ADENOCARCINOMA del PANCREAS

highlights from ASCO GI 2016

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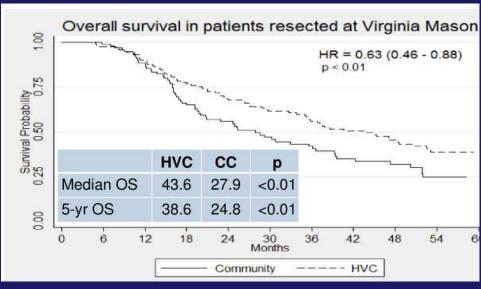
adjuvant center volume

METHODS

Patient were identified through VM cancer registry (reports to western WA SEER) and programspecific database

Eligible:	Diagnosis 2003-2014
	Primary resection at VM
	Intention to give adjuvant Rx at VM or referral to medical oncologist
Exclusions:	Neoadjuvant Rx
	Synchronous cancer
	Death, lost to follow-up or disease progression within 3 mos following surgery
	Refusal to receive adjuvant Rx
	Medical oncologist and/or receipt of Rx absent in medical record and SEER registry

	HVC* (n=139)	CC n=(106)	р
T stage (%1 or 2)	15	13	ns
Node status (% pos)	69	72	ns
Margin status (% positive)	22	20	ns
ECOG %0/	1 73/27	70/30	ns



I LINE Metastatic Locally advanced

Evofosfamide (TH-302) in combination with gemcitabine in previously untreated patients with metastatic or locally advanced unresectable pancreatic ductal adenocarcinoma: primary analysis of the randomized, double-blind phase III MAESTRO study

Eric Van Cutsem

Lenz H-J, Furuse J, Tabernero J, Heinemann V, Ioka T,
Bazin I, Ueno M, Csoszi T, Wasan H, Melichar B, Karasek P, Macarulla T,
Guillen-Ponce C, Kalinka-Warzocha E, Horvath Z, Prenen H,
Schlichting M, Ibrahim A, Bendell J

University Hospitals Leuven, Leuven, Belgium

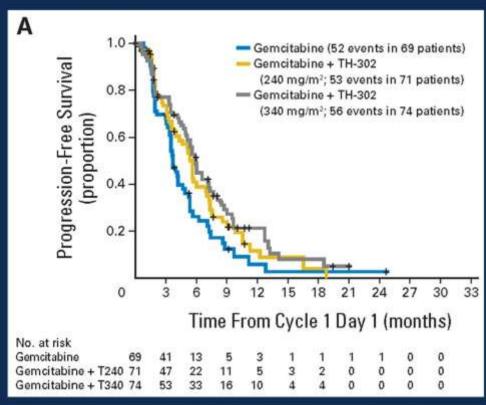
Pancreatic cancer, hypoxia, and novel therapy

- Median OS for advanced pancreatic cancer is 6–11 months^{1,2}
- The tumor microenvironment in pancreatic cancer is characterized by hypoxia, which modulates many of the key features of cancer²⁻⁴
- Hypoxia-activated prodrugs (HAPs) are designed to preferentially release chemotherapeutic agents within hypoxic tumor regions⁵
- Evofosfamide is a HAP that preferentially releases the cytotoxic bromoisophosphoramide mustard (Br-IPM) in areas of severe hypoxia^{5,6}
- Combining evofosfamide with conventional chemotherapy has the potential to induce cell death in hypoxic and normoxic tumor cells, and demonstrated activity in a randomized phase II trial⁷

Phase II primary endpoint: PFS

Median PFS

- 3.6 months for gemcitabine
- 5.6 months for G+T240 (P=0.040; HR, 0.66)
- 6.0 months for G+T340 (P=0.008; HR, 0.59)



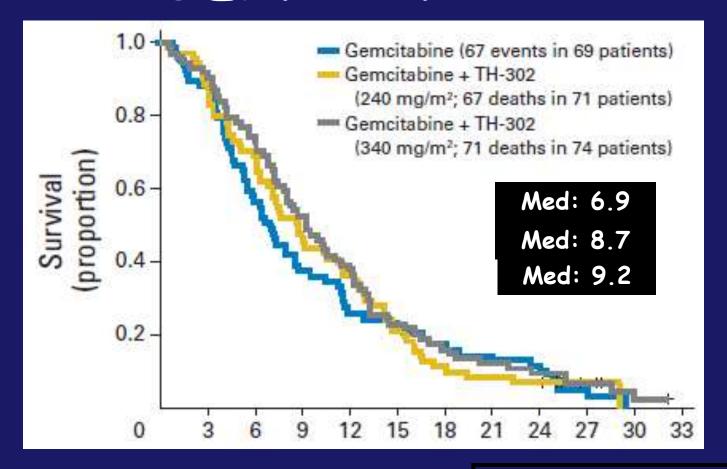
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Borad, et al. J Clin Oncol 2015

Borad et al., JCO 2014

GEM + TH-302



Gem vs gem + TH-302 (340 mg) HR: 0.86; p=0.39

Includes LAPC and MPC 😊

Gem vs gem + TH-302 (240 mg) HR: 0.95; p=0.77

Borad et al., JCO 2014

Randomized, double-blind phase III MAESTRO trial: design

Evofosfamide 340 mg/m² + gemeitabling 1 000 mg/m² Includes LAPC and MPC v cycle > Gem schedule is not the standard Unrese ued until disease advanced (-14% DI as in PRODIGE-ACCORD)! erable toxicity, or thdrawal Comaprator arm is not the standard v cvcle (n=347)

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Phase III MAESTRO trial: patient eligibility

- ≥18 years with histologically or cytologically confirmed, measurable or unmeasurable locally advanced unresectable or metastatic pancreatic ductal adenocarcinoma
- ECOG PS 0 or 1
- Acceptable liv
- No prior chen doses of 5-FL completion of <6 months pri



function

ipy other than radiosensitizing occurred ≥6 months after ant or adjuvant chemotherapy

 Patients suitable for FOLFIRINOX were ineligible; unless the patient refused FOLFIRINOX

Phase III MAESTRO trial: statistical considerations

- A sample size of 660 patients randomized 1:1
- 508 events (deaths) required to ensure 90% power to detect a HR of 0.75 for OS (median OS 8.67 vs 6.5 months) at a two-sided significance level of α =0.05

PFS and a 2-side Wrong hypothesis: this is inferior to Further expected outcome for a mixed population

edure with

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Patient demographics and baseline characteristics

Characteristic	Gemcitabine + placebo (n=347)	Evofosfamide + gemcitabine (n=346)
Median age, years (range)	65 (35–84)	66 (27–87)
Male/female, n (%)	179/168 (51.6/48.4)	191/155 (55.2/44.8)
Region, n (%) Europe Asia (Japan and South Korea) USA/Canada Rest of the world	212 (61.1) 58 (16.7) 49 (14.1) 28 (8.1)	213 (61.6) 65 (18.8) 47 (13.6) 21 (6.1)
Race White Asian Black Other	245 (70.6) 61 (17.6) 7 (2.0) 34 (9.8)	243 (70.2) 65 (18.8) 9 (2.6) 29 (8.4)

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Patient demographics and baseline characteristics (cont'd)

Characteristic	Gemcitabine + placebo (n=347)	Evofosfamide + gemcitabine (n=346)
ECOG PS, n (%)	116 (33.4)	115 (33.2)

Unsuitable for FOLFIRINOX?

≥3.5 g/dL	241 (69.5)	237 (68.5)
Hemoglobin, n (%)* <12 g/dL ≥12 g/dL	116 (33.4) 223 (64.3)	129 (37.3) 210 (60.7)
Concomitant diabetes, n (%)	125 (36.0)	146 (42.2)

^{*}Do not total 100% because data are missing for some patients

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Disease characteristics

Characteristic	Gemcitabine + placebo (n=347)	Evofosfamide + gemcitabine (n=346)
Site of primary tumor involves, n (%) Head Body Tail	189 (54.5) 115 (33.1) 83 (23.9)	187 (54.0) 123 (35.5) 89 (25.7)
Extent of disease, in (94)		
Locally advanced	74 (21.3)	75 (21.7)
Wetastatic	213 (10.1)	211 (16.5)
No. of metastatic sites, n (%) 0 1/2 >2	78 (22.5) 202 (58.2) 67 (19.3)	81 (23.4) 215 (62.1) 50 (14.5)
Site of metastases (>10% occurrence), n (%) Liver Lung Peritoneal Para-aortic lymph node	201 (73.6) 66 (24.2) 52 (19.0) 38 (13.9)	193 (71.2) 82 (30.3) 45 (16.6) 31 (11.4)

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Overview of adverse events

	Gemcitabine + placebo (n=341)	Evofosfamide + gemcitabine (n=338)
Any adverse event, n (%)	337 (98.8)	335 (99.1)
Any grade 3/4 adverse event, n (%)	273 (80.1)	308 (91.1)
Serious adverse events, n (%)	177 (51.9)	183 (54.1)
Adverse events leading to death, n (%)	37 (10.9)	31 (9.2)
Adverse events resulting in dosing interruption ≥1 study drug, n (%)	187 (54.8)	251 (74.3)
Adverse events resulting in dose reduction ≥1 study drug, n (%)	128 (37.5)	211 (62.4)

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Most commonly reported clinical adverse events*

	Gemcitabine + placebo (n=341)		Evofosfamide + gemcitabine (n=338)			
	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4
Nausea, n (%)	152 (44.6)	13 (3.8)	0	169 (50.0)	9 (2.7)	0
Decreased appetite, n (%)	118 (34.6)	10 (2.9)	0	118 (34.9)	6 (1.8)	1 (0.3)
Diarrhea, n (%)	89 (26.1)	6 (1.8)	0	114 (33.7)	15 (4.4)	1 (0.3)
Vomiting, n (%)	117 (34.3)	14 (4.1)	0	110 (32.5)	10 (3.0)	1 (0.3)
Constipation, n (%)	107 (31.4)	1 (0.3)	0	104 (30.8)	1 (0.3)	0
Fatigue, n (%)	109 (32.0)	13 (3.8)	0	99 (29.3)	15 (4.4)	1 (0.3)

^{*}According to MedDRA PTs; events occurring in ≥30% of patients in either treatment arm (apart from blood and lymphatic disorders)

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Hematologic events and biochemical toxicities

	Gemcitabine + placebo (n=341)		Evofosfamide + gemcitabine (n=338)			
	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4
Neutropenia*, n (%)	119 (34.9)	66 (19.4)	22 (6.5)	188 (55.6)	103 (30.5)	49 (14.5)
Febrile neutropenia, n (%)	2 (0.6)	1 (0.3)	1 (0.3)	7 (2.1)	7 (2.1)	0
Thrombocytopenia*, n (%)	103 (30.2)	20 (5.9)	6 (1.8)	241 (71.3)	88 (26.0)	72 (21.3)
Anemia*, n (%)	115 (33.7)	39 (11.4)	2 (0.6)	172 (50.9)	73 (21.6)	3 (0.9)
ALT increased, n (%)	30 (8.8)	19 (5.6)	0	35 (10.4)	15 (4.4)	1 (0.3)
ALP increased, n (%)	29 (8.5)	17 (5.0)	0	21 (6.2)	10 (3.0)	0

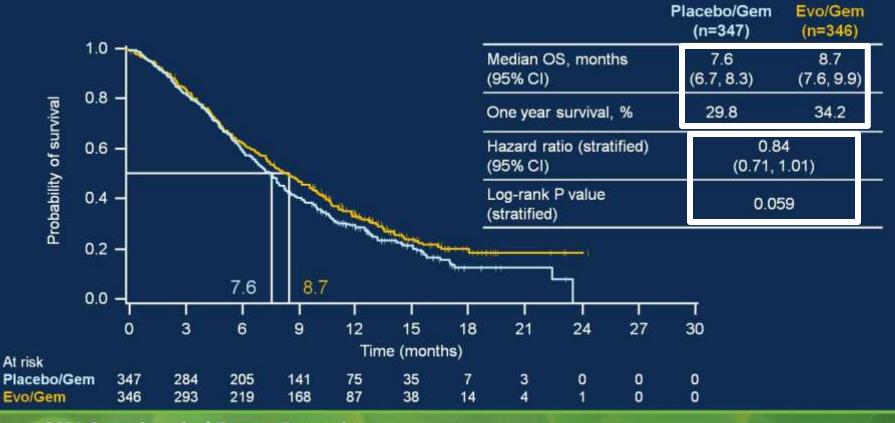
^{*}According to pooled MedDRA PTs including blood and lymphatic disorders and laboratory investigations

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Overall survival



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Progression-free survival



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Objective response rate in patients with measurable disease

	Gemcitabine + placebo (n=325)	Evofosfamide + gemcitabine (n=323)
Objective response rate unconfirmed (%)	16.3	20.4
	Odds ratio 1.32 (0.88, 1.97) P=0.17	
Objective response rate confirmed (%)	8.6	15.2
	Odds ratio 1.90 (1.16, 3.12) P=0.0086	

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Subsequent therapy

	Gemcitabine + placebo (n=347)	Evofosfamide + gemcitabine (n=346)
Patients receiving any anticancer drug therapy after study drug discontinuation, n (%)	170 (49.0)	158 (45.7)
Chemotherapy, n (%)	167 (48.1)	154 (44.5)
FOLFIRINOX	29 (8.4)	16 (4.6)
FOLFOX	27 (7.8)	24 (6.9)
Gemcitabine/nab-paclitaxel	24 (6.9)	17 (4.9)
Single-agent gemcitabine	23 (6.6)	32 (9.2)
TS-1	23 (6.6)	25 (7.2)
Other chemotherapy*	56 (16.1)	57 (16.5)

^{*}Includes GEMOX, CAPOX, FOLFIRI, carboplatin/cisplatin+ paclitaxel, single-agent paclitaxel, and single-agent capecitabine

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Conclusions

- The phase III MAESTRO trial did not meet its primary endpoint of overall survival (P=0.059)
- A signal for overall antitumor activity was observed with evofosfamide + gemcitabine in PDAC (OS, PFS and ORR)
- No new safety findings were identified and the safety profile was consistent with that in other studies
- Discontinuations, dose interruptions and dose reductions were more frequently observed with evofosfamide + gemcitabine

concurrent medications



Impact of concurrent medications use on outcome of pancreatic cancer SEER Medicare analysis.



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Division of Hematology/Medical Oncology, Department of Internal Medicine; University of Texas Southwestern Medical Center, Dallas, TX

Results

- There were 13,702 cases which met inclusion criteria and had available Part D data.
- Median age was 76 years, There were 42.5% males, 77.1% were white and 34.0% had diabetes.
- The results of the Cox proportional hazard models are summarized in table 2.
- Beta blockers, heparin, insulin, warfarin were associated were significantly with improved survival (p<0.05).

Variable	Total (%)	Diabetes (%)	No diabetes (%)
Age (years)	76	77	75
White	10,545 (77)	7118 (78)	3427 (74)
Male	5820 (43)	3739 (41)	2081 (45)
Stage 4	5906 (50)	3966 (51)	1940 (47)
Grade 3/4	1813 (44)	1143 (44)	670 (44)
Head of pancreas	6842 (50)	4491 (50)	2351 (50)
Medication			
Beta blockers	5209 (38)	3208 (35)	2001 (43)
Statin	4680 (34)	2722 (30)	1958 (42)
Insulin	2319 (17)	885 (10)	1434 (31)
Metformin	2276 (17)	565 (6)	1711 (37)
Thiazolidinediones	1037 (8)	351 (4)	686 (15)
Warfarin	1857 (14)	1185 (13)	672 (14)
Heparin	764 (6)	477 (5)	287 (6)

Table 2: Cox Proportional hazards					
	HR (CI)				
Medication					
Beta blocker	0.92 (0.88, 0.96)				
Insulin	0.89 (0.84, 0.93)				
Warfarin	0.90 (0.84, 0.95)				
Heparin	0.76 (0.70, 0.82)				
Age	1.03 (1.03, 1.03)				
Race	1.07 (1.03, 1.14)				
Stage	2.48 (2.37, 2.59)				
Charlson score	1.42 (1.24, 1.62)				
Site	1.09 (1.04, 1.13)				

Conclusions

- Concurrent medication use, particularly heparin, insulin warfarin and beta-blockers are associated with improved survival in patients with pancreatic cancer.
- Diabetes medications (metformin, TZD) did not have an impact in the multivariable model.
- Additional studies are needed to examine whether these medications may improve outcomes for patients with pancreatic cancer.

(Ir)relevance of metformin treatment in patients with metastatic pancreatic cancer: an open-label, randomized phase 2 trial Reni M, Dugnani E, Cereda S, Belli C, Balzano G, Nicoletti R, Liberati D, Pasquale V, Scavini M, Maggiora P, Sordi V, Lampasona V, Ceraulo D, Di Terlizzi G, Doglioni C, Falconi M, Piemonti L.

Clin Cancer Res. 2015 Oct 12

	PEXG	PEXG+metformin	p				
Ν	29	31					
PFS-6	52%	42%	0.61				
mPFS	6.1	4.9	0.036*				
mOS	10.4	6.8	0.13°				
PR	34.5%	35.5%					
DCR	79.5%	64.5%	0.26				
* adjus ° adjus	* adjusted p-value; HR 2.00 (1.05-3.8)						

real life

MODIFIED FOLFIRINOX

	Stein ¹	Uesugi ²	Conroy
	(# 395)	(#422)	(NEJM)
N	37	19	171
ECOG 0	46%	nr	37%
M+ liver	54%	nr	88%
CA19.9 <59 ULN	49%	nr	44%
mOS	10.2	10.3 ²	11.1
PR	35%	nr	31.6%
(stage III)	17%	na	na

- 1. OXA 85; FU 300+2400; IRI 135
- 2. OXA 85; FU 0+2400; IRI 150 includes locally advanced

II LINE

Outcome of Second-Line Treatment Following nab-Paclitaxel

+ Gemcitabine or Gem Alone for M+ Pancreatic Cancer

Outcome of Second-Line Treatment Following nab-Paclitaxel + Gemcitabine or Gemcitabine Alone for Metastatic Pancreatic Cancer

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INTRODUCTION

PC is a highly lethal malignancy, and mortality rates nearly equal incidence? = 80% of pts are diagnosed with advanced disease (52% with metastatic

 Over the past decade, treatment plans for most pile with MPC have consisted. predominantly of 1 line of therapy^{0,4}

- This may be due, in part, to the appreciate mature of the disease Improvements in 1L efficacy may permit the use of subsequent therapy
- nab*-Pacitiacel (nab-P) + Gern demonstrated superior efficiery vs Gern stone for all endpoints examined in a phase III MPC trial, including OS, the primary endpoint (median, 8.7 vs 6.8 mg, P = 0.001 P.4
- Feasibility and efficacy data are needed to guide 21, beatment decisions in MPC
- As mab-P + Gern has become a standard 1L therapeutic option for pts with MPC,2 an analysis of the regimen as part of a treatment plan is necessary

net* a a registeral transment of Ceigner Corporation

OBJECTIVE

 The current post hoc analysis investigated the feasibility and efficacy of 2L therapy emong pts from the MPACT that

STUDY DESIGN

- . In the phase III trial, pts received nab-P + Gern or Gern alone as 1L treatment as Pis were treated until disease progression, unacceptable toxicity, or pt or
- physician decision Pts were followed until discontinuation of 1L therapy, after which only dates and
- type of subsequent treatment(x) as well as date of death were collected After the closure of the MPACT trial (NCT00844649) in 2013, an observational
- extension study was initiated to gather more aurylval information on pts who were
- The data collected from the extension study is included in this cost had eveluation
- . The Kaplan-Meter method was used to calculate OS:
- Total OS: from initial randomization
- OS2 survival time from and of 1L therapy
- Multivariate analyses of total OS and OS2 were conducted using a Cox proportional hazard model to evaluate 1L treatment and use of 2L therapy adjusted for other progressic factors (at the end of TL treatment for OS2); a stagestae procedure was performed to evaluate the treatment effect and identify the possible factors associated with OS or OS2
- Total OS: In addition to 1L and 2L treatment effect, the potential influence of the following prognostic factors was assessed.
- Geographic region (North America and other), age, KPS, NLR, PC primary location, stage at diagnosis, CA10-9 level, presence of liver metestases, peritoneal cardinomatosis, previous Whippie procedure, presence of billery sterf, presence of pulmonary metestases, number of metestatic sites
- OS2. The potential influence of the following factors was assessed:
- Prognostic fectors at baseline: geographic region (North America and other) and number of metastatic sites
- Factors at the end of 1L treatment age, KPS, NLR, 1L PFS (2 median and

RESULTS

- + = 40% of pts in each treatment arm received a 2t therapy (Table 1A)
- 5-FU or cape-containing regimens were the most common 2t, therapies (> 75%).
- + Pts who received 25, treatment had a better performance status at baseline compared with those who did not receive 2L treatment (Table 1A)
- Pts treated with FOLFIRINOX as 2L therapy had better performance status at the and of 1), beatment compared with all other regimens (Tables 2A and 28)

Table 1A. Baseline Characteristics by 2L Therapy Received

			Any S. Tharney		No S. Thompy		Containing	
Vallence	1007 1000	Oint	+Gan	Oin:	1007 1000	Cien	mbP + Gen	Cim
n	431	400	170	177	281	253	132	135
Age, median, y	42.0	63.0	61.0	62.0	£3.0	64.0	59.5	82.0
KPS, % 90 - 100 70 - 80	\$6 42	62 36	55 32	76 25	51	54	64 36	76 24
CA19-0 median, Um/L ≥ 50 × ULA, %	n = 329 2294 52	11 = 371 2759 52	n = 152 2644 49	n = 952 2095 45	n = 227 1961 -43	n = 209 3664 48	n • 120 2637 51	n = 125 2172 47
No. met. sites, % 1-3 > 3	00 14	85 15	88 12	88	85 15	54 18	86 12	89 11
NER %	n • 40% 80 30	n • 425 55 35	75 25	73 27	55 46	60	74 26	72 28

Table 1B. Baseline Characteristics for Pts who Received 2L 6-FU- or Cape-Containing Combinations

	6-8'U or Cape Combe*		POLITIMOX		POLFOXICITY	
Variable	mah P s Gers	Gen	mb#+ Gare	Ours	Ours	Clere
n	88-	107	111	17	38	- 49
Age, median, y	59.0	62.0	535	55.0	55.5	54.0
KPS, % 90 - 100 70 - 80	87 33	76 24	72 26	76 24	53 47	67 30
CA18-8 median, U/mL ≥ 59 × UCM, %	n = 90 2601 61	5 € 100 2206 46	n = 16 5539 56	n • 17 2368 53	n • 33 2650 53	7. 43 2006 43
No. met. sites, % 1-3 >3	201 9	103 7	100	66 12	66 14	93 8
NUL %	1		0.0		1	The State of
×6	75	TO	72	71	70	59
2.5	25	30	25	29	72	31

Reasons for 1L Treatment Discontinuation

 Pts with any 2L treatment 50% and 74% in the nab-P + Gern and Gern-alone arms. respectively, discontinued 1L therapy due to progressive disease

- 28% and 14% discontinued 1L therapy due to edverse events

Table 2A. Pt Characteristics at End of 1L Treatment

	Any 2L	Any 2L Theopy		No III. Therapy		Grantelani	
Vermine	CHEN CHEN	Gini	Gara.	Om	mit-P+ Gem	Gass	
n:	170	177	261	283	132	135	
Age, tredlaruy	61.8	62.5	63.6	65.2	80.4	62.5	
KPS, % 80 - 100 80 70 \$ 60	43 11 11 9	n • 175 46 34 10 8	78 260 26 26 20 27	222 22 32 19 27	43 36 8	45 35 12 8	
GA18-6 median, U/mL ≥ 60 = ULN, %	n = 144 276 26	n • 131 360 32	n • 170 263 26	n = 125 1669 45	n = 112 276 28	n = 99 514 33	
NLR ≤8,%	74	n = 176 67	n = 236 69	n • 215 40	77	84	

Table 2B. Pf Characteristics at End of 1L Treatment for Pts who Received 2L 5-FU- or Cape-Containing Combinations

Vertical Control	6-FEI o Con	6-FIU or Cupe Condus		FOLFHUIDE		WOFF:
Military.	Gent Communication	Gum	Com.	Oim	Gen-	Gen
n	90	107	10	17	36	49
Age, median, y	39.8	62.5	54.4	66.2	59.5	54.7
KPS, % 90 - 100 10 70 ± 60	47 38 6	48 35 11 7	50 39 6 6	59 17 29 0	44 31 6 19	35 51 10
CA19-9 median, U/mL ≥ 50 × ULN, %	n=84 241 27	5-75 5-67 33	195 195	n • 10 401 20	n = 32 398 26	251 30
NLRSS, %	TT.	68	72	71	59	63

A Flore do Not the party of two armount of these date and respect to Art Africanson

- Fis with any 21 treatment Total OS from initial randomization) was wonificantly longer with nab-P + Gets vs Gem (median, 12.8 vs 9.9 ms; P = 0.015; Figure 1) Without 21, therepy: longer for neb-P + Gem (median, 6.2 vs. 4.7 mo; HR 0.89).
- . Pts who received a 5-FU- or cape-containing 2L therapy. Total OS was significantly longer for those in the neb-P = Gem vs Gem-stone arms (medien, 13.5 vs 9.5 mo; F
- In the nab-P + Gern and Gern-alone arms, fewer pts received 5-FU or cape mono-
- than combination therapy (34 vs 98 pts and 28 vs 107 pts, respectively) - Fewer pts who received 5-FU or cape monotherapy had KIPS 90 - 100 (32%and 36% for mab-P + Gern and Gern sions, respectively) compared with those
- who received 5-FU or cape combination therapy (Table 28) OS2 (from end of 1L therspy) for nab-P + Gern vs Gern alone
- With 21, therapy median OS similar #6.7 vs 6.4 mg; P = 0.273. Flours 21 Without 2L therapy: longer for neb-P + Gem (median, 2.5 vs. 1.8 mo; HR 0.87)

1. Not the 21, marchine E.R., Shormand, CHI-O, schopfede edger 10-2, Cape, especialme, ECCO PK, Robert Copensión Chrosing Oliva performer misst, DONNECCE, marceris, SPL (include, capital), ECCO PK, ECCO, marceris, SPL (include, capital), ECCO PK, ECCO, marceris, SPL (include, capital), and include and

Figure 1. Total OS in Pts Who Received 2L Therapy

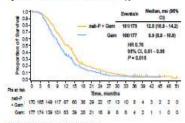
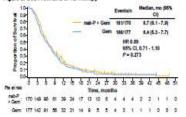


Figure 2. O82 From End of 1L Therapy



Efficacy (continued)

- · Factors significantly associated with longer total CS by multivariate analysis include 1L treatment with neb-P + Gem vs Gem alone, use of 2s therapy, better KPS at baseline (90 - 100 vs 70 - 80), no liver metastages, baseline NLR ≤ 5 vs > 5 (P < 0.001 for each), and lower CA19-9 at baseline (P = 0.005).
- Fectors significantly associated with longer OS2 by multivariate analysis (Table 3) include 1L treatment with nab-P + Gern vs Gern sione, use of 2L therapy, NLR \$5 vs > 5 at and of 1L therapy, better KPS at and of 1L therapy (P < 0.001 for each), and PFS1 ≥ 4.4 mo vs < 4.4 mo (P = 0.002)
- The longest total OS values were for pts who received 1L nab-P + Germ and 2L treatment with FOLFIRINOX (medien CS, 15.7 mo; Table 4)

Table 3. Multivariate Analysis of OS2

Constitle	HR (MY C)	Patter
Treatment group (rub-P + Gern vs Gern alone)	(88.0 - 68.0) 61.0	+0.001
21. therapy (with its without)	0.47 (0.40 - 0.54)	+0.001
NLR at end of 1L (5 5 vz > 6)	0.60 (0.52 - 0.70)	+0.001
10°C at end of 1L 80 - 100 vs ± 60 70 - 80 vs ± 60	0.46 (0.37 - 0.57) 0.57 (0.47 - 0.70)	100.00 100.00
PFS, mo (c. 4.4 vs < 4.4)*	0.78 (0.67 - 0.91)	0.002
Geographic region (North America vs others)	0.86 (0.74 - 1.00)	0.051

*In this study, the median PFS for the entire ITT population was 4.4 mo.

Table 4. Survival Outnome Summary in Pts Who Received 21. Therapy

	Median Discribios, rest				
H (%)	8	From 16. Rendered parties to First Cose of SL Tz	From First Dog of St. Ta to Dead		
(20 (38) (27 (81)	12.8	ne Al	5.3 6.2		
36 (22) 42 (24)	10.9	63	32 48		
132 (76)	13.5	67	5.7 4.5		
96 (53)	14.0	66	60		
34 (20) 20 (10)	11.9	67	47		
10 (11)	15.7	5.4 4.0	72 35		
M(21) 49(20)	13.7	50	6.4 4.5		
	170 (35) 177 (41) 30 (22) 43 (24) 135 (75) 36 (53) 107 (50) 36 (10) 10 (10) 10 (10)	170(38) (2.8 177(81) 88 30(22) 10.5 40(20) 13.5 102(75) 85 30(75) 85 30(75) 85 30(75) 85 30(75) 85 30(75) 85 30(75) 85 30(75) 85 30(75) 85	(%) (%)		

CONCLUSIONS

- · 21, treatment was feasible and beneficial for pts with MPC, with greater benefit observed for those who received 1L nati-F + Gern vs Gern alone
- A limitation of this study is that no information was available about treatment
- schedule or draw, swinty, or efficacy (beyond survival) during X, therapy
- Receiving 2L therapy was significantly associated with longer total OS, even after
- adjusting for baseline characteristics. 1L therapy may play a role in achieving optimal treatment benefit
- Total OS was significantly longer among pts who received 2L 5-FU- or capecontaining therepies following 1L nat-P + Gemive Gemielone
- Pts most likely to benefit from additional therapy include those with a longer PFS.
- during 1L treatment and lower NLPC and better PS at the end of 1L treatment The current analysis supports the use of mat-P * Gern as an appropriate 11, therapy
- onto which a treatment plan can be built

ACKNOWLEDGMENTS

The study is supported by Delgare Deposition, Surmit, by The solves needed editions and production apport in the proposition of the position for the The Studies and Associated Associated by Studies by Delgare Deposition for a collection of the proposition for all the solutions are fully responsible for all count and editional declarate for the poster.

CORRESPONDENCE

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DISCLOSURES

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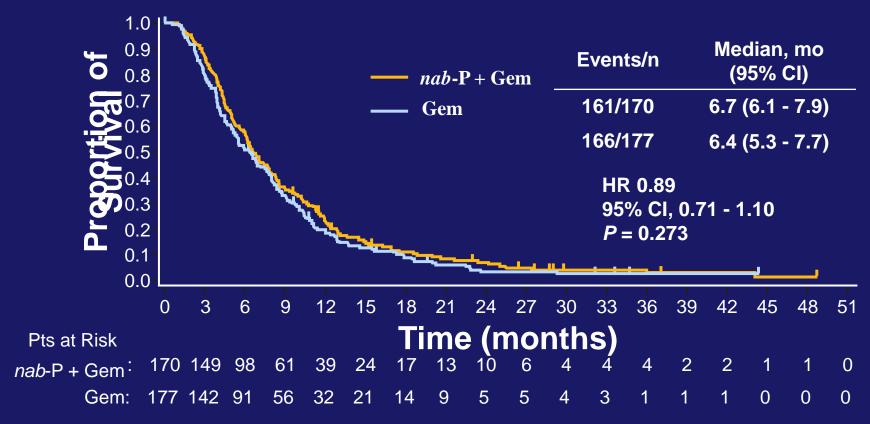
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Poster presented at the 2018 Gastrointestinal Cancers Symposium; January 21-23, 2018; San Francisco, CA

Overview of Survival Times with Duration of 1L

Variable	n, %	OS median, mo	Time from randomization to 1st dose of 2L tx, median, mo	Time from 1 st dose of 2L tx to death, median, months		
Any 2L Therapy nab-P + Gem Gem	170 (39) 177 (41)	12.8 9.9	6.6 4.1	5.3 4.5		
5FU/cape containing	ì					
<i>nab</i> -P + Gem	132 (39)	13.5	6.7	5.7		
Gem	135 (41)	9.5	4.1	4.5		
Other than 5/Fu/cape)	, ,					
<i>nab</i> -P + Gem	38 (22)	10.9	6.3	3.2		
Gem	42 (24)	11.3	4.5	4.8		
5-FU or Cape Combo						
<i>nab</i> -P + Gem	98 (74)	14.0	6.6	6.0		
Gem	107 (79)	9.5	4.0	4.6		
5-FU or Cape Mono						
<i>nab</i> -P + Gem	34 (26)	11.9	6.7	4.7		
Gem	28 (21)	9.4	5.3	3.9		
FOLFIRINOX						
<i>nab</i> -P + Gem	18 (14)	15.7	8.4	7.2		
Gem	17 (13)	7.2	4.0	3.5		
FOLFOX/OFF						
<i>nab</i> -P + Gem	36 (27)	13.7	5.6	6.4		
Gem	49 (36)	9.8	4.1	4.5		

MPACT - Pts With Second-line Therapies After AG Survival From End of 1L Therapy (OS2)



Variable	Statistic	<i>nab-</i> P + Gem n = 431	Gem n = 430	P-value BETWEEN treatment
With Any 2 nd -	n (%)	170/431 (39)	177/430 (41)	0.273
lineTherapies	Survival time, median mo (95% CI)	6.7	6.4	
Without Any 2 nd -	n (%)	250/431 (58)	226/430 (53)	< 0.001
lineTherapies	Survival time, median mo (95% CI)	2.5	1.6	
	P-value WITHIN treatment	< 0.001	< 0.001	

MPACT - Pts With Second-line Therapies After AG

Multivariate Analysis (MVA) of OS2

Covariate	HR (95% CI)	P value
Treatment group (<i>nab</i> -P + Gem vs Gem alone)	0.73 (0.63 - 0.85)	< 0.001
2L therapy (with vs without)	0.47 (0.40 - 0.54)	< 0.001
NLR at end of 1L (≤ 5 vs > 5)	0.60 (0.52 - 0.70)	< 0.001
KPS at end of 1L 90 - 100 vs ≤ 60 70 - 80 vs ≤ 60	0.46 (0.37 - 0.57) 0.57 (0.47 - 0.70)	< 0.001 < 0.001
PFS, months (≥ 4.4 vs < 4.4) ^a	0.78 (0.67 - 0.91)	0.002
Geographic region (North America vs others)	0.86 (0.74 - 1.00)	0.051

^a In this study, the median PFS for the entire ITT population was 4.4 months.

GEM vs nab-GEM

348 retrospective series MGH II line

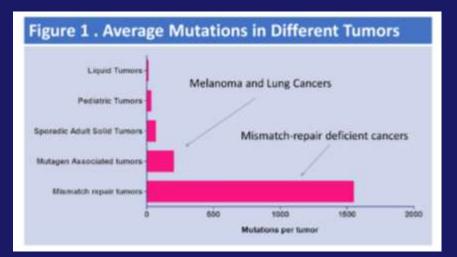
	GEM	nab-GEM	p-value
N	36	33	
mOS (days)	145	183	0.18

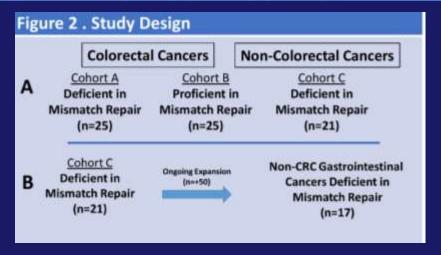
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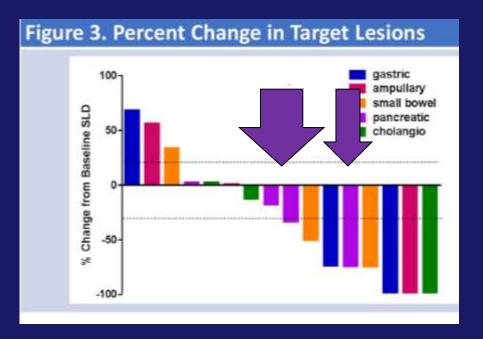
PD-1 Blockade in Mismatch Repair-Deficient Non-Colorectal Gastrointestinal Cancers

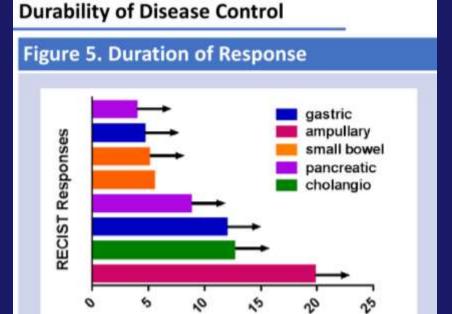
Dung Le, Jennifer Uram, Hao Wang, Holly Kemberling, Aleksandra Eyring, Bjarne Bartlett, Justin Poling, Richard Goldberg, Todd Crocenzi, George Fisher, James Lee, Tim Greten, Daniel Laheru, Nilo Azad, Ross
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Months