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Late breaking abstract

*LBA2507 First line Cetuximab and Cisplatin with or without Paclitaxel in recurrent/metastatic head and neck cancer: a randomized phase IIb trial

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Background: Cisplatin (Cis), continuous infusion 5FU and Cetuximab (Cet) (EXTREME) first-line treatment extends overall survival (OS) over Cis and 5FU of recurrent/metastatic squamous cell head and neck cancer (RM SCCHN) patients. In EXTREME, Cet has been added to a 2-drug combination, which has never shown superior OS over any single drug. In this scenario, we are left with an open question about the true value of adding 1 or 2 drugs to biotherapy. Furthermore, a significant number of pts are excluded from EXTREME for the high incidence of ≥ G3 adverse events (AEs) (>80%), most of them attributable to 5FU. Paclitaxel (P) is active and safe, both alone and with Cis. We conducted a phase IIb trial comparing a 2-drug Cet-Cis regimen with a 3-drug combination (substituting 5FU with P) in terms of progression-free survival (PFS) and tolerability.

Methods: Eligible pts had confirmed untreated R/M SCCHN. Pts were randomized to a 3 vs. a 2-drug combination (Cet + Cis w/o P) with maintenance Cet after 6 cycles. Primary endpoint was PFS; secondary end-points were overall survival (OS), response rate (RR) and toxicity. We assumed a non-inferiority margin of 1.40 as compatible with efficacy.

Results: 201 patients were randomized 1:1 to each regimen; 191 were evaluable. PFS with CetCis (median, 6 months) was noninferior to PFS with CetCisPac (median, 7 months) (HR for CetCis vs CetCisPac 0.99; 95% CI:0.72-1.36, p=0.906; margin of noninferiority [90% CI of 1.4] not reached). Median overall survival was 13 vs 11 months (HR=0.77; 95% CI:0.53-1.11, p=0.117). The overall response rates were 41.8% vs 51.7%, respectively (OR=0.69; CI:0.38-1.20, p=0.181). Grade ≥ 3 adverse event rates were 76% and 73% for CetCis vs CetCisPac, respectively, while grade 4 toxicities were lower in the 2-drug vs 3-drug arm (14% vs 33%, p=0.015). No toxic death and sepsis were reported and cardiac events were negligible (1%).

Conclusions: A 2-drug Cet and Cis regimen proved to be non-inferior in PFS to a 3-drug combination with Cet, Cis and P.
The median OS of both regimens is comparable with the 10.1 mos in EXTREME, while life-threatening toxicity rate appeared reduced.
These regimens warrant further investigation as a backbone to cancer immunotherapy.

Clinical trial identification: EudraCT number: 2011-002564-24

A*LBA2449 Extensive characterization and prognostic analyses of BRAF mutated metastatic colorectal cancer: clinical results from the "BRAF, BeCool" platform

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Background: BRAFmut assessment is routinely tested in mCRC. The unfavourable outcome of mut patients is well established and their specific clinical features have been repeatedly defined and reported. At the same time, molecular heterogeneity within the group of BRAFmut cancer was recently described. Up to now, the relatively low incidence of this alteration hampered extensive prognostic clinical analyses which would be useful for better informing physicians and patients on real disease aggressiveness and life expectations.

Patients and methods: Main eligibility criteria included: mCRC and BRAF V600E mutation as assessed on primary tumour or any metastatic site. A prognostic score was developed by an internal cross-validation procedure: the whole population was splitted in a training (67%) and in a testing (33%) sample (process repeated 10 times). Primary EP was OS. MV analysis was performed on each training sample and covariates with independent prognostic value were included in the scoring system, assigning rounded scores to the covariates.

Results: A total of 395 mCRC patients with a BRAF V600E mutation were included. At MV analysis, independent predictive factors of OS were ECOG PS (1 vs 0; 2-3 vs 0), Ca19.9 (high vs normal); LDH (≥300 vs low); neutrophil/lymphocyte ratio (>3 vs low); tumor grading (3-4 vs 1-2); liver mets (yes vs no); lung mets (yes vs no); node mets (yes vs no). Two different scoring systems were built: a «complete» score (0-18), selecting all significant covariates; a «simplified» score (0-11), excluding laboratory values. With "complete" score, proportion of patients with low (0-4), intermediate (5-8) and high (9-18) score was 39%, 46% and 15%, respectively. Median OS was 27.6, 18.7 (HR interm. vs low 1.89, 95%CI 1.25 – 2.86, p=0.003) and 6.6 months (HR high vs low 4.95, 95%CI 2.89 – 8.47, p<0.0001), respectively. Analysis adjusted for type of first-line treatment produced similar results. Median PFS was 11.1, 8.6 (HR interm. vs low 1.36, 95%CI 0.94 – 1.97, p=0.11) and 4.1 months (HR high vs low 3.50, 95%CI 1.98 – 6.20, p<0.0001). Similar results were obtained with the simplified score.

Conclusions: These results should be replicated in an independent cohort, but the internal validation makes this model robust enough to justify the effort of a confirmatory study. Strong and reliable prognostic factors in new molecular subgroups of mCRC will be determinant for properly stratifying clinical trials and for adjusting exploratory translational analyses.

B*LBA2454 Real world data from the Italian expanded access program (EAP): updated safety and efficacy results of nivolumab for metastatic renal cell carcinoma (mRCC)

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Background: Nivolumab is an anti-PD1 monoclonal antibody that has shown efficacy in patients (pts) with different tumor types and is the first checkpoint inhibitor to show a survival benefit in a randomised phase III trial in pre-treated mRCC. The experience of pts and physicians in routine clinical practice is often different from those in a controlled clinical trial

setting. The EAP provided the opportunity to treat pts in real world clinical practice before market availability of the drug. The aim of this analysis is to evaluate the safety and efficacy of nivolumab in a real world setting in pts with mRCC treated in the nivolumab EAP in Italy.

Materials and methods: Nivolumab was available upon physician request for pts aged ≥18 years who had relapsed after a minimum of one prior systemic treatment for mRCC. Nivolumab 3 mg/kg was administered intravenously every 2 weeks. Pts included in the analysis had received ≥ 1 dose of nivolumab and were monitored for adverse events using CTCAE v.4.0.

Results: Totally, 389 pts were enrolled in the EAP across 95 Italian sites, median age was 65 years (range, 34-85) with 70 (18%) aged = 75 yrs. Pts had a clear-cell RCC in 92% of cases, bone metastases in 50%, liver metastases in 33% brain metastases in 8%, and received more than one previous line in 79% of cases. At the time of this analysis, median number of doses received was 12 (1-35) and 100 (26%) pts were treated beyond progression. Among 389 pts, drug-related adverse events (AEs) were reported in 27 pts (7%). Furthermore, 18 pts (5%) discontinued treatment due to AEs which were reported drug-related only in 9 pts (2%). The best overall response rate was 22.1% including 2 complete and 84 partial responses, whereas 120 (31%) had stable disease. With a median follow-up of 9.2 months (range, 0.1 to 17), 6-month and 12-month survival rates were 80.2% and 64.1%, respectively. Furthermore, median overall survival has not yet been reached. Comparable response and survival rates were reported among pts pretreated with everolimus, primary refractory, elderly, those with bone or brain metastases, and high number of prior therapies.

Conclusions: This EAP represents the most extensive reported real-world experience with nivolumab in pre-treated mRCC pts. These data seem to confirm efficacy and safety data of the pivotal trial in a real world setting, including primary refractory, different age, site of metastases, number of prior therapies, and also pts pretreated with everolimus.

BLBA2601 Prognostic role of hemochrome parameters (neutrophil–lymphocyte ratio, platelet–lymphocyte ratio, lymphocyte-monocyte ratio and macrocytosis) in patients affected with metastatic renal cell carcinoma(mRCC) treated with Sunitinib

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Background: Few data are available regarding the impact of neutrophil–lymphocyte ratio(NLR)and platelet–lymphocyte ratio(PLR), lymphocyte-monocyte ratio(LMR) in metastatic renal cell carcinoma(mRCC) patients receiving tyrosine kinase inhibitors.Moreover, preliminary data affirm that erythrocyte's mean corpuscular volume(MCV)increase is seen during treatment with Sunitinib and that it is associated with a better outcome.

Patients and methods: We retrospectively collected and analyzed data from 73patients(pts)affected by mRCC treated with Sunitinib as first-line therapy between January 2006 until December 2016 in five Italian Oncology Unit(Varese,Busto Arsizio,Gallarate,Vigevano,Pisa).We evaluated cellular blood count at the diagnosis and periodically during Sunitinib treatment. We evaluated NLR,PLR,LMR and macrocytosis to establish the prognostic role of these factors.Considering data available from the literature, we used the following cut off:NLR>3,PLR >150,LMR<3 and macrocytosis with MCV>100 fl.Data regarding age,sex,performance status(PS),histology,BMI, previous nephrectomy,Furhman's grading,MSKCC score,Heng score and number of metastatic sites were collected.Overall survival(OS)and progression free survival(PFS)were calculated until 24 months of follow-up. Univariate and multivariate analysis using cox's regression model were performed.

Results: Of the 73patients enrolled,26 presented high NLR,31 presented high PLR,23presented low LMR at the diagnosis of metastatic disease.Ten patients developed macrocytosis (average MCV was 106fl)during sunitinib treatment.High NLR was correlated to a risk of progression and mortality: median PFS was 9 months vs 13 months (p=0.08) and median OS was 22 vs 28 months (p=0.03). Low LMR was slightly associated with worse outcome: median PFS was 11 months vs 15 months (p=0.2) and median OS was 24 vs 30 months(p=0.047). No significant differences in PFS and OS were observed between patients with high PLR and patients who developed macrocytosis. At the multivariate analysis, Heng score>3and more than two metastatic sites were associated to poor prognosis(HR=6.7, 95% IC 1.2-37.2, p=0.03 and HR=3.25, 95% IC 1.21-8.63 p=0.02, respectively); regarding the hemochrome parameters analyzed only NLR resulted associated to poor prognosis(HR 3.43, 95% IC 1.41-8.3,p=0.006).

Conclusions: High NLR was associated with shorter survival in our mRCC patients receiving Sunitinib in first-line treatment. Further prospective studies are required.

CLBA2710 Efficacy and Safety Results from the MONARCH 1 and MONARCH 2 Studies of Abemaciclib in Patients (Pts) with HR+/HER2– Locally Advanced (LA) or Metastatic Breast Cancer (MBC)

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Background: Abemaciclib, an oral, selective inhibitor of CDK4 & 6, has been studied in various breast cancer settings. MONARCH 1 (NCT02102490) was a phase 2 study of abemaciclib monotherapy in pts with HR+, HER2– MBC who progressed on or after endocrine therapy (ET) and chemotherapy. MONARCH 2 (NCT02107703) was a randomised, double-blind, phase 3 trial of abemaciclib+fulvestrant (F) vs placebo (P)+F in pts with ET-resistant HR+, HER2– LA or MBC (ET resistance defined as progression on [neo]adjuvant ET, or ≤12 mo from the end of adjuvant ET, or on 1st-line ET for MBC).

Methods: MONARCH 1: Abemaciclib was dosed continuously at 200mg BID. Primary objective (PO): objective response rate (ORR). Secondary objectives (SOs) included duration of response (DoR), progression-free survival (PFS), overall survival (OS), safety. MONARCH 2: Pts were randomised 2:1 to receive abemaciclib 150mg BID (after dose reduction from 200mg BID per amendment) or P on a continuous schedule and F 500mg IM injection per label. Pre/perimenopausal women also received a gonadotrophin-releasing hormone agonist. PO: investigator-assessed PFS. SOs included OS, ORR and safety. Final analysis was planned at 378 PFS events to provide 90% power to detect superiority of abemaciclib+F vs P+F using a log-rank test, assuming a hazard ratio (HR) of 0.703 at a one-sided alpha of 0.025.

Results: MONARCH 1: 132 pts enrolled.12 mo after last pt started treatment, ORR (investigator-assessed) was 19.7% (95%CI 13.3, 27.5), median DoR was 8.6 mo (5.8,10.2), median PFS was 6.0 mo (4.2,7.5). At 18 mo, median OS was 22.3 mo (17.7,NR). Most common grade (gr)≥3 TEAEs included diarrhoea (19.7%), fatigue (13.6%). Most common gr3/4 laboratory AEs included leucopenia (27.7%), neutropenia (26.9%). MONARCH 2: 669 pts randomised (median follow-up 19.5 mo). 379 PFS events occurred with a median PFS of 16.4 mo for abemaciclib+F vs 9.3 mo for P+F (HR 0.553 [0.449,0.681]; p<0.0000001); ORR was 48.1% vs 21.3% in pts with measurable disease. Most common gr≥3 AEs (abemaciclib+F vs P+F) included neutropenia (26.5% vs 1.7%) and diarrhoea (all gr3, 13.4% vs 0.4%).

Conclusions: Abemaciclib 200mg BID achieved durable tumour responses in pts with HR+, HER2– MBC with progression on or after ET and chemotherapy (MONARCH 1). Abemaciclib 150mg BID+F significantly improved PFS and ORR in pts with HR+, HER2– LA or MBC who progressed on ET (MONARCH 2). Most common toxicities were predominantly low grade diarrhoea and neutropenia.

CLBA2716 Prospective observational pilot study on AMH role as predictor of future ovarian function among young premenopausal women treated with adjuvant or neoadjuvant chemotherapy for early breast cancer.

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Background: Premenopausal women treated with chemotherapy (CHT) for early breast cancer (eBC) are at risk for premature ovarian failure (POF). Prospectively-validated, predictive markers of POF are needed. Some studies supporting the use of anti-Müllerian hormone (AMH) serum levels as a biomarker of the growing follicle pool to predict the degree of the ovarian follicle loss, being useful for fertility preservation strategies, fertility counselling and future family planning in patients (pts) being treated for eBC. The aim of the study was to prospectively evaluated serum AMH levels before CHT and after 2-6 and 12 months from the end as ovarian reserve predictor.

Material and methods: A prospective cohort of 15 premenopausal pts = 45 years (ys) [32-44 ys] with eBC undergoing CHT (neoadjuvant and/or adjuvant) were recruited from April 2015 to April 2017. Ovarian reserve markers (FSH, estradiol and AMH) were evaluated pre-CHT, 2 - 6 and 12 months post-CHT and correlated with age, menstrual status, CHT regimens in association or not to endocrine therapy and histological features of eBC. We considered optimal fertility AMH range values from 4 to 6.8 ng/mL, satisfactory from 2.2 to 4 ng/mL.

Results: 15 pts were evaluated. Median age at diagnosis was 38.8. 7 pts were luminal B HER2-ve; 2 pts were luminal B HER2+ve and 6 pts were triple-ve. 4 pts presented with BRCA1 mutation. 14 patients received anthracyclines, all patients received a taxane CHT regimen. AMH range of our laboratory for women from 13 to 45 ys is 0.84-9.52 ng/mL. Median AMH value at baseline was 5.49 ng/mL in <35 ys pts group; 4.32 ng/mL in 35-39 ys and 1.23 ng/mL in 40-45 ys. Older age at diagnosis was associated to lower AMH value (P value=0.04). The relationship between chemo-induced gonadotoxicity and initial AMH reduction was statistically significant (p value=0.004). For pts with longer follow up we observed a progressive recovery of AMH value using LHRH analogue during CHT with menses recovery after the end of therapy. One pt is pregnant.

Conclusions: Our study confirms the relationship between AMH values and age but the small number of pts and the current short follow up do not allow to evaluate the involvement between low AMH value and post CHT ovarian function. The study is ongoing.

E*LBA2551 Real-world results in patients with advanced non-squamous non small-cell lung cancer (non-Sq-NSCLC) treated with Nivolumab in the Italian Expanded Access Program

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Background: Nivolumab has been approved by different regulatory agencies worldwide for the treatment of non-Sq-NSCLC based on a survival benefit in a randomised phase III trial (Checkmate 057). However, the routine clinical practice outcome may be different from that of a controlled clinical trial setting. The purpose of this analysis is to evaluate nivolumab use in real world setting.

Methods and Materials: Nivolumab was available upon physician request for patients (pts) aged ≥18 years who had relapsed after a minimum of one prior systemic treatment for stage IIIB/stage IV non-Sq-NSCLC. Nivolumab 3 mg/kg was administered intravenously every 2 weeks to a maximum of 24 months. Pts included in the analysis had received ≥1 dose of nivolumab and were monitored for adverse events using Common Terminology Criteria for Adverse Events (CTCAE 4.0).

Results: From May 2015 to April 2016, 1588 pts were enrolled in the EAP in 168 Italian centers. Table shows pts characteristics. With a median follow-up of 8.1 months (1-27.4), the best overall response rate is 18%: 12 pts (<1%) with complete response and 278 pts (18%) with partial response. Stable disease has been reported in 414 pts (26%). Median overall survival (OS) is 11.3 months (10.2-12.4) and 1 year OS is 48%. Response rates and survival are comparable among pts regardless age, presence of brain metastasis and number of prior therapies. To date, median number of doses received is 7 (1-55). Among 1588 pts, 1300 (82%) discontinued treatment for any reason, with only 65 (5%) discontinuations due to related adverse events (AEs). Overall, any grade and grade 3/4 treatment related AEs occurred in 523 (33%) and 102 (6%) pts, respectively. The most frequent grade 3/4 treatment related AEs were fatigue/asthenia, dyspnea, increased transaminase and pneumonitis.

Conclusions: This EAP represents an extensive real-world experience with nivolumab in previously treated, advanced non-Sq-NSCLC. These data confirm what observed in the Checkmate 057 pivotal trial, both in terms of efficacy and in terms of safety.

Table E*LBA2551

	N= 1588
GENDER, n (%)	
Male	1029 (65)
AGE (median; range)	66 (27-89)
≥ 70 yrs, n (%)	520 (33)
≥ 75 yrs, n (%)	230 (15)
SMOKING HABITS, n (%)	
Former/current smoker	1125 (79)
Never smoker	305 (21)
NA	158
ECOG PS, n (%)	
0	648 (41)
1	815 (52)
2	108 (7)
NA	17
METASTASIS, n (%)	
Brain	409 (26)
Liver	326 (21)
Bone	626 (39)
Nodes	1168 (74)
PREVIOUS THERAPIES, n (%)	
1	378 (24)
2	562 (36)
3	332 (20)
≥ 4	307 (20)
NA	9

E*LBA2313 A randomized phase II trial of maintenance oral metronomic vinorelbine versus close observation in advanced Non Small Cell Lung Cancer (NSCLC) following platinum-based chemotherapy: MANILA trial

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Background: Several studies have proven the efficacy of maintenance chemotherapy (CT) in advanced NSCLC. The use of low dose anti-mitotic drugs (metronomic schedule) could also exert an anti-angiogenic effect while maintaining cytotoxic activity. In this study, we aimed to assess the activity of metronomic oral vinorelbine as switch maintenance treatment following platinum-based CT in patients with advanced NSCLC.

Methods: In this multicentre, randomized, controlled, phase II study, patients with stage IIIb/IV NSCLC not progressing after for to six cycles of platinum-based induction CT, received metronomic oral vinorelbine (50 mg three times per week) as maintenance treatment or close observation. Randomization with a 1:1 allocation ratio was stratified for the following factors: performance status (PS 0-1 vs 2), histology (adenocarcinoma vs other), number of CT cycles (4 vs 6). The primary endpoint was progression free survival (PFS); 98 PFS events were necessary to detect a hazard ratio (HR) of 0.60 with type I (one-sided) error rate set at 5% and power of 80%. Secondary endpoints were overall survival (OS), safety and QoL. Exploratory analysis investigated predictive correlations with serum angiogenesis biomarkers (VEGFA, THBS1) through Elisa KIT and with previous validated miRNA signature classifier (MSC) using quantitative Real-Time PCR.

Results: A total of 120 patients were enrolled from January 2013 to April 2017. Median age was 68.7; M/F: 80/40; stage IIIb/IV:19/101; adenocarcinoma/other:73/47; PS 0-1/2:113/7. After median follow up of 15.9 months, 105 PFS events were collected. Median PFS was 4.2 months for metronomic vinorelbine (ARM A) and 2.8 months for close observation (ARM B) showing no significative difference between two arms [Hazard Ratio (HR)= 0.80; 90% CI 0.58-1.10; one-sided p-value = 0.12]. The most common adverse events of grade 3-4 in ARM A were neutropenia (27%), asthenia (6%) and anemia (4%). A total of 14 patients (28%) stopped vinorelbine for unacceptable toxicity. High VEGFA and THBS1 plasma levels were found to be associated to shorter PFS as well as positive MSC expression (HR for 1000 unit, VEGF:1.58; HR for 10.000 unit, THBS1:1.17; HR for MSC pos vs neg: 1.49).

Conclusions: Switch manteinance with metronomic oral vinorelbine showed a modest PFS improvement for patients with advanced NSCLC following induction platinum-based CT which was not statistically significant. Dose adjustments are required in case of further explore this strategy.

HLBA2485 TALL/IP/2 TRIAL: feasibility of intraperitoneal adoptive cell therapy in ovarian cancer patients with minimally residual disease

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Background: Ovarian cancer is a major cause of cancer mortality with a five-year survival below 45% and, unfortunately, the majority of the patients relapses and dies even after achieving a complete response with cytoreductive surgery and platinum-based chemotherapy. Peritoneal recurrence occurs in 60% of patients. Randomized trials reported that intraperitoneal therapy significantly improves survival in optimally debulked ovarian cancer patients. Adoptive therapy with intraperitoneal administration of TALL-104 cells in patients with peritoneal carcinomatosis has shown a good safety profile with potential antitumor effect in highly pretreated patients. The aim of this analysis is to evaluate the feasibility of intraperitoneal TALL-104 cells in ovarian cancer patients enrolled in TALL/IP/2 trial.

Material and Methods: TALL/IP/2 trial is a multicentric phase II trial of intraperitoneal therapy with TALL-104 cells in patients with stage III-IV FIGO ovarian cancer with minimal or microscopic residual disease at second-look laparotomy/laparoscopy after a platinum-based first line chemotherapy. Primary endpoint is the conversion rate from minimal/microscopic residual disease to pathological complete response. TALL-104 cells are administered by intraperitoneal port-cath at day 1, 3, 5, 15 of a 30-day course at a dosage of 5 x 108/cells for each infusion. After three courses, a third laparoscopy is performed to assess the pathological response. Enrolling started from January 2015 in seven Italian centers and is still ongoing.

Results: A total of 18 patients have been screened: ten patients were considered not eligible, seven patients completed the treatment and one patient has been withdrawn after two courses for progressive disease. A total of 92 intraperitoneal infusions of TALL-104 cells have been administered with no acute adverse events. All patients experienced taste change and alitosis related to the DMSO present in the cell bags. No grade 4 toxicities were observed. One patient experienced grade 3 bacterial peritonitis requiring intraperitoneal port-cath removal and infusional antibiotic therapy. Grade 1-2 toxicities have been reported in 13% of 92 infusions.

Conclusions: These results demonstrate the feasibility and safety of intraperitoneal infusion of TALL-104 cells and the only severe toxicity appears to be catheter-related. The TALL/IP/2 trial when completed, will allow to assess the activity of adoptive intraperitoneal therapy.

HLBA2697 Dose-Dense Taxol, Ifosfamide and Platinum (TIP-DD) in treatment of advanced cervical carcinoma: a clinical effectiveness case series

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Background: Locally advanced or metastatic cervical cancer represents an aggressive tumor with a poor prognosis. To date, a dose dense chemotherapy scheme has not been assessed on this population, therefore, no data on its efficacy are currently available.

Patients and Methods: Aim of this study was to assess the efficacy and tolerability of the TIP regimen given with a dose-dense approach. We performed a retrospective review of all cases with a diagnosis of locally advanced or metastatic cervical cancer seen at the Oncology Division of the ASST of Cremona from November 2004 to May 2017. We retrospectively identified a pool of 16 patients treated with intravenous Ifosfamide 2500 mg/m2 and Mesna 2500 mg/m2, on day 1; intravenous Paclitaxel 175 mg/m2 and Cisplatin 70 mg/m2, on day 2 every 2 weeks. This regimen was applied for a maximum of 6 cycles with prophylactic granulocyte colony stimulating factor (G-CSF). Response rate was evaluated using the RECIST 1.1 criteria. Safety profile, including acute and late toxicity of chemotherapy was assessed. Morover, we investigate the time to progression (TTP) and overall survival (OS) within this population.

Results: The selected population of 16 patients had a median age of 53 years (range 40-78), PS 0-1, 15 (94%) squamous histology and 1 adenocarcinoma; FIGO Stage was IIB in 2 (12.5%), IIIA in 1 (6%); IIIB in 2 (12%) and IV in 11 (69%). Median number of TIP-DD cycles was 6 (range 1- 7). Following chemotherapy, nine patients underwent surgery (56%) and five patients received pelvic radiotherapy (31%). We observed 6 (40%) complete responses and 8 (53%) partial responses for a overall response of 93% (IC 1.06-0.81). At present, the disease recurred in 7 patients (53%) and of seven patients are still alive (36%). Four patients performed further treatments (29%). Median TTP was 14.8 months (IC 95%: 6.5-NR) and median OS was 24.1 months (95% CI: 9.3-90). Treatment was interrupted and delayed in 10 patients (62%). Toxicities included grade 3-4 neutropenia: 6% (0% febrile neutropenia), grade 3-4 thrombocytopenia: 6%, grade 2

neuropathies 12%; grade 2 asthenia/fatigue 12%, and no treatment-related deaths.

Conclusions: This retrospective case series study provides compelling results for the treatment of metastatic cervical cancer and suggest that TIP-DD might be a possible cure for this pathology. However, due to limitations of the trial design, this approach should be studied in prospective trials prior to drawing any conclusions.

MLBA2531 REGOMA: a randomized, multicenter, controlled open-label phase II clinical trial evaluating regorafenib (REG) activity in relapsed glioblastoma (GBM) patients (PTS)

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Background: There is no established treatment regimen for recurrent glioblastoma (GBM). GBMs have high expression of pro-angiogenic factors and activation of multiple signaling pathways in the tumor microenvironment, including the receptor tyrosine kinases, VEGFR, FGFR, and PDGFR. Regorafenib (REG), an oral multikinase inhibitor, inhibits these angiogenic kinases and the mutant oncogenic kinases KIT, RET, and B-RAF.

Methods: The primary aim of this academic trial was to assess REG activity in prolonging overall survival (OS) in patients (PTS) with relapsed GBM after surgery and Stupp regimen (alfa= 0.2, 1-sided; beta=0.2). Secondary objectives were disease control rate (DCR), safety, progression free survival (PFS), quality of life (QoL) and analysis of angiogenic and metabolic tissue biomarkers as possible predictors of response to REG. Eligible PTS with histologically confirmed GBM, ECOG PS 0-1, and documented disease progression were randomized 1:1 to REG 160 mg/day (3 weeks on, 1 week off) or lomustine (LOM) 110 mg/m2 (every 6 weeks) until disease progression or unacceptable toxicity. Tumor response was evaluated by gadolinium brain MRI every 8 weeks according to the RANO criteria.

Results: Between November 2015 and February 2017, 119 PTS were enrolled (n=59 REG; n=60 LOM) and stratified for surgery at recurrence; baseline characteristics were balanced. Median age was 57.3 yrs and MGMT was methylated in 47.5% and 44.1% of REG and LOM PTS, respectively. 27 PTS (22.7%) had surgery at recurrence. At the time of analysis 73 PTS had died. Median OS was 6.5 months (m) (95%CI 5.6-12.0) for REG and 5.5m (95% CI 4.7-8.0) for LOM (HR=0.64; 80% CI 0.47-0.87; p=0.028, 1-sided log-rank test). DCR (CR+PR+SD) was 44.8% and 21.1% (p=0.009) for REG and LOM, respectively. The 6 month PFS rates were 15.5% and 8.3% for REG and LOM (HR=0.69; 95% CI 0.47-1.01; p=0.051). Grade ≥3 adverse events were reported in 56% and 40% of PTS who received REG and LOM.

Conclusions: In this randomized, controlled study we report for the first time REG activity in PTS with relapsed GBM. REG significantly improved OS and DCR in recurrent GBM compared to LOM. REG dministration was feasible and safe. QoL and biomarker analyses are ongoing.

SLBA2620 INDICATORS OF SIMULTANEOUS CARE (SC) IN ESMO-DESIGNATED CENTERS OF INTEGRATED ONCOLOGY AND PALLIATIVE CARE (ESMO-DCs): WHERE DO WE STAND IN ITALY?

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Background: Over the past decade, several data have confirmed the role of SC in improving patient outcomes. To date, the benefits of such integration have become evidence-based. Since 2004 ESMO started a program to define centers of integrated oncology and palliative care (PC). In a recent international consensus, Hui et al. (Ann Oncol 2015) identified 13 major indicators of integration of PC and oncology. Based on these findings , on behalf of AIOM "Simultaneous and Continuous Care (SCC)" task force, we proposed a survey among the 41 italian ESMO DCs.

Methods: According to the 13 major indicators of SC , a web-based questionnaire developed by AIOM SCC task force was sent by March 2017 to representatives of each Italian ESMO DC. Each Center had to indicate its position about each of the 13 indicators identified by Hui et al. All 41 italian ESMO DCs were asked to return the completed questionnaire by May 2017. Data entry was performed by AIOM - SCC task force and descriptive statistics of the data were performed using Microsoft Office Excel® software, 2010.

Results: In terms of clinical structure, about 75% of DCs had both PC inpatient consultation team and PC outpatient clinic. Among the clinical processes, the vast majority of DCs had an interdisciplinary PC team (82%), made a routine symptom screening in the outpatient oncology clinic (85%), provided a routine documentation of advance care plans in patients (pts) with advanced cancer (85%) and offered an early referral to PC (98%). 72% of DCs had a SC clinic. Among clinical outcomes, 83% of pts received a pain assessment on either of the last two visits before death but about 40% of pts had 2 or more emergency room visits in the last 30 days of life and the place of death was consistent with patient's preference in 55% of cases only. Among education's indicators, 63% of DCs offered a didactic PC curriculum for oncology fellows provided by PC teams but several DCs (38%) didn't provide a routine rotation in PC to oncology fellows. A continuing medical education in PC for attending oncologists and combined PC and oncology educational activities were provided by almost 90% of DCs.

Conclusions: Despite the presence of weaknesses in some clinical outcome and education indicators , Italian ESMO DCs showed a quite satisfactory level of integration between oncology and PC: they should make efforts to further improve the efficacy of SC and promote the spread of this integrative model even in non-DCs.