PBC) population. In this study aimed at identifying clinico-pathological factors associated with PBC prescription and the corresponding outcome.

Methods: We analyzed a consecutive series of 169 EGFR and ALK wild-type NSCLC Epts (age ≥ 70) treated with first-line PBC or single-agent chemotherapy (SAC) for stage IIIB-IV disease at the Department of Oncology of Udine (Italy), from January 2010 to March 2017. Data on clinico-pathological features, comorbidities and hospitalization during 1LT were collected. Association analyses were conducted through logistic regression. Prognosis was explored with a Cox’s regression model. Kaplan-Meier analysis and log-rank test were used to compare overall survival (OS) among subgroups. A landmark analysis at 63 days (day 1 cycle 4 of PBC) was performed in the PBC group, after stratifying Epts for having received or not at least 4 cycles of PBC (4PBC vs < 4PBC).

Results: Median age was 75 years (range 70-90) and PBC was prescribed to 112/169 Epts (59.9% received < 4 cycles and 42% cisplatin). During 1LT 6/169 Epts were hospitalized (in 56.5% of cases for toxicities, experienced by 14% of Epts treated with SAC and 27.6% of Epts treated with PBC). In multivariate analysis, age was the only factor associated with lower use of PBC (OR 0.67, p < 0.001), while ECOG performance status (PS) > 0 (OR 0.38, p = 0.03) and hospitalization before progression (OR 0.19, p < 0.001) were associated to < 4PBC. Notably, in multivariate analysis, PS > 0 (HR 2.19, p < 0.001), liver metastases at baseline (HR 3.28, p < 0.001) and hospitalization for any cause (HR 1.00, p < 0.001) predicted shorter OS. No difference in OS was observed between SAC and PBC: median OS (mOS) was 12.9 months in both arms (HR 1.17, 95% CI 0.83-1.66, p = 0.36 for SAC). Comparing < 4PBC to 4PBC we found a significant difference in OS, confirming a landmark analysis at 63 days (mOS: 6.9 vs 13.7 months; HR 2.38, 95% CI 1.38-4.07, p = 0.001 for < 4PBC).

Conclusions: Old age is the only factor predicting lower PBC use. PBC > 0 and hospitalization before progression are associated to earlier PBC discontinuation. PBC > 0, hospitalization during 1LT, and liver metastases are associated with worse outcome. Further studies are needed to identify which Epts may have a benefit from PBC.
The effects of LIPUS on ctDNA release in the medium of NSCLC cell lines

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Background: Low Intensity Pulsed Ultrasound (LIPUS) application has been shown to have an encouraging effect in inducing a transient pore formation through cellular membranes. This permeability condition has been demonstrated to be useful in enhancing gene and drug delivery. Nowadays, in the management of NSCLC patients, the use of liquid biopsy has entered the clinical practice. One of the main limits in the context of analyzing tumor DNA is the low concentration rate of nucleic acids in body fluids. Ultrasound stimulation (US) has been recently demonstrated to be effective for the release of specific circulating tumor biomarkers in many mouse models. We demonstrated the role of US in inducing the release of tumor DNA fragments (rtdNA) in NSCLC without inducing any apoptotic or necrotic event.

Material and methods: EGFR wt and del19 NSCLC cells (A549, HCC827) were cultured in RPMI1640 with 10% FBS, 1% pen/strep at 37 °C and 5% CO2. The day before the sonication, the cells were seeded in a 24-well plates (20,000 cells/well HCC827; 70,000 cells/well A549). Each group was exposed at the following sonication protocol: frequencies (650 kHz, 1 MHz); acoustic pressure (250 kPa, 25 kPa); 25% duty cycle with three different exposure time points (1, 3, 7 min). After US treatment, the cells were incubated for 24h and then cell viability was performed by Cell Titer-Glo® Luminescent Cell Viability Assay. Each experiment was performed in triplicate.

Results: NSCLC cell lines have been subjected to sonoporation at different exposure time points as well as ultrasound acoustic pressures and frequencies. We evaluated the viability of cells to exclude the possibility that rDNA analysis could be affected by apoptotic or necrotic DNA fractions. In fact, after ultrasound exposure no significant reduction of cell viability, in terms of ATP content, has been shown. Moreover, the analysis of DNA fragments content, released in the medium, showed a different behaviour on the basis of EGFR mutational status. Indeed, in EGFR mutant cells the concentration of rDNA was significantly higher than control cells after performing sonoporation at 250 kPa and 1 MHz. For the EGFR wild type cell line, no variation of ctDNA at different exposure time points and pressure has been showed.

Conclusions: the assessment of ctDNA is strongly influenced by its amount. Therefore, US application to enhance the release, is of great interest not only in NSCLC but also for all the “oncogene addicted” cancers.

Thymic epithelial tumors (TETs) and additional tumors: a single Centre experience

E.27

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Background: The association of TETs and previous or secondary malignancy is frequently reported in literature. A review of several studies reported a variable percentage of additional tumors, ranging from 8 to 30%. Despite different results and methodology, all of these studies showed an increased risk for cancer in patients (pts) with TETs.

Materials and methods: From 1990 to 2017 we retrospectively collected pathological and clinical data about pts with TETs, referred to our Medical Oncology Unit and to the Thoracic Surgery Unit of our institution.

Results: 88 pts were enrolled, 74 (84%) with thymomas and 14 (16%) with thymic carcinomas (TCs). Nineteen of them (20%) experienced previous or secondary tumors, 4 (5%) skin cancers, 5 (6%) breast cancers and 2 (2%) prostate cancers. Other tumors typically reported in both liquid biopsies and tissue, and 1 case in tissue but not in liquid biopsy. TKi therapy was related to disease progression. In 11 cases, modification of EGFR mutation testing for patients was 2 (range 1-3). In 4/21 cases, T790M was performed: 3 cases in tissue but not in liquid biopsy. TKi therapy was ineffective in this patient with T790M mutation detected in tissue, but not in liquid biopsy.

Conclusion: The association of TETs and previous or secondary malignancy is frequently reported in literature. A review of several studies reported a variable percentage of additional tumors, ranging from 8 to 30%. Despite different results and methodology, all of these studies showed an increased risk for cancer in patients with TETs.

Circulating programmed death ligand-1 (PD-1-L1) in non-small cell lung cancer (NSCLC)

E.28

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Background: Since the introduction of immune-checkpoint inhibitors for Non Small Cell Lung Cancer (NSCLC) treatment, the predictive and prognostic value of programmed death ligand-1 (PD-L1) is under investigation. Aim of the present study was to define feasibility of plasma PD-L1 testing and to assess how PD-L1 expression is modified by standard treatment.

Material and methods: PD-L1 expression was evaluated in plasma samples from patients with chemo-naïve NSCLC candidate for systemic first-line therapy, irrespective of histology or any other clinical or biological characteristic. A cohort of healthy volunteers, individuals who are not affected by oncology, autoimmune, metabolic and infectious diseases, was also analyzed for plasma PD-L1 expression (Healthy control Cohort-HC). PD-L1 in plasma samples was evaluated using the Human programmed death ligand-1 (PD-L1)/CD274 ELISA kit (CUSABIO, MD, USA).

Results: A total of 56 patients with histologically proven stage IV NSCLC and 16 HC were included. The median age of the patients was 70 years (range 48-85). The majority of patients were male (67.9%), with an Eastern Cooperative Oncology Group (ECOG) performance status score of 1 (55.6%) mainly former smokers (57.1%). The majority of patients received chemotherapy as first line treatment (N = 41, 73.2%), (3.5%) received immunotherapy and 12 (21.4%) received targeted therapies (N EGFR inhibitors= 9, N anti-ALK-1). We first defined the PD-L1 plasma levels in the HC. Median PD-L1 basal level was 37.81 pg/ml (range 9.73-90.21). In patients with NSCLC median PD-L1 plasma level was 42.21 pg/ml (range 12.00-143.49). This difference was not statistically significant (p = 0.78). Interestingly, levels of PD-L1 plasma expression significantly increased during the first 3 months of systemic therapy (Wilcoxon test p = 0.04). In addition, the 5 patients with high levels of plasma PD-L1 had significantly shorter progression free survival (PFS) and overall survival (OS) than individuals with low or no plasma PD-L1 expression (PFS: 1.2 versus 6.4 months, p = 0.006; OS: 1.2 versus 9.7 months, p = 0.003).

Conclusion: Plasma PD-L1 expression is feasible and high levels of expression could correlate with worst prognosis. Additional studies exploring correlation of plasma with tumor tissue PD-L1 expression are needed.

EGFR status evaluation by liquid biopsy during first-line therapy in advanced NSCLC patients

E.29

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Background: Over the past decade, personalized management based on the molecular features of tumours in patients with advanced non-small cell lung cancer (NSCLC) has emerged routine clinical practice. The poor performance of many advanced NSCLC patients may limit invasive biopsies. The liquid biopsy is a diagnostic procedure performed on cancer-derived material obtained in blood samples. In this abstract, we will describe our experience with liquid biopsies.

Methods: In the Reggio Emilia Clinical Cancer Centre from March 2016 to December 2016, 42 patients with advanced NSCLC were analyzed that had had or had already started first line therapy. The liquid biopsy was repeated at each imaging response evaluation by thoracic abdominal computed tomography (CT) scan performed every 3 months. In the liquid biopsy, the mutational status of EGFR was analyzed with real time PCR (KIT cobas EGFR mutation test v2 CE-IVD Roche); in tissue, it was evaluated by pyrosequencing.

Results: 21/42 liquid biopsies were EGFR-mutated (12/21 exon 19 and 9/21 exon 21). In 32/1 (14.3%) cases, the tissue biopsies showed wild type (WT) EGFR. 6 liquid biopsies were also performed at time 0 (diagnosis). All liquid biopsies of EGFR WT remained WT during treatment and imaging evaluation. The median number of liquid biopsy tests for patients was 2 (range 1-3). In 4/21 cases, T790M was performed: 3 cases in both liquid biopsies and tissue, and 1 case in tissue but not in liquid biopsy. TKI therapy was ineffective in this patient with T790M mutation detected in tissue, but not in liquid biopsy. In all patients, the disappearance of the T790M mutation during TKI therapy was related to disease progression. In 11 cases, modification of EGFR mutation status during treatment anticipated CT scan evidence of disease progression (median = 3 months).

Conclusion: The liquid biopsy is an excellent resource. In our experience the liquid biopsy is the sensitive method of choice during treatment of advanced NSCLC patients. EGFR modification status during TKI therapy showed advanced disease progression.
E30 Malignant pleural mesothelioma multidisciplinary team unit: experience of one high-volume center in Italy

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Background: Malignant pleural mesothelioma (MPM) is a rare disease, although its incidence is increasing in Italy. Its diagnosis and treatment are challenging, and require the expertise of a multidisciplinary team (MDT). Due to the paucity of current treatment options, inclusion of MPM patients in clinical trials is advisable. MDTs are standard of care for several other cancers.

Material and methods: A weekly mesothelioma MDT meeting was established at our Hospital since January 2017. The core team of MDT is comprised of 4 dedicated medical oncologists, 1 palliative care physician, 2 dedicated radiologists, 1 radiation oncologist, 1 thoracic surgeon, 1 research nurse, and 2 data managers. A pharmacist, a pathologist and a lab biologist are available on call. All MPM patients referred to our Centre, diagnosis, and during treatment and follow up.

Results: From January 2014 to May 2017, 188 new patients were referred to the Medical Oncology Unit of our Clinic. Of them, 23 were referred since January 2017. Diagnostic and treatment advice was provided for all cases within 2 weeks of referral. Since the starting of MDT meetings 72/75 (30%) cases were subsequently enrolled in a clinical trial, versus 35/165 (21%) in the 2014-2016 period. Additional benefits of MDT included evaluation of all new cases by a palliative care physician since diagnosis, and implementation of modified RECIST criteria for MPM for response assessment and radiological monitoring of each patient (both within clinical trials and in everyday practice).

Conclusion: Mesothelioma MDT meetings are very effective at providing timely diagnostic and therapeutic recommendations. The rate of patient inclusion in clinical trials is improved when a dedicated MDT discusses all referred cases. Patients with MPM should be referred to high-volume Centers with adequate expertise.

E31 EGFR mutational status in determining choice of TKIs or standard chemotherapy for patients with advanced non small cell lung cancer

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Background: Tyrosine Kinase Inhibitors are important therapeutic resources for Non-Small Cell Lung Cancer (NSCLC) patients (pts) expressing EGFR-activating mutations (EGFR-m). However, pts without EGFR-addicted tumors do not display the same benefit. Nevertheless, Erlotinib can currently be prescribed to NSCLC pts after failure of a standard platinum doublet regimen, 1 thoracic surgeon, 1 research nurse, and 2 data managers. A pharmacist, a pathologist, a lab biologist and a variety of specialists are available on call. All MPM patients referred to our Centre, diagnosis, and during treatment and follow up.

Results: From January 2014 to May 2017, 188 new patients were referred to the Medical Oncology Unit of our Clinic. Of them, 23 were referred since January 2017. Diagnostic and treatment advice was provided for all cases within 2 weeks of referral. Since the starting of MDT meetings 72/75 (30%) cases were subsequently enrolled in a clinical trial, versus 35/165 (21%) in the 2014-2016 period. Additional benefits of MDT included evaluation of all new cases by a palliative care physician since diagnosis, and implementation of modified RECIST criteria for MPM for response assessment and radiological monitoring of each patient (both within clinical trials and in everyday practice).

Conclusion: Mesothelioma MDT meetings are very effective at providing timely diagnostic and therapeutic recommendations. The rate of patient inclusion in clinical trials is improved when a dedicated MDT discusses all referred cases. Patients with MPM should be referred to high-volume Centers with adequate expertise.

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Background: Tyrosine Kinase Inhibitors are important therapeutic resources for Non-Small Cell Lung Cancer (NSCLC) patients (pts) expressing EGFR-activating mutations (EGFR-m). However, pts without EGFR-addicted tumors do not display the same bene-

E32 Clinical use of immune-checkpoint inhibitors: focus on late immune-related adverse events and pseudoprogession

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Background: Immune-checkpoint inhibitors are changed the treatment’s paradigm of Non Small Cell lung cancer in second line setting and for patients with high-expression of PD-L1, they play a key role in first-line setting. The immune-based mechanism of action of these drugs determine a spectrum of adverse events called immune-related adverse events (irAEs) and a possibility of atypical response patterns called Pseudoprogession. These treatments require understanding of the management of Immune-related adverse events (irAEs) in terms of Incidence and Kinetics of onset and a characterization of atypical response (Pseudoprogession) with Immune-related criteria (irREC).

Materials and methods: Seventwo patients treated with Nivolumab Monotherapy enrolled in Expandid access program and in Clinical Practice were retrospectively studied. Incidence and Kinetics of onset and resolution of irAEs (Cutaneous, gastrointestinal, hepatic, endocrine, renal and pulmonary-effects) were evaluated. Late irAEs were defined as irAEs occurred after 12 weeks to start of therapy. Using irREC Pseudoprogession was identified.

Results: From August 2015 to May 2017 pts were treated with Nivolumab and 43 (40% ) pts are eligible for evaluation of response and later toxicities. The median age at NSCLC diagnosis was 66.5 (55–80) years. Twenty-three pts (76.7%) were male. Twenty-five pts (58.1%) were former smokers, 16 pts (37.2%) were current smokers. Squamous NSCLC was the most common histology (22 pts, 52%). Most pts received Nivolumab in Second-line therapy (31, 72%) and in 9 (21%) pts was superior to 12 months. Incidence of Pseudoprogession was very low (3 pts, 7%) and the treatment of 2 of these pts is ongoing. The Skin events was reported in 4 (9%) of pts and in 12 (25%) occurred after 40 weeks of treatment. Gastrointestinal events was reported in 11 (25%) of pts and in 5 (45%) occurred after 12 weeks, 2;40% of these occurred after 30 weeks. Endocrine events occurred in 2(11%) pts and in 2 (40%) pts occurred after 12 weeks. Pulmonary events occurred in 3(7%) and 6 of these occurred at 37 weeks.

Conclusion: Incidence of atypical response seems a rare events in patients treated with Nivolumab and seems associated with longer PFS. In our clinical practice the incidence of irAEs is very low but the time to onset is not predictable and some events often occur late.

E33 Docetaxel and ifosfamide as salvage treatment in EGFR, ALK wild type non small cell cancer lung (NSCLC)

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Background: The current standard regimen for advanced EGFR, ALK wild type non small cell lung cancer (NSCLC) is cisplatin containing regimen. Docetaxel is active durg, has shown promising activity with improvement in survival and quality of live, therefore its is indicated in second line and in successive lines. Ifofasimide is a broadly active antitumor agent. Therefore we have determined the antitumor activity (response rate) of docetaxel and ifosfamide in patients with relapsed EGFR and ALK wild type NSCLC previously treated with cisplatin based - chemotherapy and with other agents in successive lines.

Material (patients) and methods: Eligible patients with histological proven EGFR and ALK wild type relapsed NSCLC, bidimensional measurable disease, PS < 2 and adequate haematological, hepatic and renal function received Docetaxel 60 mg/m²q1d and Ifosfamide 1500 mg/m²q3d with Mesna as rescue, repeated q 21 days as blood count permitted, until disease progression or appearance of non-tolerable toxicity. Baseline data, toxicity and activity are available in 22 patients (pts) . Pts with median age 67 years (range 43-80), were treated for a median of 4 cycles (range 1-8 cycles). Sites of metastases were lung, mediastinal lymph nodes, liver, bone and adrenal glands.

Results: Out 22 evaluable patients for response, we obtained 3 partial response, 6 stable disease and 13 disease progression. The median survival was 4 months, the median DFS 2 months. The haematologic toxicity was modest. Seven pts experienced grade 3-4 neutropenia without fever, 5 pts anemia, three pts experienced thrombocytopenia grade 2 and four pts hypertontransaminasemia grade 2. Additional non-haematologic toxicities experienced include mild nausea/vomiting, alopecia and nail onycholysis.

Conclusion: Combined therapy with docetaxel low dose and ifosfamide has demonstrated preliminary clinical activity in pts with relapsed EGFR and ALK wild type lung cancer heavily pretreated. Further evaluation of this combination in this setting is warranted.
The correlation between EGFR mutation subtype and efficacy of TKIs in Treatment for elderly patients (EP) with advanced non-small cell lung cancer (NSCLC) could be an important part of daily practice. Between January 2011 and December 2016 a consecutive series of 39 EGFR-positive patients with NSCLC was treated with TKIs. Our analysis showed that TKIs may be used for treating EGFR-positive patients with aNSCLC. However, data of literature suggests better outcomes for patients with exon 19 deletions (19del) in comparison with exon 21 point mutations (L858R). Patients with EGFR-positive aNSCLC receiving TKIs as first line treatment were included in the analysis. Mutational status at diagnosis was detected on tumor tissue or circulating free tumor DNA (ct-DNA). The association between mutation subtype and clinical factors was assessed by Pearson chi square test, while differences in progression free survival (PFS) and overall survival (OS) according to mutation subtype were evaluated by Log-rank test.

Results: Between January 2011 and December 2016 a consecutive series of 39 EGFR-positive patients (all with adenocarcinoma) received a first line TKI: Gefitinib (21 pts), Erlotinib (14 pts) or Afatinib (4 pts). Most of patients, whose median age was 70 years (range 35-84), were female (67%), never smokers (74%) and with stage IV (97%). EGFR mutations were detected on tumor tissue in 37 pts and on ct-DNA in 2 pts. No correlation was found between mutation subtype and site of metastases (lung, lymph nodes, liver, adrenal, bone and brain). After a median follow up of 11.2 mos, the mutation subtype did not influence PFS (median 9.6 mos, 95% CI 3.3 – 15.9 for 19del group vs 8.3 mos, 95% CI 6.6 – 9.9 for L858R group) and OS (median 17.4 mos, 95% CI 12.3 – 23.8 for 19del group vs 18 mos, 95% CI 12.3 – 23.8 for L858R group). Anyway, it is noteworthy that 2 y PFS and OS rates were quite different according to mutation subtype being 24.8% and 36.4% in 19del pts, compared to 0% and 14.8% in L858R pts, respectively.

Conclusions: Our analysis showed that TKIs may be used for treating EGFR-positive lung adenocarcinoma regardless of mutation subtype. Despite the small sample size, the mutation subtype did not correlate with site of metastases, and no statistically significant difference was found in terms of PFS and OS between two mutation subtypes.

E35 Efficacy and safety of immune checkpoint inhibitor nivolumab and radiotherapy combination in advanced NSCLC

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In the last decade the discovery of immune checkpoint inhibitors such as PD-1 inhibitor Nivolumab had revolutionized the treatment of advanced NSCLC. The combination of radiotherapy with immunotherapy is of particular interest, due to some preliminary observations reporting additive or synergist effect in some tumors.

The purpose of this study was to retrospectively evaluate the role of radiotherapy on the effect of an immune checkpoint inhibitor (Nivolumab) in terms of activity and toxicity in pretreated locally advanced or metastatic lung cancer patients. From March 2015 to December 2016, 35 consecutive patients (15 men and 5 women) received Nivolumab for a advanced NSCLC. Fifteen received an hypofractionated radiotherapy as palliative measure, and in these patients Nivolumab was administered at least one week from radiotherapy end.

The median age was 69 years, 23 patients (65.7%) had an ECOG score 0-1. All patients had received, previously at least one systemic regimen, for only 3 (8.6%), nivolumab was a third treatment line. The two groups of treatment (radiotherapy-nivolumab and nivolumab alone) were well matched for baseline characteristics.

At a median follow-up of 7.4 months, the 1-year overall survival rates were 57.8% for patients treated with radiotherapy-Nivolumab and 27.4% for patients treated with Nivolumab alone (p = 0.043). The 1 year progression free survival was 57.8% in the radiotherapy-nivolumab group and 20.6% in the Nivolumab alone group (p = 0.049). No difference in adverse event was detected. In conclusion, radiotherapy and Nivolumab can be combined in advanced, pretreated NSCLC patients, with potential benefit in overall survival and progression free survival, without significant increase in acute toxicities. Prospective studies are needed to confirm these results.

E36 Very elderly patients and lung cancer in a tertiary care center: a real life experience

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Background: Very elderly patients with non-small cell lung cancer (NSCLC) constitute an important part of oncological practice. The peculiar features of patients with more than 75 years and the clinical pathway of patients with adenocarcinoma (ADC) or squamous cell carcinoma (SCC) have not been completely described.

The features and treatments of patients not suitable for local treatment were:

- ADC (15 patients): 3 patients had mutated EGFR (2 del-ex19 e 1 mut-ex21); 2 received 1st line afatinib with a mean PFS of 7.5 months and 1 patient with G3 rash. Among other 12 patients, 4 did not received any chemotherapy, 5 received 1st line single-agent vinorelbine and 3 platinum-based doublet (all the 3 patients had less than 77 years and EGOC PS 0-1 at diagnosis). Disease control rate (SD+PR) was globally 45% (5/11). Four patients had a treatment delay due to G2-3 toxicity, in 1 case a hospital admission was needed.
- SCC (3 patients): 1 patient had mutated EGFR and received off-label 1st line afatinib (with a PFS of 7 months and a PR), 1 patient received 1st line paclitaxel and 1 patient 1st line cisplatin/gemcitabine (with a SD). Two patients had a treatment delay due to G2-3 toxicity.

Conclusions: Very elderly patients with NSCLC could be an important part of daily practice, a significant part of them, especially those affected by ADC are in good general clinical conditions at diagnosis. Also in this population active treatments could be proposed.


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Background: Treatment for elderly patients (EP) with advanced non-small cell lung cancer (NSCLC) comprises single agent of doublet chemotherapy (CT) or tyrosine kinase inhibitors (TKI) for those harboring mutations of the epidermal growth factor receptor or translocation of anaplastic lymphoma kinase (ALK). Clinical studies show that EP (>70) physically fit to receive CT obtain from platinum-based CT similar benefits than younger patients, but with a higher risk of treatment-related toxicities; overall survival (OS) advantage with doublet CT is controversial: a meta-analysis shows an OS benefit with platinum-based doublets (Des Guetz, 2012), while other data show that OS was not significantly improved by platinum-based therapy (Qi, 2012). Single agent (SA) gemcitabine, vinorelbine, taxane are used in fragile or vulnerable patients.

Material and Methods: Results: We registered in our experience a steady increase in NSCLC cases in EP, who accounted for 47% of all NSCLC cases in 2013, 53% in 2014,
50% in 2015, 54% in 2016. We observed an increase in the percentage of EP diagnosed with advanced stage NSCLC (stage IIIB-IV): 45% of cases in 2013, 48% in 2014, 51% in 2015 and 62% in 2016. Patients’ status have been evaluated traditionally only according to the ECOG Performance Status scale, while recently patients have been evaluated more frequently using also the G8 and CGA tool (from only 20% of patients in 2013 to 47% in 2016). The use of G8/CGA evaluation allows oncologists to offer to EP a tailored therapeutic choice, with better results in term of quality of life. Upfront doublet or single agent chemotherapy have been used in 50% and 10% of EP, respectively. SA chemotherapy has been used as second-line treatment in 21% of EP in 2013, with a steady increase up to 60% in 2016. Second-line targeted therapy with TKI, when appropriate, has been given in a progressively higher proportion of NSCLC EP, rising from 3% of patients in 2013 to 11% in 2016. As for the overall NSCLC population, EP benefited from immunotherapy with nivolumab, with 60% of EP receiving the treatment in 2016.

**Conclusions:** Our experience confirms the therapeutic evidence reported in medical literature for advanced-stage NSCLC EP, an ever growing population. A better evaluation of such patients with appropriate tools (G8/CGA) will translate in safer and more effective treatments, better preservation of quality of life and reduced financial toxicity, both for patients and their caregivers.
We retrospectively collected data from metastatic Italian GIST patients treated with imatinib or sunitinib reintroduction after progression to conventional three or four lines of therapy.

Material and methods: 104 eligible advanced GIST patients, previously treated with imatinib, sunitinib and regorafenib, were collected in the present analysis from 6 cancer centers. All patients received all three lines of therapy. Imatinib dose increase as active second line or 800 mg upfront in exon 9 mutant GIST were allowed. Specific mutations were recorded if available (deletion versus others) and correlated with survival.

Results: Seventy-one patients were evaluable. 63 received imatinib 400 mg as rechallenge and 134 patients (79 M, 55 F) were considered, (65-70 y) 63%, (71-75 y) 25%, (76 - 80 y) 11%. STS histologies: mixoid and round cell liposarcomas (34%), leiomyosarcomas (25%), pleomorphic undifferentiated sarcomas (13%), Angiosarcoma (10%), Myxofibrosarcoma (6%), MPNST (4%), synovial sarcoma (2%), other histologies (6%). The patients received at least one course of chemotherapy (1-12). Median OS was the principal end point calculated from the start of chemotherapy to the last date of follow up or death. Response rate and toxicities related to type of administered chemotherapy were the secondary end points.

Conclusion: Seventy-one patients were evaluable. 63 received imatinib 400 mg as rechallenge, while 8 patients were treated with sunitinib at personalised dose and schedule according to the physician’s choice. Mutational status was available in all patients and in particular details about type of mutation were achievable. The median follow-up was 13 months (range 1-42 months). The time to progression (TTP) in patients receiving a rechallenge therapy was 5.4 months (95% CI 1.9-13.5) and Overall Survival (OS) was 10.6 months (95% CI 2.8-26.9). Apparently, in this setting a correlation between mutational status and response rate, TTP or OS was not found. On the contrary, considering only exon 11 mutated patients and comparing patients with deletion vs non deleted ones a significant difference was identified both in terms of TTP and OS (respectively, P = 0.04 and P = 0.02).

Conclusion: Our retrospective data confirm that the rechallenge of imatinib or sunitinib is a reasonable option in advanced GIST patients after failure of previous treatments. As expected, imatinib is the most frequently prescribed option in the Italian real life setting, demonstrating a TTP and OS longer than those observed in previous studies. Also the prognostic value of the specific type of exon 11 KIT mutations has been confirmed in our series.

F2

Molecular characterization and pharmacological profile of myxofibrosarcoma primary cultures

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Background: Myxofibrosarcoma (MFS) is one of the most common sarcoma of the extremities in adult patients and is characterized by a high propensity for local recurrences. Morphologically, it is a myxoid variant belonging to the heterogeneous group of malignant fibrous histiocytomas (MFH). Distinctive histologic features of MFS may include: myxoid stroma, prominent curvilinear blood vessels and pleomorphic areas. Given its relatively recent recognition as a distinct pathologic entity, the clinical behavior and outcomes for patients with MFS are uncertain, and the efficacy of chemotherapy is still not well documented, no randomized trials to guide treatment protocols. Although MFH molecular and cellular biology has been widely investigated, and a large number of human MFH cell lines are available, only a few number of MFS cell lines have been established. In an effort to improve the current understanding of the molecular biology and treatment outcomes of high grade MFS, we have conducted an analysis on a new patient derived culture.

Material and methods: Three primary or recurrent MFS were harvested intraoperatively from patients undergoing resection and the cells were brought into cell culture. The diagnostic impact of CD109 expression was evaluated and we also investigated TGF-β as a marker of chemoresistance. Moreover the efficacy of different drugs which are currently used, including ifosfamide, epirubicin, ifosfamide in combination with epirubicin or trabectedin for the treatment of soft tissue sarcoma (STS) was assessed.

Results: The results showed an overexpression of CD109 gene in all samples compared to the matched healthy tissues highlighting that CD109 could represent a promising marker for MFS diagnosis and a potential therapeutic target. Furthermore, our findings indicated that TGF-β could be involved in MFS chemoresistance. Finally, pharmacological analysis confirmed the sensitivity of the cultures to the chemotherapies. In particular the most active regimens were represented by epirubicin alone and in combination with ifosfamide which currently represent the standard treatment for advanced STS patients including MFS.

Conclusion: This work seeks to shed light on this poorly explored disease showing potential markers for diagnosis and drug resistance and sensitivity that would represent the basis for further research aimed to improve the management of MFS patients. Our results need to be confirmed in a larger case series.

F3

Elderly patients and metastatic soft tissue sarcoma (STS): a noninstitutional experience

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Background: Elderly people represent more than 50% of STS patients, but few data are available in this population and old patients in clinical studies are underrepresented or not included. Aim of this retrospective, noninstitutional study is to describe the activity and feasibility of first and second line chemotherapy in elderly patients with metastatic STS.

Methods: Patients older than 65, with metastatic STS of the scalp, trunk, girdles and extremities, treated and followed from February 1998 to December 2015 in an Italian referral Center for diagnosis and care of STS were included. Median Overall survival (OS) was the principal end point calculated from the start of chemotherapy to the last date of follow up or death. Response rate and toxicities related to type of administered chemotherapy were the secondary end points.

Results: 134 patients (79 M, 55 F) were considered, (65-70 y) 63%, (71-75 y) 25%, (76 - 80 y) 11%. STS histologies: mixoid and round cell liposarcomas (34%), leiomyosarcomas (25%), pleomorphic undifferentiated sarcomas (13%), Angiosarcoma (10%), Myxofibrosarcoma (6%), MPNST (4%), synovial sarcoma (2%), other histologies (6%). All the patients received at least one course of chemotherapy (1-12). Mono CT was the preferred administered schedule (92%of cases). Median OS was 7.3 months; at the time of this analysis only 14 patients were alive (10%). In the first line therapy we recorded 1 CR, 14 PR and 43 SD. In second line therapy no CR, 4 PR, 23 SD. PR were recorded mainly in 65-70y old patients. Bad PS, low score in Comprehensive Geriatric Assessment (CGA), vulnerability, comorbidities, number of metastasis, were negative prognostic factors. No toxic death were recorded, but 12% of the pts were recovered for febrile neutropenia, thrombocytopenia and mucositis.

Conclusions: Our study confirms that elderly patients with metastatic STS is a difficult population to be treated. Only patients less aged, with good PS, good GCA and 0-1 comorbidities can be treated with full dose of drug, generally with mono CT. Chemotherapy in elderly pts doesn’t produce a significant improvement in Median Survival and the benefit observed support the routine use of citotoxic treatment in selected good performance status population.

F4

Potential therapeutic combination of beta-blockers and trabectedin in metastatic soft tissue sarcoma and ovarian cancer

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Trabectedin has been approved as single agent for second-line therapy of soft tissue sarcoma (STS) such as liposarcoma (LS) and leiomyosarcoma (LMS) and for the treatment of patients with relapsed, platinum-sensitive ovarian cancer in combination with pegylated liposomal doxorubicin. Clinical evidence revealed that beta-adrenergic receptor antagonists such as propranolol, could increase the effectiveness of vinblastine in the treatment of sarcoma patients. In order to realize tailored therapy toward different histological subtypes of STS and of ovarian cancer, the investigation of β-adrenergic receptors (β-ARs) as appropriate targets in a combined treatment with Trabectedin was evaluated. After determining the expression of β-ARs in ovarian and sarcoma cell lines, we started combining propranolol with Trabectedin. Our results demonstrated that propranolol strongly enhances the response to Trabectedin in both A2780 ovarian cancer cells resistant to carboplatin and in the sensitive cell lines OV2008. The evaluation of the synergy among drugs was assayed both in 2D and in 3D cells models. The analysis of cell cycle showed that Trabectedin blocked the cells in S-phase and the addition of propranolol further caused the accumulation of cells in both G0/G1 and S-phase. Such effects resulted in a strong induction of apoptosis in the combination compared to single treatment. Noteworthy the efficacy of the combination was maintained in stress induced condition (10μM norepinephrine-NE). In agreement with cytotoxic results, the combination still induced apoptosis even after NE stimulation. We also tested the therapeutic potential of combining propranolol to Trabectedin in the treatment of sarcoma cells. Both drugs alone were effective in reducing cell proliferation of
LS cells stronger than LMS cells, and also the combination was more cytotoxic in LS cells than LMS cells. Interestingly, the activation with physiological concentration of β-ARs agonist Norepinephrine (NE) 100mM, did not resulted in reduced sensitivity to both propranolol and Trabectedin, while the stress induced concentration of NE 10μM resulted in reduced sensitivity to each single agent in LMS model. In conclusion blockage of β-adrenergic receptors enhances Trabectedin effectiveness, therefore further evaluation of underlying mechanisms of drugs synergism are warranted in order to provide a strong rational for suggesting this combination in the treatment of sarcoma and ovarian cancer patients.

The value of trabectedin in the treatment of soft tissue sarcoma: a monoinstitutional retrospective real-life study

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Background: Soft-tissue sarcomas (STS) are rare tumors, accounting for approximately 1% of all cancers worldwide each year. The treatment of STS is often palliative, although a subset of patients may be cured or have a good disease-free interval. Trabectedine is a novel marine-derived antineoplastic agent that is characterized by multiple potential mechanisms of action combining cytotoxic, targeted, and immunological effects. Now it’s to be consider a standard second line in not all subtypes.

Materials and methods: From January 2016 to April 2017 we treated 10 patients with STS metastatic (7 females, mean age 58.5 years, 5 liposarcoma, 1 fibrosarcoma mixed, 3 leymiosarcoma, 1 lonely pleural fibrous tumor). All patients were entered in the AIFA registry. Six patients were treated with Trabectedin as second line after failure of first line therapy containing anthracyclines. Three patients were treated in the third line and one in the fourth line. One was treated as a first line for heart problem. The dosage was 1.5 mg/m² every 21 days and was administered a total 54 cycles (media 5.4; range 1-11). All administration was performed using CVC. Every two doses (in accord with AIFA) we proceeded to perform CT revaluation.

Results: Best tumor response by RECIST to the second cycle was: PR = 5, SD = 3, PD = 2 cases, for an overall response rate (PR + SD) of 80%. A patient died after a few days of treatment for intestinal perforation. Median PFS was 8.3 months (range 1-11). Five patients are alive and two of this are still in treatment. Overall, trabectedine was well tolerated, the most common side effect G4 was thrombocytopenia. In the case of first-line treatment, hyperbilirubinemia and significant hypertransaminasemia occurred which caused the drug to be discontinued.

Conclusions: Trabectedin has consistent activity in all types of STS. It can be positioned after failure of first-line therapy with anthracyclines or in patients unfit for anthracycline-based therapy. This analysis confirms the efficacy of trabectedin in clinical practice (with a third of patients experiencing prolonged disease control). Therefore, trabectedin has become one relevant therapeutic option in metastatic STS, especially in selected histologies.
G - MELANO MA AND SK IN CANCERS

G1 A phase II trial of dacomitinib in locally advanced unresectable or metastatic skin squamous cell carcinoma

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Background: In recurrent/metastatic skin squamous cell cancer (sSCC) not amenable to radiotherapy (RT) or surgery, chemotherapy (CT) has a palliative intent and limited clinical responses. The role of pan-HER inhibitor dacomitinib in this setting was investigated within an Italian clinical trial.

Methods: Patients (pts) with diagnosis of sSCC not amenable to curative treatments were treated. Oral dacomitinib was started at a dose of 30 mg per day for 15 days, followed by 45 mg qd. Primary endpoint was response rate (RR). Tumor samples were analyzed through Next Generation Sequencing methods (pgm, Ion torrent) using a custom panel targeting 36 genes associated with sSCC.

Results: Forty-two pts (33 M, 9 F; median age 77 years, range 45-92) were treated. Brain metastases (mts) are common in MM and their prognosis is poor, with overall survival typically measured in months. Despite promising preclinical rationale, synergistic effect of RT and IT remains to be investigated within an Italian clinical trial.

Conclusion: Brain metastases (mts) are common in MM and their prognosis is poor, with overall survival typically measured in months. Despite promising preclinical rationale, synergistic effect of RT and IT remains to be investigated within an Italian clinical trial.

G2 Prognostic role of disease extent and lymphocyte-monocyte ratio in advanced melanoma

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Background: One-third of patients (pts) with early melanoma experience a disease recurrence. Previous data showed that pts with advanced melanoma (AM) treated with BRAF and MEK inhibitors with normal lactate dehydrogenase (LDH) concentration and fewer than three organ sites of metastases had better outcome. Furthermore, melano
da has been recognized as one of the most immunogenic malignancies. The lymphocyte-monocyte ratio (LMR) is a simple biomarker of host immune system and inflammation and it was suggested as a prognostic factor in different cancer types.

Patients and methods: We retrospectively analyzed 165 consecutive pts with AM between Jan 2010 and Mar 2016 treated at the Department of Oncology of Udine, Italy. The aim of the study was to evaluate the prognostic role of disease extent and LMR at baseline. Outcome was measured in terms of overall survival (OS).

Results: In our cohort 102 pts (62%) were male, 136 (82%) presented at baseline ECOG PS 0-1; 42 pts (23%) received more than 2 treatment lines. Stage classification was III, M1a, M1b and M1c in 19 (11%), 44 (27%), 18 (11%) and 84 (51%) pts, respectively. BRAF was mutated in 76% of pts (missing data in 30 pts). Overall, 69 pts (42%) received target therapy (MEK and/or BRAF inhibitors) and 43 (26%) received immunotherapy. At a follow-up of 48 months, 129 pts (78%) were died, the median OS was 3 months. LMR was significantly associated with absence of CNS-localization (p = 0.011), less than 3 metastatic sites (p = 0.015) and normal LDH level (p = 0.005). In univariate analysis, PS > 1 (HR 2.67, p = 0.0002), number of metastatic sites more than 2 (HR 2.38, p = 0.0001), lung (HR 1.97, p = 0.0004), liver (HR 2.05, p = 0.0089), and CNS-localization (HR 1.62, p = 0.0267), elevated LDH (HR 3.27, p < 0.0001), Mib and Mib stage (HR 2.13, p = 0.0271 and HR 3.70, p < 0.0001), respectively were significantly associated with worse OS; on the contrary, high LMR was associated with better OS (HR 0.71, p = 0.0004). In multivariate analysis, ECOG PS (HR 7.86, p = 0.001), LDH (HR 2.82, p = 0.004) and LMR (HR 0.75, p = 0.030) were significantly associated with OS.

Conclusions: In our study, LMR seems to be associated with extent of AM and increased risk of mortality. Further investigations are needed to confirm these data.

G3 Brain radiotherapy (RT) and immunotherapy (IT) for metastatic melanoma (MM): a retrospective single institution experience

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Background: Brain metastases (mts) are common in MM and their prognosis is poor, though recent therapeutic advances. Limited preclinical and clinical evidences have suggested a potential immune-modulatory role of RT, which may synergize with IT, and some cases of abscopal effect (i.e. response of a distant non-irradiated site) have been described. We aimed to investigate efficacy and toxicity of concomitant or sequential IT and RT in a single Institution experience.

Material and methods: We analyzed data about all pts treated at our Institution between 06/12 and 11/16 with a CI, either antiCTLA4 or antiPD1, and brain RT, either stereotactic (ST) or whole brain (WB). Only cases treated with RT within 6 months (mos) before or after IT were eligible, without any other oncologic therapies meanwhile. Progression free and overall survival (PFS and OS, respectively) were estimated according to the Kaplan-Meier method.

Results: 36 pts were identified. IT was administered as 1st line in 21 pts, 2nd line in 22, and 3rd line in 7. 23 pts received antiCTLA4, 13 antiPD1. 18 pts were treated with ST RT, 18 with WB RT. Median PFS from RT was 4.2 months (95% CI 2.3-6) and 5 months (95% CI 3.9-6.1) respectively (p = 0.22). Median OS from RT was 6.5 months (range 0.3-23) and 12 months (95% CI 9-NR), respectively. Median PFS from antiCTLA4 or antiPD1 was 4.6 months (range 1.1-11). No grade 3-4 acute reactions were observed. Neurologic adverse events were 23%, mainly consisting in fatigue (71%), headache (14%), speech disorder (11%). Long-term follow-up (median 18 mos) showed 16% of pts alive at last follow-up.

Conclusions: Despite promising preclinical rationale, synergistic effect of RT and IT does not seem to be confirmed in our experience. No cases of abscopal effect were observed and most pts underwent early progression of systemic disease after RT. Overall prognosis of this population was poor, without predictors of benefit from combination of IT and RT. Prospective data are needed to focus on this topic, given the acceptable tolerability of combined treatment.

G4 Metastatic melanoma patients treated with BRAF and MEK inhibitors: Patterns of progression. An Italian Melanoma Intergroup study

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Background: Patterns of progression after data collected from 164 consecutive pts affected by BRAF V600 melanoma metastatic disease, we analysed outcomes in pts treated with BRAF+MEK1 to characterize pts with rapid progression.

Methods: In this multivariate retrospective analysis, data were collected from 164 consecutive pts affected by BRAF V600 metastatic melanoma and treated with BRAF+MEK1 from February 2012 to April 2017. Results: 64 patients were enrolled. Baseline LDH was elevated in 68 (41%) pts, baseline number of metastatic organs were 1, 2, 3 and more in 52(32%), 52(32%), 29(18%) and 32(19%) pts. BRAF+MEK1 were administered dabrafenib+trametinib in 151 pts and vemurafenib+cobimetinib in 13 pts, and they were administered in first line in 129(79%)pts. Best response was CR, PR, SD and PD in 27, 8, 72 and 17 pts. On cutoff summary for survival responses were as follow: no progression (median 21 months), best response was CR, PR, SD and PD in 27, 8, 72 and 17 pts. On cutoff
date, progression was observed in 104 (63%) pts - 60 (37%) pts still on treatment. mPFS was 9.8 (1-54.7) months; significant difference in PFS was showed in pts with normal baseline LDH or high LDH (13.2 vs 6.3 months, p < 0.0001), and in pts with number of metastatic organs lower or higher then 2 (13,4 vs 7 months, p < 0.0001). mOS was 18.3 (1-62.5) months; significant difference in OS was showed in pts with normal baseline LDH or high LDH had (24.7 vs 10 months, p < 0.0006), and in pts with number of metastatic organs lower or higher then 2 (25.9 vs 10 months, p < 0.0003). Among 104 progressed pts, 72 (69%) pts died, mOS after progression was 2.5 months (0.5-42+ months); Subsequent treatments were administered in 44 (42%) pts. Duration of response (DR) was defined as time from BRAF + MEK 1 best response to progression of disease. Significant difference in OS after BRAF + MEK 1 progression was observed in pts with DR < 6 month (77 pts) or > 6 months (27 pts) (2 vs 8.3 months, p < 0.0023) and in pts with number of metastatic organs after progression lower or higher then 3 (4.5 vs 2 months, p < 0.022).

Conclusion: DR and extension of progression during BRAF + MEK 1 are factors that can be useful to identify pts with lower OS after progression, in addiction to known parameters like LDH and baseline number of metastatic organs.

GS Analysis of miRNAs and their correlation with early malignat melanoma (MM)

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Background: The incidence of MM progressively increases and today 14 cases/100,000 cases per year are expected in Italy. The screening campaigns led to the identification of many early forms of MM, resulting in increased incidence of the disease, but have not changed mortality. This is possibly related to the identification of MM that would have remained silent. The visit and the dermoscopy are operator-dependent methods and require long experience for their optimal use. Even in the most experienced hands, the sensitivity of these methods does not exceed 85% and 90%, respectively. It would be need to identify new effective screening methods, able to eliminate the existing limits. MM is the skin cancer with the worst prognosis, especially when discovered at advanced stages. Moreover, it would be clinically relevant to identify in advance the melanoma lesions at risk of recurrence.

Subjects and methods: In 2014 we have activated an experimental study to investigate the possible role of miRNAs in MM screening tool. All the subjects screened with dermoscopy by the "Lega Italiana per la Lotta contro i Tumori" (LILT) are invited to join the study. They underwent a blood sample collection and a panel of 15 miRNAs is analyzed. We selected miRNAs described as markers of MM diagnosis and/or to have well supported roles in its progression.

The primary objective is to compare the level of circulating miRNAs in 100 patients with MM and 100 subjects with non-neoplastic skin pigmented lesions, to evaluate their diagnostic value. The study foresees to enroll 700 subjects, to create a database, to make a multivariate analysis including selected miRNAs, personal anamnesis and exposition to known risk factors.

Results: From September 2014 to December 31, 2016, we accrued 633 subjects, with doubt of MM at the screening evaluation. We found 101 MM (16%); 36 in situ MM, 59 infiltrating (20 pT1a, 22 pT1b, 7 pT2a, 2 pT2b, 1 pT3a, 4 pT3b, 2 pT4b, 1 pTXNxM1a), 2 lentigo maligna and 4 multiple MM. At the preliminary analysis miR-199a-5p, miR-122-5p and miR-424-5p represent the most promising candidate biomarkers in terms of diagnostic efficiency in distinguishing between MM patients and healthy subjects.

Conclusions: The study gives preliminary information about the incidence of MM in a population clinically screened. Analysis of selected miRNAs and their role as diagnostic tools for early MM detection will be presented and correlated with clinical and known risk factors.
Nodal status is paramount to tailor the need of adjuvant treatments in patients affected by apparent early-stage epithelial ovarian cancer (eEOC). Here, we aimed to estimate the prevalence of nodal involvement according to various disease characteristics in order to assess the prognostic advantages to have nodal dissection in eEOC.

**Patients and Methods:** Data of consecutive patients undergoing comprehensive staging for eEOC were retrospectively evaluated. Logistic regression and a nomogram-based analysis were used to assess the risk of nodal involvement.

**Results:** Overall, 377 patients were included. Among those, 94 (74.6%) patients experienced nodal involvement, and 16 (10.9%) patients were upstaged due to nodal involvement. Pelvic and para-aortic nodal metastases were observed in 32/377 (8.6%) and 42/370 (11.3%) patients, respectively. Nodal involvement was observed in 46/136 (33.8%), 8/24 (33.3%), 15/94 (15.9%), 4/42 (9.5%) and 1/81 (1.2%) patients with serous, undifferentiated, endometrioid, clear cell, and mucinous histology (p < 0.001). Via multivariate analysis, we observed that poor differentiated tumor, FIGO grade 3, serous histology and bilateral tumors were independently associated with both pelvic and para-aortic nodal involvement (p < 0.05). Normograms displaying the risk of nodal involvement in the pelvic and para-aortic areas were built. FIGO grade, serous histology and bilateral tumors are the main characteristics suggesting node positivity. Moreover, we observed that pelvic node involvement was more frequently detected in patients affected by FIGO stage II eEOC.

**Conclusions:** Our data suggested that FIGO grade 3, serous and bilateral eEOC are at high risk of having disease harboring in the lymph nodes. After receiving external validation, this data will help to identify patients deserving comprehensive retroperitoneal staging.

**H2** Phase II study of the safety and efficacy of oral capcitabine in patients with platinum-pretreated advanced or recurrent cervical carcinoma

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**Background:** Cervical cancer is underrepresented in the gynecological clinical research. The objective of this observational study was to evaluate the activity and the safety of capcitabine in patients with platinum-resistant recurrent cervical carcinoma.

**Materials and methods:** In this phase II study we enrolled patients with advanced/ recurrent cervical carcinoma who have failed a previous platinum-based therapy. All patients signed an informed consent and were treated at the Gynecological Units of the IRCCS National Cancer Institute of Milan (Italy). All patients received a starting dose of oral capcitabine 1250 mg/m2 twice a day continuously from day 1 to day 14 every 21 days. We used RECIST 1.1 criteria to evaluate response to therapy and CTCAE 4.1 to evaluate AE. Progression-free survival (PFS) was defined as time from first capcitabine intake to progressive disease (PD) and overall survival (OS) as time from first capcitabine to cancer-related death. We performed descriptive analysis and Kaplan Meier test using SPSS 20.0.

**Results:** From Dec 2013 to Jan 2017, 20 patients were enrolled. All patients receive a combination of carboplatin/paclitaxel as first-line therapy for advanced/recurrent disease. Median age at the first capcitabine administration was 56.9 years (range 27-82). After a median follow-up of 14.3 months (range 3-96.6), 2 patients were on treatment, 18 patients experienced a PD with a median PFS of 4.7 months and 16 patients died (median OS 14.4 months). With a median exposure to capcitabine of 4.5 cycles (range 3-13), 5% complete responses, 30% partial responses and 25% stabilization of disease were reported. After capcitabine, 65% of patients received further chemotherapy (median 2 lines, range 0-5). No grade 3 adverse events (AE) were reported; the most frequent grade 2 AE were fatigue (55%), hand-foot syndrome (40%) and diarrhea (20%). Overall, 5 patients received a reduced dose of capcitabine (1000 mg/m2 twice a day) due to AE (1 grade 2 diarrhea, 2 grade 2 fatigue and 2 grade 2 hand foot syndrome).

**Conclusions:** Our study suggests that oral capcitabine should be considered an active and safe treatment in patients with platinum-resistant advanced/recurrent cervical carcinoma.

**H3** Is chemotherapy worthwhile in patients with high-risk, lymph node negative, FIGO stage 1, endometrial cancer?

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**Background:** Until the results of the ENGOT-EN2-DGCC/EORTC 55102 trial will become available, the role of adjuvant chemotherapy (CT) in patients with high-intermediate and high risk, early stage, lymph node negative (LNN), type 1 endometrial cancer is unclear.

**Methods:** We retrospectively collected patients diagnosed with endometrial endometrial cancer stage Ia and b (2009 FIGO staging), LNN, and grade 3. We performed descriptive analysis and Kaplan Meier test using SPSS 20.0.

**Results:** From March 1996 to Oct 2016, 54 consecutive patients were identified and enrolled (46 at the National Cancer Institute of Milan and 8 at the University Hospital of Udine). Median age at diagnosis was 65.4 years (range 34.2-84.9). All patients were documented to be LNN negative. 27 patients underwent pelvic lymphadenectomy (PLD), 19 PLD plus lomboaortic (LA), and 8 sentinel lymph nodes biopsy. Overall, 35 patients had lymphovascular space involvement (LVS+) and 11 had not, in 8 pathologic report this data was not reported. After surgery, 33 patients received adjuvant radiotherapy (RT): 21 patients (63.6%) received brachyRT, 8 patients (24.2%) received external RT, 4 patients (12.2%) received both; 13 patients underwent platinum-based adjuvant chemotherapy (CT): 7 only CT, 2 external RT followed by CT and 2 brachyRT followed by CT. To note, among patients who received CT, 84.4% had LVS+. After a median follow up of 51.1 months (range 6-249), 14 patients (25.9%) experienced disease relapse and 12 patients (22.2%) died (9 due to endometrial cancer, 2 breast cancer and 1 pancreatic cancer). Median disease-free survival (DFS) was 19.9 months (range 4.7-15.4). Only 1 patients who underwent CT experienced disease relapse, the relapse rate was 7.7% in CT group versus 31.7% in non-CT group (P = 0.085).

**Conclusions:** According to our study, patients with stage Ia and b, LNN, grade 3 endometrial endometrial cancer seems to derive a great benefit from adjuvant chemotherapy. This data needs to be further investigated in a large prospective clinical trial.

**H4** The impact of chemotherapy-related leukopenia on survival outcomes in locally advanced cervical cancer

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**Background:** The immune system plays an important role against tumor growth. Accumulating evidence indicates that chemotherapy might influence the activity of resident and recruited immune cells that contrast tumor proliferation. Here, we aimed to investigate the impact of hematologic toxicity and leukopenia in locally advanced cervical cancer patients undergoing neoadjuvant chemotherapy (NACT). The purpose was to determine whether there is a correlation between hematologic toxicity and survival outcomes.

**Patients and methods:** Data of consecutive patients undergoing platinum-based NACT followed by surgery were collected in order to evaluate the impact of chemotherapy-related toxicity on survival outcomes. Toxicity was graded per the Common Terminology Criteria for Adverse Events (CTCAEv4.03); Survival outcomes were evaluated using Kaplan-Meier and Cox hazard models.

**Results:** Overall, 126 patients were included. Among those, 94 (74.6%) patients experienced grade 2 hematologic toxicity; while, grade 3-4 hematologic toxicity occurred in 11 (8.7%) patients. After a median follow-up of 37.1 (inter-quartile range, 12-57.5) months, 21 (26.6%) patients experienced recurrence. Via multivariate analysis, no factor was independently associated with disease-free survival; while a trend toward worse prognosis was observed for patients experiencing grade 3-4 leukopenia at cycle 3 (HR:3.33 (95%CI: 0.94, 10.3); p = 0.06). Similarly, grade 2 leukopenia (HR:9.98 (95%CI: 1.14, 86.6); p = 0.03), lymph-node positivity (HR:14.6 (95%CI:1.0, 214.4); p = 0.05) and vaginal involvement (HR:5.81 (95%CI:1.43, 23.6); p = 0.01) impacted on overall survival, at multivariate analysis. Magnitude of leukopenia correlated with survival (p < 0.001).

**Conclusions:** The present study shows an association between the occurrence of leukopenia and survival outcomes. NACT-related immune suppression might reduce the response against the tumor, thus promoting cancer progression.
Background: Approximately 18% of patients with high-grade ovarian cancer (inclusive of epithelial ovarian cancer) harbour a deleterious germline BRCA1 or BRCA2 mutation, and approximately 7% harbour a somatic mutation. In high-grade ovarian cancer, about 5% of patients have a somatic BRCA1 or BRCA2 mutation (Pennington et al. Clin Cancer Res. 2014;20:764-75). The poly(ADP-ribose) polymerase (PARP) inhibitor rucaparib is approved in the United States for treatment of patients with deleterious BRCA mutation (germline and/or somatic) associated advanced ovarian cancer who have been treated with ≥2 chemotherapies. Data comparing PARP inhibitors to standard of care for treatment of relapsed ovarian cancer are limited. ARIEL4 (EudraCT 2016-00816-14; NCT02855444) is evaluating rucaparib versus standard of care chemotherapy as treatment for patients with relapsed, high-grade ovarian cancer (regardless of histology) and a deleterious germline or somatic BRCA1 or BRCA2 mutation who have received ≥2 prior chemotherapy regimens.

Materials and methods: Patients (n=345) stratified by progression-free interval after their most recent platinum regimen will be randomised 1:1 to receive rucaparib 600 mg BID or chemotherapy. Patients with platinum-resistant (progressive disease ≥2 to ≤6 months after last platinum) or partial platinum-sensitive disease (progressive disease ≥6 to <12 months after last platinum) will receive rucaparib or weekly paclitaxel; patients with platinum-sensitive disease ≥12 months after last platinum) will receive rucaparib or investigator’s choice of platinum-based therapy (single-agent or doublet). Patients receiving chemotherapy may cross over to rucaparib upon radiographic disease progression. The primary endpoint is investigator-assessed progression-free survival (per RECIST version 1.1 criteria). Secondary endpoints include overall survival, investigator-assessed objective response rate per RECIST criteria, objective response rate per RECIST/C1a-125 criteria, duration of response, and patient-reported outcomes. Safety will be summarised descriptively using standard adverse event reporting.

Results: ARIEL4 is actively recruiting patients.

Conclusions: Randomised studies such as ARIEL4 are needed to assess the benefit-risk profile of PARP inhibitors versus standard of care as treatment for relapsed, high-grade ovarian cancer.

Ref: Retrospective analysis of 77 patients with ovarian cancer undergoing genetic testing for BRCA1 and BRCA2 mutations

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Background: Ovarian cancer (OC) is still a big killer in the field of female neoplastic disease, placing itself fifth as cause of death. In recent years, some genetic mutations have been analyzed within high grade serum OC. BRCA1/BRCA2 genes mutation is the most commonly observed in a proportion of patients with ovarian cancer not necessarily belonging to families expressing such alterations.

Material (patients) and methods: A retrospective cohort of 77 OC patients were selected between 2014-2017. All patients samples were collected with appropriate consent and tested for germline BRCA1 and BRCA2 mutations after genetic counselling at the Department of Medical Genetics unit of University Hospital of Careggi in Florence. Genomic DNA was isolated from blood using FlexGene DNA Kit. Targeted library preparation of BRCA1 and BRCA2 was performed using hybridization capture probes or multiplex PCR. Post PCR Illumina sequencing was carried out on the Illumina MiSeq following the manufacturer’s instructions. Data analysis, including alignment to the hg19 human reference genome and variant calling was done using GATK or SeqNeat software package. All pathogenic germline variants were validated by Sanger sequencing.

Results: Pathogenic mutations in BRCA2 genes were found in 23 out of 77 (29.9%) high grade malignant epithelial OC. 20 of them were in BRCA1 while 3 in BRCA2. The remaining 54 patients were wild type. Patients, after cytoreductive surgery, had chemotherapy of line according to the carboplatin-paclitaxel scheme for 6 cycles. All 23 mutated patients, except for a platinum-resistant case (4-month progression time), had platinum sensitivity over 6 months. 16 patients over 20 with BRCA1 and BRCA2 mutations, received a chemotherapy II of line. Of these patients, 13 had a PFS greater than 6 months and 3 patients were resistant platinum. Ca 125 basal marker was positive (range of normality from 0-35) in more than 78.2% of cases, while Ca 125 on relapse was positive in 95.7% of cases.

Conclusions: The differentiation of patients in subgroups related to the presence or absence of BRCA1 and BRCA2 genes and their variants, has allowed to identify in the mutated population a higher platinum sensitivity, also in subsequent lines of therapy and to undertake treatments with innovative molecules for OC such as PARP14-16 inhibitors, that partially modified the prognosis of this neoplasia by increasing the disease-free interval.

First line treatment with carboplatin-paclitaxel-bevacizumab in ovarian cancer: retrospective review of a single institute experience

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Oncology unit, Azienda Ospedaliera Arcispedale Santa Maria Nuova - IRCSS, Reggio Emilia; Oncology unit, Azienda Ospedaliera Arcispedale Santa Maria Nuova, Reggio Emilia

Purpose: Carboplatin- Paclitaxel- Bevacizumab has become the standard first line treatment of ovarian cancer (OC) at high risk of progression (IIIB, IIIC, IV). The purpose of this study was to investigate the efficacy and safety of this combination in our first 35 patients (pts) treated with this combination.

Materials and methods: This is a retrospective analysis of 35 consecutive OC pts undergoing carboplatin, paclitaxel and bevacizumab chemotherapy regimen, from February 2013 to January 2017, in Reggio Emilia Clinical Cancer Center.

Results: Thirty-five consecutive pts were included in this analysis who received at least one cycle of the combination. Median patient age was 58 years (range 41-73). Except one patient who had an endometroid G3 tumor, the rest had a papillary serous G3 type. Eight pts had a BRCA mutation (22%), 4 BRCA1 and 4 BRCA2. Eighty percent were stage IIIC, one patient was stage IIIB and 6 pts (17%) were stage IV. A median of 6 cycles of carboplatin-paclitaxel-bevacizumab was delivered (range 3-18). A median of 18 cycles of bevacizumab in maintenance was delivered (range 3-24). Twelve of them are still in bevacizumab maintenance therapy. Eleven pts received neoadjuvant chemotherapy without bevacizumab with 25% of partial responses, one complete response and one stable disease. Fifty-seven percent of the pts reached an optimal cotermination and 43% a suboptimal one. The median progression-free survival was 22,7 months (range 3,97-48,07) (95% 21,5-23,9 CI). Median overall survival has not been reached with a median follow up of 45,5 months (95% 42,3-48,8 CI). Grade 1-4 hematologic toxicity was seen in 33% of the pts, mainly neutropenia G2 (5 pts, 14%) and G3 (3 pts, 8,5%). The most frequent G1-4 non- hematologic toxicity were: paresthesia 44%, myalgia 25%, constipation 25%, asthenia 25%, arthralgies 13%, nausea 10% and vomiting 19% as well as anemia 14%. Main G4-3 toxicities were neutropenia 11% and asthenia 8%. During the bevacizumab maintenance treatment the most frequent toxicities were hypertension (5 pts) 13%, in 2 cases G3 (5,7%), 2 cases of epistaxis G1 (5,7%) and 1pt (2,8%) with peridontal bleeding G1. No bowel perforation was notified.

Conclusion: In this study, our purpose is to provide enough evidence that the use of bevacizumab as part of first-line treatment of patients with ovarian cancer at high risk of progression has demonstrated higher rates of efficacy comparable with those obtained in clinical trials, without unexpected toxicities.

Prognostic impact of CA15-3 pre-treatment levels in ovarian cancer patients


Background: In ovarian cancer (OC) patients (pts), CA15-3 represents the pivotal serum tumor marker with a well established role in diagnosis, response to treatment and follow-up. CA15-3 is a breast cancer-associated antigen also expressed in some other ovarian cancer and gynecological malignancies, even if its role is still not well clarified. The aim of this study is to evaluate the prognostic role of CA15-3 at diagnosis in OC patients.

Patients and methods: OC pts treated in our Center from 2009 to 2017 were eligible for analysis. We retrospectively collected data regarding histopathological type, treatment (CA125 and CA15-3 levels during treatment, and CA15-3) and tumor markers information. We performed CA15-3 cut-off values (greater than 35 U/
patients were divided into a group with high CA 15-3 at diagnosis and a group with normal levels. The two groups were compared with regard to clinical and survival measures, including overall survival (OS) and first-line progression-free survival (PFS). Survival distribution was estimated by the Kaplan–Meier method. The association between categorical variables was tested by Fisher exact test and by Chi-square test. OS was defined as the interval between the start of chemotherapy to death or last follow-up visit, while first-line PFS was defined as the interval between the first-line chemotherapy and progression.

Results: Out of 72 OC eligible pts, CA 15-3 serum levels at diagnosis were evaluated in 38 pts. Among them, 16 (42%) had elevated CA 15-3 level at diagnosis. Analyzing the prognostic impact of CA15-3, a significant difference in terms of OS was found: OC patients with elevated CA 15-3 at diagnosis showed a worse OS when compared with patients with normal CA 15-3 levels (median OS: 30.9 months vs 65.72 months; HR: 3.0179; 95% ci 1.0346–8.8030; p = 0.0164) whereas no difference in terms of first-line PFS was observed. High CA 15-3 levels were not associated with histotype or BRCA mutation status, while a statistically significant correlation was found with higher stage at diagnosis (p = 0.0124).

Conclusions: Our data suggest that high CA15-3 levels at diagnosis in OC patients could represent a poor prognostic factor. High CA15-3 levels also seem to be related with an advanced stage at diagnosis. Further prospective and multicentric studies are needed to confirm the prognostic role of CA15-3 in OC patients.
L1 Different signatures of HPV-related oropharynx cancer (OPC) correlate with patients outcome
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Background: HPV-related OPC patients have different epidemiologic, clinical and outcome behaviors in comparison with HPV-negative OPC, having HPV-related OPC patients a 70% of reduction in their risk of death. Smoking exposure and bulky neck nodes are negative prognostic factors, however the reasons of treatment failure are almost unknown in HPV-related OPC. In the last years high-throughput gene expression assays allowed to identify predictive signatures in several tumor types. Our objective is to seek whether exists a predictive signature in HPV-related OPC.

Methods: publicly gene expression data for HPV-positive OPC were searched by a literature revision, through a systematic search, performed in the following databases: PubMed, ArrayExpress, Embase, and GEO meta-analysis. Only studies with HPV status confirmed by DNA sequencing or qPCR were considered eligible. Patients outcome will be described using Kaplan-Meier curves.

Results: 346 available cases from 11 studies were merged through a meta-analysis approach and 324 gene-sets have been investigated. An unsupervised subtype analysis provided evidence that this dataset can be split in four main clusters (Table 1). The clinical relevance of this classification was tested for its association to overall survival. Kaplan-Meier analysis demonstrated that Cluster 3 has the worst behavior, while Cluster 1 has the better one. The four HPV clusters show remarkable different molecular profiles: the most relevant involved pathways include proliferation and the activation of several immune pathways.

Conclusions: Our analysis demonstrated the existence of a molecular heterogeneity within the HPV-related OPC that correlates with patients outcome. Further analyses to validate our gene expression data are already planned.

Table: L1

<table>
<thead>
<tr>
<th>Cluster</th>
<th>Relevant dysregulated pathway</th>
<th>5-yr OS</th>
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</thead>
<tbody>
<tr>
<td>Cluster 1</td>
<td>EMT</td>
<td>89%</td>
</tr>
<tr>
<td>Cluster 2</td>
<td>Inflammatory Response</td>
<td>54%</td>
</tr>
<tr>
<td>Cluster 3</td>
<td>Hyponxia</td>
<td>28.5%</td>
</tr>
<tr>
<td>Cluster 4</td>
<td>Proliferation</td>
<td>62.2%</td>
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</tbody>
</table>

L2 Gene-expression profiles of primary and metastatic lesions in head and neck squamous cell carcinoma
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Background: Mechanisms of tumour spread and the deregulation level existing in distant metastatic lesions, in comparison with primary disease, are not fully understood in head and neck squamous cell carcinoma (HNSCC). We would test at molecular level the hypothesis that the development of the metastatic disease is linked to the biologic characteristics of the primary tumour more than to the degree of regional nodes involvement.

Materials and methods: We identified 27 HNSCC patients with available tissues of either primary tumor and distant metastasis (DM). As control, a series of 26 cases with out DM was matched according to subsite, HPV status and TN stage. Whole-transcriptome profiling was performed by microarray analysis using the DASL assay and BeadArray Chips (Illumina). To identify expression pattern related to patients with or without DM, we applied sparse Partial Least Square – Discriminant Analysis (sPLS-DA). We analysed the potential biological pathways differentiating primary tumors and metastases through Gene Set Enrichment Analysis (GSEA) and interrogating the Hallmark Gene Set Collection database.

Results: sPLS-DA disclosed gene-expression patterns between patients who developed or not DM. sPLS-DA defined a set of genes discriminant for patient’s DM status. Starting from those genes, we developed a signature following the Bayesian Compound Covariate Predictive (BCCP) algorithm. A core including 10 genes entered in our model and was able to predict patients who develop DM reaching AUC=0.85. To investigate the biological patterns associated to primary tumours of patients who developed or not DM, functional analysis was performed and the gene expression matrix was deconvoluted in 18x18 metagenes. We identified two networks involving a number of gene-ontology terms enriched in patients without DM, related to inflammation and keratinocyte differentiation. We investigated the genes differentially expressed between the primary tumors and the corresponding metastatic lesions and a total of 239 genes were identified. Functional pathway analysis was performed by GSEA and hallmark database was investigated resulting in 14 gene-sets enriched in metastasis imposing FDR<0.1.

Conclusions: Our analysis of matched HNSCC primary tumours having or not developed DM highlighted a 10-gene signature able to stratify patients whose relevance deserves further validation.

L3 Can the salivary microRNA expression profile help to identify novel biomarkers for oral squamous cell carcinoma detection?
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Background: Oral squamous cell carcinoma (OSCC) is the most frequent malignant tumor of the oral cavity with low survival rate, accounting for more than 95% of all head and neck cancers. Generally, fewer than 50% of patients survives more than 5 years, because this tumor is often detected at a late stage. Since saliva has been shown to be a non-invasive, accessible, and highly efficient diagnostic medium, the analysis of salivary biomarkers may provide an efficient tool for oral cancer early detection. The main aim of our study was to analyze the salivary microRNA expression profile in OSCC patients, in order to investigate the molecular mechanisms and signaling pathways responsible for the development and progression of this tumor.

Materials and methods: Total RNA and miRNAs were isolated using the miRNeasy Mini Kit, and their quality and quantity were assessed using the 2100 Bioanalyzer and spectrophotometer NanoDrop ND-1000. Using a TaqMan Low Density Array Human microRNA microarray assay, the expression profile of 377 miRNAs was analyzed in saliva of ten OSCC patients and ten healthy individuals. In addition, the expression of specific salivary miRNAs was analyzed in other independent samples from fifteen OSCC patients at different stages of disease, using real-time PCR analyses.

Results: Microarray analysis showed that a subset of twelve miRNAs, such as let-7g, miR-27a, miR-31b, miR-133a, miR-135b, miR-148b, miR-183, miR-199a-3p, miR-328, miR-361-5p, miR-486-5p, involved in several cancer-related pathways, including TGF-b, PI3K/Akt, Wnt, MAPK signaling, was differentially expressed in saliva of OSCC patients. Among these deregulated salivary miRNAs, eight were found to be up-regulated in their expression and four down-regulated. Finally, expression analysis of hypothetical miRNA gene targets involved in the same cancer-related pathways confirmed the coherence of our results.

Conclusions: Recent findings reported in literature regarding variations in expression of some miRNAs involved in proliferation, metastasis development, and therapy response in OSCC have confirmed the coherence of our results.

L4 Plasticity of PD-L1 expression between nodal metastases and primary tumors in p16 negative squamous cell carcinoma of the oral cavity

Background: the recent achievements of immunotherapy in many different areas (melanoma, kidney, lung and bladder carcinoma) stimulate the investigation about the action of checkpoint inhibitors in tumors, particularly in cases of tumors with an high mutational load, that are potentially responsive to immunotherapy approaches, like p16 negative oral squamous cell carcinoma. Phase III studies are ongoing, and there are also preliminary data about the PD-L1 tissue expression, in correlation with tumor grade and stage. However, investigations concerning the possible up/down regulation of this ligand in primary vs nodal metastasis are still largely inadequate.

Materials and methods: 16 oral squamous cell carcinoma T2-T4, node positive (N1), p16 negative, moderately differentiated (G2), underwent immunostaining with anti PD-L1 rabbit MoAb SP 142, using a VENTANA BenchMark Ultra platform with
**abstracts**

OptiView detection kit. Both primary tumors and nodal metastases were immunostained. Results were evaluated according to Roche PD-L1 (SP142) scoring system. In particular, neoplastic cell immunoreactivity (TC) and immune cells (lymphocytes, macrophages, dendritic cells and granulocytes) intratumoral and peritumoral immunoreactivity (IC) were evaluated. CD3 immunostaining of both primary tumors and nodal metastases were also performed, in order to facilitate the interpretation of the results.

**Results:** The entire group of 16 cases showed PD-L1 expression in perineoplastic IC, ranging from 1% to 50%, according to the scoring. No significant variations of expression between primary and secondary nodal sites were observed in all cases but one. Conversely, 10 out of 16 showed no expression of PD-L1 on TC (0%) both in primary tumor and nodal metastasis. The other six cases showed: case 4: T 0%, N 50%; case 5: T 80%, N 5%; case 6: T 70%, N 5%; case 11: T 50%, N 0%; case 13: T 30%, N 0%; case 16: T 40%, N 1%.

**Conclusions:** In the light of the relevance of PD-L1 expression in terms of immunotherapy efficacy in other areas (lung and bladder carcinoma), this documented plasticity (37.5% of cases) might be an interesting information for future trials.

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**L5**

**A single institution twenty-year experience of recurrent or metastatic epithelial non-glandular sinonasal cancer**

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**Background:** Sinonasal cancers (SC) are rare and heterogeneous tumors, whose natural history depends on histology and stage. Clinical trials (ClinicalTrials.gov: NCT02099175, NCT02099188. AJOI. 2013-000075-33) are ongoing to evaluate the role of multimodal therapies (MMT, consisting in induction chemotherapy -iCT- followed by locoregional therapy) as upfront treatment. Few data about the outcome of patients with SC progressing after MMT to gather data about treatment outcomes. Results were evaluated according to the WHO 2005 histotypes and according to the criteria of Adverse Events (CTCAE) v 4.0.

**Methods:** Among 106 pts with SC treated at our Center from 1997 to 2016 (median follow-up: 26 months -, range 5-192), 50 (48%) patients relapsed after MMT. Median age was 55 years (range 16-73). WHO 2005 histotypes were: 36% undifferentiated carcinoma (SNUC), 34% squamous cell carcinoma (SCC) and 30% neuroendocrine cancer (SNEC). Among them, 41 pts (82%) with stage IV, only 39% (16/41) had a potentially resectable disease at diagnosis. However surgery was part of the initial curative treatment in 32% of pts. Results were evaluated according to the WHO 2005 histotypes and according to the criteria of Adverse Events (CTCAE) v 4.0.

**Results:** Among 106 pts with SC treated at our Center from 1997 to 2016 (median follow-up: 26 months -, range 5-192), 50 (48%) patients relapsed after MMT. Median age was 55 years (range 16-73). WHO 2005 histotypes were: 36% undifferentiated carcinoma (SNUC), 34% squamous cell carcinoma (SCC) and 30% neuroendocrine cancer (SNEC). Among them, 41 pts (82%) with stage IV, only 39% (16/41) had a potentially resectable disease at diagnosis. However surgery was part of the initial curative treatment in 32% of pts. Median time from to first relapse after MMT was 15.5 mm. Median OS was 13 mm: 19 mm in SCC, 16 mm in SNUC and 6 mm in SNEC (p < 0.001). Relapse occurred as distant metastasis in 40%, as nodal recurrence in 6% and at primary site in 54% of cases. First line salvage treatment was surgery in 38%, CT in 30%, RT in 8%, best supportive care in the remaining pts. Median OS was 13 mm in surgically treated pts and 4.8 mm in those receiving CT (p < 0.001). Median OS was longer in pts with disease control after iCT than in pts with PD (15.4 ± 1.5 mm, p = 0.07). Median OS was 29.6 mm in pts with CR after definite treatment, 7.1 mm in those with PR and 3.4 mm in those with PD (p = 0.002). Pts with an objective response to palliative CT had a longer median OS than those with PD (20 vs 4.5 mm, p = 0.002).

**Conclusions:** About 50% of locally advanced SC actually experiences a recurrence, within a relatively brief time from treatment start. Factors associated with better outcomes are feasibility of salvage surgery, objective response to prior definitive treatment and response to palliative CT. OS after recurrence is poor, so understating the need of new treatment approaches in this setting.

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**L6**

**Subsite-dependent prognostic impact of age in patients with nasopharyngeal and oropharyngeal cancer**

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**Background:** Outcome results in elderly head and neck cancer (HNC) patients (pts) treated with concurrent chemoradiation are controversial. Comparative effectiveness analyses showed a lack of benefit in multimodal treatment; however, retrospective highly selected series reported older patients to have similar outcome compared to younger ones albeit with high burden of toxicities.

**Material and methods:** Locally advanced oropharyngeal (OPC) and nasopharyngeal cancer (NPC) pts treated at our institution with concurrent platinum based chemoradi- therapy (CHT) and intensity modulated radiation therapy (IMRT) techniques from 2004 to 2015 were retrospectively evaluated. Overall survival (OS) and Relapse Free Survival (RFS) Kaplan-Meier curves were estimated and compared with the log-rank test; acute toxicity rate >G3 according to Common Toxicity Criteria Adverse Event v4.0 was also analyzed, distinguishing between patients >65 years old (elderly) and ≤65 old. HPV status was recorded in all OPC patients.

**Results:** 375 pts received IMRT-CHT, 215 in OPC and 160 in NPC cohort. Elderly pts represented 26% and 11% of OPC and NPC pts, respectively. OPC HPV positive cases were similarly represented in older (73% of the cases) and younger pts (66%); HPV positivity maintained a significant prognostic role independently of age and also across different age group. On the contrary, age did not significantly impact on survival in OPC. Five years RFS was 68% in older versus 76% in younger patients (p = 0.59); the corresponding figures for OS were 93% versus 87% (p = 0.54). There was no significant difference in cumulative acute toxicity rate = G3 (39% in elderly vs 36% in younger p = 0.78). When analyzed separately, no difference was shown for what concerns dysphagia and mucositis. NPC pts showed a different outcome according to age both in terms of RFS (5-years probabilities 41% in elderly vs 80% in younger pts, p < 0.001) and OS (48% vs 90%, p = 0.001), which turned out to be a negative prognostic factor in this disease. Also for NPC pts, the two age subgroups did not significantly differ in acute toxicity rate = G3 (56% vs 61%, p = 0.88). No different platinum total dose was adopted in OPC and NPC elderly pts.

**Conclusion:** We observed a subsite-specific impact of age on treatment outcome: older NPC pts showed markedly worse survival than the younger counterparts, while in OPC pts such an effect was inconsistent. HPV status was confirmed to be a positive prognostic factor independently of age.

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**L7**

**Skin rash and response to cetuximab treatment: a retrospective single-center analysis**

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**Background:** The standard of care for patients with recurrent/metastatic head and neck squamous cell cancer (R/M HNSCC) not susceptible for surgery or reirradiation is chemotherapy with 5-FU and cisplatin plus cetuximab. Skin rash (SR) is a common adverse event of cetuximab. In patients treated with cetuximab for colorectal cancer there is strong evidence of a better outcome in those who undergo moderate or high grade of SR, and some retrospective data seem to confirm this finding in HNSCC. We report our experience.

**Materials and methods:** We retrospectively reviewed 107 patients treated with cetuximab for R/M HNSCC from January 2014 to December 2016. Patients were divided in two groups by the grade of SR (G0-1 and G2-4), conforming to Common Terminology Criteria for Adverse Events (CTCAE) v 4.0. Progression-free survival (PFS) was computed as time of progression or death since the date of assessment of recurrent/metastatic disease. Overall response rate (ORR) was computed as the sum of partial and complete responses and evaluated according to RECIST 1.1. PFS and ORR were correlated to the grade of rash.

**Results:** 67 patients were evaluable for PFS; among them PFS was significantly longer (p = 0.0014) in those who underwent a G2-4 rash (9.3 months) vs G0-1 (4.9 months).

**Conclusion:** Our results support data of literature on improved outcome according to the development of skin rash in HNSCC. SR might be considered a predictive marker of response in these patients; nonetheless further ad hoc studies would be interesting.
M - BRAIN TUMOURS

**Gender and MGMT methylation in glioblastoma patients: interactions in the PERNO prospective study**


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**Background:** Glioblastoma (GBM) remains an incurable disease. Radiotherapy and chemotherapy have a limited role in GBM treatment. The role of gender and MGMT methylation status on overall survival (OS) has been recently highlighted.

**Methods:** Ninety-three consecutive GBM with IDH mutation and codel were included. The median follow up (FU) was 96.1 months. Mean age was 40 yrs (range: 25-66); 8 pts (8.6%) underwent biopsy, 61 pts (65.6%) partial resection, 24 pts (25.8%) complete resection. 84 pts (90.3%) were considered high risk using RTOG criteria (40 years and/or incomplete resection). Fifteen pts (17.3%) received only surgery, 17 pts (18.3%) received chemotherapy (CT), 18 pts (19.4%) received radiotherapy (RT), 9 pts (9.6%) received RT + CT. Median OS (mOS) was 59.6 months (95%CI: 41.8-77.4) and was significantly longer in pts who received post-surgical treatments than those who received postsurgical therapy (79.5 months, 95%CI: 66.4-92.7) than pts who received FU (46.3 months, 95%CI: 36.0-56.5; P = 0.001). mOS was 50.8 months (95%CI: 17.4-84.3), 103.6 months (95%CI: 11.7-195.6) and 120.2 months (95%CI: 40.5-199.8) in pts treated with CT alone, RT alone and RT + CT, respectively.

**Results:** Gender and MGMT methylation status showed a median OS (mOS) of 120.2 months. mOS was 50.8 months (95%CI: 17.4-84.3), 103.6 months (95%CI: 11.7-195.6) and 120.2 months (95%CI: 40.5-199.8) in pts treated with CT alone, RT alone and RT + CT, respectively.

**Conclusions:** We report a prospective study on gender and MGMT methylation status in GBM treated with temozolomide concurrent with and adjuvant to radiotherapy. COX regression analysis showed that receiving a post-surgical treatment (P < 0.001) had a significant impact on OS. Multivariate analysis showed that receiving a post-surgical treatment (P = 0.043) was significantly correlated with PFS.

**Table M1**

<table>
<thead>
<tr>
<th>Gender</th>
<th>n</th>
<th>median OS (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>methylated male</td>
<td>31</td>
<td>16.3 (9.2-23.4)</td>
</tr>
<tr>
<td>unmethylated male</td>
<td>41</td>
<td>15.6 (11.8-19.5)</td>
</tr>
<tr>
<td>methylated female</td>
<td>26</td>
<td>17.0 (11.8-22.2)</td>
</tr>
<tr>
<td>unmethylated female</td>
<td>21</td>
<td>17.0 (11.8-22.2)</td>
</tr>
<tr>
<td>total</td>
<td>119</td>
<td>17.0 (15.2-18.9)</td>
</tr>
</tbody>
</table>

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We evaluated adult LGG patients (pts) which occurred from 1991 to 2015, at our oncological center, Veneto Institute of Oncology, between January 1988 and December 2015, we prospectively enrolled 111 consecutive pts; median age 60; 69 PTS were male and 36 PTS aged 40 years with complete resection, and 176 (82.6%) were subtotal resection, 64 pts (30%) gross-total resection. According to RTOG criteria 37 pts (17.4%) were low-risk (<40 years with complete resection), and 176 (82.6%) were high-risk. IDH1/2 mutation was found in 93% of pts. 1p/19q codeletion was found in 50.8% of pts. MGMT methylation in 65.3% of pts. Median progression free survival (PFS) was 47.8 months. Median survival was 211.0 months (95%CI: 185.7-236.3) and 164.0 months (95%CI: 123.0-203.0) in low risk and high risk patients respectively. Significant factors in univariate analysis are listed in the table. Multivariate analysis showed that PFS was influenced by extent of resection (P < 0.001), IDH mutation (P < 0.001) and treatment. IDH mutation (P < 0.001) and extent of resection (P = 0.029) were significantly correlated with overall survival in multivariate analysis.

Conclusions: The definition of LGG outcome is complex. Both clinical and molecular factors are needed to determine prognosis and treatment strategies.

<table>
<thead>
<tr>
<th>Table: M3</th>
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<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>IDH mutation</td>
</tr>
<tr>
<td>1p19q codelletion</td>
</tr>
<tr>
<td>MGMT methylation</td>
</tr>
<tr>
<td>Surgery (complete vs biopsy)</td>
</tr>
</tbody>
</table>

M4 Worsening of quality of life (QoL), cognitive functions (CF) and psychological status (PSY) can predict radiologic progressive disease (RPD) in glioblastoma (GBM) patients (PTS) treated with radiation therapy (RT) and temozolomide (TMZ): a mono-institutional prospective study

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Background: Almost all of GBM PTS treated with RT and TMZ relapse during and after treatment. We performed a prospective study to assess if deterioration of QoL, CF, and PSY is a predictor of RPD.

Methods: PTS with newly histologically diagnosed GBM treated with RT and TMZ as first-line therapy and KPS>60 were enrolled. PTS received TMZ for 12 cycles of until unacceptable toxicity or progressive disease. All questionnaires were given to PTS for self-assessment before performing MRI. Macdonald criteria were used for radiological evaluation. We assessed QoL, CF and PSY before starting treatment, at the end of RT and every 3 months until 9 months after the end of RT using EORTC-QLQ-C30-BR-20, MMSE and HADS questionnaires. Brain MRI were performed at the same times.

Results: At our oncological center, Veneto Institute of Oncology, between January 2013 and December 2015, we prospectively enrolled 111 consecutive PTS; median age was 59; 69 PTS were male and 36 PTS aged >65. PTS showing a RPD reported lower physical functioning (p = 0.018), minor role function (p = 0.0007) and a lower global health status (p = 0.01) than patients without RPD. In addition, they reported greater uncertainty in the future (p = 0.007), increased drowsiness (p = 0.013), increased itchy skin (p = 0.005) and greater weakness in the legs (p = 0.027) compared with PTS without RPD. PTS with RPD resulted more anxious (p = 0.001) than the other PTS. The two groups significantly differed in the CF (p = 0.0007) especially, after 1 and 6 months after RT reporting worse results in the MMSE for PTS with RPD.

Conclusions: Worsening of QoL, CF and PSY can predict RPD in GBM PTS treated with RT and TMZ

M5 The role of treatments in IDH mutant molecular astrocytomas

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Background: Low grade gloma (LGG) is a heterogeneous disease. Recently, the 2016 WHO classification of brain tumors has underlined the role of genetic and molecular features. Molecular astrocytomas have been defined as grade II tumors with IDH mutation and without 1p19q codelletion.

Methods: We evaluated 213 consecutive patients with LGG who received surgery or biopsy and had adequate tissue to assess molecular characterization. IDH mutations were assessed by immunohistochemistry (IHC) and next generation sequencing (NGS) in IHC negative cases, MGMT methylation status was assessed by polymerase chain reaction (PCR) and 1p19q deletion was assessed by fluorescence in situ hybridization (FISH).

Results: 198 patients (93.0%) showed IDH mutation. Ninety patients (49.2%) were 1p19q non codelleted (molecular astrocytomas). The median follow up was 98.3 months, 25 pts (11.7%) underwent biopsy, 124 pts (58.2%) were diagnosed at time of treatment, but only follow-up, 31 patients (34.4%) received post-surgical treatments: 20 pts (9.0%) received radiotherapy (RT) and 11 pts with a high grade (67% and 79%, respectively). Based on semiquantitative analysis of 18F-DOPA uptake in the lesion (identified by MRI) higher than controlateral striatum 75% patients had a positive PET/CT result, in particular 4 with a low grade glioma and 14 (70%) patients had a positive PET/CT result, in particular 4 with a low grade glioma and 14 (70%) patients had a positive PET/CT result, in particular 4 with a low grade glioma and 14 (70%) patients had a positive PET/CT result. Median progression-free survival (PFS) was 44.3 months. Significant differences in PFS were observed between treated and untreated patients (64.8 vs 35.7 months p = 0.004) and treated with RT versus follow-up (60.0 vs 35.7 months p = 0.004). Multivariate analysis confirmed the treatment after surgery as an independent prognostic factor (HR 0.456, p = 0.005). Median overall survival (OS) was 164.0 months. At time of analysis no significant differences in OS were available.

Conclusions: Post-surgical treatment after resection of IDH mutant molecular astrocytomas is an independent prognostic factor. A longer follow-up is needed for worthy results in terms of OS.

M6 Suspicious for recurrent low and high grade glioma and indeterminate MRI: the role of 18F-DOPA PET/CT

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Background: The aim of present study was to assess the role of 18F-DOPA PET/CT in patients who had a suspicious for recurrent low and high grade glioma but with an indeterminate MRI.

Materials and methods: From a monocentric database, we retrospectively analyzed 21 patients (median age: 60 yrs; 19-80) who underwent 18F- DOPA PET/CT for the restaging of low and high grade glioma. All PET/CT images were re-examined by two nuclear medicine physicians. Both visual and semiquantitative analysis was used for the interpretation of images. At visual analysis, PET/CT was defined as positive in case of a DOPA uptake in the lesion (identified by MRI) higher than controlateral striatum uptake. For the semiquantitative analysis, the ratios between SULmax of the lesion and SULmax of the striatum (T/S) or normal brain tissue (T/B) equal to 1 and 2 were used. Clinical reassessment consisted of standard evaluation including MRI and assessment of neurological symptoms. The agreement between visual and semiquantitative analysis was obtained by k statistical analysis. Diagnostic performance was calculated by standard methods.

Results: Six patients had a low grade glioma and 14 a high grade. At visual analysis, 15 (75%) patients had a positive PET/CT result, in particular 4 with a low grade glioma and 11 with a high grade (67% and 79%, respectively). For semiquantitative analysis, 14 (70%) and 14 (70%) patients had a positive PET/CT, respectively for T/S and T/B. The agreement between visual and semiquantitative analysis was 88% (p < 0.001). In accordance with clinical reassessment, 11 patients, 10 subjects had recurrence of disease. Sensitivity, specificity, positive and negative predictive value of PET/CT based on visual and semiquantitative analysis were 90%, 100%, 100% and 75% versus 80%, 100%, 100% and 60%, respectively.
Conclusions: In patients with suspicious for recurrent low and high grade glioma, DOPA PET/CT has a high sensitivity and specificity. Therefore, in case of indeterminate MRI, DOPA PET can anticipate the presence of recurrent disease useful for the treatment planning.

18F-sodium fluoride (18F-NaF) PET/CT scan for the assessment of brain metastases (BMs)
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Background: 18F-NaF does not distribute to normal brain but it can be uptaken by BMs. This data suggests that it can cross the blood-tumor barrier (BTB). However, whether the 18F-NaF uptake is reflective of BTB permeability, possibly indicating the entity of drugs penetration into BMs and therefore representing a predictive tool of response, is still unknown. We did the present study with the aim to investigate the potential predictive and/or prognostic role of the 18F-NaF uptake by BMs.

Patients and methods: From November 2014 to July 2016, 28 patients (pts) with MRI-documented BMs from different solid tumors (13 lung, 9 breast, 4 genitourinary, 2 other primaries) were enrolled in the study and underwent a 48-minute dynamic acquisition protocol. Area under the curve (AUC) of SUVmean was calculated for BMs (AUC BM) and for internal carotid artery (AUC ICA). We used the AUC BM/AUC ICA ratio (BM/ICA ratio) for estimating 18F-NaF penetration of BMs. The median value of BM/ICA ratio was established as the cut-off, with a value higher than the cut-off indicating high 18F-NaF penetration. Pts received investigator-choice treatment for BMs and response was assessed by brain MRI according to RECIST criteria.

Results: 18F-NaF PET/CT scan identified 75 out of the 130 BMs with a diameter ≥ 5 mm (i.e. PET spatial resolution) detected with MRI with a sensitivity of 0.58 and a positive predictive value of 1.0. A patient with only 1 BM less than 5 mm had a negative 18F-NaF PET/CT scan. Among 27 evaluable pts, 11 pts had 1 BM, 8 pts 2-3 BMs and 9 pts ≥ 3 BMs. The BM/ICA ratio cut-off was 0.53. As treatment for BMs, 4 pts received chemotherapy alone, 10 radiotherapy alone, 1 surgery alone and 12 had a multi-modal treatment. There was no significant difference in terms of RR, PFS or OS according to chemotherapy alone, 10 radiotherapy alone, 1 surgery alone and 12 had a multi-modal treatment. There was no significant difference in terms of RR, PFS or OS according to chemotherapy alone, 10 radiotherapy alone, 1 surgery alone and 12 had a multi-modal treatment.

Conclusions: To our knowledge, this is the first study of 18F-NaF PET/CT scan for the assessment of BMs. BM/ICA ratio indicating 18F-NaF penetration of BTB was not predictive nor prognostic in pts with BMs. However, pts enrolled in this study were widely heterogeneous in terms of primary tumor, number of BMs and treatment, and such heterogeneity could have affected the results.
Prognostic relevance of VEGF, VEGFR, IGF and IGFR immunohistochemical expression in gastroenteropancreatic neuroendocrine tumours


Clinica Oncologica - Ospedali Riuniti Ancona, Ancona; Anatomia Patologica - Ospedali Riuniti-Ancona, Ancona

Background: angiogenesis represents a peculiar trait of gastroenteropancreatic neuroendocrine tumors (GEP-NETs). We aimed to analyze the immunohistochemical expression of angiogenic markers on tumor tissue and their potential prognostic role in GEP-NETs.

Methods: we selected 28 patients with available material (excluding biopsies and small samples). The immunohistochemical evaluation involved the use of 6 monoclonal antibodies: anti-VEGF, Flt-1, Flk-1, Flt-4, IGF-1 and IGF-1R.

Results: Median age was 60 (range 29-79), 24 cases (85%) were pancreatic NETs and 17 neuroendocrine carcinomas (NEC) of the lung are usually associated with a dismal prognosis. Few studies evaluated the impact of platinum/etoposide combination in NEC, including those of lung origin. However, little advances have been made in the last few decades and it is still unclear whether the outcome of such patients (pts) has been improved. The aim of our study was to evaluate the outcome of pts with advanced NEC of the lung treated at two Italian institutions with a platinum/etoposide combination.

Patients and methods: We retrospectively evaluated 68 consecutive pts with histologically-confirmed advanced/metastatic neuroendocrine carcinomas of the lung treated with platinum/etoposide chemotherapy between September 2006 and December 2016. We collected clinic-pathologic characteristics, treatments, and outcome of all pts.

Results: We included in the present study 68 pts with pulmonary NEC (82% SCLC; 18% LCNEC). Median age was 67 years (range 45-80 years), 81% were male and 19% were female, ECOG PS was 0-2 in 97% of pts and 3 in 3%. Stage distribution at diagnosis: stage IV 91%, stage III 9%. Symptoms at diagnosis were present in 63/68 pts, including cough (25%), tumor pain (35%), dyspnea (36.5%). Cisplatin/etoposide was used in 50% of pts, and carboplatin/etoposide was used in 50% of pts. Median number of chemotherapy cycles was 4 (range 1-8). 18% of pts required a dose reduction. Major toxicities in evaluable pts were as follows: hematological 70.5%, gastrointestinal 26.5%, and fatigue 18%. ORR was 39% (5% CR), DCR was 73%. Pts receiving a second line therapy after progression were 44%. Fifteen percent of pts were still alive at the time of the present analysis. Median PFS with platinum/etoposide was 5.0 months (mos) (range 1-70). Median OS was 9.0 mos (range 1-70). Median PFS and OS did not differ between cisplatin and carboplatin groups (p = 0.192 and p = 0.191, respectively).

Conclusions: Data presented here confirm the poor outcome of pts with lung NEC in a large retrospective cohort confirming the results of previous reports in a similar population. Moreover, our data did not evidence any significant difference in terms of efficacy. These data suggest that cisplatin- and carboplatin-based chemotherapy at the moment remain the standard of therapy for advanced lung NEC, but novel therapeutic strategies should be pursued.
Breast cancer (BC) is commonly diagnosed at early stage and more than 80% of patients (pts) are long-term survivors. Most cancer society guidelines recommend a non-intensive follow-up, that, after 5 years from diagnosis, consists of annual medical history, physical examination and surveillance mammography. The role of family physician in the management of BC follow-up is still under discussion.

Material and methods: Since 2013, we have launched a shared BC survivor follow-up program involving family physicians working in the Province of Lecce. Pts with diagnosis of early BC have been referred to their family physician to continue surveillance with annual physical examination and mammography at the completion of adjuvant treatment and after at least 5 years of follow-up, if no clinical evidence of disease recurrence was present. In case of suspicious disease recurrence, a direct access to our oncology unit has been offered.

Results: From May 2013 to March 2017, 643 women have been enrolled in our program. All pts were disease-free (as per clinical assessment), had completed adjuvant treatment and at least 5 years of follow-up at the time of enrollment. 11% of pts had ductal carcinoma in situ, 66% invasive ductal carcinoma, 7% invasive lobular carcinoma and 16% other histologic subtypes. 11% was hormonal receptor negative and 7% was HER2 positive. 44% was G2 and 34% G3. 23% received chemotherapy followed by hormonal treatment. 9% received adjuvant chemotherapy alone and 61% received hormonal treatment alone. Median follow up time was 8 years (range 5-23 years). 10/643 (1.6%) pts experienced recurrent BC: 3 had distant metastases, 4 unmetastatic breast recurrent and 3 contraterral. Those with local recurrence underwent breast surgery followed by adjuvant chemotherapy in 1 case, chemotherapy and hormonal treatment in 1 and hormonal treatment alone in 5. Pts with distant metastases are still alive and currently on treatment (1 with chemotherapy, 2 with hormone therapy).

Conclusion: This preliminary analysis has shown the feasibility of our program with a significant number of pts referred to their family physicians, reducing the need for specialist follow-up. Only a small proportion of pts experienced subsequent relapse requiring reassessment by the treating oncologist. Further analysis is planned to define the adherence to the shared follow-up.

Post-survey data about “I do not smoke it”, smoking prevention campaign addressed to schools

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Introduction: According to Il fumo in Italia (DOXA-Italian Institute of Health survey, 2016), most smokers try their first cigarette in the range from age 15 to age 17 (56.8%). The main reason why people start smoking is emulation (60.7%). There is the need to strengthen the work of the healthcare professionals in preventive care about cigarette smoking. Considering these, WALCE (Women Against Lung Cancer in Europe), since 2011, promotes “I do not smoke it” – We shall try to see things clearly in the smoky speeches”, an information campaign on damages of smoking, aimed at 9-11 year-old pupils in Primary schools.

Materials and methods: After the administration of a questionnaire and the use of the educational kit we asked to some teachers to administer a post-survey to pupils, in the 2015-2016 school year. We analyzed 253 surveys: 76 questionnaires from 9 years-old Primary school pupils; 137 from 10 years-old Primary school pupils; 40 from 11 years-old Lower Secondary school pupils. Surveys were filled in by 130 male (51.38%) and 123 female pupils (48.62%), in schools of 3 different Italian regions (Piemonte, Veneto and Emilia). Results: 81% of pupils believes that this type of intervention is useful as prevention action. 8.7% thinks that cigarette smoke only harms those who smoke, 1.6% thinks that smoking improves performance in sports and 9.5% thinks it can help to lose weight. Answers to the question “I do not smoke it”, are encouraging: 77% responded “Yes”, 21% “No”. Analyzing in the different classes the reasons why people start smoking: “to be cool”, with percentages of 60.5%, 76.6% and 82.5%, in the fourth, fifth grade of Primary school and in the first grade of Lower Secondary school, respectively. Other reasons reported in high percentages were: “to imitate adults” and “to feel accepted”. When asked, “What do you think is more dangerous for you?”, “smoking a cigarette” was the most answered response.

Conclusion: Several health education studies have shown that prevention programs addressed to school are more effective if conducted by the teachers. It is known that young people, especially during the adolescence, try to put in practice behaviors that allow them to affirm their identity and build a network of social and affective relationships. For this reason, health promotion and behavioral prevention activities, implemented in schools and at home by families are crucial to avoid to endanger the well-being of tomorrow’s adults.

Genetic counseling for BRCA1/BRCA2 testing

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Background: Increasing evidence supports the benefit of identifying BRCA1/2 mutations in Hereditary Breast and Ovarian Cancer (HBOC) either for implementing prevention strategies and for the recent availability of target therapies.

Material and methods: From May 2013, a Multi-disciplinary Counseling (medical oncologist, geneticist, psychologist) has been offered. Screening for select individuals to be tested is carried out through a multistep process by collecting a detailed personal and family history, drawing the family tree and determining the genetic risk. The BRCA1/2 genes were analyzed by DNA-sequencing and by Multiplex Ligation-dependent probe amplification. From May 2013 to April 2017 a total of 251 patients (pts) and 99 healthy individuals have been seen. The 251 cancer pts were: 187 Breast (BC): 178 women < 56, 36 Ovarian (OC), 16 Colon (CC), 6 Thyroid (TC), 3 Uterine (UC), 1 Gastric (GC), 1 Pancreatic, 1 Lung (LC). Eighty of the 187 pts with BC had another tumor: 6 OC, 6 TC, 2 UC, 1 NHL, 1 HL, 1 LC, 1 RCC. One of the 16 pts with CC had a Prostate cancer (PC) too. One triple tumor was studied: PC + OC + TC.

Results: BRCA1 pathogenic variants (BRCA1+) were detected in 10.3% (26/251) of pts: 14 women BC, 8 OC, 1 TC, 1 LC. Two more pts had a double tumor (BC+OC). BRCA2 pathogenic variants (BRCA2+) were detected in 17.1% (18/251) of pts: 12 women BC, 1 male BC, 3 OC. Two more women had a double tumor: BC + LC, BC + TC. A total of 19 BRCA1+ and BRCA2+ families were studied: BRCA1+ and BRCA2+ were seen in 10 and 11 healthy individuals, respectively. Prophylactic bilateral mastectomy (PM) + bilateral salpingo-oophorectomy (SO) were performed in a healthy woman BRCA1+ during a single operative session. PM was performed in a OC BRCA1+ and in a OC BRCA2+. The SO was performed in 2 BC: 1 BRCA1+ and 1 BRCA2+.

Conclusions: Clinical testing for mutations in BRCA1/2 remains the most prominent example of the use of human genetic variation to prevent cancer and reduce disease risk. The goal of pre-test genetic counseling is to ensure the patients having sufficient information to make a decision about being tested. On the other hand, at results disclosure, during post-test genetic counseling, individuals can learn from our Department, along with information about cancer risks and surgical and medical management options. In our opinion, the clinical BRCA1/2 testing programs should include pre- and post-test genetic counseling.

Hypercoagulable state as marker of occult cancer in healthy blood donors: data from HYPERCAN Prospective Study

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Background: HYPERCAN is an ongoing prospective Italian, multicenter, observational study structured in two sub-projects that involve non-cancer and cancer subjects. Aim of this part is to establish whether the persistence of a hypercoagulable state in healthy subjects as detected by laboratory thrombosis markers, may predict for an increased risk to develop cancer.

Material and methods: Healthy Italian blood donors from Bergamo and Milan areas are enrolled. In your opinion, is it possible to quit smoking?” are encouraging: 77% responded “Yes”, 21% “No”. Analyzing in the different classes the reasons why people start smoking: “to be cool”, with percentages of 60.5%, 76.6% and 82.5%, in the fourth, fifth grade of Primary school and in the first grade of Lower Secondary school, respectively. Other reasons reported in high percentages were: “to imitate adults” and “to feel accepted”. When asked, “What do you think is more dangerous for you?”, “smoking a cigarette” was the most answered response.

Conclusions: Several health education studies have shown that prevention programs addressed to school are more effective if conducted by the teachers. It is known that young people, especially during the adolescence, try to put in practice behaviors that allow them to affirm their identity and build a network of social and affective relationships. For this reason, health promotion and behavioral prevention activities, implemented in schools and at home by families are crucial to avoid to endanger the well-being of tomorrow’s adults.
collected. In addition, subjects are asked to fill in a questionnaire about their lifestyle. Identification of all malignant tumors is carried out every 6 months.

Results: Between April 2012 and April 2017, 7,328 blood donors (71% males; median age 48 yrs) have been recruited. Most of the donors had biochemical and hematological parameters within the normal range. The analysis reveals that 59% of the donors were not smokers, 15% regular smokers, 28% ex-smokers; 49% of them were moderate alcohol consumers (≥2 drinks/day; now, after a median follow-up of 2.8 years, we recorded a total of 56 cancer cases (35M/13F). The most frequent tumor type in male donors is prostate (27.0%), followed by colorectal (16.2%) and thyroid (10.8%) cancers, while in females, the most frequent is breast cancer (41.6%). Both in males and females the most frequent tumor is the same compared to the general population in Bergamo and Milan area. Interestingly, we observed that the occurrence of tumor correlate with educational status (p = 0.05). According to hematological parameters, tumor cases had significantly lower red blood cell counts and higher values of glycemia and cholesterol compared to healthy population (p < 0.05).

Conclusions: The enrollment of healthy donors and follow-up is ongoing, as well as the investigation on tumor incidence.

P5 Occurrence of ultrasound-detected symptomatic and asymptomatic central vein catheter-related thrombosis in pediatric oncology patients

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Background: Pediatric oncology patients are more likely to develop venous thromboembolic events CVC-related, but the incidence of CVC-related thrombosis (CRT) is still under debate. For this reason, we performed a retrospective study of single-center to investigate the incidence of symptomatic and asymptomatic CRT using Doppler Ultrasound and evaluate the possible risk factors linked to this pathology.

Methods: This study was performed on all pediatric patients with cancer, aged <18, requiring CVC implantation for chemotherapy infusion, from October 2015 to December 2016 in Istituto Nazionale Tumori di Milano. All patients underwent US examination at 15, 30, and 90 days after implantation.

Results: A total of 114 medium-long term CVC were inserted into 104 patients (median age: 9.5; 0-14.7 years). Patients have been followed up for an average of 269 (range: 11-503) days. Incidence of asymptomatic CRT was 0.11 (0.03-0.33) events for 1000 catheter-days. Only three cases of thrombosis were identified with Doppler Ultrasound screening. In no patient symptomatic DVT occurred. The only common risk factor in these cases was the presence of a previous catheter-related infection (p-value = 0.00018).

Conclusion: Despite the high risk of CRT associated with the considered sample, the incidence of symptomatic and asymptomatic thrombosis in our patients is very low, especially when compared to other studies. Following these results, the role of US surveillance for the prevention of CRT could be evaluated, perhaps limiting it to patients with previous CVC-related complications. Possible limitations of this study are the limited number of patients and the limited follow up.

P6 Observational case-control study about the adherence to the Mediterranean diet in elderly oncological patients in Salento

Silvani L, Leone S, Chiara L, Anna Maria G, Accettura C, Saracino V.

Ospedale Vito Fazzi, Leccese, “La Chiesa d’Argentina Onlus, Leccese, University of Salento, Leccese

Background: Mediterranean Diet (MD) is the only alimentary model that could prevent degenerative chronic disease and cancer. We analyzed the alimentary habits of elderly oncological patients (pts), compared to healthy elderly pts, to evaluate the correlation between the adherence to MD and cancer development, due to the high incidence of tumors in Salento.

Material(s) and methods: 293 (155 males, 138 females) oncological pts (≥70 years) were enrolled in the Oncology Unit of Vito Fazzi Hospital in Lecce and 135 elderly pts (≥70 years) without cancer diagnosis. Predimed test was used to evaluate the alimentary habits and to define the adherence to MD, using 14 questions (score 0-14). A value ≥7 was estimated as low adherence, 8-9 as median adherence, ≥10 as high adherence. Oncological pts showed the subsequent diagnosis: lung, prostate, breast, urinary tract, gastric, colorectal cancer.

Results: The main source of diet in extra virgin olive oil (98% of pts). 37% of pts eat almost 2 times/die vegetables and 50% almost 3 times/die fruit. 71% of pts eat less than 1 time/die red meat, hamburger and sausages and 86% eat less than 1 time/die butter, margarine or cooking cream. During a week, 43% of pts drink ≥7 glasses of red wine, ≥2 glasses of white wine/day. 13% of pts eat fish more than 4 times/week; 34% eat 25% red meat and 90% eat 2 times/week vegetables, pasta or rice. Low adherence to MD is showed for oncological pts and healthy pts in 46% and 15% respectively, median adherence 25% and 48%, high adherence 28% and 46%.

Conclusion: In healthy pts a higher adherence to MD was observed and they eat more vegetables, fruit and red wine, compared to oncological pts. Both pts groups eat low quantity of fish and legumes. Pts with urinary tract cancer shows a diet rich of vegetables (more 2 times every day): this could be related to the ingestion of pesticides used in farming. Gastric cancer pts showed a low use of onion and garlic, so an protective role in development of this disease is confirmed (as previously demonstrated in literature). Healthy women drink more red wine than breast cancer pts: red wine polyphenols could prevent the breast cancer disease. The results of this study suggests that could be a relationship between the adherence to MD and the incidence of tumor, but further studies, in a several number of pts, are necessary to confirm this hypothesis.

P7 The follow-up and lifestyle (FUCSAM project), Oncology Network of Piemonte and Valle d’Aosta: update 2017


1Dipartimento Rete Oncologica Piemonte e Valle d’Aosta - AOU Città della Salute e della Scienza, Torino

Background: Lifestyle factors can benefit not only the quality of life of cancer survivors, but also overall survival, and decrease the risk of recurrence from cancer. Integrating life-style support into standardised models of aftercare for cancer survivors is a challenging purpose.

The FUCSAM project (observational study) aims to assess the impact of an intervention designed to change the lifestyle of patients in follow-up after treatment of colorectal and breast cancer followed by different Interdisciplinary Groups and Care.

Material and methods: Eligible patients: diagnosis of breast or colorectal cancer (histologically confirmed), at first follow-up after surgery and adjuvant medical therapy (if indicated), free of disease, able to walk and with informed consent. Data detected: personal, therapies, comorbidity, stage at diagnosis, anthropometric, clinical and biometric parameters, adherence to programs on lifestyle, changes carried out by local Patients Associations. All patients were handed information brochures and recommended adherence to specific programs, if any. The collection of information has been replicated at subsequent follow-up visit.

Results: Until now 19 local hospitals have joined the FUCSAM project after the ethics committee approval. Patients enrolled are 1615 (504 colorectal cancer, 1313 breast cancer) and 78% are <70 years old. Among 1265 women in the mammography screening age group (50-69 years) 352 (28%) had the diagnosis through the local screening program, while among 289 subjects in the colorectal cancer screening age group (36-70 years) 42 (15%) subjects were diagnosed through the organized program.

Information brochures were delivered to 95% of the patients in the study.

Conclusions: Although at the beginning, the first study results show that the introduction of lifestyle recommendations within the follow-up protocols is feasible. After diagnosis of cancer, people are more inclined to consider the relationship between their behavior and the effects on health. To encourage the adoption and maintenance over time of new habits, the Oncology Network of Piemonte and Valle d’Aosta will plan to provide practical guidance for the realization of the desired changes.

P8 Breast cancer secondary prevention: get it to feel healthy


Clinica di Oncologia Medica e Centro Regionale di Genetica Oncologica, Università Politecnica delle Marche, Ancona, AOU Ospedali Riuniti-Ancona, ITALY, ANCONA, Dipartimento di Scienze Biomolecolari, Università degli Studi di Urbino Carlo Bo, ITALY, URBINO, Clinica di Neuroradiologia, Università Politecnica delle Marche, Ancona, AOU Ospedali Riuniti-Ancona, ITALY, ANCONA, Medicina Riabilitativa, AOU Ospedali Riuniti-Ancona, ITALY, ANCONA, Dietetica e Nutrizione Clinica, AOU Ospedali Riuniti-Ancona, ITALY, ANCONA

Background: Healthy lifestyle, including caloric restriction, balanced diet and physical activity, is important in primary and secondary prevention of breast cancer (BC). It is known that Mediterranean diet reduces metabolic syndrome and insulin resistance that are associated with increased risk of BC onset and recurrence. Physical activity decreases BMI, blood concentrations of testosterone, estrogens, insulin, its resistance and strengthens anti-inflammatory pathways against tumor cells.

The aim of our study was to evaluate the clinical impact of healthy lifestyle promoted by a project named “Lifestyle Programme” created in our Centre.

Patients and methods: 67 women with BC who underwent primary surgery in our Centre were enrolled between January 2014 and July 2016. We included the ones who had high risk of recurrence due to BMI ≥25, increased levels of testosterone and/or insulin and metabolic syndrome and we evaluated them every six months after first diagnosis. The project involved oncologist (performing oncologic anamnesis, laboratory and HADS score for anxiety and depression), dietitian (performing...
nutritional anamnesis and providing an hypocaloric diet) and physiatrist (questioning about ordinary physical activity, applying 6 minutes walking test, brief fatigue inventory test and Borg respiratory and muscular score and providing a personalized physical activity program). All collected data were analyzed by Chi-square test assuming statistical significance at $p < 0.05$.

**Results:** Most of BC had positive hormonal receptors (Luminal phenotype 85.1%) and high proliferative index (62.7% with Mib-1 $> 20$%); 55.2% of patients were in stage I. We observed a statistically significant reduction of BMI, body weight and waist circumference between every single evaluation. These results are associated with a significant reduction of glycemic ($p = 0.0405$) and insulin levels ($p < 0.0001$) in the first six months of observation. Total HAD score and the specific one for anxiety were significantly reduced during the first six months of observation ($p < 0.0001$ and $p < 0.0064$). 72% of patients increased their physical activity levels in the first six months of observation and 20% of them referred a clinical benefit regarding arthralgia ($p = 0.4459$).

**Conclusions:** BC in overweight women have aggressive features despite early stage. These data demonstrate that healthy lifestyle can reduce risk factors implied in disease recurrence and assure psychological benefit improving quality of life.

**Three-monthly dynamic evaluation of CEA and CA15-3 and 18-FDG PET vs usual practice in the follow-up of early breast cancer patients: a prospective, multicenter, randomized trial (KRONOS – Patient-Oriented New Surveillance-Study Italy)**

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1Policlinico S. Orsola-Malpighi, SSD Oncologia Medica “Addarii”, Bologna; 2Centre for the Study of Biological Malignancy Markers, Mestre; 3Istituto Nazionale Tumori, Milan; 4University of Munich, Institute of Clinical Chemistry, Monaco di Baviera; 5Policlinico S. Orsola-Malpighi, U. O. di Medicina Nucleare, Bologna; 6Zentrumklinik Bad Berka, Bad Berka; 7STRATIFYER Molecular Pathology GmbH, Colonie; 8Policlinico S. Orsola-Malpighi, SSD Oncologia Medica, Bologna

**Background:** Current guidelines for breast cancer (BC) surveillance in asymptomatic patients (pts) recommend only annual mammography and periodical physical examination. These recommendations arise from trials conducted in the 1980’s: since then our knowledge on breast cancer biology, diagnosis of metastases and treatment has deeply improved. The aim of this prospective randomized trial is to verify if the serial measurement of CEA and CA15-3 followed by 18-FDG PET can anticipate the diagnosis of BC recurrence compared to control arm by estimation of the difference of restricted mean survival time (RMST) between the two arms. If the end point will be met a subsequent extension trial will investigate the impact of the earlier diagnosis of distant metastases on survival.

**Methods:** Pts diagnosed with stage I-III BC, who underwent adequate surgery are eligible. Special histologies and low-risk cases according to St. Gallen criteria are excluded. The study includes pts at the beginning of the follow-up after the conclusion of primary treatment (cohort 1), and pts that have concluded without relapse the first 5 years of follow-up (cohort 2). Eligible pts will be randomized in a 1:1 ratio to follow-up according to local practice (control arm) or to three-monthly serial dosing of CEA and CA15-3 and subsequent 18 FDG-PET only in case of an increase of CEA and/or CA 15.3 greater than a critical difference compared to baseline (experimental arm). The following stratification factors will be used: node negative vs positive, HER2 negative vs positive, ER positive vs negative. Eight-hundred pts will be enrolled over 3 years. For such a calculation, we made the assumption of a 20% baseline 5-year incidence of relapse. The target reduction of three months in RMST implies a median time of diagnostic anticipation, conditional on having BC recurrence, of 10 months. The follow-up will continue until 10 years from surgery. Since 23rd October 2014 625 pts have been enrolled. The present trial was approved by the Ethical Committee of each participating centre and is registered on clinicaltrials.gov (NCT02261389).
Convergent findings indicate the need for broadening the vision of cancer. Patients were asked to respond to some self-reported questionnaires (State-Trait Anxiety Inventory, Visual Analog Scale for Pain intensity) and physiological parameters were registered (blood pressure, heart rate, respiratory rate). Pre- and post-test data were thus collected. Measurements on the experimental group were recorded twice: prior to T0 and after music medicine intervention, which was characterized by passive listening to pre-recorded music for a period of 45 minutes (T1) during chemotherapy administration. Measurements on the control group were also recorded twice at the same time points, but without music.

Results: Statistically significant differences were observed in mean change of State-Trait Anxiety Inventory scores between the music and the control group (p = 0.003). Although significant decreases were observed in heart rate (p = 0.027), no significant differences were seen as regards blood pressure, respiratory rate or pain perception.

Conclusion: Music intervention during chemotherapy administration decreased the state of anxiety levels and heart rate in oncological patients, showing that a simple environmental intervention can promote psychological well being and quality of life improvement.

Acknowledgement: This study was carried out within the PhD program in Experimental Medicine and Systems (XXIX cycle, Medical Oncology Course).

R2 Evaluating depression in elderly patients with cancer

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Background: Depression is one of the most common psychiatric disorders in elderly people, especially among oncologic patients, yet it often goes unrecognized. Performing a comprehensive geriatric assessment (CGA) is recommended to identify medical, psychosocial, and functional limitations of a frail older person. The aim of the present study was to assess associations between depressive symptoms and other variables of CGA in a population of elderly oncologic patients.

Patients and methods: We considered all patients who underwent a CGA in the Geriatric Clinic of Trieste Maggiore Hospital over 2 years on request of the oncologist. We registered age, sex, cancer type and evaluated functional, cognitive, nutritional, comorbidity and affective status respectively through ADL (Activities of Daily Living), IADL (Instrumental Activities of Daily Living), MNA (Mini Nutritional Assessment), GIRS (Cumulative Illness Rating Scale), MMSE (Mini Mental State Examination) and GDS (Geriatric Depression Scale). First we identified associations between the presence of depressive symptoms (i.e. GDS > 5) and CGA variables through Wilcoxon’s non parametric test; then we used a generalized linear model to test independence. Finally we evaluated the ability of two screening tools that are commonly used to detect anxiety among elderly oncologic patients to identify depressive symptoms (G8 screening tool and Vulnerable Elderly Survey 13).

Results: 147 patients completed G8. Of these 39 (26.5%) had significant depressive symptoms. Worse functional, nutritional, cognitive and comorbidity status was significantly associated (p < 0.05) with depressed mood, but only nutritional status was an independent predictor. G8 screening tool and VES 13 had a sensitivity and specificity respectively of 92, 22% and 54, 72%.

Conclusions: Our study confirmed that among elderly patients with cancer depression is associated with cognitive, nutritional and functional decline and greater comorbidity burden. The significant association with MNA highlights the vicious circle between malnutrition and depression. Given its high sensitivity, G8 screening tool could be a useful instrument to identify as soon as possible this condition with use of specific assessment scales.
Results: Preliminary correlational analyses showed a negative correlation between the intensity of prenatal attachment and negative affective states, particularly depression (r = -0.78, p < .001) and anxiety (r = -.81, p < .001). Moreover, a positive correlation between maternal attachment quality and perceived benefit by their partner (r = .804, p = .016) was found. Finally, the more pregnancy is perceived as a turning point in their life, the better the quality of prenatal attachment (r = .926, p = .016).

Conclusions: These preliminary data indicate that in addition to providing medical support to these patients it will be important to consider their experiences, their psychological adaptation to pregnancy as well as the perceived social support. It will be necessary to implement research in this direction, considering possible intervening variables, in order to structure targeted interventions aimed at supporting parenthood in the prenatal and postnatal period.

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**Evaluation of psychological aspects of taking care cancer patients: a multicentre study on a sample of caregivers**

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Every day about a thousand people receive a cancer diagnosis (AIOMAIRTUM, 2016). The cancer is one of the disease that most of all represent a serious danger for the human life and arises as one of the most stressful and traumatic events with which who is hit must deal with. When a pathology hits a person, immediately the whole family and all his internal and external relations are involved. The family is the first relational network and the first subjective dimension of the individual, indeed, when a member is hit from an ontologic pathology, the whole family ‘lives’ the disease and this could play a determinant role on how the illness is faced and lived. The oncological disease forces the family to face an incredibly amount of stress or changes on daily activities. Supporting caregivers so they can deal with their relatives’ cancerous condition is usually impossible, both patient care and collaboration with medical teams. San Raffaele Hospital’s Clinical and Health Psychology Service, developed a study to make a psychological evaluation of who attend the patient during course of the disease. This multicentred study is in line with the intervention model “action research”. In a sample of 201 caregivers (mean age=54.46±14.92) (M=72, W=129) Short Form Health Survey (SF-36), Zanit Burden Interview (ZBI), Coping Orientation Problems Experienced (COPE), Experience Close Relationship (ECR) were administered to evaluate respectively Quality of Life, perceived emotional Burden (B), Coping styles and Attachment styles. The sample takes care his/her partner (P) (n=85), parent(PA) (n=68), son/daughter (SD) (n=7), brother/sister (BS) (n=19), or others (O) (n=22).

Preliminary results show a main effect of type of relationship between caregiver and patient for “Mental Health Index” (MFI; F(4,191)=4.150;p<.003). In particular P (m=35.28;sd=1.38) and PA (m=36.25;sd=1.53) reported worse levels of MHI than O (m=45.23;sd=2.68). MHI and Anxiety attachment style average were significantly correlated (r=-.522;p<.05). Furthermore a main effect of type of relationship between caregiver and patient was found for B (F(4,190)=4.091;p<.003). Specifically P reported higher levels of B (m=23.31;sd=1.39) than O (m=14.24;sd=2.78). P, PA, SD reported mild or moderate levels of Burden.

On the basis of the results, the relationship is a relevant element in the experience of caregiving. The final aim is increasing the knowledge about specific oncological caregivers’ needs, in order to improving psychological interventions.

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**Evaluation of QoL as a predictor of chemotherapy-induced toxicity**

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1Medical Oncology Unit of the Tor Vergata Clinical Center, Rome

Background: The increased number of quality of life (QoL) studies in the oncology set- ting highlighted the negative effects of chemotherapy administration, including toxicity, on health-related (HR) QoL during or after treatment. However, the predictive value of pre-treatment HRQoL assessment on the subsequent occurrence of chemotherapy- related side effects, has never been tested. The present study aimed to investi- gate whether baseline patients’ perception of well-being, as HRQoL index, could influence both subject perception of chemotherapy-induced side effects and objectively measured parameters of toxicity.

Methods: A total of 110 cancer patients (41% male, mean age 62 ± 10.49 years) treated at the Medical Oncology Unit of the Tor Vergata Clinical Center, were enrolled. Primary tumors were gastrointestinal (53%), breast (32%), head/neck/lung (10%), urologic (5%). The self-reported questionnaire was administered before chemotherapy start: 1) the National Comprehensive Cancer Network Distress Thermometer (NCCN-DT) and 2) the FORTQ-QLQ-C30. Chemotherapy-related tox- icity was recorded in medical records according to NCI-CTC v4.0 criteria. Data were analyzed using MedCalc statistical software. The predictors of side effects toxicity was assessed using logistic regression analysis. Primary endpoint was overall toxicity inci- dence grade 0-2 vs. grade 3-4. The following variables were analyzed: age, sex, primary tumors, Karnofsky Performance Status, Global Health Status (GHS) and Distress. The effect size of predictors was estimated using adjusted odds ratio (OR) with 95% CI. A p-value lower than 0.05 was considered as statistically significant for all tests.

Results: GHS values were stratified in three categories, low (0-25), medium (26-49) and high (50-100) levels of QoL. Patient distribution according to GHS levels were 7.3% in the low, 13.6% in the medium and 79.1% in the high QoL category. In the whole population, age, sex and GHS were found significantly associated to chemotherapy- induced toxicity at the univariate analysis (p = 0.01, p = 0.02, p = 0.03, respect- ively). However, at multivariate analysis GHS was the only independent predictor of the occurrence of chemotherapy-related side effects (AOR: 2.78, 95% CI: 1.01-7.62; p = 0.04), particularly of grade 3-4 toxicity.

Methods: Pre-chemotherapy evaluation of health-related QoL parameters, might represent a useful tool to predict common chemotherapy-related side effects occurrence.
Patients and methods: Chinese cancer patients referring to the LCMD set up at Istituto Nazionale Tumori of Milan (INT) between July 2016 and April 2017 were evaluated. The LCMD guarantees the presence of a LCM who supports Chinese patients during the admission to the hospital and/or diagnostic assessment, offering a service of counseling to healthcare professionals and to the patient and his/her family. General practitioners located in specific neighborhoods of Milan were provided with Chinese language brochures and posters in order to expand this service to the broader Chinese community. The linkage project was supported by an AIOM grant.

Results: From July 2016 to May 2017, 42 Chinese cancer patients referred to the LCMD. The distribution of the population based on the main characteristics is summarized in Table 1. Overall 33 patients (78.6%), out of 42 Chinese cancer patients accepted and underwent treatment proposed by the physicians while 9 (21.4%) didn’t follow the indications. 26 out of these 33 subjects started a treatment at INT (78.8%), while the remaining 21.2% followed the treatments indicated at other hospitals.

Conclusions: After only 10 months from the beginning of the LINKAGE PROJECT, our findings showed a positive impact on qualitative standards regarding the access to healthcare services and the patient-caregiver interaction by Chinese cancer patients. Data showed that the vast majority (80%) of Chinese cancer patients referring to our LCMD accept to receive a treatment at INT.

Table 1: Main characteristics of Chinese cancer patients who referred to the LCMD.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Median SD</th>
<th>Range (1-76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>26</td>
<td>62</td>
</tr>
<tr>
<td>Female</td>
<td>16</td>
<td>38</td>
</tr>
<tr>
<td>Tumor type</td>
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<td></td>
</tr>
<tr>
<td>Breast Cancer</td>
<td>8</td>
<td>19.05</td>
</tr>
<tr>
<td>Cervical Cancer</td>
<td>4</td>
<td>9.52</td>
</tr>
<tr>
<td>HCC</td>
<td>4</td>
<td>9.52</td>
</tr>
<tr>
<td>CNS Cancer</td>
<td>4</td>
<td>9.52</td>
</tr>
<tr>
<td>Gastric Cancer</td>
<td>4</td>
<td>9.52</td>
</tr>
<tr>
<td>Other</td>
<td>18</td>
<td>42.86</td>
</tr>
<tr>
<td>Metastasis status at diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M-</td>
<td>14</td>
<td>33.3</td>
</tr>
<tr>
<td>M+</td>
<td>28</td>
<td>66.7</td>
</tr>
<tr>
<td>Type of treatment at diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>11</td>
<td>26.2</td>
</tr>
<tr>
<td>Medical</td>
<td>10</td>
<td>23.8</td>
</tr>
<tr>
<td>Surgery+Medical</td>
<td>14</td>
<td>33.3</td>
</tr>
<tr>
<td>Unknown</td>
<td>7</td>
<td>16.7</td>
</tr>
</tbody>
</table>

Results: From January to May 2016 we screened for distress 106 new oncologic patients. The application of expressive forms of art in oncology is considered an accepted method to measure distress and unmet needs of oncologic patients. At the first visit, a brief interview with a psychologist and the Distress Thermometer, our psychologists were able to individuate distress very quickly. This allowed us to perform fast intervention thus improving the quality of life and adherence to the oncologic plan.

Background: Routine screening for distress is today recognized as a standard of care in oncology practice, given the high incidence and the high negative impact on quality of life. It is demonstrated that a quickly identification of distress may led to prompt treatment and consequently to a better adherence to the oncologic plan.

Methods: Our principal aims were to identify factors associated with distress and propose a simple and accurate method to measure distress and unmet needs oncologic patients. At the first visit, we proposed a test battery (Pro.spera, Designing My Future, Resilience Scale) to 26 patients with lung cancer. The project has been designed in a holistic view of the complex and multidimensional relationship (14 patients under TKI or Chemotherapy; 12 patients under TKI or Chemotherapy). We proposed a test battery (Pro.spera, Designing My Future, Resilience Scale) to 26 patients with lung cancer.

Results: Most recognized strengths are Courage, Social Resources and Family Cohesion (Table 1). Vulnerability areas are, like expected, Optimism, Hope and Future planning. Anyway, over the 50% of participants recognize the presence of resources for all dimensions investigated. Using the Mann-Whitney statistic, however, no significant differences emerge between different therapeutic conditions or different ages (p < 0.05).

Conclusion: Results show that the elements of positivity are greater than those of vulnerability. Medical staff can better understand which dimensions help to cope and maintain good levels of compliance in patients with lung cancer, also in older ones. It seems useful to enhance them and increase vulnerability areas. Future studies are suggested.

Table 9: People who recognize themselves in these 3 areas. Values expressed in %

<table>
<thead>
<tr>
<th>Resilience</th>
<th>Optimism</th>
<th>Hope</th>
<th>Courage</th>
<th>Life Satisfaction</th>
<th>Development</th>
<th>Family Cohesion</th>
<th>Social Resources</th>
<th>Planned Future</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pro.spera</td>
<td>24</td>
<td>64</td>
<td>12</td>
<td>84</td>
<td>84</td>
<td>62</td>
<td>62</td>
<td>12</td>
</tr>
<tr>
<td>Designing My Future</td>
<td>28</td>
<td>72</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Resilience</td>
<td>12,5</td>
<td>58</td>
<td>29,5</td>
<td>58</td>
<td>58</td>
<td>58</td>
<td>58</td>
<td>12</td>
</tr>
<tr>
<td>Courage</td>
<td>-</td>
<td>38,5</td>
<td>61,5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Life Satisfaction</td>
<td>16</td>
<td>84</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Resilience</td>
<td>29</td>
<td>50</td>
<td>21</td>
<td>-</td>
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<td>-</td>
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<tr>
<td>Resilience</td>
<td>4</td>
<td>58</td>
<td>38</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Perception of Self</td>
<td>1</td>
<td>65</td>
<td>23</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Planned Future</td>
<td>27</td>
<td>58</td>
<td>15</td>
<td>70</td>
<td>15</td>
<td>15</td>
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<tr>
<td>Social Competence</td>
<td>19</td>
<td>62</td>
<td>19</td>
<td>-</td>
<td>-</td>
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<td>-</td>
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</tr>
<tr>
<td>Family Cohesion</td>
<td>12</td>
<td>50</td>
<td>38</td>
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<td>-</td>
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<tr>
<td>Social Resources</td>
<td>-</td>
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</table>

Table 10: The thermometer of distress in oncology

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>M0</th>
<th>M1</th>
<th>M2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric Cancer</td>
<td>4</td>
<td>9.52</td>
<td>9.52</td>
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<td>Medical</td>
<td>10</td>
<td>23.8</td>
<td>23.8</td>
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<tr>
<td>Surgery</td>
<td>11</td>
<td>26.2</td>
<td>26.2</td>
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<tr>
<td>Surgery+Medical</td>
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Background: The application of expressive forms of art in oncology is considered an integral part of patient care and the theatre seems to be a powerful resource for training, personal growth and rehabilitation. At the Medical Oncology Department of “S.G. Moscati” Hospital in Avellino, within a humanization program of cancer care a rehabilitation project of theatre therapy for cancer patients has been carried out for 8 years. The project has been designed in a holistic view of the complex and multidimensional care.

Methods: All cancer patients with at least 1-year of life expectation referred at the Division of Medical Oncology, have been selected for inclusion. Enrolled patients are identified by the psycho-oncologists with clinical and motivational interviews. The first
phase is characterized by the selection of potentially eligible patients. After the inter-
views, the selected patients complete a registration form and receive the MAC entry-
questionnaire. The second phase involves the formation of the group and the ‘start up’
of the workshops. It uses pre-expressive techniques and post-expressive techniques.
All the activities are characterized by the group mode. Is very important the presence of
men in the group.

Results: Quantitative Analysis: As the therapy theater experience of our U.O. came in
2016 to the ‘eighth edition of the project it has been decided to make an assessment of
half of the course and evaluate the analysis results for the fourth edition. The sample
consists of 10 women with an average age of 52 (Minimum age 36 - maximum age 68),
of which 9 were suffering from breast cancer and an ovarian cancer and 3 males of aver-
age age of 46, of a 30 year boy with a testicular cancer and two others of 50 and 59
respectively with seminoma testicular with colon carcinoma. All patients gave their
Informed Consent before starting the therapy theater activities.

Qualitative Analysis: From semi—structured interview analysis of patients who partici-
pated in the theater therapy it emerges that participation to these forms of art, leads to
a quality of life improvement, but also to the acceptance of the disease and medical
maintenance.

Conclusion: From the analysis of the results of the experience of the year 2013, which is
in the middle of our path, a substantial improvement in the style of adaptation to the
patient disease who took part in the theater therapy emerges and, in particular, this
result appears to be more evident after the final performance.

R12 Incidence of alcoholism among cancer patients undergoing active

treatment

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Background: Substance abuse was frequently underdiagnosed among patients in onco-

logy treatment and palliative care. Alcoholism occurs in approximately 8% of the gen-

eral population, being more frequent among hospitalized patients (approximately up
to 20%). It has been described as a poor prognostic factor for cancer symptoms man-
agement. Previous studies focusing on frequency of alcoholism in advanced cancer patients admitted to palliative care unit in Italy detected this condition for only a
minority of patients (4%). Aim of our study is to determine the incidence of alcoholism
among patients with advanced cancer admitted to two Oncology Units for active cancer
treatment, using a simple and validated assessment instrument.

Methods: We present an unplanned interim analysis of a prospective cohort study.

From August 2015, all consecutive eligible patients completed the Catt down, Annoyed,
Guilty, Eye-opener (CAGE) questionnaire. Baseline symptom assessment and quality
of life were also evaluated by Edmonton Symptom Assessment System (ESAS) and
EORTC-QLQ-C30 questionnaires. Demographic data, cancer disease and extension
features, disease-oriented treatment and all medical information were collected.

Performance Status was evaluated according to Karnofsky (KPS).

Results: In total, 117 patients were evaluated. The mean age was 63.3 (SD 12) years and 66
(56.4%) were males. The mean KPS was 68.3 (SD 16). Lung and Gastrointestinal cancers
were the majority. The mean ESAS was 23 (SD 14.8) points and the mean BMI was 24.5
(SD 3.7). The CAGE questionnaire was positive in 38% of patients. In this population
the mean age was 61.7 (SD 11.1), the mean KPS was 69.2 (SD 16.2). Furthermore, the
mean ESAS was 18.3 (SD 13.7) and the mean BMI was 24 (SD 5.2) points.

Conclusions: First preliminary data prove that alcoholism is highly prevalent and
underdiagnosed among patients undergoing active cancer treatment, compared with other
studies in palliative and home care settings reported in the literature. Independent of
diagnosis and performance status, CAGE—positive patients are more likely to be male,
as described by other studies. Other demographic data from this sub-
group are equally represented.

R13 “I have a cancer, I am ill, it’s Sunday, my oncologist is not here, I am despairing.” How a telephone call can resolve a great difficulty of cancer patients

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Background: Cancer is a multifaceted illness that includes physical as well as psychoso-
cial challenges. The ability to cope effectively with cancer is heavily influenced by psy-
chological challenges, such as distress. For patients, unresolved distress is associated
with anxiety, adjustment, and depressive disorders. In order to reduce the patient’s
and caregiver’s distress, avoiding referral to the Emergency Department (ED) for non-
urgent conditions and to supply the patient and needs, we have performed a procedure
to listen to the patient needs through a phone call.

Methods: The telephone calls are told that they will be able to contact the Oncology
Unit (OU) by telephone regarding problems. During the weekend and when the
outpatient clinic is closed, the nurse on call of the OU will answer to phone call, and
then the needs of the patient is registered on a specific form. If the nurse can solve the
problem, the patient is provided with all the information needed and the form is filled
in; if the problem requires the consultation of an oncologist, the nurse notifies the doc-
tor on call. When paged by phone, the doctor on call may decide whether to give tele-
phone advice to the patient or to the caregiver in order to handle the problem at home,
to arrange an urgent hospitalisation or to send the patient to the ER.

Results: Between January and March 2017, 55 calls from 44 patients were registered in
the OU. The main problems were related to gastroenterology symptoms (18,18%),
pain (16,36%), fever (14,55%) and hypo/hyperglycaemia (10,91%). 61,82% of the calls
ended with the resolution of the problem simply thanks to telephone advice; in
27,25% of the cases, the patient went to the ED, and in 3,64% of the cases, the patient
went directly to the OU. The resolution of the problem was carried out by telling the
patient to take medications or to change therapy (32.73%), advising the patient go to
the ED (14.55%), to the OU (1.82%) or giving simple advice on how to handle the
problem (10.91%).

Conclusions: The possibility of receiving immediate support is useful for both the
patient and caregiver, who feel protected and supported during the entire course of
the disease. Through a phone call, the healthcare staff can intervene on symptoms before
they become unmanageable and manage the problems and the possible changes, such
as additional calls to the oncologist before the next visit, unscheduled visits, visits to
the ED and hospitalisations.

R14 Music and its influence on affectivity and relationships in oncologic and
hematologic patients

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Background: Cancer mortality has decreased in the last 10 years, but surviving onco-
hematologic patologies does not relate necessarily to a good quality of life: several studies
have demonstrated that symptoms like anxiety, depression, stress can persist after
recovery, and the impact of the disease on familiar, sexual, working relationships is very
strong. According to the American Music Therapy Association, Music Therapy is the
clinical and evidence—based use of music by credentialed professionals to address phys-
ical, emotional, cognitive, and social needs of individuals; it can find application in
many clinic contests. Considering the previous problems, it can be effective also for
neoplastic patients.

Methods: Objective of this qualitative study was to evaluate changes on affectivity and
relationships in a sample of oncohematologic patients who took part in 12 Music
Therapy group sessions. Being adults (age > 18) and participating at least in 7 sessions
were the only inclusion criteria. After consent to participation and to the use of per-
sonal data, 7 patients were interviewed on themes like quality of life, coping, relation-
ships with relatives and health workers. To better indentify changes during sessions,
questions were divided in 3 areas: pre, intra and post Music Therapy treatment.

Interviews were recorded, transcribed and finally analyzed with a phenomenological
approach: 3 researchers read interviews, underlining words and sentences considered
relevant, then they compared what was highlighted by each one. Products of the com-
parison were put together, creating and developing common themes.

Results: Seven common themes were identified: knowing the diagnosis and its conse-
quences; loneliness; the experiences during Music Therapy sessions; the role of the
therapist; the relationship with the other members of the group and relatives; meta-
phors to describe the sessions; the redesign of life.

Conclusions: Thanks to Music Therapy, patients have increased self awareness and
have found coping techniques to deal with their disease and its outcomes. Music
enhanced relationships especially between patients who took part to the sessions with their
caregivers; also the relationships among participants and between them and the
Music therapist were strongly positive. It is desirable that health workers apprise
patients of these treatments, in order to make therapeutic offer more complete.

R15 Evaluation psychological distress in elderly cancer patients

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Background: Comorbidities and disabilities coexist in elderly cancer patients (age = 70
years old). Depression and anxiety are also common and they can lead to weight loss,
fatigue, affecting the perception of their own quality of life, the compliance with thera-
pies and perhaps the outcome. Aim: our mono-institutional experience has evaluated
relevant, then they compared what was highlighted by each one. Products of the com-
parison were put together, creating and developing common themes.

Results: Seven common themes were identified: knowing the diagnosis and its conse-
quences; loneliness; the experiences during Music Therapy sessions; the role of the
therapist; the relationship with the other members of the group and relatives; meta-
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Conclusions: Thanks to Music Therapy, patients have increased self awareness and
have found coping techniques to deal with their disease and its outcomes. Music
enhanced relationships especially between patients who took part to the sessions with their
caregivers; also the relationships among participants and between them and the
Music therapist were strongly positive. It is desirable that health workers apprise
patients of these treatments, in order to make therapeutic offer more complete.
imperium; living alone; history of psychiatric disorder; alimentary behavior; sleep/ wake; rhythm; family/community supports; awareness about their diagnosis.

Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL). ADL are activities in which people engage on a day-to-day basis. These are everyday personal care activities that are fundamental to caring for oneself and maintaining independence; IADL are activities related to independent living and are valuable for evaluating the potential value to the affection and the family and the experiences that have contributed to building their identity. The introduction of topics such as dignity, searching for meaning, has proved to be a valuable tool for the development of the true meaning of one's life, despite the changes in the disease. Moreover, in some cases, it has contributed to allowing the person to find a way of self-reliance in relation to loved ones.

Conclusion: In our experience, DT showed to be a new promising therapeutic intervention for suffering and distress at the end of life. The literature review finds robust evidence for DT’s overwhelming acceptability, rare for any medical intervention, especially in psychosocial-spiritual care.

Cancer as family disease

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Background: Cancer disease doesn’t only affect the patient, but also his family. Many studies have shown that caregivers have to deal with multiple difficulties, developing psychosocial reactions such as anger, anxiety, depression, fatigue, that is caregiver burden. These evidences have led us to think that the family is an integral part of family care process, and it’s need to be supported in turn to provide adequate support to his loved one.

Material (patients) and methods: In our Oncological Department Day Hospital, sited in Firenze (Institute Toscana Nikko, IT) we have been thinking of widening the psychological support, already provided to patients, also to families. So they can meet psychologist that evaluates caregiver burden with clinical interview and Caregiver Burden Inventory (CBI), a multiple choice self-administration questionnaire composed of 24 items, 5 sub-scales, each of which measures a type of burden/reductions in personal time (Time-Dependence Burden, T/dep-B), failure of hopes and expectations (Developmental Burden, Dev-B), physical stress (Phys-B), work and family conflicts (Social Burden, Soc-B), negative feelings towards patient (Emotional Burden, Emot-B). Score range is 0-4 for each item, 0-20 for each dimension, whereas total score is between 0-100. 57 caregivers (38 women,19 men) have agreed to answer to CBI in an outpatient setting, while waiting for their family members to visit or therapies. The median age of the caregiver was 55.93 (range 33-77), while that of the patients 73.40 (range 45-86).

Results: CBI total score varies between 0 and 62 (M 20.93), with highest scores respectively for T/dep-B (M 7.07, range 0-18), Dev-B (M 6.25, range 0-20) and Phys-B (M 4.75, range 0-16) while the lower ones for Soc-B (M 1.81, range 0-10) and Emot-B (M 1.05, range 0-10).

Conclusions: CBI results show the most subjective burden in time required by caregiving, the sense of failure of hopes and expectations and perception of fatigue and health problems, while role conflicts and feelings towards the patient can cause lower scores. We have not provided detailed quantitative data because the research is still ongoing and sample of caregivers is too small to be able to make inferences of any kind. Starting from these data, specifically for the dimension of psychological reaction, the opportunity to avail of a psychological support is given to families, to improve their psychological well-being, patient relationship, and coping strategies of this Family Disease.

Screening of distress in hospitalized patients: the experience of medical oncology department

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Background: Despite the numerous studies on the topic and the clear guidelines that recommend routine distress assessment in cancer patients, this psychological parameter is often not recognized or debated at all. The aim of our study is to determine whether the Distress Thermometer (DT), used in each patient’s hospitalization, may favor a more targeted takeover of the patient’s real needs and faster monitoring of the symptoms in the various stages of illness.

Methods: We analyzed 371 [57.7% male, 42.3% female] patients (pts) between 23 and 91 (median 63.2) years old who completed DT during hospitalization through the cooperation of suitably trained and motivated nurses. They almost represent the total population of pts taken over in a 16-month period by an in-out patient of the Department of ASST Sette Laghi of Verona. These pts are randomly characterized by heterogeneity of tumors and staging of disease. The ANOVA (Analysis OF Variance) method was used for data analysis to test the differences between scores at DT (0-10) and the presence/absence of other problems or disturbances (39-item) in the last week.

Results: 49.6% of pts show DT scores between 6 and 10 (11% =) 10. ANOVA (One-way) shows significant differences between DT scores averages in different type of

image and self-esteem: a photo-therapy program to improve body image, increase self-awareness and the expression of emotions in breast cancer patients. A pilot study

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Background: Conventional breast cancer therapies often provoke consistent changes in patients’ body image that can negatively impact their self-perception and social relationships. Photo-therapy consists in the use of personal snapshots, magazine pictures and photos taken by others, under an expert therapist guide to reduce painful psychologic symptoms, facilitate the process of change, improve body image, self-consciousness and encourage the manifestation of emotions, better than words alone.

Methods: In photo-therapy each patient chooses one of a set of images that represents her, to introduce herself to the group and to increase emotional awareness; Photo-collage consists in cutting and pasting images on a individual poster to explore cancer related experiences and to recognize changes; in Photo-dialogue patients select a photo, on a set, that represents how they perceive their body in order to create an individual story; Self-portrait consists in comparing pictures of the patients taken by themselves with those taken by other people, to understand how they perceive themselves and how they are seen by others. Basic Self-Esteem scale (SE), Positive and Negative Affect Scale (PANAS), FACIT Fatigue scale, NRS pain score, Distress Thermometer (DT), and two anxiety/depression tests (HADS and STAI-V) were administered at the beginning and end of the course.

Results: From 12/2016 to 03/2017 6 breast cancer patients, median age 54 (47-72), attended 16 weekly sessions of Photo-therapy, 3 of them in adjuvant hormonal therapy after surgery and chemotherapy, 1 in chemotherapy for advanced disease. Before Photo-therapy Basic Self-Esteem was >75 percentiles in 1/6 cases; after the course 3/5 pts, who returned final test, scored >75 percentiles. Median PANAS-positive score showed an increase (from 23.7 to 27.3 points) and PANAS-negative a decrease (from 18.5 to 16.8). Fatigue, pain, anxiety, depression and distress evaluations did not show any change.

Conclusions: This pilot study of an image-based therapy suggests possible advantages of this technique in breast cancer patients to improve self-esteem and emotions. Larger studies are recommended.

Dignity Therapy: a new psychotherapeutic approach for people facing advanced disease

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Background: The fear of loss of dignity is a recurring concern among oncological patients, especially in the advanced stage of illness, for those who are in advanced stage of their disease. Chochinov has made the model of Dignity Therapy (DT) used primarily with people who were terminally ill. It consists of a 16-weeks psychotherapy process, and it’s need to be supported in turn to provide adequate support to his loved one.

Methods: Since 2016 we applied to 4 patients the DT in the perspective of simultaneous care with metastatic disease, in psychological therapy and still in chemotherapy. We are using the Italian validated version of semi-structured interview. The intervention takes place in 3-4 meetings, lasting 1 hour each, after informed consent. The interview uses 10 core questions and the responses are used to create a written legacy document to family members. The DT session is audio-recorded, transcribed, edited and given back to the patient. Content includes lifetime events that are most significant in the life of the patient, who can later personalize adding photos, images, titles or more.

Results: Because the our small sample, we do not have a statistically relevant data, but we have noticed that the common themes that emerge in patients mainly concern the attributed early-stage of the disease and family and the experiences that have contributed to building their identity. The introduction of topics such as dignity, searching for meaning, has proved to be a valuable tool for the development of the true meaning of one’s life, despite the changes in the disease. Moreover, in some cases, it has contributed to allowing the person to find a way of self-reliance in relation to loved ones.

Conclusion: In our experience, DT showed to be a new promising therapeutic intervention for suffering and distress at the end of life. The literature review finds robust evidence for DT’s overwhelming acceptability, rare for any medical intervention, especially in psychosocial-spiritual care.
Background: In developed countries, including Italy, the immigrant population with cancer is growing and wide disparities in cancer prevention and treatment have been demonstrated between migrants and native populations. Here we report preliminary data of a project aimed to create a dedicated service for immigrants affected by cancer in order to reduce health disparities in this subgroup of patients (pts) by implementing the right and access to healthcare as an opportunity for integration and social inclusion.

Patients and methods: In September 2016, a specific service for migrant oncology pts consisting of a dedicated outpatient clinic was started at our Medical Oncology Unit. From then, any foreign born accessing our hospital with a suspicion or a diagnosis of cancer was referred to our dedicated clinic. This project is supported by AIOM.

Results: From September 1st 2016 to April 30th 2017 a total of 72 pts (20 male and 52 female) accessed our dedicated service. Most pts (66 pts) were from Less Developed Countries (Eastern Europe, Africa, Asia, Central/Southern America), whereas a minor of them (6 pts) was from Developed Countries (United Kingdom, France, Australia, Japan). 52 pts were managed in the outpatient clinic whereas 20 needed hospitalization. The most common diagnosis was breast cancer (36 pts), followed by gastrointestinal (9 pts), gastrointestinal (8 pts), gynecological (8 pts), lung (6 pts), head and neck (3 pts), skin (1 pt), and hematologic cancer (1 pt). 53 pts underwent curative surgery, 37 received chemotherapy, 29 in adjuvant/neoadjuvant setting, 3 with curative intent, 5 in palliative setting, 46 received chemotherapy (27 in adjuvant/neoadjuvant setting, 3 with curative intent, 16 in metastatic setting) 24 received endocrine therapy (20 in adjuvant setting, 4 in metastatic setting), 10 received supportive care. Most patients reported that financial, social, and logistical support would help them to comply with the diagnostic/therapeutic pathway.

Conclusions: These preliminary results showing high attendance of migrant cancer pts at our clinic suggest that a dedicated service could provide migrants greater access to cancer care. Further multidisciplinary interventions directed to psychologic and social needs of these pts should be implemented, in order to ensure that each migrant have a full access to high-quality health care, without discrimination on the basis of national origin, religion, gender or race.

R21 Preliminary data for assessing the impact of psychological stress on the development of primitive tumors or relapses of disease

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Background: The relationship between psychological and immune systems in the development of chronic inflammatory and cancerous diseases has already hypothesized. In particular, the presence of strong emotional stress has been considered as a cause for development of neoplasms such as breast cancer, melanoma, and gastrointestinal tumors. What is still unknown is how stress of nervous origin can influence the chain of molecular events leading to cell proliferation, leading primarily to the development of tumors and, subsequently, the occurrence of relapses. The present study aimed to investigate risk factors for early onset of primary cancer or cancer relapse, that arise from lifestyle and psychological stress.

Methods: Between January and September 2017, we provided a questionnaire to 100 patients followed at the University Hospital in Cagliari and San Marcellino Hospital in Muravera, regardless of tumor histology, disease stage, and ongoing therapy. The questionnaire was focused on a biopsychosocial diagnosis, onset time, relapse time, and the quality of life reported over the last three years. The surprising news is that 94% of patients reported the presence of a highly stressful/painful event in the three years prior to diagnosis, whether they were in adjuvant therapy or after relapse of the disease: altogether 46% of patients reported a strong psychological stress due to family mourning (29%) or serious illness (17%) in a close relative (parent, brother/sister, son/daughter); 15% reported a heavy emotional burden caused by work stress (incompatibility with leader or colleagues) and 10% reported family problems caused by economic reasons related to inheritance.

Conclusions: Although psychological stress is difficult to assess, this preliminary analysis suggests the need for a wider study with a control arm to confirm our hypothesis and, if so, to identify clinical and instrumental parameters that allow us to customize the control of subjects potentially at risk of relapse.
important emotional experiences related to the memory of the disease and the need to rebuild daily life.

**R24 Patient relationship training in an integrated perspective: guidelines for psychological intervention**

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The world of Oncology is now facing new challenges in the need for multidisciplinary work. Our work aims to identify a model to improve the skills of each professional in an integrated perspective. Training is an area of psychology that in recent years has had more attention by the clinicians, for its implications on Care and Health Promotion. The group is an elective tool for this job, as it works as a natural container that expresses aspects of the worker identity through coping and identification mechanisms. The specificity of the techniques used established a link and became contact facilitators with the primitive expression of emotion. The matters encountered dealt with both the relationship with cancer and terminally ill patients, and with the management of internal team dynamics. To identify the Training model, the contributions of all the professionals have been fundamental, in particular of oncologists, psychologists, psychotherapists, nurses and coordinators.

25 health workers (3 males (12%), 22 females (88%); mean age: 43.55, SD = 8.36) years of service M = 19.13, SD = 8.68) were enrolled at the Department of Medical Oncology at “Presidio Ospedaliero” of Saronno, ASST Valle Olona, Italy. Nurses were tested three times with (A) Maslach Burnout Inventory, (B) Coping Inventory for Stressful Situations and (C) SF-36. Cronbach’s alphas ranged from 0.58 to 0.91.8 health workers didn’t want to change work, 15 thought about that and 2 reported the intention of changing. 11 health workers reported the desire to be moved to other department (D). Preliminary results show a significant main effect of the possibility of changing work for “vitality” of SF-36 [F(1,22) = 4.571; p = .022]. Furthermore, a significant main effect of the desire to be moved to other department was found for “Emotional Exhaustion” (EE) [F(1,22) = 5.634; p = .027]. D (M = 19.27; SD = 8.90) reported more EE than who didn’t want to move to other department (M = 11.69; SD = 6.74). D showed moderate levels of EE. Results evidence statistically significant association between years of service and “Personal Accomplishment” of MBI [b = .453; p = .034; F(1,21) = 5.157]. The team of highly specialised oncologists, nurses, healthcare assistants, radiotherapists, psychologists and head nurses has to work together towards the development and care of a relational ability for interaction in a group. Results of this study could permit better understand psychological aspects of taking care oncological patient, in order to improve relationships trough different member of the group.
Early palliative care has been shown to improve outcomes in patients with advanced cancer such as quality of life, mood, end-of-life care. In accordance with American Society of Clinical Oncology (ASCO) and AOM recommendations of implementing palliative care early in the course of illness for patients with metastatic cancer along with active cancer treatment a Simultaneous Care Clinic (SCC) was set up at Istituto Oncologico Veneto (IOV) in Padova since 2014.

Methods: Data of pts referred to the SCC at IOV from March 2014 to November 2016 were retrieved from a prospectively maintained database. Data collected included cancer type, status of disease, performance status, ongoing oncological treatment, psychological evaluation, social evaluation, nutritional evaluation. Collected data included activation of home territorial services and/or Palliative Care services, use of other health services after a first visit and place of death.

Results: 533 pts were evaluated by a multidisciplinary team (oncologist, palliativist, nutritionist, psychologist, radiation therapist, nurse, case manager). Overall symptom burden was low with baseline symptom scores (ESAS) highest for fatigue, lack of appetite and depression. Nutritional evaluation revealed 224 pts (42%) with nutritional problems, the most frequent being weight loss (n = 121). Some form of psychological distress was present in 185 pts (35%). Social issues were present in 26 pts (5%) and were dealt with activation of social services (n = 9) or volunteer territorial services (n = 8). Patients deemed in need of home care services after the first access to the SCC were 177 (33%) and for these a formal request for Home Care services activation was sent to the Local Health Territorial Unit (Distretto ULSS). After the first visit 141 patients referred to Emergency Room for intervening problems with median time of 41 days. Globally 290 pts (54%) died with 53% of deaths occurring at home. The median time from first visit in the SCC to death was 85 days. For pts who were receiving active oncological treatment at the time of first visit, median time from first visit in the SCC and death was 126 days. We are also evaluating a score for priority for access to SCC.

Conclusion: Early integrated SC may be most effective if targeted to the specific needs of each patient population.

Background: The main goal of palliative care (PC) is to improve the quality of life of patients and their families facing life-threatening illness, with a special attention to achieve high quality end of life (QoELC) care. Here we report about caregiver perceived quality of care in the last week of life, a secondary outcomes from a randomized controlled trial comparing systematic versus on-demand early palliative care (SPC vs ODPC) in patients with pancreatic cancer.

Methods: Informal caregivers of patients enrolled in the main study (NCT01996540) and died within the period 31.10.2013 to 31.12.2016, were eligible for this mortality follow-up. Six to twelve months after patients’ death, bereaved caregivers were contacted to ask for informed consent to study participation. Accepting caregivers were interviewed over the telephone by a trained psychologist. The summary scales of the Toolkit of Instruments to Measure End-of-Life Care, namely patient and family information, respect for patient treatment preferences, symptom control, death with dignity, family emotional support and global QoEOL were used for assessing caregiver scores. Scale scores are reported on a range from 0 (worst) to 100 (best end-of-life care). Student t-tests for independent samples were used to compare SPC vs ODPC pts on the questionnaire scale scores.

Results: 118 pts were eligible for the present survey, 71 of them (58%) it was possible to contact the main caregiver, who accepted to be interviewed in 65 cases (34%). Interviewed caregivers were most often females (65%), with a mean age of 57 years. Respondents were more often partner (51%) or son/daughter (33%) of the decedent. Percentages of patients dying with EOL PC were the majority in both SPC and ODPC groups (72% and 60%). Global QoEOL care was fairly good in both groups (64 vs 68 vs 65, group difference 0.9 vs 0.8). Similarly, other scale scores were rather high (all average scores above 80, but family emotional support which scored 74) and the comparison of the two groups did not show any treatment effect (all group differences not statistically significant and ranging from -1 to 3.4).

Conclusions: While the main study results shows a benefit of SPC vs ODPC during the first 3 months from diagnosis of pancreatic cancer, the fairly high QoEOL scores found for both groups suggest that the management of EOL care is relatively uniform and good in this patient population.
Our results suggest to consider symptom burden, ECOG PS, disease stage (HR = 3.1, p = 0.005), dyspnea (HR = 2.5) and cough (HR = 2.2). The multivariable model confirmed independent prognostic value for ECOG PS, disease stage and pain. On Dec, 31, 2015, 25/98 patients were still alive, 65/98 had died and 8 patients were lost at follow up. Among patients who died, 39 (29%) were admitted to the hospital in the last 30 days of life, 56 (86%) did not receive chemotherapy in the last 30 days of life, 40 (61%) died with hospice or home care.

Conclusions. Our results suggest to consider symptom burden, ECOG PS, disease stage among the screening criteria for referral to palliative care in patients with lung cancer.

Simultaneous Home Care project for frail advanced cancer patients: a model of integration between no profit and Public Health System

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1Uo Oncologia Medica AOO Settelaghi, Varese; 2Aree Settelaghi, Varese

Background: Despite widespread evidence reported in literature and attention by Health system, limited research exists evaluating principles and effectiveness of cancer patients-centered home management according on patients’ needs rather than on prognosis. Our Simultaneous Home Care (SHC) project represents both an opportunity for patients referred to palliative care and may benefit from home care, but present physical and social problems coming to day hospital and a model of integration between “no profit” and Public Health System.

Methods: The Oncology Department of AOO Settelaghi Varese with the support of Varese per l’Oncologia, a non-profit organization, a grant from Regione Lombardia and according to the general practitioners, has conducted from May 2014 to April 2017 a pilot project of a SHC, a dedicated home-based service for frail advanced cancer patients. We included patients with advanced disease, treated with oral or subcutaneous,ousy biological agents and zoledronic acid, with limiting day-hospital access co-morbidities and at least six months life expectancy. Home care was provided by a high qualified team including three oncologist with expertise in palliative care, four nurses, a psychologist and a physiotherapist; home care was available 12 hours a day and included an on call oncologist everyday of the year.

Results: a total of 115 patients, median age 72 years (range 38-84), affected by advanced solid tumors or hematological malignancies were enrolled. All of them had metastatic disease and received both supportive care and anticancer treatment as outpatients. 95% received a cancer therapy. The median length of simultaneous care was 155 days (range 7-825). A total of 187 (range 169-198) nursing and 148 (range 142-155) medical visit were performed a year, with an average of 1.4 and 1.8 visits a month respectively. The median number of in-line patients were 20 (range 17-23). Hospitalization occurred in 18.4%. Blood transfusions at home was delivered in 2 patients and parenteretics in 8. One third of them died at home.

Conclusions: Our experience within SHC shows that the integration of supportive care and cancer treatment in home setting is effective. Hospitalization rate is lower than other studies. If confirmed in prospective pharmaco-economics studies, our data suggest that SHC provides high quality of assistance to frail. Integration with no profit was successful. Model can be replicated in other settings.

Efficacy of neurokinin-1 receptor antagonists in the prevention of Chemotherapy-Induced Nausea and Vomiting (CINV) in patients receiving carboplatin-based chemotherapy: a systematic review and meta-analysis

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1Dipartimento di Oncologia, Università degli Studi di Torino, AO Ordine Mauriziano, Torino; 2Dipartimento di Oncologia, Università degli Studi di Torino, AOU San Luigi Gonzaga, Ossattano (TO); 3Oncologia Medica, Dipartimento di Medicina, Università di Verona, Azienda Ospedaliera Universitaria Integrata di Verona, Verona; 4Oncologia Medica, AO Ordine Mauriziano, Torino; 5Oncologia Medica, Azienda Ospedaliera “Santa Maria”, Temi

Background: Carboplatin was traditionally included among moderately emetogenic chemotherapy agents. According to 2016 guidelines of the Multinational Association of Supportive Care in Cancer (MASCC) for chemotherapy-induced nausea and vomiting (CINV), a combination of a NK1 receptor antagonist (RA), dexamethasone and a 5-HT3 RA is recommended to prevent carboplatin-induced emesis, with moderate level of confidence and moderate dosing recommendations. Our aim was to perform a literature based meta-analysis of all randomized trials (RCTs) evaluating the addition of a NK1 RA in the prevention of emesis for patients treated with carboplatin-based chemotherapy.

Methods: A systematic review of articles published or presented at major meetings was performed in January 2017. RCTs comparing NK1 RA + dexamethasone + 5-HT3 RA vs. dexamethasone + 5-HT3 RA in patients receiving first cycle of carboplatin-based CT were included. Outcome was complete response (CR), defined as no emesis and no use of rescue medication. CR was measured in day 1 (acute phase), days 2-5 (delayed phase) and days 1-5 (overall period). A random effects model was applied.

Results: 9 trials were potentially eligible (7 appretatin, 1 fosaprepitant, 1 dolasetron): 6 were RCTs including patients receiving carboplatin, and 3 were subgroup analyses of patients receiving carboplatin within RCTs including various MEC. Data of CR were available in 8 trials (1598 patients). The addition of NK1 was associated with a significant improvement in CR during acute phase (94.5% with NK1 RA vs 90.1% with control, Odds Ratio 1.75, 95%CI 1.19-2.59, p = 0.005), during delayed (95.5% with NK1RA vs 61.7% with control, Odds Ratio 2.04, 95%CI 1.64-2.55, p < 0.0001) and during the overall period (75.3% with NK1RA vs 60-4% with control, Odds Ratio 2.04, 95%CI 1.64-2.54, p < 0.0001). There was no significant heterogeneity among trials.

Conclusions: In patients receiving carboplatin-based chemotherapy, triple therapy with NK1 RA, 5-HT3 RA and dexamethasone is associated with a statistically significant and clinically relevant improvement in CR, compared to 5-HT-3 RA plus dexamethasone. An individual patient data meta-analysis could help to identify patients who are likely to obtain the higher improvement from the addition of NK1 RA.

Medication-Related Osteonecrosis of JAW (MR-ONJ) After Bisphosphonates, Denosumab and other Drugs in Advanced Cancer Patients: Recent Experience Data from Rete Oncologica Piemonte – Vallet D’aostra (North-West Italy Cancer Network)

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1Azienda Ospedaliera di Alessandria, Alessandria; 2Dental School, Torino; 3Rete Oncologica Piemonte- VdA, Torino; 4Centro Documentazione Osteonecrosi, Alessandria

Background: Data concerning incidence of Osteonecrosis of JAW (ONJ) are scarce. As an almost unique experience, since 2005 a multidisciplinary study group collected data of ONJ cases in patients receiving Bisphosphonates (BP) due to metastatic bone disease in oncology and hematology centers of a regional network, and followed in the main dental care and maxillofacial surgery centers of the area. By December 2008, 221 cases were registered (Fusco et al, ISRN Oncology 2013); the number of new ONJ cases per year in cancer and myeloma patients increased since 2004 until 2006 and then reduced (till to 21 cases on 2008). Several possible reasons of this “up and down” trend (shift from pamidronate to zoledronic acid; increase of ONJ awareness; diffusion of preventive dental measures; late modifications of BP prescriptions) were hypothesized.

In recent years, literature data showed increasing numbers of ONJ cases after denosu- mab or after other drugs (bevacizumab, suitinib, etc), so that the new term Medication Related – ONJ (MRONJ) was introduced. Consequently, we decided to repeat the survey to verify the time trend in advanced cancer and myeloma patients.

Patients and methods: We asked for new ONJ cases observed between January 2009 and March 2016. We identified cases after cross-checking reports from medical oncol- ogy, haematology, and oral care centers to avoid double count.

Results: We received partial data about 335 cancer patients: 72% were female and 28% male; primary neoplasm was breast cancer 151 (46%), myeloma 78 (23%), prostate cancer 42 (13%), lung 17 (5%), renal cell 11 (3%), and other types of cancer or not specified 34 (10%). The median number of new cases per year was 39 (range 30-49) in years 2009-2015. Local visits to collect complete data of all cases (duration and doses of therapy; concomitant treatments and diseases; oral health risk factors) are ongoing.

Conclusions: Preliminary data show an unexpected increase of new ONJ cases per year, in spite of measures prescribed to reduce the ONJ risk (dental visit and oral care before antiresorptive treatment). Possible recommendations include: introduction of antiresorptive treatment in bone metastatic patients; larger use of biological agents potentially inducing ONJ; longer survival of some subsets of cancer patients (eg, lung and renal cell cancer, etc.); higher risk from antineoplastic plus antiangiogenics drugs.

The collection of full clinical data is warranted to explore these suggestions.

The tailored nutritional counseling in early cancer patients

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Background: The benefits of a nutritional support in patients diagnosed with meta-static cancer is well recognized. Evidences suggest that nutritional care should be an integrated part of the global oncology care of the patients, especially during chemother-apy administration. Therefore, the aim of the current study was to examine the unique impact of a tailored nutritional counseling on patients during adjuvant or neo-adjuvant chemotherapy.

Methods: Patients diagnosed with early stages cancer were included before starting adjuvant or neo-adjuvant treatment. After obtaining the patients informed consent, they obtained anthropo-metric parameters (see Table) at baseline (T0) nutritional visit. A personalized diet prescription was delivered and patient revaulation at 3 weeks (T1), 3 months (T2) and 6 months (T3), was scheduled. Data were analyzed by non-parametric statistical analysis by applying Student’s test (for paired data) with a SPSS 15.0 software.
Results: Within a six-month period, 10 patients (7 women and 3 men; mean age 61.5 ± 10.3 years) followed at the Medical Oncology Unit of the Tor Vergata Clinical Center, were considered eligible for the present study. Statistically significant improvement of strength (F), resistance, muscle mass (MM), left arm circumference (AC), phase angle, control of symptoms (nausea and dysphagia); Functional Assessment of Chronic Illness Therapy Trial Outcome Index (FACT-T-TOI); Functional Assessment of Anorexia/Cachexia Therapy (FAACT) and Quality of Life (QoL) (EORTC scale) were reported (see Table).

Conclusion: This study provides suggestive evidence of a favorable effect of a tailored mind-body counseling during chemotherapy.

Acknowledgement: this study was carried out within the PhD program in Experimental Medicine and Systems (XXIX cycle, Medical Oncology Course).

Table: S8

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*statistically significant; FFM: fat free mass

S8 Sunitinib, hypertension and renal function: a monocentric experience

G.P. Dognini, F. Petelli, M. Destro, M. Ghidini, K. Borgonovo, M. Cabiddu, S. Lencioni

Background: sunitinib and other antiangiogenetics (AAG) have been shown to sigificantly increase blood pressure (BP). AAG-related hypertension (AAG-HTN) may be a new diagnosis of HTN because of uncontrolled BP. Importantly, a new diagnosis of HTN before sunitinib treatment among patients with solid and hematologic malignancies was reported (see Table).

Methods: This retrospective study was carried out in an Italian oncology center, in a cohort of patients treated with sunitinib and other antiangiogenetics (AAG) (considered as the threshold dose) irrespectively of primary cancer site or treatment line, undergoing to regular cardiovascular monitoring by echocardiography and without any evidence of cardiac toxicity. All pts but 3 underwent radical nephrectomy, 2 pts had also colorectal adenocarcinoma. All pts but 3 underwent radical nephrectomy, 2 pts had also colorectal adenocarcinoma. All pts but 3 underwent radical nephrectomy, 2 pts had also colorectal adenocarcinoma. All pts but 3 underwent radical nephrectomy, 2 pts had also colorectal adenocarcinoma.

Results: From 10/2016 to 4/2017, 79 pts asked for mind-body programs. Males(M) 8/79 were diagnosed with HTN before sunitinib introduction (20%). A part of cancer patients (pts) ask for IO. We assess their basal traits to support can guide IO organizations.

Conclusions: The high rate of HTN diagnosed before sunitinib introduction (20%) and that of AAG-HTN (70%) suggest the crucial role of a careful multidisciplinary basal evaluation of pts. Renal function should be carefully monitored, but in most of pts e-GFR is stable or even improved. These results suggest that sunitinib and RAAS inhibitors may be used safely, thus resulting in a better management and outcome of pts.
Peripheral neuropathy is one of the main side effects of chemotherapy, especially taxane-based, greatly impairing patients’ quality of life and often leading to dose delay, dose reduction or treatment discontinuation. Incidence of CIPN is 1-12%. Taxanes may induce sensory neuropathy with paresthesia and neuralgia, as they cause blockage of axonal microtubules and peripheral demyelination. Anaplus HP is a dietary supplement based on L-acetylcarnitine, N-acetyl-L-cysteine, inositol and α-lipoic acid, used to prevent and treat CIPN. This study was to evaluate the role of Anaplus HP in prevention of CIPN in patients affected by breast cancer treated with taxane-based adjuvant chemotherapy.

Patients and Methods: Since September 2015 to January 2016, we administered 2 capsules per day of Anaplus HP to 25 patients affected by breast cancer treated with taxane-based adjuvant chemotherapy. Average age of enrolled patients was 60 ys (range 39-75 ys). 16 patients were undergone to 4 cycles of EC chemotherapy, followed by 12 weekly cycles of paclitaxel; the remaining 9 patients were undergone to 3 cycles of FEC chemotherapy, followed by 3 cycles of docetaxel, administered every three weeks. The 12 Her-2+ tumors were also treated with trastuzumab for one year. We evaluated incidence and severity of CIPN by administering patients the EORTC-QLQ-CIPN20 survey at the beginning of taxane treatment, after each cycle of chemotherapy with docetaxel or after each cycle of three paclitaxel weekly doses, and finally three and six months after the end of taxane treatment. Neurotoxicity was recorded according to CTC-NCI 3.0.

Results: 3 patients (12%) treated with weekly paclitaxel showed G1-G2 paresthesia of the lower limbs. Paresthesia appeared between eighth and eleventh cycle of paclitaxel, resulting in no delays, no dose reductions, no additional therapies required and disappeared within three months after the end of chemotherapy. The remaining 22 patients (88%) didn’t exhibit the typical symptoms of taxane-induced peripheral neuropathy (pain, numbness, paresthesia).

Conclusions: Although enrolled patients are few, our experience highlighted the efficacy of Anaplus HP as prophylaxis of taxane-induced peripheral neuropathy in patients undergone to adjuvant chemotherapy for breast cancer. Because of small sample size and the absence of a control arm further randomized studies are needed to better assess the impact of Anaplus HP on CIPN.

Micetrin has proven to help traditional supportive care in the prevention of side-effects of adjuvant chemotherapy in breast cancer, especially nausea and fatigue.

Background: Chemotherapy of neoplastic disease often causes many side effects. Among these, we should consider fatigue and nausea that, thanks to the new antiemetic therapies, rarely results in vomiting. A high incidence of fatigue and nausea is observed among patients affected by breast cancer treated with anthracycline-, taxane- and alkylating-based adjuvant chemotherapy. Micetrin is a nutritional supplement consisting of fungi (Lentinula edodes, Ganoderma lucidum, Grifola frondosa), C vitamin, magnesium bisglycinate and superoxide dismutase, which can be used to mitigate the side effects of adjuvant chemotherapy in breast cancer, due to its antioxidant and immunomodulatory properties. This study was to evaluate the role of Micetrin in the prevention of nausea and fatigue in patients affected by breast cancer treated with adjuvant chemotherapy.

Patients and Methods: Since February 2015 to April 2016, we enrolled 30 patients with stage II and III breast cancer treated with adjuvant chemotherapy. They received 4 cycles of EC chemotherapy every 21 days, followed by 12 weekly cycles of paclitaxel. Patients with Her-2 + breast cancer were treated with trastuzumab. We administered Micetrin (1 sachet per day) to 15 patients from 2 days before the beginning of adjuvant chemotherapy until a month after last dose of chemotherapy. The remaining 15 patients received only supportive care. To evaluate nausea and fatigue, we administered enrolled patients EORTC-QLQ-C30 survey (Version 3.0) at the beginning, during (after three months) and at the end of adjuvant chemotherapy. Nausea and fatigue were assessed according to the criteria CTACE (version 4.0).

Results: Average age of the patients enrolled in Micetrin arm was 55 years (33-72), in the control arm was 51 years (32-70). Nausea was less frequent in Micetrin than control arm (fatigue G1 47% vs 33%, fatigue G2 33% vs 60%). Micetrin was well tolerated with no significant side effects.

Conclusions: Micetrin has proven to be able to help traditional supportive care in the prevention of side-effects of adjuvant chemotherapy in breast cancer, especially nausea and fatigue.
**T1** Thrombin generation (TG) and D-dimer levels for the identification of cancer patients at higher VTE risk enrolled in the HYPERCAN study


**Background:** Identification of cancer outpatients who might benefit from primary thromboprophylaxis is still actually a major challenge for cancer patient management. A promising approach is the stratification of patients according to their risk of thromboembolic risk assessment models that include clinical parameters and biomarkers. Aim of this study is to assess whether in a cohort of newly diagnosed metastatic non-small cell lung, gastric, colorectal and breast cancer patients, enrolled in the ongoing HYPERCAN study (Thromb. Res. 2014), the measurement thrombin generation assay (TG) and D-dimer, may be predictive of VTE and may help physician in the better treatment of cancer patients.

**Methods:** As of September 2016, overall 739 patients with metastatic cancer have been enrolled. Blood samples of patients are collected at enrollment (before starting chemotherapy treatment) after 3 and 6 chemotherapy cycles, and at end of treatment or earlier if VTE occurrence or cancer disease progression. We measured TG, fibrinogen, and D-dimer at enrollment from the first 433 patients (NSCLC—50.1%, gastric—11.5%, colorectal—20.6%, breast—17.8%). TG was measured by the Calibrated automated thrombogram (CAT assay, STAGO, France) at 1PM TF and results expressed as Peak of thrombin; fibrinogen and D-dimer were measured by commercial assays (Q.E.A. thromb; D-dimer HK, Werfen, Italy).

**Results:** In our group of patients, VTE incidence is 25%. At enrollment, patients have Peak, fibrinogen and D-Dimer levels significantly greater than that of healthy subjects (p < 0.01). Pre-chemotherapy levels of D-dimer > 493 ng/ml or Peak > 407 nm are associated with increased VTE rates (p < 0.05). Differently, fibrinogen levels are not associated with an increased VTE risk. Khorana score fails to identify HYPERCAN patients at higher risk of VTE. We tried to modify the Khorana score adding D-dimer and Peak, assigning 1 point to each biomarker over the cut-off value. Integration of the Khorana score with these biomarkers allowed us to identify those patients at higher VTE risk.

**Conclusions:** This study supports the hypothesis that measurement of plasma coagulation markers can improve the identification of cancer subjects at high VTE risk. These subjects may probably be best candidate for primary thromboprophylaxis.

Project funded by AIRC “StMILLE” n. 12237 grant from the “Italian Association for Cancer Research ( AIRC)”.

**T2** Thrombin generation for prediction of early cancer recurrence in breast cancer patients undergoing post-surgical adjuvant therapy: data from the prospective HYPERCAN study


**Background:** Screening for breast cancer has greatly increased early diagnoses, leading to anticipated cancer treatments by surgery and systemic adjuvant chemotherapy (SAC) and reducing the risk of disease recurrence (DR). However, local relapses and distant metastasis may occur in 2-7% and 20% of resected patients, respectively, in the 10 years following surgery. In this setting, the identification of high-risk patients who might most benefit from more aggressive therapy is fundamental. Aim of this study is to evaluate whether some hematostatic biomarkers may be prognostic of early (first two years) disease recurrence (EDR) in a group of breast cancer patients undergoing post-surgical SAC.

**Methods:** Plasma samples from 690 limited-resected breast cancer patients (10M/ 680F), enrolled in the Italian, prospective, multicenter HYPERCAN study, were obtained at enrollment before starting SAC and after 1, and 2 years follow-up. Samples were tested for fibrinogen, D-dimer, and thrombin generation (TG). Clinical data and information regarding surgery, cancer subtype, and treatment were recorded. DR was routinely monitored by imaging during post-treatment surveillance.

**Results:** At enrollment, fibrinogen levels were in the normal range (316±87 mg/dl), while D-dimer and endogenous thrombin potential (ETP) were increased (respectively 257±353 ng/ml and 1680±377 nM·min) compared to a control group of healthy subjects. During follow-up, D-dimer significantly diminished over time, while no modifications occurred in the other biomarkers. After 2 years follow-up, 5.7% of patients presented with EDR. Kaplan-Meier analysis revealed that an ETP value ≥1670 nM·min at enrollment was an independent risk factor for EDR (HR = 3.65; 95% CI 1.60-8.34; p < 0.01). Differently, EDR was not associated with fibrinogen and D-dimer levels. A risk assessment score for the identification of breast cancer patients at higher risk of EDR has been created using ETP, hemoglobin level and triple negative subtype variables, that were found to be independent risk factor of EDR in multivariate analysis.

**Conclusions:** We showed, for the first time, the prognostic significance of measuring pre-chemotherapy TG levels on the risk of EDR in resected breast cancer patients. After a proper validation, this biomarker could be a candidate to tailor a risk-adapted adjuvant treatment.

Project funded by AIRC “StMILLE” n. 12237 grant from the “Italian Association for Cancer Research ( AIRC)”.

**T3** Increased frequency of acute reactions to iodinated contrast media after anti-CTLA-4 immunomodulating antibodies in cancer patients


**Background:** The aim of this study was to investigate whether cancer immunotherapy, in particular with immune checkpoint inhibitors, increased the incidence of allergy-like immediate adverse reactions to iodinated contrast media (ICM) with respect to “standard” cancer chemotherapy or targeted therapy.

**Methods:** We retrospectively evaluated the incidence of contrast-enhanced computed tomography (CECT)-related immediate adverse reactions (ARs) in cancer patients undergoing treatment. Using an institutional radiological database (Elefantia, Agfa), we identified all consecutive cancer patients who performed at least one CECT after starting any medical cancer treatment at our institute between January 1, 2006 and December 31, 2014. All patients were outpatients and with a performance status of 0-1 by ECOG scale. Each ICM-related AR was classified according to the American College of Radiology Manual on Contrast Media, version 10.1 as “allergy-like” or “physiologic” and graded as mild, moderate, or severe.

**Results:** The final database included 3,521 patients who underwent first- or second-line systemic treatment for metastatic disease and were re-evaluated at the end of treatment with CECT. Fifty-nine of the 3521 patients received ipilimumab (Ipi), 75 received cytotox- kines (Cy), and the remaining 3,387 received non-immunologic agents (CHT). The mean number of CT scans performed before the index CT scan did not significantly differ between groups (p = 0.190). Overall, 71 (2%) patients developed ICM-ARs. The distribution of events among the groups was: 11.9% of reactions in Ipi patients (7/59), 5.3% in t(4/75), and 1.8% in the CHT ones (603/3.878) with a p = 0.001 that indicates a significant statistically difference between treatment groups and reactions number.

All the ARs registered in the Ipi and Cy groups were allergy-like reactions, while 10% of the ARs observed in the CHT group were of the physiologic type (6/66).

**Conclusions:** Our data show that immunomodulating cancer treatments, Ipi in particular, considerably increase the risk of developing CECT-related immediate adverse reactions with respect to non-immunologic agents. Although these findings now need to be validated in larger prospective studies, they serve as a “wake-up call” to radiologists to closely monitor patients who have previously received cancer immunotherapy with anti-CTLA-4 antibodies when using ICM in order to reduce the risk of potentially severe immediate adverse reactions.
However, the national collective health contracts allow the employment of these professionals only through atypical contracts that, due to “jobs act”, will soon be banned, causing a large professional vacuum. Before the deadline extension granted by the Government, we decided to map how much the problem was widespread among the CRGs.

Methods: In November 2016 an anonymous web survey has been addressed to CRGs from Gruppo Italiano Datamanager. The survey, preceded by a brief written description of the aims, was composed by 7 items focused on the problem of the imminent expiration of contracts.

Results: 231 CRGs completed the survey, with a prevalence of participants from Emilia (32%), Lombardia (24%), Piemonte (19%) and Veneto (10%). The majority of respondents (78%) worked through an atypical contract, while few can count on more stable type of employment (7.4% fixed term contract and 14.6% open-ended one). The most virtuous region is Emilia Romagna (37.5%) of the open-ended contracts, followed by Piemonte (21.9%) and Lombardia (18.8%). The 67.5% of respondents will be affected by the jobs act problem, with multiple contract expiration timing: 32% from January to April 2017; 23% from May to August 2017; 23% from September to December 2017; 17.3% from Jan 18; 4.7% unknown. Interestingly, about 50 CRGs were unwilling to participate in the survey, now demoralized from the age-issue of the lack of professional recognition.

Conclusions: The recent extension granted by our Government has only postponed a problem that should be quickly resolved. Where a such large number of CRGs will remain unfilled, it would create a vacuum of skilled work force that can hardly be covered by physicians. Whereas these numbers are understated and the problem also affects another big ghost of clinical research (research nurses), in the absence of a permanent solution, Italy is unlikely to meet the quality standards imposed by Europe. This will be reflected in a loss of appealing to the pharmaceutical market but mostly in a slump of therapeutic options for patients.

The pre-emptive screening of multiple polymorphisms in gene-encoding dihydroxyprymidine dehydrogenase (DPD) improve prevention of toxicity on patients candidate for fluoropyrimidines based-chemotherapy. 

A. Damato,1 C. Bonelli,1 C. Romagnani,2 M. Banzi,1 D. Nicoletti,1 E. Farnetti,2 B. Casali,2 C. Pinto2

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Background: Fluorouracil is one of the most used anti-tumor chemotherapeutic agents in oncology and dihydroxypyrimidine dehydrogenase (DPD) plays a key role in the metabolism of this drug. In patients with DPD deficiency the use of standard dose of fluorouracil can produce life-threatening toxicities. Deletious polymorphisms in gene-encoding DPD (DPYD) may result in the severe reduction of DPD enzymatic activity. DPYD*2A (IVS14 + 1G > A) is the most common single-nucleotide polymorphism (SNP) associated with critical DPD deficiency. At present, most of the evidence supports screening for at least 3 SNPs (DPYD*2A, c.2846 A > T, c.1679T > G). The aim of this study is to confirm that the detection of additional polymorphisms of DPYD could enhance prevention of fluoropyrimidine toxicity.

Methods: In 2011, we began to screen DPYD*2A in patients candidate for fluoropyrimidine based-chemotherapy. As the first step of the evaluation, we selected all cases of DPYD*2A wild type, from 2011 to 2013, who developed CTC-NCI-V.3 toxicity (grade 3 or 4). In these patients, we researched the other 3 SNPs (c.2846 A > T, c.1679T > G, c.2194G > A). Mutational status was analysed with real Time PCR.

Results: From 2011 to 2016 we pre-emptively screened DPD deficiency in 1,863 patients. Thirty two subjects (1.6%) were carriers of the DPYD*2A mutation. As the first step of the evaluation, 917 subjects were assessed from 2011 to 2013. Of these 917 wild type cases, 127 presented toxicities > G3. In this subgroup, 24 patients (19%) proved to be mutated for the other SNPs of DPYD, p <.0001. The results are expected to be clarified further in the second step, which is ongoing.

Table T5

<table>
<thead>
<tr>
<th>SNPs</th>
<th>No. of pts</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>c.2846 A &gt; T</td>
<td>1</td>
<td>0.79</td>
</tr>
<tr>
<td>c.1679T &gt; G</td>
<td>2</td>
<td>1.57</td>
</tr>
<tr>
<td>c.2194G &gt; A</td>
<td>21</td>
<td>16.53</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>24</td>
<td>18.89</td>
</tr>
</tbody>
</table>

Conclusions: Preliminary data show that in 24 (19%) of 127 patients who presented severe toxicity which was not correlated with DPYD*2A, we found other polymorphisms of gene encoding DPD. Out of the 3 SNPs evaluated, c.2194 G > A proved to be the most frequent, although it is the polymorphism that is least known and least studied. Such results suggest that the evaluation of additional polymorphisms could enhance the prevention of fluoropyrimidines toxicity. The results are expected to be clarified further in the second step, which is ongoing.

Table 16

<table>
<thead>
<tr>
<th></th>
<th>Strongly disagree %</th>
<th>Slightly agree %</th>
<th>Moderately agree %</th>
<th>Strongly agree %</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>before</td>
<td>after</td>
<td>before</td>
<td>after</td>
<td></td>
</tr>
<tr>
<td>I clearly know the difference between alternative and complementary medicine</td>
<td>24.1</td>
<td>5.3</td>
<td>27.6</td>
<td>4.4</td>
<td>33.9</td>
</tr>
<tr>
<td>Alternative medicine is a valid alternative to conventional medicine</td>
<td>34.5</td>
<td>67.2</td>
<td>41.6</td>
<td>26.5</td>
<td>20.35</td>
</tr>
<tr>
<td>Even if alternative medicine does not work, it does not do damage</td>
<td>25.9</td>
<td>63.3</td>
<td>35.7</td>
<td>25.9</td>
<td>29.4</td>
</tr>
<tr>
<td>Alternative medicine can be dangerous</td>
<td>10.2</td>
<td>3.4</td>
<td>17.6</td>
<td>5.6</td>
<td>51.8</td>
</tr>
<tr>
<td>Use of alternative medicine can hinder a correct therapeutic path</td>
<td>10.6</td>
<td>1.8</td>
<td>25.7</td>
<td>4.4</td>
<td>38.9</td>
</tr>
<tr>
<td>I would do or I do use CAM</td>
<td>28.8</td>
<td>52.9</td>
<td>27.9</td>
<td>19.2</td>
<td>28.8</td>
</tr>
</tbody>
</table>

Conclusions: Final results from CAMEO-PRO study: complementary and alternative medicine in oncology, physicians inform oncological patients

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Background: The role of Complementary and Alternative Medicine (CAM) in oncology is heavily debated. It is estimated that about half of cancer patients use at least one form of CAM in their life but there is a strong unwillingness of patients in talking about CAM with their oncologist. Primary aim of this study was to inform patients about CAM, focusing on their supposed benefits, toxicities and interactions with conventional therapeutic agents. The study also explored patient’s perception about CAM and ascertained the level of CAM its use among cancer patients of an Italian academic hospital.

Methods: From April 2016 to April 2017, the observational pilot trial “CAMEO-PRO” prospectively enrolled 239 cancer patients that were invited to attend a tutorial about CAM at the Department of oncology, University Hospital of Udine, Italy. Before and after the informative session, patients were asked to fill a questionnaire reporting their knowledge and opinion about CAM.

Results: Overall, 163 (70%) women and 70 (30%) men were enrolled. Median age was 61 years. At study entry, 168 (72%) patients declared they had never been interested to the topic previously; 24 patients (11%) revealed the use of a type of alternative therapy and 58 (28%) revealed the use of complementary therapy. In total, 139 (55.2%) patients attended the informative session. Table 1 shows the percentage of response and the opinion’s change about CAM before and after the tutorial. All patients that participate to the session reported that the session was moderately (16%) or very (83%) helpful.
Informative sessions seem to have an impact on patients’ perceptions and opinions about CAM.

**Economic burden of cancer: a population-based cost analysis**

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**Background:** Cancer poses a substantial economic burden on health care systems. Cost-of-illness analysis allows for a comprehensive estimation of the costs of cancer care and for the identification of relative costs of specific subgroups of diseases, informing future decisions for governmental budgets allocation.

**Methods:** We ran a population-based cost analysis in the Forli-Cesena province (396,696 inhabitants) in 2016, using a government perspective (direct health care resources only). We considered 6 subgroups of cancers, using the International Classification of Diseases, 10th rev.: hematologic, gastrointestinal, breast, urogenitological, thoracic, rare tumours and others. We included five categories of services: inpatient, outpatient, emergency, and end-of-life care, drugs. We used National and Regional official charges for the valuation of care settings. For drugs, we used the national pharmaceutical formulary by AIFA. We estimated per capita (PC) cost by dividing the total cost for cancer subgroup for the total number of residents in the Forli-Cesena Province.

**Results:** Total costs equaled to more than 98 million euro. Among cancers subgroups, hematologic absorbed the largest share (28%, 70.6 PC costs), followed by gastrointestinal (20%, 49.6 PC costs). Thoracic accounted for 12% of total costs, but per patient costs were the highest (€99349). Lowest per patient costs were in breast. Cost absorption is uneven referring to health care services, too: eg. gastrointestinal cancer absorbs about 30% of total inpatient care cost compared to only 8% for breast, which however accounts for 30% of total outpatient care whereas thoracic only 8%.

**Conclusions:** Our analysis sets the basis for better understanding total costs in cancer care and resource allocation among cancer subgroups and care settings. Benchmarking is feasible for the use of administrative databases.

**Table T7**

<table>
<thead>
<tr>
<th>Type</th>
<th>ALL</th>
<th>Hematology</th>
<th>Breast</th>
<th>Gastrointest</th>
<th>Uro-Gyn</th>
<th>Thoracic</th>
<th>Rare, Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>11,931</td>
<td>4,388</td>
<td>2,759</td>
<td>1,849</td>
<td>1,457</td>
<td>600</td>
<td>877</td>
</tr>
<tr>
<td>In-pat. Care*</td>
<td>34,107</td>
<td>8,341</td>
<td>2,721</td>
<td>10,142</td>
<td>5,604</td>
<td>3,901</td>
<td>3,395</td>
</tr>
<tr>
<td>Drugs*</td>
<td>26,864</td>
<td>10,624</td>
<td>5,496</td>
<td>2,444</td>
<td>3,238</td>
<td>2,753</td>
<td>2,308</td>
</tr>
<tr>
<td>Out-pat. Care*</td>
<td>17,889</td>
<td>3,955</td>
<td>5,381</td>
<td>2,623</td>
<td>2,578</td>
<td>1,672</td>
<td>1,677</td>
</tr>
<tr>
<td>End-of-life care*</td>
<td>18,722</td>
<td>4,802</td>
<td>1,707</td>
<td>4,328</td>
<td>2,407</td>
<td>3,220</td>
<td>2,257</td>
</tr>
<tr>
<td>Emer-G. Care*</td>
<td>764</td>
<td>286</td>
<td>98</td>
<td>153</td>
<td>91</td>
<td>69</td>
<td>64</td>
</tr>
<tr>
<td>Total (€)*</td>
<td>98,348</td>
<td>28,010</td>
<td>15,404</td>
<td>19,692</td>
<td>13,920</td>
<td>11,617</td>
<td>9,702</td>
</tr>
<tr>
<td>Resident Popul. 396,696</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Per Capita Costs</td>
<td>€2,27,9</td>
<td>€70,6</td>
<td>€38,8</td>
<td>€49,6</td>
<td>€35,1</td>
<td>€29,3</td>
<td>€24,5</td>
</tr>
<tr>
<td>%</td>
<td>100%</td>
<td>28%</td>
<td>16%</td>
<td>20%</td>
<td>14%</td>
<td>12%</td>
<td>10%</td>
</tr>
<tr>
<td>PER PATIENT COSTS</td>
<td>€8,243</td>
<td>€6,383</td>
<td>€5,583</td>
<td>€10,650</td>
<td>€9,553</td>
<td>€19,349</td>
<td>€11,067</td>
</tr>
</tbody>
</table>

(*) Costs in thousands of €
Osteonecrosis of jaw (ONJ) after antiresorptive treatment (bisphosphonates, denosumab) of cancer-treatment induced bone loss (CTIBL): a negligible risk?

A. Gambino1, M. Cabrera1, V. Fusco1, O. Bertetto1, D. Martino1, M. Alessia2, G. Numico2

1Dental School, Turin; 2Azienda Ospedaliero di Alessandria, Alessandria; 3Rette Oncologica Piemonte- VdA, Turin; Centro Documentazione Osteonecrosi, Alessandria

Background: CTIBL is a concern for breast and prostate cancer patients (pts). Treatments proposed for prevention and/or treatment of CTIBL include: oral alendronate (70 mg/week); oral risedronate (35 mg/week); iv ibandronate (3 mg/ q/month); oral ibandronate (150 mg monthly); ibandronate iv (4 mg q/months); yearly iv zoledronic acid (5 mg qI2months); sc denosumab (60 mg qmonths). All these agents showed possible induction of ONJ, described by some Authors as “rare” (1/1,000-1/10,000, according to WHO) or “very rare” (<1/100,000). Actually, evaluations about the individual ONJ risk are uncertain, due to bias in old trials (unknown ONJ, short-term follow-up, etc) and in recent trials (very restricted ONJ definition; limited follow up time). Vice versa, real life ONJ cases after bisphosphonate (BP) and/or denosumab treatment in osteoporosis pts are not so rare (even if probably underdiagnosed), exceeding the ONJ cases in metastatic cancer pts in some countries (eg, Korea). Since 2005 a multidisciplinary study group collected data of cases of ONJ in pts treated with BP in oncology and hematology centers of a regional network (Piemonte – Valle d’Aosta), and among pts followed in the main dental care and maxillofacial surgery centers of the area. Between 2004 and December 2008, out of 241 total ONJ cases (203 out of 239 non EU citizens), 70% were 1st cycle. 28% had ONJ diagnosis after BP therapy of bone disease different from bone metastases or myeloma (ie, osteoporosis, osteopenia, Rheumatoid Arthritis, Paget’s disease, etc) (Fusco et al, ISRN Oncology 2013).

Patients and methods: The survey was repeated, asking for ONJ cases observed between January 2009 and March 2016. We identified cases after cross-checking reports from medical oncology, haematology, and oral care centers to avoid double count and to integrate data.

Results: We received partial data about 440 cases: 335 advanced cancer pts (76%) and 105 pts treated for other diseases (24%). The median number of cases per year was clearly increased in years 2009-2015, especially in osteoporosis patients. Local visits to collect complete data of all cases (duration and doses of therapy; concomitant treatments and diseases; oral health risk factors) are ongoing.

Conclusion: Preliminary data show increase of ONJ cases in pts receiving BP or denosumab for osteoporosis. The cancer patients receiving antiresorptive drugs to treat or prevent CTIBL need oral care measures to reduce the ONJ risk.

Safety and metabolic effects of the fasting mimicking diet (FMD) in cancer patients

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1 Fondazione IRCCS Istituto Nazionale dei Tumori, Milan; 2Istituto FRC di Oncologia Molecolare (IFOM), Milan

Background: Preclinical studies have shown that a plant-based, low-calorie, low-protein, low-carbohydrate diet, also known as fasting mimicking diet (FMD), modifies systemic metabolism and displays significant antitumor effects. Nonetheless, no clinical data are available yet. In this study, we explored the safety and metabolic effects of the FMD in cancer pts.

Methods: We prospectively evaluated cancer pts who followed a 5-days FMD (700 kcal on day 1 and 800 kcal on days 2-5) every 21-28 days. Inclusion criteria were: pts with any cancer type (except for small cell lung cancer), stage and concomitant antitumor therapy. Main exclusion criteria were: BMI <20 kg/m², recent unintentional weight loss >5%, insulin dependent diabetes and severe comorbidities.. Before and at the end of the FMD, we collected blood and urine samples to measure changes in metabolites and growth factors. We show data of FMD safety and metabolic effects at the end of the first cycle.

Results: We recruited 29 pts from November 2016 to April 2017, 20 had metastatic disease, and 27 received concomitant anticancer treatment. Breast (12), lung (3), prostate (3) and pancreatic (3) cancer were the most represented tumors. All pts completed at least one cycle of FMD. Based on the analysis of diet diaries, compliance to the diet was good, with only minor deviations (±10%) in the quantitative intake of permitted aliments. 79% of pts reported G1-G2 AEs, in particular fatigue (72%) and headache (10%), more likely to be related to the diet. One patient experienced G2 symptomatic hypoglycemia that required sucrose intake; No G3-G4 toxicities were observed. Relative weight loss during the first cycle was 4.65% (range 2.5-6.5%). The FMD reduced median glycemia by 15.6%, IGF-1 blood levels by 27% and insulin levels by 32%, while median triglyceride, total cholesterol and uric acid levels increased by 31.5%, 11% and 80%, respectively; finally, we observed an increase of average urine ketone body levels from 0.38 mg/dl (range 0-10) to 62 mg/dl (range 20-100).

Conclusions: Our interim analysis suggests that the proposed FMD scheme is safe and significantly modifies systemic metabolism in a heterogeneous population of cancer pts.

The impact of social factors on oncology: The Experience of the Reggio Emilia Clinical Cancer Center

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Background: After treatment for the acute phase of the disease, patients (depending on clinical condition) can be transferred to other sub-acute wards, discharged to home or released to local care facilities. This process is frequently hampered by social problems. The aim of this study is to highlight non-clinical factors that reduce the capability of the oncology wards.

Methods: We analyzed 265 hospital discharge records in our department. We assessed nationality, age, diagnosis, causes of admission, length of hospital stay and reasons for delayed discharge, if any.

Results: From October 2016 to April 2017, we observed 265 hospitalizations for a total of 2665 days of stay and a median of 10.07d. 139(90%) were EU citizens and 26(10%)-non-EU. Of these, 171(65%) were useful for initiating or continuing active oncological treatment, 33(12%) for managing toxicity during cancer therapy, 33(12%) for dealing with clinical deterioration and 28(11%) for performing diagnostic tests. In 31 cases(12%), we observed delayed discharge resulting in an average increase in stay of 7.35d. This translated into a median prolongation of 0.94d for all hospitalizations, corresponding to a total of 228(9%) for non-clinical needs. The average length of stay of non-EU citizens was 11.4d, while that of EU nationals was 9.5d. The average delay in discharge was greater for non-EU citizens (2.5d) than for those in the EU(0.5d). The delays were caused by waiting for relocation to local care facilities(LCF 34%), inadequate support of caregivers(ISC 31%) virtually all due to the lack of a suitable home), waiting for home medical devices(HMD 22%) and transfer to other departments (13%).

Conclusions: The above analysis revealed an acute care that is burdened by social problems, the complexity of providing external care to patients and the impact of these factors on the cost effectiveness of health care, especially for non-EU patients. The data suggests the need to strengthen assistance on the local level and to identify caregivers and possible assistance-related social difficulties as early as possible.

Table T12

<table>
<thead>
<tr>
<th>Total days of hospitalization</th>
<th>2665</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age(9)</td>
<td>60(22-88)</td>
</tr>
<tr>
<td>Nationality(%)</td>
<td>239 EU(90)</td>
</tr>
<tr>
<td>Major non-EU nationalities(%)</td>
<td>26 non-EU(10)</td>
</tr>
<tr>
<td>Most frequent diagnoses(%)</td>
<td>Ukraine(27)</td>
</tr>
<tr>
<td>Soft tissue sarcomas(14)</td>
<td>Ghana(19)</td>
</tr>
<tr>
<td>colorectal(11)</td>
<td>Morocco(15)</td>
</tr>
<tr>
<td>Breast(10)</td>
<td>Georgia(12)</td>
</tr>
<tr>
<td>Average length of all hospitalizations(d)</td>
<td>10.1(EU:9.9-non-EU:11.4)</td>
</tr>
<tr>
<td>Average delay in discharge(d)</td>
<td>0.9(EU:0.7-non-EU:2.5)</td>
</tr>
<tr>
<td>Total days for non-clinical needs</td>
<td>228</td>
</tr>
<tr>
<td>Average waiting time(d)</td>
<td>LCF(7)</td>
</tr>
<tr>
<td>HMD(6)</td>
<td>ISC(9)</td>
</tr>
</tbody>
</table>

Blood stream infection in cancer patients—device management and epidemiology: the BSIDE study

F. Cortella1, D. Basile1, I. Genesta1, M. Bonotto1, E. Ongaro1, S.K. Gnetto1, V. Fanetto1, M. Cattaneo1, V.I. Andreotti1, A. Pannaforte1, R. Cocco1, D. Pecor1, G.G. Cardi1, M. Casagrande1, P. Ermacotta1, M. Giovannoni1, D. Iacono1, F. Puglisi1, A. Aprile1, N. Pella1, G. Pasola1

1Department of Oncology, University Hospital of Udine, Italy; 2Department of Medicine, University of Udine, Italy; 3Clinical Management staff, University Hospital of Udine, Italy; 4Department of Infectious Diseases, University Hospital of Udine, Italy; 5Department of Clinical Management, University Hospital of Udine, Italy; 6Department of Infectious Diseases, University Hospital of Udine, Italy; 7Department of Oncology, University Hospital of Udine, Italy; 8Department of Oncology, University Hospital of Udine, Italy; 9Department of Infectious Diseases, University Hospital of Udine, Italy; 10Department of Oncology, San Bortolo General Hospital, Vicenza, Italy

Background: Cancer patients are at a high risk of sepsis, and infection management is a major issue in this setting.

Methods: We retrospectively analyzed 55 consecutive cancer patients diagnosed with primary blood stream infection (BSI), according to CDC/NSHN Surveillance Definitions, at University Hospital of Udine from June 2013 to December 2016.

Annals of Oncology

Volume 28 | Supplement 6 | October 2017

96 | T - Miscellaneous
Patients’ characteristics were collected at the hospital admission. Statistical descriptive analyses were performed on the whole population. Kaplan–Meier estimator and Log–Rank test were performed for survival analysis among patients with a central line (CL).

Results: The study population consisted of 52 patients (3 patients were lost on follow-up); 20 (38%) women and 32 (62%) men, median age 68 years. The most represented sites of the primary tumor were lung (21%), pancreas (17%) and stomach (13%); 85% of the patients had stage IV disease and, overall, 37 (52%) were on active anticancer treatment. ECOG PS was distributed as follows: 0 (4%), 1 (40%), 2 (52%), 3 (4%), 47 (90%) patients had a CL, 23 (44%) carried an infuse-a-port, 19 (37%) a peripherally inserted central catheter, 5 a central venous catheter. S. Epidermidis was the most frequent microorganism involved in the infection (36%), followed by S. Aureus (19%). Multi Drug Resistant pathogens represented the 23% of the microorganisms. In the 58% of the infections the antibiotic therapy was started after knowing the blood culture results, in the other cases the empiric therapy was confirmed. Nineteen (40%) patients removed the CL after the antibiotic therapy has been started, 21 (45%) retained the CL. For 7 patients the management of the device was not known. Percentage of patients alive at 36 days after diagnosis was higher in the group who had the CL removed: 17 (89%) patients vs 11 (52%) (OR: 7.1 p = 0.0078). After the resolution of the infection, considering the whole population, 19 patients (37%) received further active cancer treatment.

Conclusion: The study suggests a survival advantage for cancer patients who removed the CL after the BSI, compared with those that retained the device. Further investigations are needed to confirm these findings and contribute in improving the manage- ment of sepsis in the oncologic context.

T14 The continuing training program of oncology network of Piemonte and Valle d’Aosta: a model for improving the management of oncologic patients

M. Valade1, M. Mistrangelo1, T. Caristo1, A. Carobene1, E. Gretri1, M. Pezzin1, O. Bertetto1
1Dipartimento Rete Oncologica Piemonte e Valle d’Aosta - AOU Città della Salute e della Scienza, Turin

Background: One of the goals of Oncologic Networks is to organize training courses for operators involved in the diagnostic and therapeutic pathways of cancer patients, in order to update everyone of them about innovations introduced every year.

Methods: We yearly plan a training offer, both as residential and “on field” education, allowing to earn credits within the “continuous medical education program”. These courses have the dual purpose of technical-scientific updating and of raising relational and communicative skills.

Results: During 2017 the Oncology Network of Piemonte e Valle d’Aosta has organized 31 educational courses dedicated to medical doctors, 10 to nurses, 5 to district directors and territorial nurses, 2 to biomedical technician lab, 7 to psycho-oncologist, administrative employees and social assistants. Reguarding “on field education”, 32 courses have been conducted, characterized by 5 lessons/year and 20 CME credits: 18 for cancer-site specific groups, including 2 for hematologists, 5 for groups engaged in trasversal topics such as cardiooncology, support therapies, late toxicities, geriatric oncology and palliative care, 1 for nurses and 1 for hospital pharmacists.

Moreover, 8 study groups composed of pathologists have been formed to allow clinical cases discussions and to enhance diagnostic uniformity. 108 recommendations and 17 consensus documents have been drafted during the last 5 years, and they are entirely published on Oncology Network web site (www.reteoncologica.it). Since 2016, P.I.C. O. network has been delivering a DRS to grow up consensus.

Conclusions: Continuous medical education is an effective and basic tool to enhance operators’ knowledge. It allows to decrease mistakes and time and money waste, to improve and uniformize clinical assistance; training enables operators to acquire high innovative value information and to recognize their limits. Patients benefit by CME programs, and their negative experiences can reduce.

T15 Can the use of clinical decision support system (CDSS) affect the number of adverse drug reaction (ADR) reports in the oncological patient? A preliminary evaluation of the status quo in Reggio Emilia Oncological Center (CORE) and future perspectives

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1Medicina ad indirizzo Oncologico-azienda ospedaliera ASMn, Reggio Emilia

Introduction: The new legislation (D.M. 4/30/2015) reaffirmed the obligation to report suspected adverse drug and vaccine reactions promptly and set strict time limits within which healthcare operators are required to report to the local network and agency. An internet site (www.vigifarmaco.it) was developed (AIFA, 2015/07/16).

Objective: Monitoring of ADRs is a challenging research issue. Our belief is that there is little attention and information about this subject. We evaluate the state of reporting ADR in both oncologic and non- oncologic settings.

Methods: On 5/22/2017 we collected the data from a survey sent to 400 medical doctors in our Hospital, by email on 5/11/2017. The survey included 8 questions in language age, sex, department, number of total ADR reports in 2016, number of ADR reports due to oncological drugs in 2016, number of ADR reports due to biological oncological drugs in 2016, the kind of reactions to report on and the knowledge of www.vigifarmaco.it site.

Results: 165 doctors completed the survey (41%), of whom 39 in the oncological departments (24%); 88 female (53.2%) and 76 male (46.8%); the most represented age range was from 31 to 40 (n = 63 (41.2%); 25 (10.5%), 6-18(3.1%), 11-15(1.9%), 16-20(2.0%); >20 (0%); the number of reports/year for oncologic drugs was 0 (88.1%), 1 (5.6%), 2-5 (4.4%), 6-10 (1.9%); >10 (0%); the number of reports/year for biological oncologic drugs was 0 (93.6%);1-10(6.4%); >10(0%). No difference in the oncological or general doctors group. To the question “What kind of reactions are to be reported?” the right answer “mild and severe, known and unknown” was chosen by 38%, only “if severe” by 41.7% and only “if by 20.3%. 80.4% do not know the official site, 13.9% knows it but do not use it, only 6% knows and uses it.

Conclusion: Despite a strong commitment to awareness and information of doctors, adherence to ADRs is unacceptable; low doctors do not know the criteria for sending reports and are not up to date on new tools, created to encourage the delivery of ADRs. It is essential to develop a simple and automated tool that will enable doctors to send all ADRs report. Our next step will be to set up an instrument with this characteristics and to study its impact in clinical practice.
We conducted a retrospective analysis of 358 consecutive patients aged ≥75 years with nonmetastatic cancer who received an adjuvant treatment at Sant’Andrea Hospital in Rome and San Camillo dei Lellis Hospital in Rieti.

Results: Median age at diagnosis was 77 years. At the histological breast (65.6%) and colorectal (22.3%) cancer were the most represented ones. Comorbidities emerged in 81% of patients not resulting in a significant correlation with disease free survival (DFS) hazard ratio (HR), 1,1; 95% confidence interval [CI], 0.72-1.71; p = 0.63).

We didn’t report any association between increased age and adverse events on chemotherapy. Risk analysis for DFS showed that female gender (HR,0.53; 95% CI, 0.37-0.78; p = 0.0081) and a better performance status (PS) according to ECOG scale (PS1 vs PS0: HR,1.60; 95% CI, 1.08-2.34; p = 0.02 and PS2 vs PS0: HR, 3.31; 95% CI, 1.32-8.28; p = 0.01) had a significant lower risk for replace or death. Increased age (HR, 1.1; 95% CI, 0.77, 1.61), and colorectal (CR) cancer (HR, 2.39,95% CI, 1.58-5.39; p < 0.0001) were associated with a shorter DFS.

Conclusions: This real-life multicenter experience identified four (gender, PS, age, CR histology) prognostic factors among elderly patients who received an adjuvant treatment. Prospective trials are necessary to select and customize chemotherapy in this group of patients.

T10 Preventive dose reduction of capecitabine in elderly population

A. Gaudio1, A. Luciani1, G. Pagliani, B. Bocci1, C. Careni1, M. Volatì1, M. Blasi1, M. Narcacci1, V. Bordin1, S. Caldera1, G. Zamparelli1, S. Zonato1, G. Cassinelli1, D. Ferrari1

1ASST Sant’Paolo e Carlo – Ospedale San Paolo, Milan

Background: Nowadays life expectancy is longer than a few decades ago and entails an increase in elderly population, defined as people over the age of 65. Since old age is a well known risk factor for developing neoplasia, in the future we can expect an increase in elderly cancer patients, a different population as far as the pharmacodynamic and pharmacokinetic processes are concerned. The objective of this retrospective, mono-institutional study is to compare the efficacy and tolerability of the oral drug capecitabine among patients over 75 years compared to the reported data in literature.

Patients and methods: 117 pts older than 75 years treated with capecitabine as monotherapy (67% of patients) or in combination with other anti tumor drugs (33%) from 2006 to 2016 were evaluated. Colon, breast and stomach cancers were the most represented tumors (76%, 13% and 11% respectively). 48% were stage IV, All therapeutic regimens (adjuvant and advanced stage treatments) containing capecitabine were considered. A dose reduction of 25% of capecitabine was preventively applied at the beginning of the treatment.

Results: In this series, the median age was 80 years, ECOG PS 0-1. The median number of comorbidities was 2.8, DCR, PFS and OS were evaluated and compared to randomized trials in literature, DCR in this study was much lower (48% vs 67.2%), but PFS and OS were not different (PFS: 5 vs. 5.7 months, OS: 11 vs. 13 months). Adverse Drug Reactions (ADR) were evaluated to assess tolerability. 3% of our patients had hematological ADR (grade III) and 24% of them non-hematological ADR (including diarrhea, asthenia, mucositis of grade III). In literature ADR are much more frequently reported (13% of hematological and 43% of non-hematological ADR).

Conclusions: Capecitabine is an oral anti tumor drug largely used in a variety of diffuse cancers (colon-rectum, stomach, breast). Elderly patients, with their physiologically altered metabolism processes, represent a current and future challenge in the treatment of a part of population increasing over time. In our study we found that a preventive 25% dose reduction of capecitabine reduces ADR, but at the same time it implies a reduction in efficacy. Further prospective studies are needed to understand if this reduced efficacy is due to pharmacological alterations peculiar of the elderly patients or to the numerous associated comorbidities, and if combination therapy is safer than monotherapy in this subset of patients.
Annals of Oncology

(18 dementia/Alzheimer’s disease, 7 heart disease, 3 SLA, 1 multiple sclerosis, 1 kidney disease). In the first 4 months of 2017 47 patients, 14 (29.3%) non-oncologic (9 dementia/Alzheimer’s, 2 heart disease, 2 liver cirrhosis, 1 SLA).

Conclusions: The number of patients admitted for a terminal condition because non-oncological disease has been increasing in our hospice over the years considered to demonstrate that there is a change in palliative care with increasing sensitivity and attention to final stages of the patients regardless of their pathology. A desired and desirable change to further increase, in order to give the needed treatment in a palliative home care course or in a protected environment such as Hospice to all terminal patients. In particular the most common non-oncologic illness with a higher percentage were dementia/Alzheimer’s and heart disease. Specifically dementia/Alzheimer’s were 45.4% in 2015, 60% in 2016, 64.2%, while heart disease in 2016 was 18.2%, 23.3% in 2016.

Table T23

<table>
<thead>
<tr>
<th>ACCESS total</th>
<th>96.961</th>
<th>oncologic pts hospitalized in:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total of admission</td>
<td>15.587</td>
<td>- internal medicine</td>
</tr>
<tr>
<td>Total of oncologic patients (pts)</td>
<td>356</td>
<td>- other departments</td>
</tr>
<tr>
<td>oncologic pts resigned at home</td>
<td>30</td>
<td>- oncology total: 241</td>
</tr>
<tr>
<td>oncologic pts sent in hospice</td>
<td>11</td>
<td>males 133</td>
</tr>
<tr>
<td>oncologic pts who refuses hospitalization</td>
<td>17</td>
<td>females 108</td>
</tr>
<tr>
<td>oncologic pts who voluntarily left the emergency room</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

Reasons for Hospitalization:

| Blood Dyscrasias | 33 | Dyspnea |
| Neurological Symptoms | 34 | Cachexia |
| Pleural Effusion/Ascites | 33 | Intestinal Symptoms |
| Pain | 31 | Jaundice |
| Fever | 28 | Other |

Distribution By age group/number/pts

| 45-50 | 13 | 71-80 | 73 |
| 51-60 | 25 | 81-85 | 20 |
| 61-70 | 101 | >85 | 9 |

Conclusions: The Admission of oncologic patients to emergency care continues to be a health problem. Our survey shows: 1. Patients with potentially manageable home illness access the emergency room; 2. Need to provide adequate information to patients about the different health options (hospital, territory, home care, hospice); 3. Improve treatment procedures against pain; 4. Increase efforts for better therapeutic continuity.

T24 Nutritional counseling

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The growing scientific evidence on links between lifestyle and cancer incidence as well as the recommendations that research institutes like WCRF (World Cancer Research Fund International) and AICR (American Institute for Cancer Research) have compiled guided us in organizing an outpatient nutritional counseling for cancer patients. Nutritional counseling is done by a biologist specializing in science of nutrition and dietitian. At the first meeting we collect the medical history and lifestyle with emphasis on eating habits and of physical activity, we evaluate the BMI (Body Mass index) and waist circumference. Bearing in mind the recommendations of the WCRF and AICR we give specific guidance for:

- introduce or increase consumption of whole grains, advising preparation methods
- increased consumption of vegetables especially for those vegetables at a higher content of protective nutrients, advising the methods best suited to preserve the nutrients in the culinary preparations
- encourage a regular consumption of seasonal fruit-enter or increase consumption of vegetables as a source of vegetable protein
- insert the bluefish 1-3 times weekly
- insert the nuts according to individual requirements
- limit consumption of red meat and dairy products, avoid sausages
- limit the simple sugars and high caloric density foods
- avoid sugary drinks
- limit your intake of salt.

We recommend physical activity adapted to play regularly.

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Meetings are scheduled monthly or quarterly evaluation nutrition to make sure the objectives of change in eating habits, assessment of BMI and waist circumference. We enrolled 25 patients; the 46% have made at least one control. Patients are interested and cooperating. Among the overweight patients on 15% of controls has reduced the BMI at least of 1 point, the 90% of patients who presented to the following weight loss at 2 times a week. The food education project also foresees the organization of themed group activities to help patients to greater awareness in food choices.

**Oncogeriatic assessment of older patients with cancer in the ASL Cuneo 2**

D. Marocco1, B. Carlucci1, E. Nicola1, C. Garenpra1, M. Elisabetta1, C. Ortega1
1Ospedale, Bra

Marocco D, (a), Carlucci B, Nicola E, (b), Canavero GP, (b), Marocco E, (a), Ortega C, (a): (a) ASL Cn2, SOC di Oncologia Alba e Bra; (b) ASL Cn2, SOC di Medicina Generale Bra

**Introduction:** The number of oncologic elderly patients has increased with global aging. Close collaboration between oncologist and geriatricians becomes necessary to evaluate the health status and the residual reserves of old patient, to provide adequate approach and therapy. The G8 screening has been specifically developed and validated to screen for frailty and identifies patients who may benefit Multidimensional Geriatric Assessment (MGA). G8 consists of 8 items concerning nutritional status, body mass index, motor skills, psychological status, number of medications, and self-perception of health. The score ranges from 17 (not at all impaired) to 0 (heavily impaired). A score lower or equal to 14 requires MGA.

**Methods:** The Outpatient Oncogeriatic Service of the ASL Cn2 started in January 2017. If the G8 screening results are lower or equal to 14, the patient is sent to our Service and a MGA is carried out.

**Results:** We evaluated 25 patients (11 women and 14 males). Average age was 83 years (range 76-96). The G8 average score was 10.7; 8 patients had urololgic cancer, 7 patients had colon cancer, 4 had breast cancer, 4 had lung cancer, 1 had pancreatic cancer, and 1 had vulvar cancer. 11 patients had metastasis when evaluated in our outpatient. The 44% of patients knew their health status, 28% had partial consciousness and 28% had no awareness of cancer. After our evaluation 19 patients resulted less frail: 13 received conventional therapy and 6 had personalized protocols, whereas 6 patients were sent to palliative care because too frail.

**Conclusions:** Our initial experience points out that multidisciplinary approach in the elderly is important in detects frailty and leads to tailored oncology treatments. Cognitive impairment, the advanced stage of cancer and inadequate social situation are the factors that most influencce in deciding not to treat the patient (Table 1).

**Table:** Table T25. Patients’ characteristics

<table>
<thead>
<tr>
<th>Less frail</th>
<th>Frail</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 19</td>
<td>N = 6</td>
</tr>
</tbody>
</table>

Average age (range) 82 (76-96) 84 (75-93) 0.30

G8 (± SD) 11 ± (2.9) 9 ± (2.2) 0.59

ADL 1 ± (1.8) 1.8 ± (1.8) 0.62

IADL 9.4 ± (4.3) 5.3 ± (3.6) 0.56

SPMSQ 1 ± (3.2) 3 ± (4.0) 0.00

BMI 25.1 ± (3.6) 21.0 ± (2.1) 0.09

CIRS-G 5.4 ± (2.9) 5.0 ± (2.9) 0.71

Metastasis (%) 42 68 0.53

Illness awareness (%) 46 50 0.54

Social situation (%) 61 17 0.05

**Surgery and the elderly: when an apparent overtreatment becomes safe and effective**

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1Dipartimento di Oncologia-Ematologia, Ospedale Guglielmo da Saliceto, Piacenza; 2Dipartimento di Oncologia-Ematologia, Ospedale Unico della Val d'Arda, Piacenza; 3AOU Cagliari, Cagliari

**Background:** There are unique issues to consider when caring for an older with cancer. Since their patients with cancer are under-represented in clinical trials, there are less evidence-based data to guide the treatment. The challenge of managing older patients is to assess whether the expected benefits of treatment are superior to the risk in peoples with decreased life expectancy and tolerance to stress.

**Methods:** Our approach for identification of fit patients match the comprehensive geriatric assessment with a multidisciplinary evaluation of older patients. At the roundtable there were the oncologist and the surgeon, a radiologist, internist with expertise in pulmonology, geriatrician, anesthesiologist with expertise in nutrition, psychologist, physi- ariotrist, oncologic nurse, the geriatrician and caregiver of the specific patient, social worker. Starting from a careful analysis of medical history, physical examination, biochemical and instrumental exams the team proceeded applying the comprehensive geriatric assessment and balancing risks and benefits of all possible therapeutic options; the final decision was made taking into account the opinion of general practitioner and caregiver. Thereafter, the decision-making process was completed through a discussion with the patient in order to explain the risk-to-benefit ratio of surgery and to better understand wishes, hopes and unmet needs.

**Results:** In the last year we were able to identify as fit, forty-five very old oncologic patients. Whiat an aggressive surgical approach all the patients are free of disease and their quality of life is ameliorated. Notably, for six patients the surgical approach was firstly excluded for age and tumor burden as evidenced on Computed Tomography at another oncologic hospital with high surgical volumes. After our re-evaluation, all six patients were deemed as fit and surgery was radical for all. The length of hospital stay was of three days for two of them, seven days for other three; for a patient with nutritional problem, the total parenteral nutritional support was prolonged for ten days.

**Conclusions:** Aging and increased life expectancy mean that cancer in the older is becoming an increasingly common problem. Proper selection of patients is mandatory to administering effective and safe oncologic treatment. Advanced age alone should not preclude an effective cancer option that could improve quality of life or extend survival.

**LibroBluApp: a mobile app to improve cancer care**

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**Background:** Libro Blu was born in 2012 as an effort to coordinate Oncology practice in our institution and consisted of recommendations deriving from Italian and international guidelines. After its first publication, periodic updates were made until 2015, when a major revision took place, involving also consultants from many fields other than Oncology in order to also improve supportive care. Our next goal was developing a mobile app to make consultation easier and to share this tool with physicians from other institutions.

**Methods:** After the 2015 revision, Libro Blu was updated, with the inclusion of new recommendations based on new scientific evidence; it was also submitted for review by a number of Italian oncologists from other institutions. The mobile app development, based on the updated version of Libro Blu, has been realized, with an unconditioned support from Eli Lilly, by Medica Editoria e Diffusione Scientifica, a company involved in medical publishing and education.

**Results:** Since its debut in 2015, the new version of Libro Blu received a positive feedback from physicians in our institution; the review from other Italian oncologists ensured its adherence to good clinical practice. The mobile app development resulted in LibroBluApp, a mobile app for iOS devices (both iPhone and iPad are supported), that was finally released for download in April 2017. A version for Android devices is currently being developed and will be released.

**Conclusions:** Libro Blu was our first effort to establish a common standard of care in Oncology practice in our institution. The development of the LibroBluApp has made consultation easier and will allow to share this tool with oncologists and physicians from other institutions (in this regard, Eli Lilly Medical Information will contribute writing to 1680 Italian oncologists). The mobile app will be periodically updated with emerging scientific evidence and upon the approval of new treatments. We think that LibroBluApp will be a useful tool to coordinate Oncology practice, ensuring up-to-date information, and this is of particular relevance at this moment, in which Oncology is facing rapid innovations.

**CREAM study: Clinical correlation between immunotherapy-related colitis And intestinal Microbiote in metastatic patients**

L. Organo1, A. Cubeddu1, R. Maccia1, E. Lai1, M. Desai1, E. Pedditizi1, P. Pizzardi1, E. Sabia1, V. Palmis1, T. Camboni1, E. Masa1, G. Astara1, A. Manzin1, C. Maddeddu1, M. Sciarrotti1
1AOU Cagliari, Cagliari; 2ASL Cagliari; PO Muravera, Muravera; 3ASL Nuoro, PO Lanusei, Lanusei; 4ARO, PO Oncologico, Cagliari

**Background:** Today’s it’s well known that the composition of intestinal flora is able to influence the development of inflammatory gastrointestinal diseases, even though the association of inflammatory diseases with specific intestinal microbes is still unknown, because the inflammation itself and its treatment can change the composition of the microbiota. Surely some bacterial species are essential to maintain the mucosal
physiological tolerance, although species such as Bacteroides, Clostridium and Faecalibacterium can induce the up-regulation of T-cells and stimulate the production of anti-inflammatory cytokines. Innovative therapies such as Ipilimumab, Nivolumab and Pembrolizumab, a monoclonal anti-CTLA-4 antibody and inhibitors of the PD-1 receptor, respectively, are particularly involved in the up-regulation of lymphocyte system; among their side effects, the most relevant are those immune-mediated such as hypophysitis, thyroiditis and colitis. In particular this last one usually occurs within 16 weeks from the start of treatment: about one third of patients develop intestinal inflammation (of any grade) as a result of dysregulation of the immune system of the intestinal mucosa. Therefore, the high incidence of colitis in patients treated with immunotherapy offers the possibility to characterize the intestinal microbiota before the development of immune-mediated inflammation.

**Trial design:** Our study is a single-center observational study of clinical and biological parameters prospectively stratified. Specifically, we collect from patients eligible for immunotherapy a blood sample to analyze serum cytokines levels and a sample of fecal material at baseline and at least after 3 administrations of treatment: actually we enrolled 12 out of 40 planned patients; we suppose to complete the enrollment in approximately 4 months. According to preliminary data already published in the literature, we expect to find an alteration of the intestinal microbiota in metastatic treated with immunotherapy. Once we’ll identify the presence of an alteration of the microbiota, we want to assess whether there is any correlation with the patient’s clinical outcome.

**T29 Cost-effectiveness of a cancer diagnosis on frail elderly cancer patients**


**Background:** Elderly patients admitted to the hospital with a suspect of cancer are often offered a complete diagnostic. However some of them are not referred to an oncologic department. We analyzed the variables that could potentially have interfered with this decision.

**Patients and methods:** Electronic charts of older patients with an admittance or discharge diagnosis of cancer were analyzed. The inclusion criteria were as follow: age older than 70 years old; hospitalization at the medical area department (including Oncology, internal medicine, Nephrology, Pneumatology, hepatology and neurology); at least a cancer diagnosis in the dismissing codes. For every patient we had: type of hospitalization, polypharmacy, comorbidities, oncologic diagnostics, status of disease (metastatic or not) and destination after discharge. The end points were as follows: find a frailty profile for older patients, explore the elements that influence the approach to oncological department or not, the role of a cancer diagnosis in this type of patients.

**Results:** 838 patients were included in the analysis, 721 (86%) with cancer as main oncological diagnosis and 117 with another non oncological disease as main diagnosis at the dismissal. 461 (55%) were metastatic, 648 (77.3%) patients received some form of cancer diagnosis. Of these 243 (37%) were referred to an oncological department. 154 out of patients were admitted to the hospital with an oncological diagnosis 85.8% and 44% of patients had cardiovascular and metabolic comorbidities respectively. In the logistic regression, male sex (p 0.001, OR 1.68), metastatic disease (p 0.0001 OR 1.79), number of comorbidities and a complete oncological diagnostic e (p 0.001 OR 0.88 e 0.38 respectively) were the parameters significantly associated with an oncological course after dismissal.

**Conclusions:** More than 70% of patients received some form of oncological diagnosis (complete or partial) and among them only 37% had an oncological route after dismissal. Some efforts should be done to improve the identification of those patients that have to be excluded from an oncological diagnosis. This approach could be helpful to reduce costs and distress for patients that are not able to receive cancer treatment.
**U1**

Breakthrough-pain likelihood scoring system in cancer patients

M. Gonnellini¹, R. Cherubini¹, P. Bini¹, R. Rossetti¹

¹Umbria 1, Perugia

**Aim of investigation:** Breakthrough cancer pain (BTP) shows variable prevalence in different clinical settings. BTP diagnostic tools with demonstrated reliability, validation and prognostic capability are lacking. Samolysky Dekel validated a diagnostic/prognostic tool, the IQ-BTP, for BTP likelihood (‘High’, ‘Intermediate’ or ‘Low’) recognition among chronic pain (CP) patients. Using IQ-BTP scoring system and the Naive Bayes classifier we evaluated its performance on correct classification of BTP in cancer patients with CP.

**Material and methods:** Patients competent with Italian language, age > 18yrs and cancer CP treated by strong opioids were included. Using the IQ-BTP we assess potential presence of BTP and its characteristics. Then, we computed, for each selected predictor, the score for each likelihood level. We repeat the questionnaire once a month (± 10 days) for each patients for 3 times. The developed BTP-likelihood scoring system, is being used in a national multicenter impact study (n = 400 patients). We report the preliminary results of our first 33 recruited patients.

**Results:** Baseline patients characteristics are listed in table 1. Potential-BTP was found in 36% (n = 12) of patients. In 75% (n = 9) of them, potential-BTP was present in 2 or more visits. The likelihood for BTP diagnosis was ‘high’ in 25% (n = 3), ‘intermediate’ in 50% (n = 6) and, ‘low’ 83% (n = 10) of patients. BTP was predictable in 54% of cases. Only patients with high potential or recurrent intermediate likelihood-BTP level in two or more visits received rapid onset opioids.

**Conclusions:** The IQ-BTP scoring system may enable, in cancer patients, the detection of potential-BTP and its likelihood with significant relevance to BTP correct management.

<table>
<thead>
<tr>
<th>Table: U1. Baseline characteristics of patients (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics</td>
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<tr>
<td>Mean age, 69 years (range: 49-89)</td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Median Karnofsky index score 60 (range: 40-100)</td>
</tr>
<tr>
<td>Place of assessment</td>
</tr>
<tr>
<td>Outpatients</td>
</tr>
<tr>
<td>Home care</td>
</tr>
<tr>
<td>Primary tumor site</td>
</tr>
<tr>
<td>Pancreas</td>
</tr>
<tr>
<td>Lung/mesothelioma</td>
</tr>
<tr>
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</tr>
<tr>
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</tr>
<tr>
<td>Gastrointestinal</td>
</tr>
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<td>Others</td>
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</tr>
<tr>
<td>Therapy</td>
</tr>
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</tr>
</tbody>
</table>

**U2**

BTPC: Retrospective study on integrated hospital care between palliative care and oncologist

C. DeFerrari¹, N. Rossetti¹, E. Molinari², M. D’Amico¹, A. De Censi¹, M. Luzzani¹

¹Ospedale Galliera, Genoa

**Background:** Breakthrough Cancer Pain (BTPC) is distinguished in idopathic or spontaneous, accidental or procedural. Prevalence of BTPC reported in literature is 40-80%. Presence of BTPC has a negative impact on the quality of life and is a prognostic factor of hard to treat pain. Diagnosis and therapy of chronic pain and its exacerbations are fundamental aspects of the patient’s care pathway. In recent years, several studies have demonstrated how effective is simultaneous care approach of palliative care in oncology. We undertook a retrospective study regarding simultaneous care experience in Oncology Day Hospital (ODH), in presence of Palliative Care (PC) clinician, with attention to diagnosis, characterization and treatment of BTPC.

**Material and methods:** Patients who have performed PC visit in ODH setting, have been recruited from 1 January 2017 to 30 April 2017. Data were analyzed consulting patients’ clinical folders and reporting the following variables: demographics, pathology, therapy, ECOG-Performance Status, features of chronic pain and BTPC and specific therapies prescribed.

**Results:** 36 patients who performed at least 3 progressive PC-visits (F = 16, M = 20, mean age 67 ± 10 days) were included. The IQ-BTP scoring system may enable, in cancer patients, the detection of potential-BTP and its likelihood with significant relevance to BTP correct management. The IQ-BTP was found in 36% (n = 12) of patients. In 75% (n = 9) of them, potential-BTP was present in 2 or more visits. The likelihood for BTP diagnosis was ‘high’ in 25% (n = 3), ‘intermediate’ in 50% (n = 6) and, ‘low’ 83% (n = 10) of patients. BTP was predictable in 54% of cases. Only patients with high potential or recurrent intermediate likelihood-BTP level in two or more visits received rapid onset opioids.

**Conclusions:** The IQ-BTP scoring system may enable, in cancer patients, the detection of potential-BTP and its likelihood with significant relevance to BTP correct management.

**U3**

Fentanyl pectin nasal spray for breakthrough cancer pain treatment: a single center experience

E. Lai¹, S. Tolu¹, R. Mascia¹, V. Impara¹, A. Pretta¹, N. Lisica¹, A. G. Fredi¹, G. Pusole¹, L. Demurtas², P. Ziranu², E. Molinari¹, C. Madeddu¹, G. Astaldi¹, M. Scartozi¹

¹Medical Oncology, University of Cagliari, Cagliari, Italy, CAGLIARI
²Medical Oncology, University of Cagliari, Cagliari, Italy, CAGLIARI

**Background:** Breakthrough cancer pain (BTPC) is defined as a temporary exacerbation of algesic symptomatology occurring in patients with controlled chronic cancer pain. Typically BTPC arises with rapid onset, high intensity and has an average duration of 30 minutes. From 64% to 89% of patients with chronic cancer pain have episodes of BTPC and most episodes are unpredictable. Episodes of BTPC are usually treated with short-acting opioid analogues. Fentanyl, an highly liposoluble opioid molecule, showed efficacy and feasibility in treatment of BTPC in different formulations, including transmucosal and nasal administration. Intranasal fentanyl was reported to be often preferred by patients because of easy spray delivery of the drug and it seemed to be more helpful than transmucosal one in patients with oral mucosal disorders. In our center we studied compliance and satisfaction of patients treated with fentanyl pectin nasal spray for BTPC.

**Material (patients) and methods:** We retrospectively studied 48 patients attending our Oncology Unit from May 2014 to April 2015. They were affected by various types of tumors (mainly gastrointestinal and non-small cell lung cancer) and they were already taking maintenance opioid therapy for chronic cancer pain. They received fentanyl pectin nasal spray 100 mcg or 400 mcg for BTPC episodes. Patients were asked to report the effect of intranasal fentanyl on pain intensity according to a numerical rating scale (NRS), the action time, the grade of satisfaction (from 0 to 5) and how many times they fentanyl pectin nasal spray in relation to BTPC episodes.

**Results:** Most patients obtained a significant reduction of pain intensity with intranasal fentanyl: 70% (33) had a reduction of 7-8 points according to NRS scale, 31% (15) had a reduction of 2-3 points in NRS. 50% (24) showed pain relief within 5-10 minutes after administration, 44% (21) within 15 minutes. 67% of patients reported a grade of satisfaction from 5 to 3, with feasibility and efficacy as the most frequent referred reason. 90% of patients used fentanyl nasal spray for most episodes of BTPC obtaining an improvement of daily life quality.
The ANT Foundation is implementing a cloud computer platform. In the course of 2016, 6607 new cancer patients were enrolled in the 20 ANT Foundation. This innovative project is able to provide reliable information on the efficiency and in deceased patients.

Conclusions: Our patients showed high compliance towards fentanyl pectin nasal spray, thanks to its ease use and the quick release from breakthrough cancer pain, which had also a good impact on quality of life.

Methods: The project envisages that doctors working in the 20 ANT Home Care Hospitals (HCHs), record pain presence and intensity at each home visit in the Vitaveer® platform via the personal smartphone. Pain intensity was assessed by the NRS scale, and the pain intensity (‘physician’ assessment according to the class of analgesic drugs used). In this way a database is continuously updated and real-time information on the prevalence, intensity and evolution of the symptom in individual patients, individual HCHs and in the whole case can be obtained. The present analysis is based on three indicators: 1) actual efficiency achieved (percentage of visits with NRS reported), 2) effectiveness (difference between the first and the last NRS score) and 3) appropriateness (difference in the percentage of patients taking strong opiates between the first and the last ANTE score). Indicators 2 and 3 were evaluated only in HCHs with > 75% efficiency and in deceased patients.

Table: US

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<th>pain score at discharge</th>
<th>pain reduction after treatment</th>
<th>information about pain treatment during hospitalization</th>
<th>patients satisfaction about pain management</th>
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Conclusions: The “Comitato Ospedale senza dolore” program reached in all patients considered in Medical Dept a reduction of pain score from admission to discharge (reduction pain score over two points for exception of 4%). In all patients there is a good level of satisfaction about pain treatment, pain management and informations obtained, and this result was maintained along five years. We think that is necessary a periodically re-train for nurses and physicians to maintain high the sensibility for this problem.

Methods: In the course of 2016, 6607 new cancer patients were enrolled in the 20 ANT HCHs. The median age was 76, the median KPS 50, the main primary tumor sites were GI (33%), Lung (20%) Breast and Gyn (19%). Five out of 20 HCHs had an optimal efficiency rating (indicator 1). Patients evaluated for indicators 2 and 3 were 945. In these, pain was significantly reduced at the last evaluation (mean NRS from 3.1 to 2.4 and from 5.7 to 3.3 when initial NRS ≥ 4) (P = 0.01). At the same time, there was a reduction by almost 35% of patients with severe pain (NRS 7-10). The percentage of patients taking opiates shifted from 44% at the first home visit to 66% at the end of the assistance.

Background: The pain’s evaluation and treatment are relevant for the management of patients with cancer. The pain’s evaluation and treatment are relevant for the management of patients with cancer. The pain’s evaluation and treatment are relevant for the management of patients with cancer. The pain’s evaluation and treatment are relevant for the management of patients with cancer. The pain’s evaluation and treatment are relevant for the management of patients with cancer. The pain’s evaluation and treatment are relevant for the management of patients with cancer.

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Manipulative scar treatment and orthopaedic manipulative treatment for pain, shoulder motion and quality of life in post-mastectomy pain syndrome (PMPS). A randomized clinical trial

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Background: PMPS affects about 25% of breast cancer survivors. Drugs, sometimes ineffective, carry risks of adverse events.

Purpose: This study assesses the effect of Manipulative Scar Treatment (MST), with/without Orthoopaedic Manipulative Treatment (OMT), on pain, shoulder range of motion in external rotation (ROM-RE), distress and Quality of Life (Qol.).

Methods: Upon informed consent, 18 (mean age 52.88, SD 10.92) PMPS patients, attending oncologic follow-up, were randomized during 5 weekly sessions of treatment MST + OMT (9 patients vs MST-alone (9 patients)). Pain-quality/interest was assessed with Short-form McGill Pain Questionnaire (SF-MPQ) and Douleur Neuropathique-4 (DN-4); Distress with Distress Thermometer (DT); Qol, with 36-item Short-Form Health Survey (SF-36); ROM-RE of the shoulder with an universal goniometer. Data were collected before the 1st (T0), 2nd (T2), 3rd (T3) sessions, and monthly thereafter (F1,F2). Wilcoxon, Paired t test, Mann-Whitney test and Two-sample t-test were used for statistical analysis.

Results: 18 patients attended the entire schedule until F1 and 17 patients until F2. Both groups improved their condition concerning pain intensity at T4, F1 and F2 vs T0: SF-MPQ overall score at F2 vs T0 decreased in group MST + OMT (mean change -5.88, SD 3.72; P = 0.009) and MST (-5.62, SD 3.51; P = 0.020); SF-MPQ Visual-analogue scale at T2 vs T0 decreased in group MST + OMT (-23.33, SD 14.43; P = 0.007) and MST (-28.25, SD 21.49; P = 0.017). DN-4 score decreased at F2 vs T0 in group MST + OMT (-2.33, SD 1.58; P = 0.008) and MST (-2.12, SD 3.35; P = 0.11). DT score improved in F2 vs T0 in group MST + OMT (-3.77, SD 2.65; P = 0.007) and MST (-2, SD 2.13; P = 0.040). ROC-RE significantly improved in MST + OMT vs all intervals (F2 vs T0: +0.10, 5.55; P < 0.001), but not in MST. Qol, by SF-36 improved at F2 vs T0 in group MST + OMT, with significant differences in physical functioning (11.11, SD 9.27; P = 0.016), pain (23.66, SD 16.79; P = 0.011), social functioning (+24.88, SD 19.77; P = 0.017), emotional role (+37.11, SD 38.88; P = 0.026) and emotional well-being (+12.44, SD 15.15; P = 0.008), while group MST showed no significant change in scales, at all intervals. Between-group differences in F1 vs T0 were observed in general health (P = 0.037), energy/fatigue (P = 0.002), emotional role (P = 0.007). Conclusion: Our results suggest a reduction in pain and distress in all patients, with/without OMT, maintained at 2 months, and an additional improvement in range-of-motion and Qol in MST + OMT group. A larger study is required to confirm these results.

Procedural pain: acknowledgement of the issue by palliative care professionals

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1Hospital villa speranza, Rome

An optimal pain control is a constant challenge for palliative care professionals. As with all treatment and medical assistance processes, palliative care patients can undergo potentially painful procedures. Procedural pain is therefore a form of breakthrough pain that should be averted and treated adequately in order to improve the quality of life of terminally ill patients.

Detection and control of procedural pain can be effectively achieved only if medical operatives have the necessary training. In order to assess the knowledge and awareness of this issue, palliative care workers of the home care and residential care staff of our Hospice were given a specific questionnaire to complete.

27 doctors and 36 nurses were interviewed. 96% of doctors and 90% of nurses indicated knowledge of the definition of procedural pain. Among doctors, 85% state that they prescribe a medication for intense breakthrough pain, although only 65% of nurses claim to be able to find them amongst available prescriptions. For both operative categories, procedural pain affect the quality of life of patients, but only 68% of doctors and 77% of nurses interviewed ordinarily detect it. The procedure most commonly believed to be a source of procedural pain is mobilisation, followed by medication. Overall, operatives think that in 84% of the situations, procedural pain is appropriately managed in their own setting.

Our results show evidence of high levels of awareness about procedural pain by palliative care professionals. However, this does not seem to be reflected in its systematic detection at the bedside nor in a regular prescription of appropriate medication to control it, which results in a sub-optimal management of this type of breakthrough pain. Although the majority of the operatives apply their theoretical training to their medical practice, an increasing appreciation of the importance of procedural pain remains an important goal to improve these results, which will be compared to the findings of a targeted survey shortly to be conducted among patients.

Management of breakthrough cancer pain in patients with oral mucositis

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1Medical Oncology, Sapienza University of Rome - University of Cagliari, Italy, Cagliari; 2Medical Oncology, Sapienza University of Rome - University of Cagliari, Italy, Cagliari; 3Medical Oncology, Sapienza University of Rome – University of Cagliari, Italy, Cagliari; 4Medical Oncology, Sapienza University of Rome - University of Cagliari, Italy, Cagliari; 5Medical Oncology, University of Cagliari, Italy, Cagliari; 6Medical Oncology, University of Cagliari, Italy, Cagliari

Background: Oral mucositis, which typically appears with erythematous and ulcerative lesions of the oral mucosa, is a common affection in cancer patients as a consequence of chemotherapy or radiotherapy or cancer itself. It can compromise nutritional status and quality of life, being a cause of pain, especially during swallowing and inhibiting proper feeding. Furthermore, inflammatory state of oral mucosa negatively affect absorption of therapy, especially analgesic drugs, causing insufficient efficacy. So alternative administration routes need to be investigated to control algic symptomatology. Intranasal fentanyl formulation is recommended for breakthrough cancer pain (BTCP), it provides fast pain relief and it may be a valid treatment option for these patients, in particular the assumption immediately before meals can allow a better feeding. We investigated efficiency of fentanyl pectin nasal spray in a subset of patients with oral mucositis and its impact on quality of life.

Material (patients) and methods: We retrospectively studied 31 patients attending our Oncology Unit from August 2015 to April 2017, with many tumor sites, with oral mucositis and non controlled BTCP, treated with fentanyl pectin nasal spray 100 mcg/ D or 400 mcg/D, assumed during the BTCP episodes and before meals. We asked the patients to report the effect of fentanyl pectin nasal spray on pain intensity (using NRS scale) and on feeding (0 = no improvement 1 = slight improvement 2 = good improvement). We asked if the use of fentanyl pectin nasal spray had effects on quality of life too (0=N0 1=Yes).

Results: 58% of patients (18) had a pain reduction of 2-3 point of NRS scale, 25% (8) had a pain reduction of only 1 point, 17% didn’t have benefits (5). 65% (20) of patients had a slight or good improvement of feeding; 68% of patients report positive effects on their life’s quality.

Conclusions: Fentanyl pectin nasal spray led to better pain control in patients with oral mucositis; its administration before meals, allowing improved feeding and provided a better quality of life.
V - ONCOLOGY NURSING

V.1 Observational study on the effectiveness of the Dragon Boat in reducing the risk of incidence of lymphedema in women with breast cancer

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Introduction: In women with breast cancer undergoing sentinel node biopsy and axillary lymph node dissection, the ipsilateral upper extremity lymphedema is one of the most disabling complications. The gold standard for the treatment of this condition is physiotherapy, called complete decongestant therapy, but also constant exercise is an important element of prevention. The Dragon Boat, a very popular rowing activity, has been reported to be of clinical benefit and improve quality of life in some studies.

However, given that studies lacked to demonstrate the effectiveness of this Dragon Boat in reducing the incidence of lymphedema, this study’s objective was created to precisely assess this influence in women with lymphedema, as well as the impact on quality of life and on the possible predictors of this condition.

Materials and methods: Observational study of two groups: women who participate in the Dragon Boat activity for at least six months and women who practice different physical activities both biweekly. For the collection of epidemiological and clinical data a questionnaire constructed ad hoc was used for the assessment of QoL the EORTC QLQ-C30, and a tape measure was used for the local measurement of lymphedema. Data were collected at the Hospital Physiotherapy Institutes of Rome (IPo) and the lake of Castel Gandolfo (RM) from June to October 2016, upon approval from the Central Ethics Committee IFO. A comparison of categorical variables with the Chi-square test and statistical significance with p < 0.05 through the software Statistical Package for the Social Sciences (SPSS), version 19.0 was used.

Results: The sample consisted of 100 women, equally divided between the two groups. The presence of lymphedema was detected mainly in the group of women who did not practice the Dragon Boat (26% vs 4%), confirmed by measuring limbs before and after exercise. From the data obtained through the Questionnaire EORTC QLQ-C30, it is clear, moreover, how the Group of the Dragon Boat present a better quality of life (p = 0.008), and reduced presence of fatigue (p = 0.005), insomenia (p = 0.001), pain (p = 0.003), and dyspnaxia (p = 0.03) in women who practice the Dragon Boat that ultimately have a lower BMI and a more balanced lifestyle.

Conclusions: Practicing Dragon Boat reduces the risk of onset of lymphedema and improves QoL. The possible predictive factors: high BMI, reduced physical activity and high protein diet, rich in carbohydrates and fats.

V.2 Efficacy of cryotheraphy in paclitaxel-induced nail toxicity: Final results from a Phase II Clinical Study

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1Centro di Riferimento Oncologico di Aviano, Aviano

Background: Taxanes are cytotoxic agents that induce nail toxicity, including severe effects such as pain and discomfit. Cryotherapy, causing temporary vasoconstriction, is a successful approach in preventing nail toxicity. However, so far, few studies, have described cryotherapy and its effects on nails.

Materials and methods: We conducted a phase II clinical study to investigate the efficacy of cryotherapy in preventing nail toxicity in breast cancer patients treated with paclitaxel. The study, conducted in a Multidisciplinary Day Hospital at CRO Aviano from October 2015 to September 2016, was planned to enroll 62 women to estimate a 40% to 25% reduction in nail toxicity (a p = 0.05; b = 0.20). The study included women diagnosed with breast cancer, with no previously nail disease, treated with weekly chemotherapy and weekly paclitaxel. The study, conducted in a Multidisciplinary Day Hospital at CRO Aviano from October 2015 to September 2016, was planned to enroll 62 women to estimate a 40% to 25% reduction in nail toxicity (a p = 0.05; b = 0.20). The study included women diagnosed with breast cancer, with no previously nail disease, treated with weekly chemotherapy and weekly paclitaxel.

Results: G2-G3 nail toxicity was reported in 13 women (21.0%, 95% confidence interval – CI: 11.7-33.2), which was significantly lower than the expected 40% (p = 0.002). Nail toxicity was more frequent in women aged ≥50 years (31.0%, 95% CI:15.3-50.8) than in younger ones (12.0%, 95% CI: 3.4-28.2). The study included women diagnosed with breast cancer, with no previously nail disease, treated with weekly chemotherapy and weekly paclitaxel having hourly paclitaxel for the first time for 3 cycles. Specifically excluded were women with Raynoud’s syndrome and those previously treated with taxanes. Participants wore finger gloves (temperature: 5°C to 6°C) on hands and feet during drug infusion for a total of 70 minutes. Nails condition was assessed weekly by trained nurses. Nail changes, including pain, were evaluated using CTCAE 4.03 grades and through photographs.

Conclusion: This study indicates the efficacy of cryotherapy in reducing the incidence of nail toxicity in breast cancer patients treated with paclitaxel.

V.3 Italian translation of a nursing instructor helping the patient to treat oral antineoplastic medicine: the MOATT

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Introduction: In recent years, the introduction of oral therapeutic formulations has contributed to making oncologic patients responsible, in the first place, for the assumption and management of the therapeutic plan. This “empowerment” required reflects the need for better information to manage side effects and favor adherence to therapeutic treatment. The nurse appears to be the figure mainly involved in the therapeutic education of patients, so they need more and more tools to guide them in favoring the correct intake of prescription drugs. Among those encouraging/guiding therapeutic education about taking oral antineoplastic drugs is the MasC Oral Agent Teaching Tool (MOATT), created by the Multinational Association of Supportive Care in Cancer (MASCC), consists of four sections and is present in 16 different languages with the exception Italian.

Objective: To translate the MOATT into Italian.

Methods: A forward-backward translation was performed following the guidelines provided by Beaton et al for transcultural adaptation of self-report questionnaires. The stages of the translation process were: authorization request, forward translation (two translators with good knowledge of both languages), creation of a new version and backward translation (concluded with the approval of the MASCC).

Discussion: The main issues arise in the individual translation phase are largely dependent on the presence of Anglo-Saxon terms in Italian which provide more than one translation. It was useful in this regard to resort to a comparison between the translators, which made it possible to reach a unique choice of Italian terms best suited to replace the original ones, as well as to the cultural adaptation that will ensure the optimal use of the instrument in clinical practice.

Conclusion: The MasC Oral Agent Teaching Tool from 2015 is available in Italian and can also be consulted through the official website: http://www.mascc.org/assets/Guidelines-Tools/moatt_italian_2015.pdf. This version can become a valid means of patient support and a tool for simplifying nursing educational work, useful in achieving a form of empowerment-based therapeutic education and therefore aimed at self-management of the disease and especially treatment.

V.4 Development and psychometric testing of a measure of perception of care dependency in cancer patients

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1Research Unit Nursing Science Campus Bio-Medico di Roma University, Rome; 2Research Unit in Nursing Science, Campus Bio-Medico di Roma University, Rome; 3OncoPalliative Care Unit Nursing Science Campus Bio-Medico di Roma University, Rome

Background: The number of patients with comorbidities and cancer related disabilities is expected to increase in the near future. Care dependency is central to nursing and can be associated with suffering, humiliation, but also with positive balances and personal developments. Understanding the patients’ perception of care dependency enables nurses better to meet patient’s needs. No instrument is available to evaluate patient’s perceptions about their dependency experience.

Material and methods: This study is part of an ongoing project aimed to develop and validate an instrument to measure the patient’s perception of nursing care, in particular the patient’s basic emotions anger, guilt, shame and sadness. The project follows the European Statistical System’s Guidelines for Instrument Development including five steps: conceptualization, questionnaire design, pre-field and field testing, final validation. Conceptualisation implied the formation of concepts from a meta-synthesis and
From an initial pool of 63 items questionnaire design produced a 25-item draft. We enrolled 13 patients for pre-field test and 12 patients for field test. After pre-field and field test the wording of several items, the questionnaire layout and the answers’ structure were modified to increase clarity and 6 items were removed producing a 19-item tool.

Conclusions: The final questionnaire is being validated in a multicenter study. This study will provide oncology nurses with an instrument based on patients’ accounts, valid and reliable to assess the patient’s perceptions of care dependency, enabling them to better meet the dependent patient’s needs through personalized quality care.

The predictive role of toxicity induced by chemotherapy: systematic review on relationship between toxicity and effectiveness

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Background: The toxicity of chemotherapy is the major problem for the continuity of treatments. Despite this, they may be used as a guide to treatment response as demonstrated by various studies in the literature. The purpose of the review is to deepen the relationship between the side effects and the effectiveness of chemotherapy in order to improve the management.

Material and methods: We have performed several literature research by the following internet databases: PubMed, The Cochrane Library and Toxnet, Biomed Central, Trip Liberating the literature. The research was performed linking search words: “correlation toxicity and efficacy chemotherapy”, “toxicity markers correlation”, “body markers and oncology toxicity”, “prognostic toxicity and chemotherapy”. The correlation between toxicity and survival was evaluated according to the PFS and OS. We have applied the following filters: human species and 5 years. Inclusion criteria: Our research was not limited by study design or outcomes. We have been included full-text and abstract, until January 2017. We have included patients with all types of tumor and toxicity, both adult and pediatric, subjected to every type of chemotherapy.

Exclusion criteria: We have been excluded all articles not written in English or Italian language. For the fulfillment of this review it has been possible to formulate the question with Pico model.

Table: V5

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<th>PATIENT</th>
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<th>COMPARISON</th>
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<tr>
<td>Patients with chemotherapy-related toxicity</td>
<td>/</td>
<td>Patient without chemotherapy-related toxicity</td>
<td>Best response to treatment</td>
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Results: For review we found 33 articles, but only 21 meet the inclusion criteria (for a total of 6537 patients). The review supports the hypothesis that there is a correlation between toxicity such as hand-foot syndrome, rash, hypersensitivity, myelosuppression, proteinuria and the effectiveness of the treatment. There was no correlation between treatment efficacy and hypertension, cachexia, nausea and vomiting. Furthermore, in a few trials, the correlation between the degree of toxicity and the best therapeutic response has been demonstrated.

Conclusions: Although there are studies in the literature, it is necessary to deepen with works of greater statistical value and sampling, identifying efficacy classes based on the degree of toxicity. It is also necessary to identify time-related landmarks that predict the efficacy of treatment, promote continuity and improve nursing management of side effects.

Observational study on dietary habits and quality of life in patients with colorectal cancer

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Introduction: Colon cancer is the second leading cause of cancer death in Western countries after lung cancer and male breast cancer. Numerous studies report the effectiveness of a healthy diet in reducing the risk of developing colon cancer or its recurrence. Although the literature provides us with some indications of the most appropriate foods to be used to reduce the risk of developing the cancer or its recurrence, there are not many scientific studies that allow us to understand whether the quality of life of people diagnosed with carcinoma of the Colon can be improve by following healthy eating habits. By virtue of this, the objective of this study was to observe the eating habits and quality of life in patients with colorectal cancer.

Materials and methods: Observational study on a sample with age > 18 years and diagnosis of colorectal cancer at the Oncology Clinic of an IRC5 in Rome. For the collection of socio-demographic and clinical data (including anthropometric data, blood type and eating habits), an ad hoc questionnaire was used, while EORTC QLQ-C30 was used for QoL (version 3.0). The data were then analyzed using the SPSS (version 9.0) program and represented by tables describing the frequency of the variables under consideration.

Results: 69 patients with an median age of 62 years were recruited, mainly married, with a low average medical title, with a BMI (Body Mass Index) 25 and a predominantly type A blood type 36%. The sample included many animal based foods, especially chicken meat (77.1%), beef (73.2%) and raw ham (77.6%) but not dairy (15.8%) or fish (20.3%), and few food of origin Vegetable (27.4%). Drinking sparkling beverages (1.3%) and alcohol (12.3%) is also limited. Despite the presence of some disorders, such as insomnia (43.5%), abdominal swelling (55.5%) and anxiety (37.4%), the QoL of the sample being tested is average (57.6).

Conclusion: The study found that patients with colorectal cancer did not follow a balanced diet regime. It is therefore necessary to raise the awareness of patients to take on foods that can reduce the disturbance and bring quality of life to higher levels.

Distress in the hospitalized oncological patient: a study observation

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Background: Distress is an unpleasant emotional experience of a psychological, social, and/or spiritual nature that may interfere with the ability to cope with the disease. This phenomenon appears to be very common in cancer patients, especially during hospitalization, and is therefore considered to be the sixth vital parameter in oncology. The literature also reports a significant association between distress and patient compliance on the therapeutic plan. It is therefore important for the nurse to constantly monitor patient distress during hospitalization. In practice, the NCCN Guidelines provide an algorithm for identifying it with an analogue visual scale, known as the Distress...
Thermometer (DT), with a score ranging between 0 to 10. A result greater than 5 requires counseling with a psycho-oncologist: therefore its early detection is fundamental.

**Objective:** To evaluate distress in hospitalized cancer patients.

**Materials and methods:** A quantitative descriptive study was used. Patient enrollment took place at an IRBCS in Rome between February and April 2016. Inclusion criteria included age >18 years and hospitalization for an oncology pathology. Cognitive impaired patients who could not provide active participation in the study were excluded. A data-demographic, clinical dataset and the distress thermometer (DT) were used for data collection. The collected data, a descriptive analysis and an association of categorical variables (statistical significance with p < 0.005) were performed with the Chicago Statistical Package for Social Science (SPSS) program 19.

**Results:** The sample consists of 77 patients, predominantly women (53%) with medium-high level of education (70%). The average distress score was 5.79. The most present emotions experienced were fear (51%), nervousness (55%) and worry (70%). Individuals in the high age group have a lower level of child-related distress (p=0.006) and work (p=0.016), despite being the most depressed (p<0.005) and with the following Physical problems: constipation (p=0.017), urinary disorders (p=0.09), tingling of hands and feet (p=0.007). Patients with a medium to low cultural level experienced significant disorders such as swelling and diarrhea (p=0.034).

**Conclusion:** Hospitalized patients requiring counseling with a psycho-oncologist, had scores higher than 5. DT should be used by nursing staff in clinical practice focusing on significant problems present in the patient’s therapeutic pathway.

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**V9 Nutritional status in elderly cancer patients: Prospective observational study**

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**Background:** The cancer impact on nutritional status of the affected persons. Weight loss is usually severe, precocious and related in frequency and extent, with the disease stage. The most common weight loss related cancers are pancreatic and gastric. Malnutrition is associated with increased incidence of adverse drug-related reactions, reduced response to therapy and poor prognosis. An inadequate nutritional status in cancer patients, is a frequent problem over 65 years old. Despite this evidence, the attention to weight loss and consequences remains largely insufficient. The aims of this study are to assess the prevalence of malnutrition in a sample of elderly cancer patients in the Hospital of Novara and, if necessary, to propose a tool for the evaluation and monitoring of the condition during hospitalization.

**Material and methods:** A prospective observational study was carried out between April the 1st and December the 30th 2016. Inclusion criteria were: older 65 years, affected by cancer and agreement to participate in the study. It was used the MNA questionnaire property of Nestle Nutrition Institutes. Data analysis by Microsoft Excel 2010.

**Results:** The used tool showed 44% of malnourished patients and, 50% of potentially malnourished. These results are in line with the literature findings, showing high prevalence of malnourished cancer patients, while no studies were found that consider potentially malnourished patients. If we consider potentially malnourished patients, we are almost at the totality of the enrolled sample. It would be useful to stratify the sample for kind of cancer as the consulted studies show very variable prevalence depending of cancer-affected district. This stratification was not possible for the smallness of the sample.

**Conclusions:** There is a high prevalence of malnutrition in elderly cancer patients. Cancer and its chemotherapy may favour this condition that negatively impacts on the treatments outcome. Attention to weight loss and negative impact on prognosis of elderly cancer patients remains largely inadequate. In Italy, malnutrition prevalence data are missing in the elderly cancer patients and, the few available data refer to types of non homogeneous patients in different stage of illness and treatment. In the clinical setting, its use of detection tool such as the MNA, could be encouraged to allow timely intervention to provide adequate nutritional support, prevent further deterioration and improve patient’s safety.

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**V10 Intensive mucositis management in head and neck cancer patients treated with concomitant chemo-radiotherapy: the pivotal role of the nurse**

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**Background:** Treatment-induced oral mucositis affects 90% of head and neck cancer patients undergoing concomitant chemo-radiotherapy (CHT-RT) leading to a impairment in food intake in up to 50%-70% of the cases. This translates in significant weight loss, dehydration, malnutrition and prolonged hospitalization, hampering the continuation of treatment plans. We considered that an early and continuous toxicity monitor could provide better outcomes.

**Methods:** Since May 2016, all patients diagnosed with locally advanced squamous carcinoma of head and neck cancer were included in the present study. The nurse performed her first evaluation concomitantly to the first visit with the oncologist. Oral cavity, skin and nutritional screening, social and family background were assessed. During CHT-RT, the toxicity assessment was performed three times a week: the nurse detected body weight, oral mucosal and skin hydration status, oral pain and dysphagia. The nurse was in close contact with patients and their caregivers, the oncologist and the nutritional team, as medical/nutritional measures were undertaken with her input.

**Results:** 13 patients were included in our analysis: five received CT-RT after surgery, eight as an exclusive treatment. Weekly Cetuximab, weekly Cisplatin (CDPP) 40 mg/m2, high-dose q4w CDPP 100 mg/m2 were administered concomitantly to RT in three, seven and three patients, respectively. All the patients completed the programmed treatment plan. 12 patients had minimal weight loss (<5%) during the treatment, with significant weight loss observed in only one case, associated to early disease progression. One patient required hospitalization because of the lack of familiar and social environment; we moreover recorded a death due to massive pulmonary embolism. The median cumulative dose of weekly CDPP was 220 mg/m2; the three patients treated with high-dose CDPP received a total of 300 mg/m2 as planned; Cetuximab was administered without interruption. The scheduled program of RT was accomplished in all cases.

**Conclusions:** Our design is based on the early nurse involvement; this allows a multidimensional and early identification of patients with major risk of developing treatment complications. The early and continuous nursing monitoring entails an efficient toxicity management in this high-risk population, whose final results are treatment completion in all patients, prevention of severe adverse events and a low rate of hospitalizations.

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**V11 Efficacy and patient acceptability of the DigniCap ScalpCooler to prevent hair loss in breast cancer patients receiving adjuvant chemotherapy**

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**Background:** Alopecia is a common and distressing adverse effect in breast cancer (BC) patients (pts) receiving adjuvant chemotherapy. The aim of the study was to assess the effectiveness and safety of this device to prevent chemotherapy-induced alopecia in early breast cancer patients (EBCP) receiving adjuvant chemotherapy. The quality of life of pts was also evaluated.

**Patients and methods:** From January to December 2016, a sensor-controlled scalp cooling system (DigniCap; Systex Europe GmbH, Norderstedt, Germany) was proposed to a consecutive group of EBCP submitted to adjuvant chemotherapy at the Breast Unit of Spedali Civili Hospital of Brescia. Degree of hair loss was assessed by two nurse using Dean’s alopecia scale by digital photographs at baseline and each chemotherapy cycle. EORTC QCQ-30 questionnaire and self-reported visual analogical scale (VAS) of symptoms (anxiety, tone of mood, fatigue, nausea, well-being, activity) were collected at baseline and after the first two cycles of chemotherapy.

**Results:** 70 pts were enrolled and 49 (70%) completed the chemotherapy plan and were evaluable. Median age was 51 years, 8 pts (16%) received neoadjuvant and 41 pts (84%) adjuvant chemotherapy, 21 (43%) were treated with a cycle of chemotherapy (TC, EC or paclitaxel alone), and 28 (57%) with sequential chemotherapy with antracycline and taxane + trastuzumab. Fifteen pts (30%) stopped the treatment because of loss of hair in 9 pts, for headache in 4 pts and for other problems in 2 pts.

At the end of chemotherapy, 13 pts (29%) had loss of hair (Dean score 0), 25 pts (51%) had a minimal loss of hair (Dean score 1), 9 pts (18%) had a 50% hair loss (Dean score 2), 2 pts (4%) had a 75% hair loss (Dean score 3). No pts reported hair loss more than 75% (Dean score 4). There wasn’t a significant difference between mean score value of QLQ-C30 at baseline and after chemotherapy and between the groups with and without hair loss. VAS documented an increase of fatigue and decrease of anxiety from baseline to final evaluation. The side effects presented with the use of DigniCap were the following: headache in 32% of pts and cold feeling in 57% of pts.

**Conclusion:** Scalp cooling with cold caps appears to be effective in preventing CIA among the majority of women undergoing treatment chemotherapy. The quality of life did not change in scalp-cooled patients.

**Acknowledgments:** a thank you to the EIA association that donated Dignicap to Oncology Department.

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**V12 Prospective qualitative study on the emotional experience of the patient undergoing radical prostatectomy**

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**Background:** In Italy, prostate cancer is currently the most frequent cancer in humans from the age of 50 onwards. To date, prostatectomy is the only treatment used for localized prostate cancer that has shown a reduction in overall mortality and that is tumor-specific, as...
A hermeneutical phenomenological prospective study was performed on 62 patients > 18 years of age, with prostatic carcinoma undergoing radical prostatectomy at the Urology-Oncology Clinic of the National Regulatory Tumor Institute of Rome. A 12-month follow-up is being conducted to investigate patients' experiences over time. The study is being conducted at a Multidisciplinary Day Hospital at CRO Aviano in Italy.

Background: The incidence of nausea during chemotherapy (30%-70%) is mainly related to the emetogenic potential of chemotherapeutic drugs associated with a high degree of variability of the individual and the drug. The study aims to evaluate the efficacy of cryotherapy in reducing CINV in patients undergoing chemotherapy. The study will be conducted in a Multidisciplinary Day Hospital at CRO Aviano from September 2017 to April 2018. Overall 384 patients are needed (192 per arm) to estimate a reduction of CINV from 60% to 45% (p = 0.05; b = 0.20). The study will include all patients undergoing chemotherapy for first time, with no previously psychiatric disease, limited understanding of physiopathology, lack of validated instruments, inefficient record of the event from patients, failure of nurses to assess its impact on patients' life. Empowerment of patients in the identification of CINV and in its reporting will be helpful to improve therapy adherence; nurses may play a role in this context. Despite the great number of studies investigating the efficacy of different antiemetic drugs in reducing CINV, no study focused on patients' educational program through written information about CINV.

Material and methods: We will conduct a phase II randomized clinical trial to investigate the efficacy of written and oral information (experimental arm) versus oral information alone (control arm) about CINV, in patients undergoing chemotherapy. The study will be conducted in a Multidisciplinary Day Hospital at CRO Aviano from September 2017 to April 2018. Overall 384 patients are needed (192 per arm) to estimate a reduction of CINV from 60% to 45% (p = 0.05; b = 0.20). The study will include all patients undergoing chemotherapy for first time, with no previously psychiatric disease, limited understanding of physiopathology, lack of validated instruments, inefficient record of the event from patients, failure of nurses to assess its impact on patients' life. Empowerment of patients in the identification of CINV and in its reporting will be helpful to improve therapy adherence; nurses may play a role in this context. Despite the great number of studies investigating the efficacy of different antiemetic drugs in reducing CINV, no study focused on patients' educational program through written information about CINV.

Material and methods: We will conduct a phase III randomized clinical trial to investigate the efficacy of written and oral information (experimental arm) versus oral information alone (control arm) about CINV, in patients undergoing chemotherapy. The study will be conducted in a Multidisciplinary Day Hospital at CRO Aviano from September 2017 to April 2018. Overall 384 patients are needed (192 per arm) to estimate a reduction of CINV from 60% to 45% (p = 0.05; b = 0.20). The study will include all patients undergoing chemotherapy for first time, with no previously psychiatric disease, limited understanding of physiopathology, lack of validated instruments, inefficient record of the event from patients, failure of nurses to assess its impact on patients' life. Empowerment of patients in the identification of CINV and in its reporting will be helpful to improve therapy adherence; nurses may play a role in this context. Despite the great number of studies investigating the efficacy of different antiemetic drugs in reducing CINV, no study focused on patients' educational program through written information about CINV.

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usually receive hospital care in protective isolation until neutrophil recovery. This means for the patient staying alone in a germ-free room with positive pressure and having limited contact with the outside world and with loved ones. However, isolation-related loneliness might increase patient suffering. Thus, the aim of this study was to develop and psychometrically test a self-report questionnaire to assess the patient’s perception of protective isolation.

**Material and methods:** We developed 18 items according to three dimensions emerged in a metasynthesis: Suffering, Relating to oneself, and Missing the relationship with others. Item selection was performed through focus group, comparison with the findings of two phenomenological studies, and content validity with 22 experts. A total of 17 items yielded an adequate content validity index (CVI). The CVI of the questionnaire was 0.88. Cognitive interviews with 5 patients were used to verify face validity. A validation study was conducted in 10 Italian centers. Participants included 123 adult patients receiving autologous (55%) or allogeneic (45%) HSCT in protective isolation. Patients completed the questionnaires between 7 and 9 days post-transplant. Dimensionality was tested through Exploratory factor analysis (EFA).

**Results:** The scale yielded adequate psychometric properties, with the exception of 3 items, which were eliminated. The EFA yielded a three-factor solution explaining 49% of the variance. The more patients felt supported by nurses, the less they suffered because of isolation, as they were more able to relate to themselves in a positive way (Table 1).

**Conclusions:** Nurses can help patients live their isolation with greater serenity and mitigate their suffering. Risk factors for a negative isolation experience should be taken into account in order to avoid unnecessary patient suffering. Future studies should test the psychometric properties of the questionnaire through confirmatory factor analysis and verify its trans-cultural validity.

### Table: V16. Correlation matrix (n = 123)

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suffering</td>
<td>2.6 (0.9)</td>
<td>(0.90)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relating to oneself</td>
<td>3.1 (0.8)</td>
<td>-1.5</td>
<td>(0.60)</td>
<td></td>
</tr>
<tr>
<td>Missing the relationship with others</td>
<td>3.0 (1.0)</td>
<td>0.64</td>
<td>(.043 (0.80)</td>
<td></td>
</tr>
<tr>
<td>Support from nurses</td>
<td>6.4 (0.7)</td>
<td>-1.97</td>
<td>0.29 (0.80)</td>
<td></td>
</tr>
</tbody>
</table>

*p < .05, **p < .001, (1) range 1-5, (2) range 1-7

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**V18 Sleep and hematopoietic stem cell transplantation: a pilot study with sleep questionnaire in the intensive care unit**

D. Brusati1, D. Rosa1
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**Introduction:** Over 50% of the patients have trouble sleeping before hematopoietic stem cell transplantation (HSCT), 82% during hospitalization and 43% after the resig- nation, prevalence rates much higher than the general population. Sleeping less than 300 minutes per night increases the risk of mortality by 4 times.

**Aims:** Change the rating scale “Sleep in The ICU Questionnaire” used in ICUs for patients undergoing HSCT.

**Materials and methods:** The administration of the questionnaire: May/September 2016. The average time of administration for each individual patient is 15 minutes. The interviews were carried out 33, but the number of questionnaires that have been ana- lyzed are 30. The interviews were carried out in adult Bone Marrow Transplantation Unit, Hematology, Hematology Clinic of some Hospitals in Northern Italy.

**Results:** Questionnaires administered to 30 patients (17 men, 13 women). considered most bothersome symptoms: waking at night to go to the bathroom (63.38% of respondents rated this disorder with 10 points and 13% with a score of 9) consequence of liquid doses required for the type of transplantation; followed by the alarm of the infusion pump with the 16.7% that said a disorder equal to 10 and 20%, equal to 9. Degree of sleepiness: increases to half of the period of hospitalization and decreases for more than half of patients close to resignation. On a scale where 1 is unable to stay awake and 5 corresponds to fully alert and awake, judgment 10 was given by 36.7% for the first night in the ward, from 0.00% to half of the period and from 6.66% towards the end of the period of hospitalization. Since, however, point out that the median between the middle and end of the period of stay is the same. The median of sleep quality during hospitalization is equal to 5, with 0% results equal to 1 (which is very bad) and the 33.30% equal to 0.

**Conclusions:** Patients have provided many ideas for further and more detailed analysis. Some survey items seemed to them unnecessary or wasteful while other fundamental deserving of further study to eliminate noise. In addition to reducing the baselines and noise that lead to continuous nocturnal awakenings, during service with this patient, we should also focus on decreasing anxiety and stress and the increase of activities based on the strength and the will of patients can stimulate it by reducing the feeling of isola- tion and boredom that impact negatively on the need for sleep and rest.

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**V19 Narrative review of quality of life in survivors of colorectal cancer**

S. Laura1, D. Rosa1
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**Introduction:** The quality of life of survivors of colorectal cancer after five years of diagnosis, seems to have a slow deterioration, due to the emergence of long-term symptoms in particular in the population of survivors with ostomy.

**Aims:** Investigate and identify the variables that affect the overall quality of life.

**Material and methods:** PICO method. Databases: Pubmed, Scopus, Cochrane, CINAHL, Johanna Briggs Institute (JBI), a journal: Journal of Advanced Nursing. Search terms: surveys and questionnaires, colorectal cancer survivors, long-term survi- vors, quality of life, patient continuity, cancer care questionnaire, perception, social, con- tinuity of patient care. Inclusion criteria were age ≥18 years, survivors of colorectal cancer, finished chemo/radio therapy, ostomy vs. no permanent ostomy, questionnaires that investigated the QoL, articles published in the last 10 years. Exclusion crite- ria: articles absent in the national catalog, items that only take in the studio-men or only women survived to the CRC. Evaluation of the quality of the articles: STROBE, PEDro, PRISMA statement.

**Results:** Focus identified: socio-demographics variables, physical health status variables, clinical, psychosocial variables, sexual dysfunction associated with demographic, medi- cal and psychosocial aspects in stoma care.

**Conclusions:** The oncology nurses are essential in all phases of cancer care but their role in caring for the survivors is unclear. The identified focus, must be taken into account by the nurses from taking charge of the patient and be re-evaluated at each fol- low-up in order to identify actual problems and potential in order to improve their quality of life.
progestrone receptor, for which treatment is selected with Tamoxifen or Aromatase inhibitors orally for 5-10 years. One of the side effects associated with these drugs, which mostly affects the female sex, is weight gain. This condition, if associated with unhealthy food styles, can also cause an increase in cancer-related morbidity and morality. Nevertheless, the correlation between eating habits and the response to hormonal treatments still remains an unexplored area today. The aim of this narrative review is to describe the studies in literature on dietary habits in women with breast cancer in endocrine treatment.

Method: A narrative review of literature on online databases was performed with: PubMed, CINHAL, Scopus. The proposed Mesh string on PubMed, from which the free words used in the second phase are then identified, is: (“Breast Neoplasms”[Mesh] AND “Antineoplastic Agents, Hormonal”[Mesh]) AND (“Diet, Food, and Nutrition”[Mesh] OR “diet therapy”[Subheading]). All the studies published in English between 2006 and 2016 included studies on adult humans.

Results: Out of the 229 items identified, 10 items of interest were added to the eligibility criteria. These articles include: three systematic reviews, five cohort studies, one case-control study, and one related to creating guidelines. The most investigated elements are soy, coffee, alcoholic beverages, and lifestyle-related factors.

Conclusions: Given the limited number of studies and the ineffectiveness of the results, it cannot be established with certainty whether there is a real association between the intake of particular foods and the response to the treatment. For the future, it is recommended to repeat the review by expanding the number of databases consulted and leading a multicenter observational study to assess dietary habits and the quality of life of endocrine-treating breast cancer patients.
focused on caring body-mind-spirit in a complex, taking care of the whole person. Shiatsu is a complementary mind-body treatment; it can be considered like a psychological help during oncology disease. It could also be considered as a resource for well being, relaxation, and life quality improvement.

The aim of this observational study is to describe shiatsu effects in cancer patients and connection between this treatment and improvement on psychophysical well-being and quality of life (QoL).

The study involved 21 oncological patients of Day Hospital. These patients voluntarily took part in shiatsu treatment offered by an association that works in prevention and rehabilitation area. The study participants answered a questionnaire and EORTC-QLQ C-30 to respectively evaluate shiatsu effects on psychophysical well-being and QoL.

Shiatsu treatment improved health perceptions in patients, 65% of attendees declared that shiatsu activated changes in perception of themselves and their body. 85% showed psychophysical relaxation and the 75% felt general well-being. Subjective perception of fatigue decreased (-35%), like emesis (-35%), anxiety (-20%), depression (-15%); also parasthesias decreased, sleep quality and perceptions of energy of body and mind increased. The relationship between shiatsu professional and patient is rest on trust (95% of cases) because patients declared to feel embraced and well liked from the shiatsu professional. 45% of sample adopted a well-being oriented life style during and after shiatsu treatment. The 75% of sample felt benefits days after treatment. 65% of attendees adopted at least one CAM in the past and during the study 50% was adopting at least one type of CAM.

Shiatsu is a holistic treatment which shows multidimensional effects for well-being on the whole person. It could be considered a treatment that activate healing process, it could be integrated in the medical oncology care.

V25 Massage therapy and quality of life of cancer patient in palliative care: literature review

M. Pacei1, L. Casarighi1, M. Skok2, D. Rossa

1 Fondazione Don Gnocchi, Milan, 2 Fondazione Carlo Gnocchi, Milan

Introduction: The object of assistance to cancer patient, bearers of overall suffering, is to take care of the whole person, to ensure quality of life and accompany a peaceful death. Physical and psychological means of communication, going beyond words, it allows you to heard and be heard, reassure and demonstrate emotional participation.

Aim: Identify techniques and approaches complementary, such as massage therapy, and assess whether, with the traditional therapy, can improve the comfort of the person with advanced oncological disease, treating as a whole. Reference is made to concept of total pain not only physical suffering but also psychological, social and spiritual.

Material and methods: We have consulted databases such as: Reiki, therapeutic touching. Articles published before 2000 were exclude.

Results: The literature review 13 articles have been considered.

Conclusions: Because the literature is not documented adverse events related to massage therapy, it is considered and economic tool, non-invasive, easy to access and reach good levels of effectiveness, facilitating and establishment of an empathetic relationship. The evidence found allows the nurse to expand the knowledge and training of caring personal care that is more holistic and improve the quality of life.

V26 Narrative Medicine: from words ... to actions

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1 AO Ordine Mauriziano di Torino, Turin, 2 Fondazione Don Carlo Gnocchi, Milan

Background: "Narrative Medicine" (NM), also known as “Narration-based Medicine” (NBM), can be considered as a clinical-care intervention method that makes possible to define a personalized care pathway; furthermore, it allows all healthcare professionis to develop and improve their empathic, reflexive, listening ability with the purpose of taking care of the person, as well as cure the disease.

The nurse, responsible for the care process, all along is intended to take care of the person and, for education, to consider it as a whole. For nurses, thinking about their action is a duty, not only about technical and organizational aspects (based on the use of valid scientific instruments), but also about relationship and communication with the patient.

Here we report a direct professional experience in the NM field, based on the reading of a book written by the husband of a patient we have taken care for eleven years.

Methods: The book “Mentre aspetta vivo” ("While I wait live") tells how despite a terrible illness, judged “incorlicable” since diagnosis, one can live a life defined “a fantastic adventure” and testifies how, even with the knowledge that “cancer” has arrived and is scary, you may be unwilling to spend life waiting for the worst. The book, gave by the author, was read voluntarily by some nurses who took care of the lady. This has led to professional considerations resulting in improvement actions.

Results: This NM experience has brought several results in our clinical practice. Firstly, the awareness of how written words give voice and dignity to the sick people who are the protagonists of the care process (empowerment). Secondly, the recognition by the health team of the value of NM, so that health professional can optimally assist the patient in his/her history of illness. Finally, this experience allowed the realization of an organizational model aimed at creating moments of communication with patients.

Conclusion: NM helps those who live a disease experience to rebuild the new identity that ensues and allows the health team to know aspects of the quality of patients’ and caregivers’ life that cannot be evaluated with quantitative instruments, but only through their testimonies. The relationship, based on dialogue and narration requires proper training and should be integrated with Evidence-Based Medicine, to make clini-cal care decisions more complete, personalized and effective.

V27 “Cure alopecia”: results on the first period of use of the Dignicup system in the AORMN

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Background: Preventing hair loss during chemotherapy has always been the goal of the oncologist’s nursing, physician and the patient who has to undergo this treatment. Chemotherapy-induced alopecia, although reversible, is one of the most impacting psychological effects in treatment patients, but the woman’s patient has an impact, if possible, even greater. Psychosocial implications and alteration of the body image may affect the acceptance of chemotherapy treatment. (Kome et al, 2013, The Oncologist). Since 1970, various cooling systems have been used to prevent hair loss but with poor results and a high discomfort for the patient. Thanks to the improvement of technology, DigniCup is now used routinely in several centers of excellence in Italy and Europe.

The first results showed the following alopecia data:

- Treatment was positive in 81.2% of cases where hair loss was modest (G1 = 2 women, G2 = 7 women, G3 = 3 women); while in 18.8% of the cases the treatment failed (G4 = 2 women, G5 = 1 woman), but they continued treatment until the end of the therapy.

Among patients who have suspended the treatment: 4 patients with hair loss (G4)

1 patient for change therapy

1 patient for cold cough failure

1 patients for cold intolerance + hair loss (G4)

1 patients per intervention

Our partial experience shows that an effective cooling of the scalp and the use of a technologically advanced device such as Dignicup, favoring women in treatment: better collaboration between nurses and patients, better acceptance of chemotherapy, acceptance of its own body image that tends to not change, the maintenance of its daily and social activities.

It is clear from the reported data that patients have achieved satisfactory results; The percentage of patients leaving treatment does not give up on a tool that keeps patients more confidence in themselves and in their own image.

V28 A try to positively influence the quality of life of patients undergoing stem cell transplantation in protective isolation with the use of a tablet

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Background: Patients with Multiple Myeloma who undergo autologous stem cell transplantation (HCT) are often hospitalized in protective isolation in a single room. They cannot leave it and just one visitor can visit them for a short time. This situation might negatively affect their QoL. It was hypothesised that the use of a tablet during their hospital stay in isolation could improve their QoL, by reducing the distance with the external world and increasing their activities in the isolation room.

Material and methods: This was a pre-post study with two patient groups. A total of 8 patients completed the FACT-BMT questionnaire at admission and at discharge. Among these, 5 participants were provided with a tablet with Internet during hospital stay. Among these, 3 participants were provided with a tablet with Internet during hospital stay.

Results: After a 10-day treatment, tablet users showed a more significant improvement in FACT-BMT scores compared to non-users, with a 21% increase in total score for tablet users (p < 0.05). There was a significant increase in social and physical well-being scores for tablet users (p < 0.05). Tablet users also showed a significant increase in the ability to carry out daily activities (p < 0.05). Tablet users also showed a significant increase in the ability to carry out daily activities (p < 0.05). Tablet users also showed a significant increase in the ability to carry out daily activities (p < 0.05). Tablet users also showed a significant increase in the ability to carry out daily activities (p < 0.05). Tablet users also showed a significant increase in the ability to carry out daily activities (p < 0.05). Tablet users also showed a significant increase in the ability to carry out daily activities (p < 0.05).
Results: At discharge patients who used the tablet showed an improvement in the Social/Family Well-Being and their Physical/Social/Relational Limitations remained stable. The QoL of patients without a tablet worsened in these aspects. In particular patients with tablet referred to feel close like before to their caregivers, to feel closer than before to their friends and less far than before from people. They also reported that the tablet helped them to maintain a visual contact with the external world in an active way during the isolation. They used mostly applications to communicate, to read news and to play games. Although the tablet did not show a positive effect on caregivers’ anxiety and depression, they believed that the experience was positive because the tablet facilitated the relationship with the external world and family virtual contact.

Conclusions: Since protective isolation can worsen patients’QoL, nurses should help patients to find effective strategies to spend their time in a positive way and to reduce the isolation burden.

<table>
<thead>
<tr>
<th>Table: V28</th>
<th>Table: V28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well-Being</td>
<td>TABLET (n = 3)</td>
</tr>
<tr>
<td></td>
<td>TO</td>
</tr>
<tr>
<td>Physical</td>
<td>23 (1.73)</td>
</tr>
<tr>
<td>Social/Family</td>
<td>18.3 (6.42)</td>
</tr>
<tr>
<td>Emotional</td>
<td>19.3 (1.15)</td>
</tr>
<tr>
<td>Functional</td>
<td>15.6 (6.65)</td>
</tr>
<tr>
<td>Bone Marrow</td>
<td>28.3 (4.72)</td>
</tr>
<tr>
<td>Transplant Subscale</td>
<td>41.3 (8.32)</td>
</tr>
</tbody>
</table>

V29 "Feel beautiful to feel alive"

C. Tonnini¹, A. De Papa², F. Loiacono², G. Ricci¹, M. Romero¹, R. Giampiesi¹, M. Pistelli¹, A. Savini¹, M. Francoletti¹, R. Berardi¹
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Background: On March 8, 2016, the first Pink Day has been held at the Pink Room of the Department of Medical Oncology of our institution. The Pink Room is a literally pink ambulatory, involving internal hospital specialists and external professionals, who provides their professional skills free of charge to help women during anti-cancer treatment. The aim of the project is to help women recapture the physical image and psychological identity through complementary pathways to oncological therapies.

Materials and methods: A questionnaire investigating what is the perception of the body image as well as the unmet needs of the patients was administered to all the consecutive patients admitted to the Pink Room. The first part of the questionnaire included both personal data and medical data, while in the second part there were questions exploring the body image both before and after the illness and the unmet needs.

Results: The study included 86 patients with a median of 56 years of age. From the questionnaire, the following data emerged:

1. 96.2% of women who benefited the Pink Room are Italian;
2. 54.7% are married, 17% are nubile, 7.5% are divorced, 3.8% are cohabiting;
3. 39.6% have a high school diploma, 34% have a university degree and 26.4% have a lower or elementary secondary school license;
4. 47.2% declare to have a job, 32.1% are retired, 11.3% are unemployed and 9.4% are housewives;
5. 58.5% is in a post-menopausal state and 41.5% is in pre-menopausal state;
6. 62.3% have a diagnosis of breast cancer, 20.8% a gastrointestinal tumor, 5.7% an ovarian cancer and 1.9% a lung cancer;
7. 29.3% has required aesthetic advice, 20.3% breast cancer counseling, 12.2% hair styling and yoga counseling, 7.3% dermatological and nutritional advice, 6.5% psychological counseling, 2.4% endocrinological advice and 0.8% a plastic surgery consultancy;
8. 100% of women feel less physically attractive after the illness and the treatments.

Conclusion: As Jane Cook, breast cancer survivor, once said "breast cancer change you and the change can be beautiful". The pink room has the main goal of returning the patient’s self-confidence, respect and love to one’s own body. Aesthetic treatments, in a field like oncology, become true complementary therapies to the medical ones: “feel beautiful to feel alive” and to deal with the difficulties of the disease.

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D

D'Alonzo, A. (C1*) vi25, (C6) vi26
D'Aros, F. (G4) vi68
D'Alonzo, A. (A10) vi6
D'Ambrosio, L. (F1) vi66
D'Alonzo, A. (A19) vi8, (A8) vi15
D'Alonso, A. (C6) vi26
D'Amico, M. (C26) vi32, (C39) vi35, (C57) vi40, (U2) vi102
D'Amico, R. (3*) vi76
Dane, S. (3*) vi1
D'Ambrosio, L. (F1) vi66
Dalmolin, G. (C4) vi32, (C6) vi26
D'Amore, A. (C14) vi28, (C26) vi32, (C33) vi34, (C6) vi26
D'Arienzo, P. (D11) vi47
D'Amore, S. (A19) vi8
D'Amore, S. (A18) vi8, (A45) vi15, (B23) vi24, (C27) vi32, (C52) vi39, (E35) vi64
D'Ambrosio, L. (F1) vi66
D'Alonzo, A. (C6) vi26
D'Amore, S. (A18) vi8, (A45) vi15, (B23) vi24, (C27) vi32, (C52) vi39, (E35) vi64
D'Alonzo, A. (C6) vi26
D'Amore, S. (A18) vi8, (A45) vi15, (B23) vi24, (C27) vi32, (C52) vi39, (E35) vi64
D'Ambrosio, L. (F1) vi66
D'Alonzo, A. (C6) vi26
D'Amore, S. (A18) vi8, (A45) vi15, (B23) vi24, (C27) vi32, (C52) vi39, (E35) vi64
D'Ambrosio, L. (F1) vi66
D'Alonzo, A. (C6) vi26
D'Amore, S. (A18) vi8, (A45) vi15, (B23) vi24, (C27) vi32, (C52) vi39, (E35) vi64
D'Ambrosio, L. (F1) vi66
D'Alonzo, A. (C6) vi26
D'Amore, S. (A18) vi8, (A45) vi15, (B23) vi24, (C27) vi32, (C52) vi39, (E35) vi64
D'Ambrosio, L. (F1) vi66
D'Alonzo, A. (C6) vi26
D'Amore, S. (A18) vi8, (A45) vi15, (B23) vi24, (C27) vi32, (C52) vi39, (E35) vi64
D'Ambrosio, L. (F1) vi66
Gervasio, C. (L4) vi73
Ghesdi, A. (V7) vi103
Ghedini, P. (B21) vi23
Ghiandini, M. (L7) vi74
Ghidini, M. (D22) vi50, (D23) vi50
Ghiuggioli, A. (G10) vi6, (A35) vi13
ghiardi, M. (S9) vi91, (V5) vi103
Ghiotto, C. (C25) vi39
Ghiomi, E. (C33) vi59
Giaccherini, C. (P4) vi79, (T1) vi93, (T2) vi93
Giacinti, S. (T7) vi97
Giaj Leva, M. (E13) vi58
Giampieri, R. (A14) vi7, (A22) vi9, (A27) vi11, (C7)
vi26, (D19) vi49, (D24) vi50, (D5) vi45, (H8) vi7, (V29)
vii12
Giannetta, M. (E11) vi58, (E13) vi58
Giardino, N. (S5) vi90
Giannarelli, D. (C8) vi27, (E08) vi56, (T17) vi97, (V1')
vi105, (V7) vi106
Gianni, L. (C43) vi37, (D1') vi44, (D3) vi44
Giannini, R. (E07) vi56
Giannoni, G. (D11) vi73
Giannoni, G. (C53) vi39, (D30) vi52
Giannoncelli, L. (E30) vi63
Giampiero, C. (D25) vi100
Giaquinto, A. (C21) vi31, (C48) vi38, (C31) vi41, (R19)
vii6
Giaretto, L. (S3) vi89
Giarratano, G. (T2) vi99
Giarratano, T. (C4) vi12, (C20) vi31, (C31) vi39
Giavarra, M. (E25) vi61
Giglio, E. (D19) vi49
Gili, A. (E05) vi56
Gilli, M. (E21) vi60
Gini, S. (A5) vi4
Ginocchi, L. (C60) vi41
Giombelli, E. (M1) vi75
Gion, M. (P9) vi81
Giordani, P. (A1*) vi3
Giordani, S. (C22) vi31
Giordano, L. (P7) vi80
Giordano, M. (C2') vi52, (C25) vi32, (C33) vi34, (L4)
vi73
Giorgi, C. (E35) vi64
Giorgi, G.A. (C51) vi39
Giorgi, G. (T3) vi93
Giotta, F. (3') vi4
Giovanni, B. (D14) vi48
Giovanni, M. (A24) vi10, (D4) vi48, (D18) vi49,
(T13) vi96
Garcia-Saez, J.A. (C3) vi25
Garcia, M. (G3) vi66
Garcia-Arias, A. (C58) vi41, (H7) vi71
Garetta, S. (A2) vi3
Geppi, V. (3') vi41, (C55) vi40, (E02) vi54
Gedge, D. (B20) vi23
Gelbter, A. (C5) vi26, (D27) vi51
Gelmi, M. (V11) vi107
Gelsomino, F. (A22) vi9, (A23) vi10, (A37) vi13, (A6)
vi5, (E20) vi60
Generali, D. (C32) vi34
Genestreri, M. (G2) vi57, (M3) vi75, (M5) vi76
Genova, C. (E24) vi61
Gennari, F. (T6) vi71
Genta, S. (C53) vi39
Gentili, G. (T4) vi93
Gentili, M. (T7) vi95
Geremia, S. (V24) vi110
Geron, M. (E06) vi56
Goretti, S. (D29) vi52
Gottardi, C. (M20) vi31, (E09) vi57,
(M7) vi77, (R20) vi87, (R8) vi83
Gorti, S. (G7) vi62
Gottardo, G. (V22) vi110
Granata, R. (G1) vi68, (L2) vi73, (L5) vi74, (L6) vi74
Graneli, R. (T20) vi110
Grassi, E. (H17) vi97
Grassi, R. (C37) vi35, (C63) vi42
Gravina, A. (C40) vi16
Graziano, F. (A1') vi3, (A3) vi3
Graziano, V. (C5) vi26
Grazzella, P. (C61) vi41
Gregori, V. (E08) vi56
Gregori, D. (E23) vi61
Grigioni, S. (P4) vi79, (R11) vi84
Gritti, E. (T4) vi97
Grimignani, G. (F1) vi66
Grigsgolo, G. (C20) vi31, (C51) vi39, (C9) vi27
Griz, G. (C56) vi40
Grisi, F. (E26) vi62
Grisetti, R. (T21) vi98
Grotti, E. (D3) vi5
Grossi, F. (E01') vi54, (E02) vi54, (E24) vi61
Grosso, D. (C51) vi39, (V22) vi110
Grosso, F. (E17) vi59
Giuatti, G. (C50) vi38
Gualtieri, A. (D4) vi45, (L3) vi73
Gualtieri, A.A. (E26) vi62
Guerrieri, V. (3') vi14, (C14) vi28, (C2') vi25, (C20)
vi31, (C35) vi25, (C51) vi39, (C9) vi72
Guerrera, A. (T4) vi93
Guerrini, G. (C3) vi68
Guerrera, F. (E12) vi58
Guiglielmi, A. (D29) vi52
Guiglierti, L. (S1) vi89
Guirgis, J. (B1*) vi5
Guidi, F. (M1) vi79
Guida, L. (T21) vi98
Guida, M. (C14) vi60, (F04) vi66
Guidi, A. (T18) vi98, (T29) vi110
Guidelli, M. (T11) vi102
Guirneri, L. (D29) vi52, (R2) vi82
Gutman, G. (L7) vi74
Guzzo, M. (L5) vi74

H
Hamazi, A. (B7) vi81, (B8) vi19
Harusha, E. (A10) vi6, (A35) vi13
He, S. (E06) vi56
Hentrich, D. (B8) vi19
Hendlitz, A. (A2) vi3
Hengeler, M. (E21) vi60
Hill, A. (A2) vi3
Hollebecque, A. (E04) vi55
Howard, I. S. (B20) vi23
Hurvitz, S. (C3) vi25
Huscher, A. (C36) vi35

I
Iachetta, F. (T5) vi94
Iacobazzi, R.M. (F04) vi66
Iacono, D. (A24) vi10, (A32) vi12, (C18) vi30, (D18)
vi19, (C2) vi60, (R12) vi85, (T13) vi86, (T6) vi94
Iacono, G. (C6) vi26
Iacorossi, L. (V1*) vi105, (V12) vi107, (V14) vi108,
(V20) vi109, (V3*) vi105, (V4*) vi105, (V7) vi106,
(V8) vi106
Vandone, A.M. (C14) vi28, (C36) vi35
Vanella, P. (C36) vi35
Vannini, A. (C37) vi35, (C63) vi42
Vannini, F. (A5) vi4
Vannini, L. (H6) vi71
Varamo, C. (G5) vi69
Varea Menendez, R. (E03) vi54
Vargas, J. (E30) vi63
Vasile, E. (D11) vi47, (D13) vi48, (D8) vi46, (E07) vi56
Vasassali, L. (V11) vi107
Vasuri, F. (D12) vi47
Vatrano, S. (E12) vi58
Vavassori, V. (E30) vi63
Vecchiarelli, S. (E05) vi56, (E15) vi59, (E28) vi62
Veccia, A. (E34) vi64
Veltri, E. (A3) vi3
Veneziani, M. (E20) vi60
Ventriglia, J. (D25) vi51, (D26) vi51
Ventruto, M.L. (P3) vi79
Ventrila, S. (E12) vi58
Vergallo, S. (T23) vi99
Vernet, L. (E30) vi63
Vitale, M.G. (B1*) vi17, (B4) vi18, (C10) vi27, (C18) vi30, (C19) vi38, (C29) vi33, (C30) vi33, (D16) vi49, (G2) vi68, (H3) vi70, (T5) vi94
Vite, A. (E3) vi4
Vittorio, S. (T23) vi99
Vittone, M. (M2) vi75, (M3) vi75
Volante, M. (A16) vi8, (E12) vi58
Wassim, A. (B20) vi23
Waxman, J. (B15) vi21
Wirtz, R. (P9) vi81
Zainoni, E. (A12) vi6, (A21) vi9, (A22) vi9, (A6) vi5, (C38) vi35, (R17) vi86
Zanini, A. (R14) vi85, (V24) vi110
Zanlari, L. (T26) vi100
Zanocchi, M. (C51) vi39
Zanotto, L. (B14) vi21, (B17) vi22, (C31) vi33
Zanotti, L. (C38) vi35
Zapater, O. (A30) vi12
Zerbi, A. (D1*) vi4
Zhou, K. (C54) vi39
Ziaire, S. (A20) vi9
Zicarelli, D. vi6
Zimmermann, A. (E03) vi54
Zinoli, L. (B14) vi21, (B17) vi22, (C31) vi33
Zirar, P. (A22) vi9, (A42) vi15, (U10) vi104, (U3) vi102
Ziro, F. (C61) vi41
Zitella, A. (B13) vi20
Zito, C. (C49) vi38
Zivin, P. (B15) vi21
Zonta, S. (T18) vi98, (T29) vi101
Zoppoli, G. (A10) vi6, (A35) vi13
Zincari, D. vi6
Zimmermann, A. (E03) vi54
Zinoli, L. (B14) vi21, (B17) vi22, (C31) vi33
Zirar, P. (A22) vi9, (A42) vi15, (U10) vi104, (U3) vi102
Ziro, F. (C61) vi41
Zitella, A. (B13) vi20
Zito, C. (C49) vi38
Zivin, P. (B15) vi21
Zonta, S. (T18) vi98, (T29) vi101
Zoppoli, G. (A10) vi6, (A35) vi13
Zorza, O. (A30) vi12
Zucali, P. (B7) vi18, (B8) vi19
Zucchelli, G. (A4) vi4, (A5) vi4, (A9) vi6
Zucchi, L. (E17) vi6
Zunarelli, E. (M1) vi75
Zustovich, F. (E09) vi57
See you at the

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