GI SLIDE DECK 2016

Selected abstracts on **Non-Colorectal Cancer** from:

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esdo european society of digestive oncology

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Letter from ESDO

DEAR COLLEAGUES

It is my pleasure to present this ESDO slide set which has been designed to highlight and summarise key findings in digestive cancers from the major congresses in 2016. This slide set specifically focuses on the **American Society of Clinical Oncology Annual Meeting 2016** and is available in English and Japanese.

The area of clinical research in oncology is a challenging and ever changing environment. Within this environment, we all value access to scientific data and research that helps to educate and inspire further advancements in our roles as scientists, clinicians and educators. I hope you find this review of the latest developments in digestive cancers of benefit to you in your practice. If you would like to share your thoughts with us we would welcome your comments. Please send any correspondence to info@esdo.eu.

Finally, we are also very grateful to Lilly Oncology for their financial, administrative and logistical support in the realisation of this activity.

Yours sincerely,

Eric Van Cutsem
Wolff Schmiegel
Philippe Rougier
Thomas Seufferlein

(ESDO Governing Board)

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ESDO Medical Oncology Slide Deck
Editors 2016

COLORECTAL CANCERS



Prof Eric Van Cutsem	Digestive Oncology, University Hospitals, Leuven, Belgium
Prof Wolff Schmiegel	Department of Medicine, Ruhr University, Bochum, Germany
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PANCREATIC CANCER AND HEPATOBILIARY TUMOURS


Prof Jean-Luc Van Laethem	Digestive Oncology, Erasme University Hospital, Brussels, Belgium
Prof Thomas Seufferlein	Clinic of Internal Medicine I, University of Ulm, Ulm, Germany

GASTRO-OESOPHAGEAL AND NEUROENDOCRINE TUMOURS


Emeritus Prof Philippe Rougier	University Hospital of Nantes, Nantes, France
Prof Côme Lepage	University Hospital & INSERM, Dijon, France

BIOMARKERS


Prof Eric Van Cutsem	Digestive Oncology, University Hospitals, Leuven, Belgium
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esdo

Glossary

1L	first line
2L	second line
5FU	5-fluorouracil
AE	adverse event
ADC	adenocarcinoma
BSC	best supportive care
CI	confidence interval
CIV	continuous intravenous
CR	complete response
(m)CRC	(metastatic) colorectal cancer
CT	chemotherapy
DCR	disease control rate
DFS	disease-free survival
(m)DOR	(median) duration of response
ESCC	esophageal squamous cell carcinoma
ECOG	Eastern Cooperative Oncology Group
EORTC QLQ	European Organisation for Research and Treatment of Cancer quality of life questionnaire
EOX	epirubicin, oxaliplatin, capecitabine
ESCC	esophageal squamous cell carcinoma
FDG	2-deoxy-2-[fluorine-18]fluoro- D-glucose
GC	gastric cancer
GEJ	gastroesophageal junction
GEP-NET	gastroenteropancreatic neuroendocrine tumour
GI	gastrointestinal
HCC	hepatocellular carcinoma
HER2	human epidermal growth factor receptor 2
HR	hazard ratio
ITT	intent-to-treat
IV	intravenous
LAR	long-acting release
Lu	lutetium
mAb	monoclonal antibody
MDCT	multiple detector computed tomography
MMR	mismatch repair
NET	neuroendocrine tumour
OR	odds ratio
ORR	overall response rate
(m)OS	(median) overall survival
PD	progressive disease
PD-L1	programmed death-ligand 1
PEG	poly(ethylene glycol)
PET-CT	positron emission tomography–computed tomography
(m)PFS	(median) progression-free survival
PK	pharmacokinetics
PO	oral administration
PR	partial response
PS	performance status
q(1/2/3/4/5)w	every (1/2/3/4/5) weeks
qd	once daily
QoL	quality of life
RCT	randomised controlled trial
RECIST	Response Evaluation Criteria In Solid Tumors
RT	radiotherapy
S-1	tegafur/CDHP/oteracil
SBRT	stereotactic body radiotherapy
SD	stable disease
SoC	standard of care
SSA	somatostatin analogue
SSTR	somatostatin receptor
TACE	transarterial chemoembolisation
TRAE	treatment-related adverse event
TTP	time to progression
(m)TTR	(median) time to treatment response
(m)TUDD	(median) time until definitive deterioration
WBC	white blood cell
WHO	World Health Organization

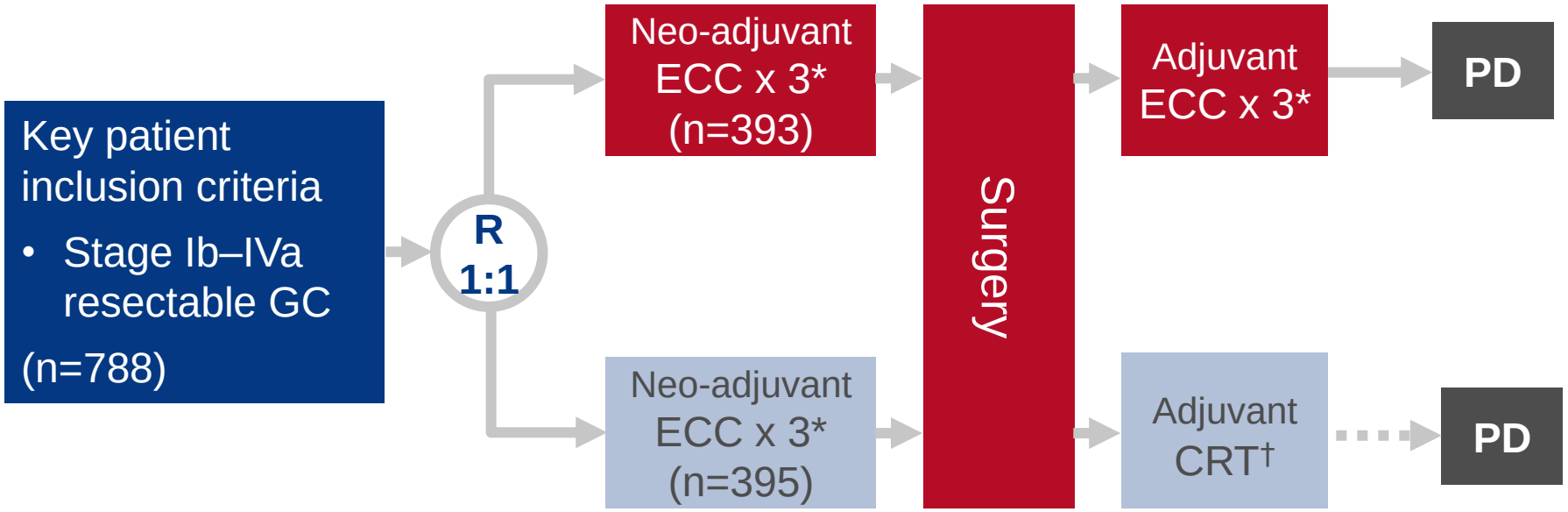
Contents

OESOPHAGEAL, ADENOCARCINOMA OF THE OESOPHAGOGASTRIC JUNCTION & GASTRIC CANCER

4000: A multicenter randomized phase III trial of neo-adjuvant chemotherapy followed by surgery and chemotherapy or by surgery and chemoradiotherapy in resectable gastric cancer: First results from the CRITICS study – Verheij M, et al

Study objective

- To investigate the efficacy and safety of CRT vs CT following neo-adjuvant CT and surgery in patients with resectable GC



PRIMARY ENDPOINT(S)

- OS

SECONDARY ENDPOINTS

- DFS
- Safety, QoL

*3 cycles of ECC (epirubicin, cisplatin/oxaliplatin + capecitabine);
†45 Gy in 25 fractions + cisplatin q1w + capecitabine qd.

Note: Based on data from abstract only

Verheij et al. J Clin Oncol 2016; 34 (suppl): abstr 4000

4000: A multicenter randomized phase III trial of neo-adjuvant chemotherapy followed by surgery and chemotherapy or by surgery and chemoradiotherapy in resectable gastric cancer: First results from the CRITICS study – Verheij M, et al

Key results

- Treatment completed: 46% with CT vs 55% with CRT
- After a median follow-up of 50 months, 405 patients had died

	CT	CRT
5-year OS, %	41.3	40.9
p-value	0.99	

Grade ≥3 AEs	CT	CRT
Haematological, %	44	34
p-value	0.01	
Gastrointestinal, %	37	42
p-value	0.14	

Conclusion

- **Only ~50% of patients completed the treatment**
- **No significant difference in OS was observed between postoperative CT vs CRT in patients with resectable GC**

Note: Based on data from abstract only

Verheij et al. J Clin Oncol 2016; 34 (suppl): abstr 4000

LBA4001: FAST: An international, multicenter, randomized, phase II trial of epirubicin, oxaliplatin, and capecitabine (EOX) with or without IMAB362, a first-in-class anti-CLDN18.2 antibody, as first-line therapy in patients with advanced CLDN18.2+ gastric and gastroesophageal junction (GEJ) adenocarcinoma – Al-Batran SE, et al

Study objective

- To assess the efficacy and safety of 1L EOX ± IMAB362 (first-in-class anti-CLDN18.2 mAb) in patients with advanced GC

Key patient inclusion criteria

- Advanced GC or GEJ ADC
- No prior CT; ECOG PS ≤1
- CLDN18.2: $2^+/3^+$ intensity in ≥40% tumour cells

(n=246)

R 1:1:1

- EOX* alone (n=84) → PD
- EOX* + IMAB362 800 mg/m^2 bolus, then 600 mg/m^2 d1, q21d (n=77) → PD
- Exploratory endpoint† EOX* + IMAB362 1000 mg/m^2 (n=85) → PD

Stratification

- CLDN18.2 positivity
- Measurability of disease

PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

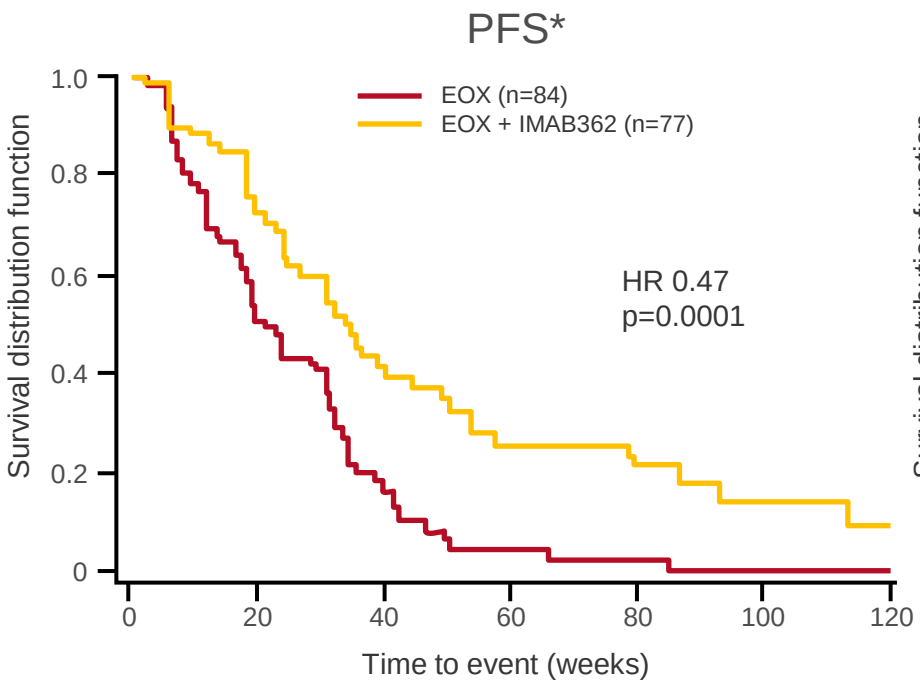
- OS, ORR, Safety

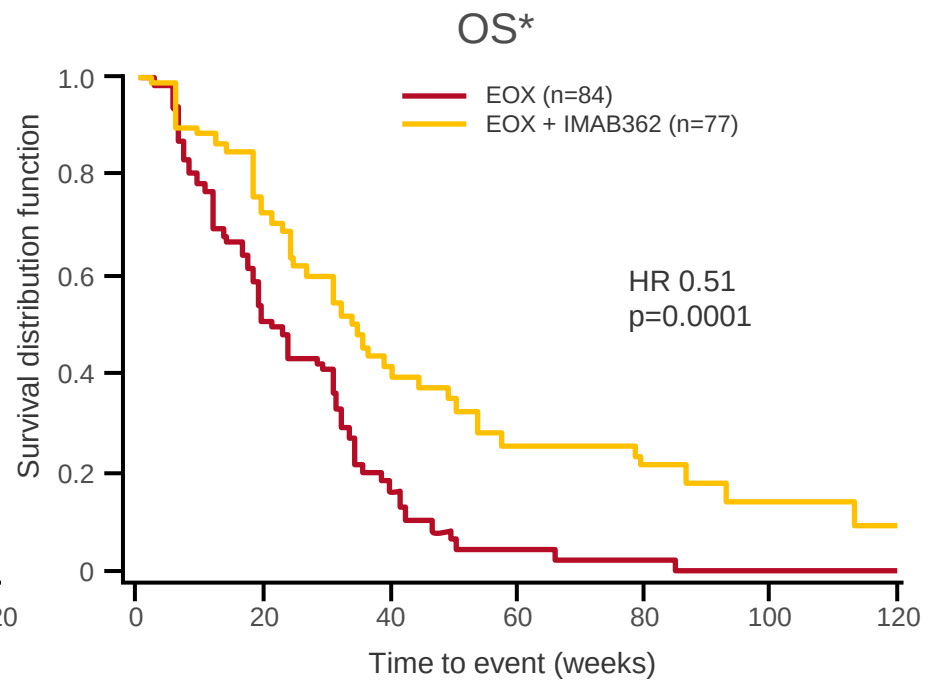
*Epirubicin 50 mg/m^2 + oxaliplatin 130 mg/m^2 d1 + capecitabine 625 mg/m^2 bid d1–21; †Not reported here.

Al-Batran et al. J Clin Oncol 2016; 34 (suppl): abstr LBA4001

LBA4001: FAST: An international, multicenter, randomized, phase II trial of epirubicin, oxaliplatin, and capecitabine (EOX) with or without IMAB362, a first-in-class anti-CLDN18.2 antibody, as first-line therapy in patients with advanced CLDN18.2+ gastric and gastroesophageal junction (GEJ) adenocarcinoma – Al-Batran SE, et al

Key results





	EOX (n=84)	EOX + IMAB362 (n=77)
mPFS, months (95% CI)	4.8 (4.1, 7.2)	7.9 (5.7, 10.4)
HR	-	0.47 (0.31, 0.70)
p-value	-	0.0001

	EOX (n=84)	EOX + IMAB362 (n=77)
mOS, months (95% CI)	8.4 (7.0, 10.3)	13.2 (9.7, 18.9)
HR	-	0.51 (0.36, 0.73)
p-value	-	0.0001

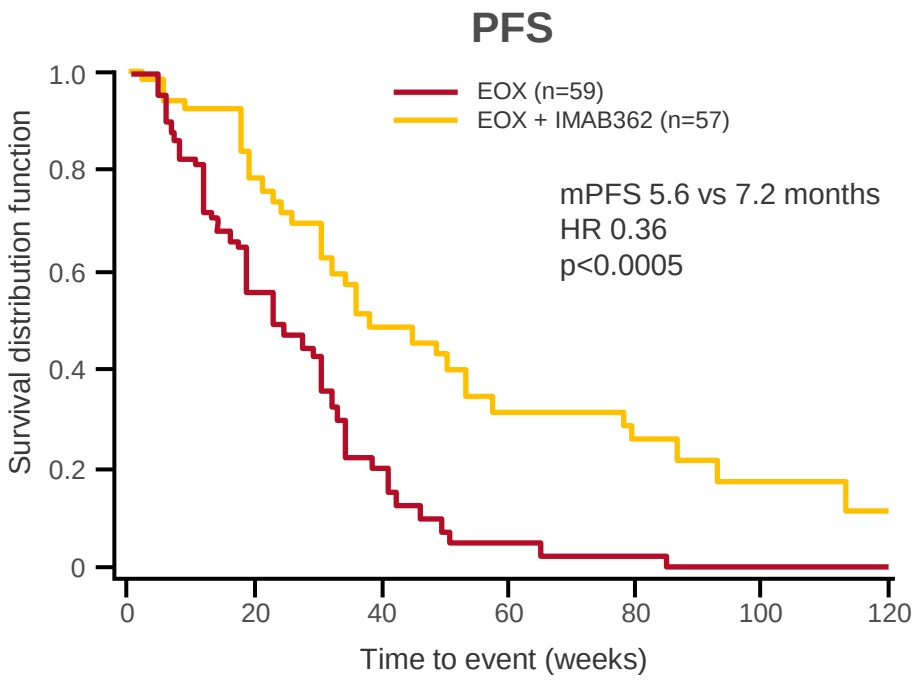
*$2^+/3^+$ CLDN18.2 staining in ≥40% tumour cells.

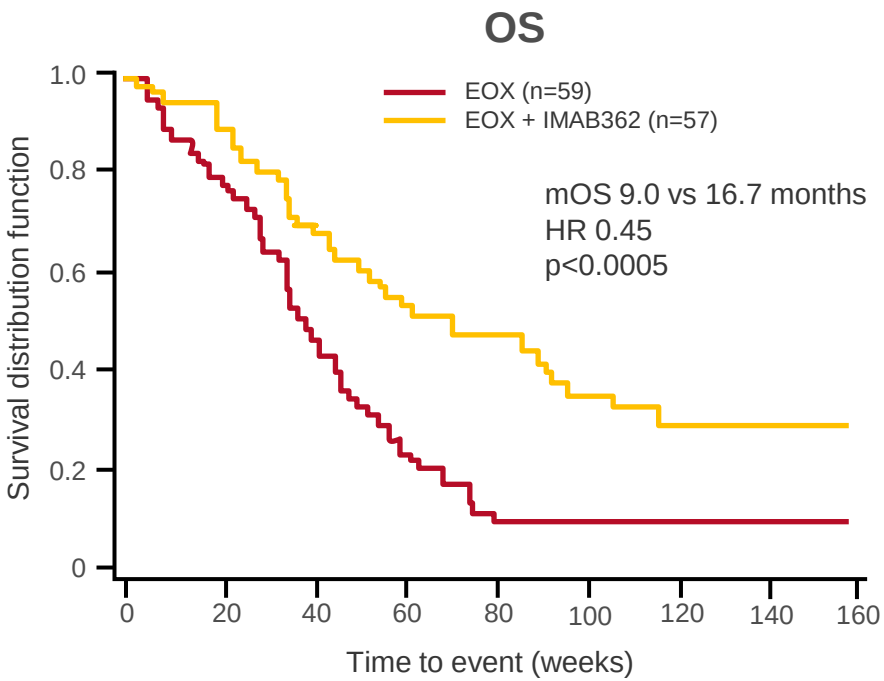
Al-Batran et al. J Clin Oncol 2016; 34 (suppl): abstr LBA4001

LBA4001: FAST: An international, multicenter, randomized, phase II trial of epirubicin, oxaliplatin, and capecitabine (EOX) with or without IMAB362, a first-in-class anti-CLDN18.2 antibody, as first-line therapy in patients with advanced CLDN18.2+ gastric and gastroesophageal junction (GEJ) adenocarcinoma – Al-Batran SE, et al

Key results (continued)

$2^+/3^+$ CLDN18.2 staining in ≥70% tumour cells





Al-Batran et al. J Clin Oncol 2016; 34 (suppl): abstr LBA4001

LBA4001: FAST: An international, multicenter, randomized, phase II trial of epirubicin, oxaliplatin, and capecitabine (EOX) with or without IMAB362, a first-in-class anti-CLDN18.2 antibody, as first-line therapy in patients with advanced CLDN18.2+ gastric and gastroesophageal junction (GEJ) adenocarcinoma – Al-Batran SE, et al

Key results (continued)

Response rate (RECIST v1.1), n (%)	EOX (n=84)	EOX + IMAB362 (n=77)
ORR	21 (25.0)	30 (39.0)
CR	3 (3.6)	8 (10.4)
PR	18 (21.4)	22 (28.6)
SD	43 (51.2)	34 (44.2)
PD	10 (11.9)	4 (5.2)
NE/missing	10 (11.9)	9 (11.7)

NE, not evaluable.

Al-Batran et al. J Clin Oncol 2016; 34 (suppl): abstr LBA4001

LBA4001: FAST: An international, multicenter, randomized, phase II trial of epirubicin, oxaliplatin, and capecitabine (EOX) with or without IMAB362, a first-in-class anti-CLDN18.2 antibody, as first-line therapy in patients with advanced CLDN18.2+ gastric and gastroesophageal junction (GEJ) adenocarcinoma – Al-Batran SE, et al

Key results (continued)

Selected Grade 3–4 AEs, n (%)	EOX (n=84)	EOX + IMAB362 (n=77)
Anaemia	6 (7.1)	9 (11.7)
Leukopenia	5 (6.0)	6 (7.8)
Neutropenia	18 (21.4)	25 (32.5)
Thrombocytopenia	3 (3.6)	0
Diarrhoea	3 (3.6)	3 (3.9)
Nausea	3 (3.6)	5 (6.5)
Vomiting	3 (3.6)	8 (10.4)
Asthenia	2 (2.4)	2 (2.6)
Fatigue	3 (3.6)	5 (6.5)
Infections	2 (2.4)	0

Conclusions

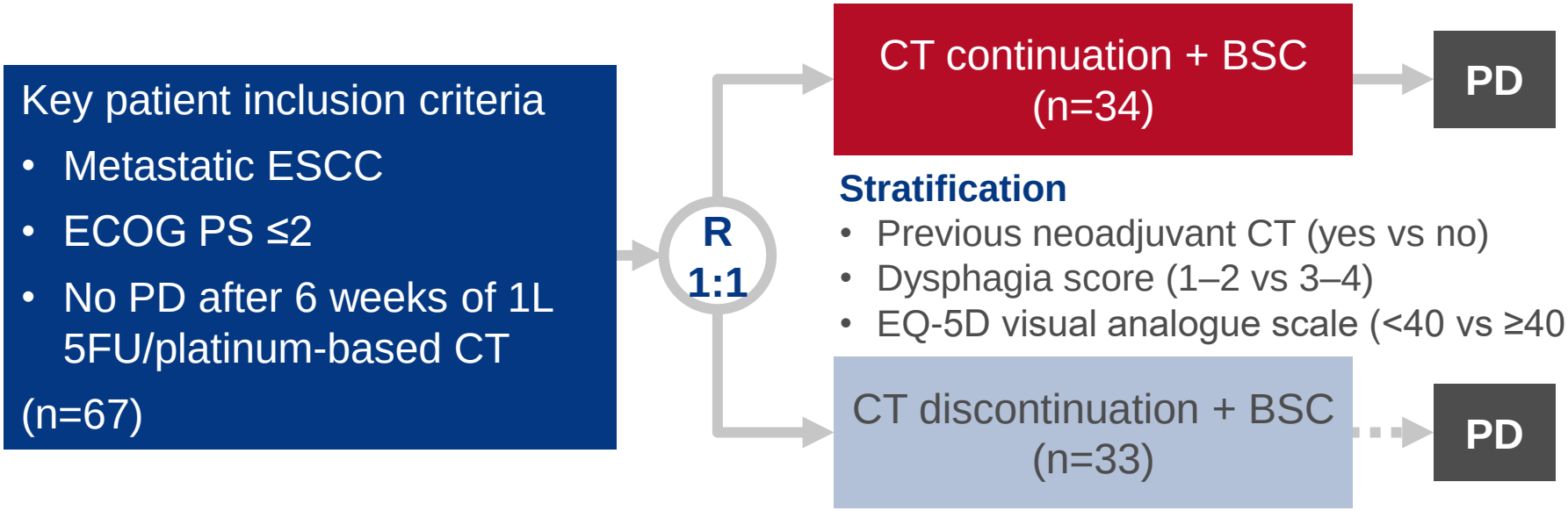
- **IMAB362 significantly improved PFS and OS, and the trial met its primary endpoint**
- **IMAB362 was feasible and well tolerated**
- **This study provides a strong rationale for a confirmatory Phase III trial**

Al-Batran et al. J Clin Oncol 2016; 34 (suppl): abstr LBA4001

4002: Discontinuation of first-line chemotherapy (CT) after 6 weeks of CT in patients (pts) with metastatic squamous-cell esophageal cancer (MSEC): A randomized phase II trial – Adenis A, et al

Study objective

- To assess the efficacy and safety of CT continuation vs discontinuation following 6 weeks of 1L CT in patients with metastatic ESCC



PRIMARY ENDPOINT(S)

- 9-month OS

SECONDARY ENDPOINTS

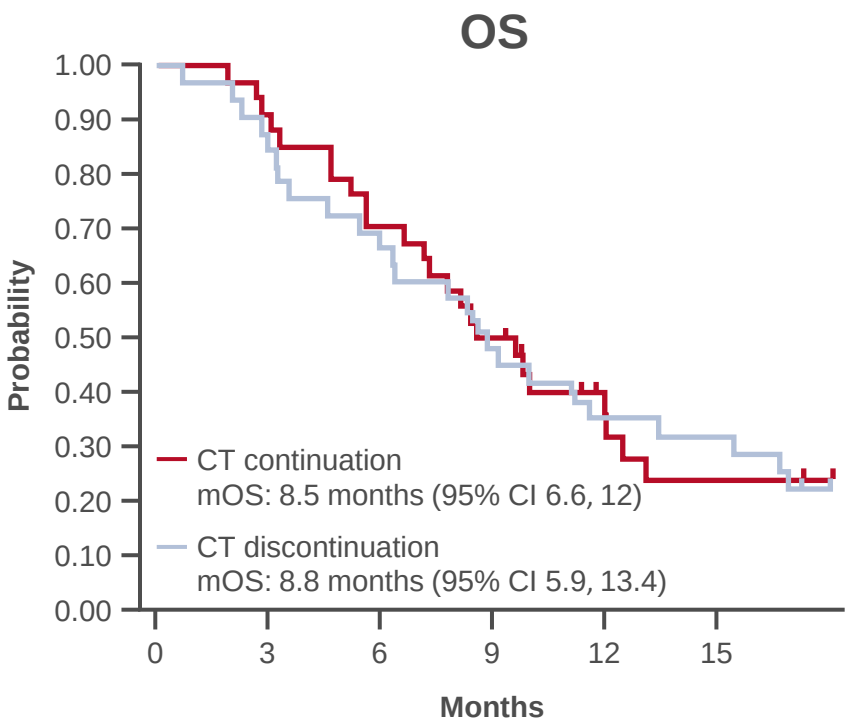
- OS, PFS
- Safety, QoL, medical costs

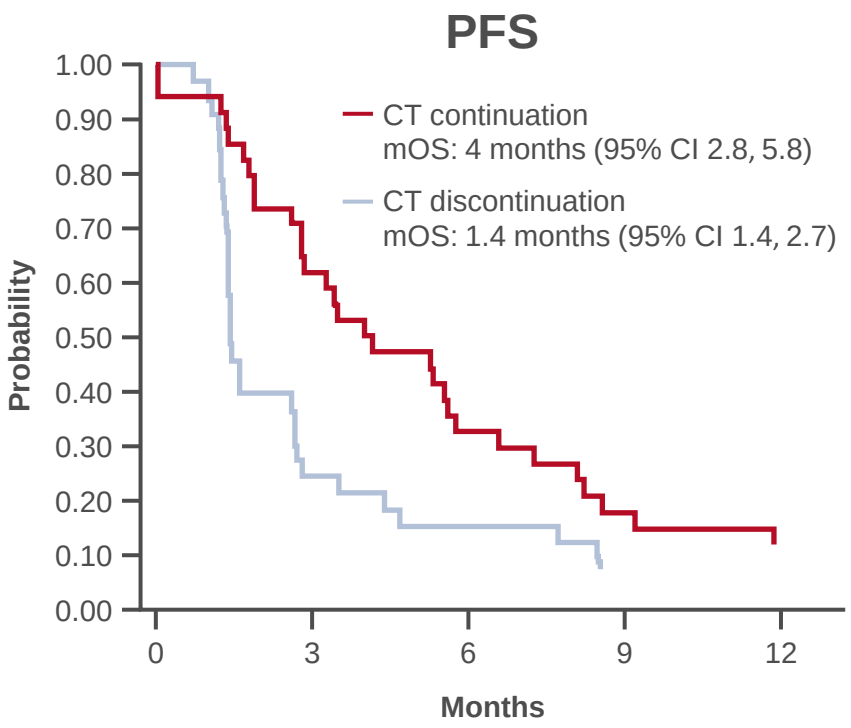
Adenis et al. J Clin Oncol 2016; 34 (suppl): abstr 4002

4002: Discontinuation of first-line chemotherapy (CT) after 6 weeks of CT in patients (pts) with metastatic squamous-cell esophageal cancer (MSEC): A randomized phase II trial – Adenis A, et al

Key results

	CT continuation (n=34)	CT discontinuation (n=33)
9-month OS, % (85% CI)	50 (37, 62)	48 (35, 60)





Adenis et al. J Clin Oncol 2016; 34 (suppl): abstr 4002

4002: Discontinuation of first-line chemotherapy (CT) after 6 weeks of CT in patients (pts) with metastatic squamous-cell esophageal cancer (MSEC): A randomized phase II trial – Adenis A, et al

Key results (continued)

AEs, %	Grade 0	Grade 1–2	Grade 3	Grade 4
CT continuation (n=31)	1	17	12	1
CT discontinuation (n=33)	18	12	3	0

Global health status*	CT continuation (n=31)	CT discontinuation (n=33)
mTUDD, months (95% CI)	6.7 (3.3, 11.9)	4.4 (2.9, 6.3)

Conclusions

- **In patients with metastatic ESCC, OS was similar in patients who continued vs discontinued CT, although PFS and QoL favoured CT continuation**
- **CT continuation and discontinuation both appear to be adequate standard treatments in this patient population**

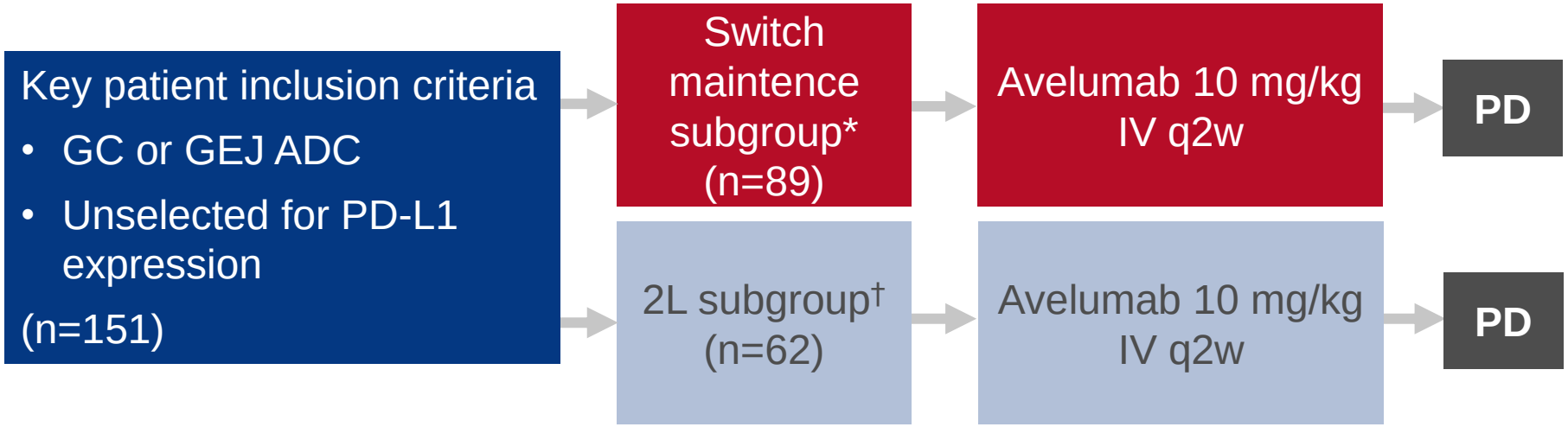
*Assessed by EORTC QLQ-C30.

Adenis et al. J Clin Oncol 2016; 34 (suppl): abstr 4002

4009: Avelumab (MSB0010718C; anti-PD-L1) in patients with advanced gastric or gastroesophageal junction cancer from JAVELIN solid tumor phase Ib trial: Analysis of safety and clinical activity – Chung HC, et al

Study objective

- To investigate the efficacy and safety of avelumab as a 1L maintenance or 2L therapy in patients with advanced GC



ENDPOINTS

- Safety
- PFS, ORR
- PD-L1 expression

*No PD on 1L therapy; †PD on 1L therapy.

Chung et al. J Clin Oncol 2016; 34 (suppl): abstr 4009

4009:Avelumab (MSB0010718C; anti-PD-L1) in patients with advanced gastric or gastroesophageal junction cancer from JAVELIN solid tumor phase Ib trial: Analysis of safety and clinical activity – Chung HC, et al

Key results

Best overall response	Maintenance subgroup (n=89)	2L subgroup (n=62)
ORR, % (95% CI)		
Overall	9.0 (4.0, 16.9)	9.7 (3.6, 19.9)
*PD-L1^{+}	10.0 (1.2, 31.7)	18.2 (2.3, 51.8)
*PD-L1^{-}	3.1 (0.1, 16.2)	9.1 (0.2, 41.3)
Overall DCR, %	57.3	29.0

mPFS, weeks (95% CI)	Maintenance subgroup (n=89)	2L subgroup (n=62)
Overall	12.0 (9.9, 17.6)	6.0 (5.7, 6.4)
*PD-L1^{+}	17.6 (6.0, 24.1)	6.3 (5.4, 18.0)
*PD-L1^{-}	11.6 (5.7, 14.1)	10.4 (4.1, 21.9)

*Based on ≥1 tumour cell staining.

Chung et al. J Clin Oncol 2016; 34 (suppl): abstr 4009

4009:Avelumab (MSB0010718C; anti-PD-L1) in patients with advanced gastric or gastroesophageal junction cancer from JAVELIN solid tumor phase Ib trial: Analysis of safety and clinical activity – Chung HC, et al

Key results (continued)

TRAEs in ≥5% of patients, n (%)	Maintenance subgroup (n=89) Any grade	2L subgroup (n=62) Any grade	Overall (n=151) Grade ≥3
Any TRAE	54 (60.7)	35 (56.5)	15 (9.9)
Infused related-reaction	14 (15.7)	5 (8.1)	1 (0.7)
Fatigue	9 (10.1)	7 (11.3)	2 (1.3)
Nausea	5 (5.6)	5 (8.1)	0

Conclusions

- **Avelumab had an acceptable safety profile**
- **1L maintenance or 2L avelumab therapy demonstrated promising clinical activity in patients with advanced GC, particularly in patients with PD-L1^{+} tumours**
- **These data represent the largest study of anti-PD-L1 agents in patients with GC/GEJ**
  - **Two Phase III RCTs of avelumab in GC are currently underway**

Chung et al. J Clin Oncol 2016; 34 (suppl): abstr 4009

4010: CheckMate-032: Phase I/II, open-label study of safety and activity of nivolumab (nivo) alone or with ipilimumab (ipi) in advanced and metastatic (A/M) gastric cancer (GC) – Janjigian YY, et al

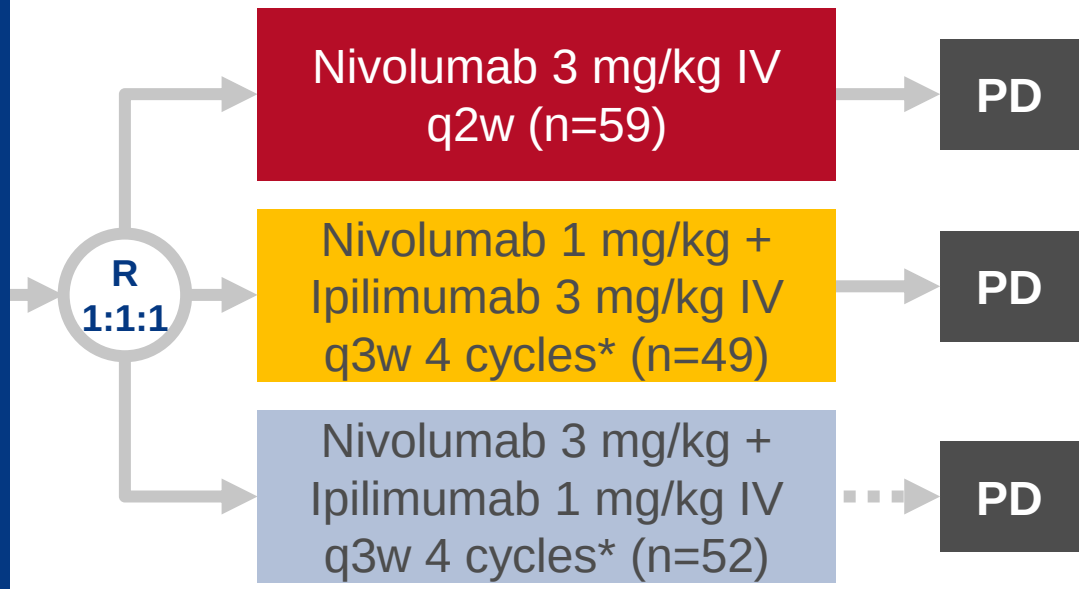
Study objective

- To assess the efficacy and safety of nivolumab ± ipilimumab in patients with advanced GC

Key patient inclusion criteria

- GC, oesophageal/GEJ ADC
- Stage IV; 'RECIST v1.1 measurable disease
- PD after ≥1 prior CT
- ECOG PS ≤1
- No autoimmune disease or immune therapy

(n=160)



PRIMARY ENDPOINT

- ORR (RECIST v1.1)

SECONDARY ENDPOINTS

- OS, PFS, duration of response
- Safety

*Followed by nivolumab 3 mg/kg IV q2w.

Janjigian et al. J Clin Oncol 2016; 34 (suppl): abstr 4010

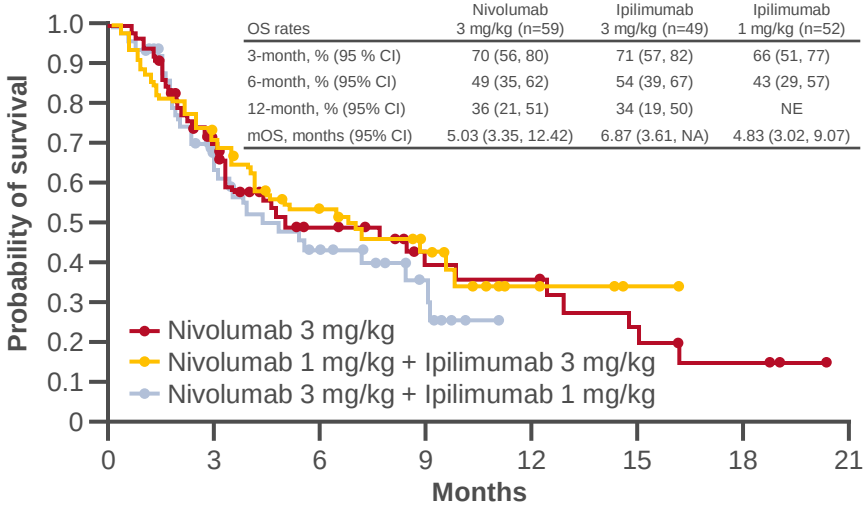
4010: CheckMate-032: Phase I/II, open-label study of safety and activity of nivolumab (nivo) alone or with ipilimumab (ipi) in advanced and metastatic (A/M) gastric cancer (GC) – Janjigian YY, et al

Key results

	NIVO 3 mg/kg (n=59)	NIVO 1 mg/kg + IPI 3 mg/kg (n=46)	NIVO 3 mg/kg + IPI 1 mg/kg (n=49)
ORR, n (%)	8 (14)	12 (26)	5 (10)
DCR, n (%)	19 (32)	20 (43)	20 (41)
mTTR, months (range)	1.6 (1.2–4.0)	2.6 (1.2–4.1)	2.6 (1.2–4.1)
mDOR, months (95% CI)	7.1 (3.0, 13.2)	5.6 (2.8, NE)	NE (2.5, NE)

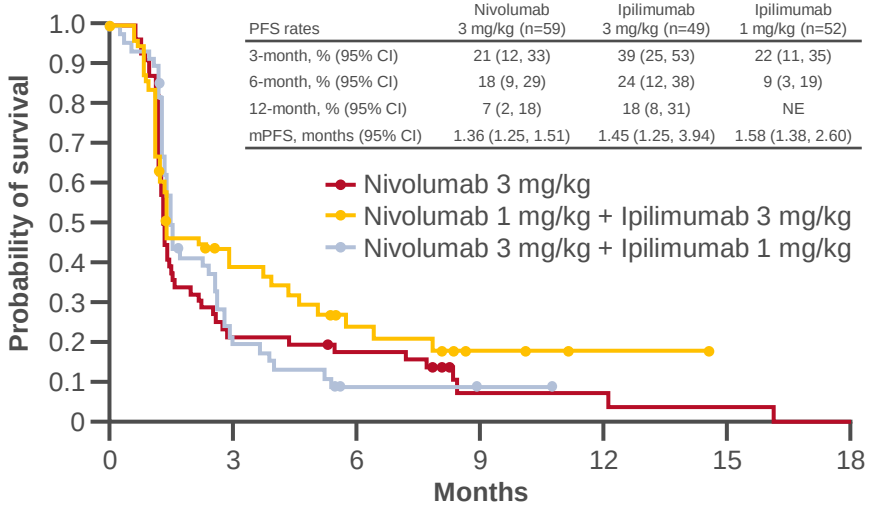
OS

OS rates	Nivolumab 3 mg/kg (n=59)	Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg (n=49)	Nivolumab 3 mg/kg + Ipilimumab 1 mg/kg (n=52)
3-month, % (95 % CI)	70 (56, 80)	71 (57, 82)	66 (51, 77)
6-month, % (95% CI)	49 (35, 62)	54 (39, 67)	43 (29, 57)
12-month, % (95% CI)	36 (21, 51)	34 (19, 50)	NE
mOS, months (95% CI)	5.03 (3.35, 12.42)	6.87 (3.61, NA)	4.83 (3.02, 9.07)



PFS

PFS rates	Nivolumab 3 mg/kg (n=59)	Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg (n=49)	Nivolumab 3 mg/kg + Ipilimumab 1 mg/kg (n=52)
3-month, % (95% CI)	21 (12, 33)	39 (25, 53)	22 (11, 35)
6-month, % (95% CI)	18 (9, 29)	24 (12, 38)	9 (3, 19)
12-month, % (95% CI)	7 (2, 18)	18 (8, 31)	NE
mPFS, months (95% CI)	1.36 (1.25, 1.51)	1.45 (1.25, 3.94)	1.58 (1.38, 2.60)



IPI, ipilimumab; NE, not estimable; NIVO, nivolumab.

Janjigian et al. J Clin Oncol 2016; 34 (suppl): abstr 4010

4010: CheckMate-032: Phase I/II, open-label study of safety and activity of nivolumab (nivo) alone or with ipilimumab (ipi) in advanced and metastatic (A/M) gastric cancer (GC) – Janjigian YY, et al

Key results (continued)

ORR by PD-L1 status, % (95% CI)	NIVO 3 mg/kg (n=59)	NIVO 1 mg/kg + IPI 3 mg/kg (n=49)	NIVO 3 mg/kg + IPI 1 mg/kg (n=52)
≥1%	27 (8,5)	44 (14, 79)	27 (6, 61)
<1%	12 (3, 31)	21 (8, 40)	0 (0, 13)
≥5%	33 (4, 78)	0 (0, 98)	25 (1, 81)
<5%	15 (5, 31)	27 (14, 44)	6 (1, 20)

TRAEs, %	NIVO 3 mg/kg (n=59)	NIVO 1 mg/kg + IPI 3 mg/kg (n=49)	NIVO 3 mg/kg + IPI 1 mg/kg (n=52)
Any	70	84	75
Grade 3–4	17	45	27
Serious	43	23	10

Conclusions

- **Nivolumab 1 mg/kg + ipilimumab 3 mg/kg resulted in encouraging clinical activity and OS in patients with PD-L1^{+} and PD-L1^{-} CT refractory advanced GC**
- **TRAEs for nivolumab + ipilimumab were consistent with previous studies**
- **A Phase III advanced GC trial of nivolumab 1 mg/kg + ipilimumab 3 mg/kg is planned**

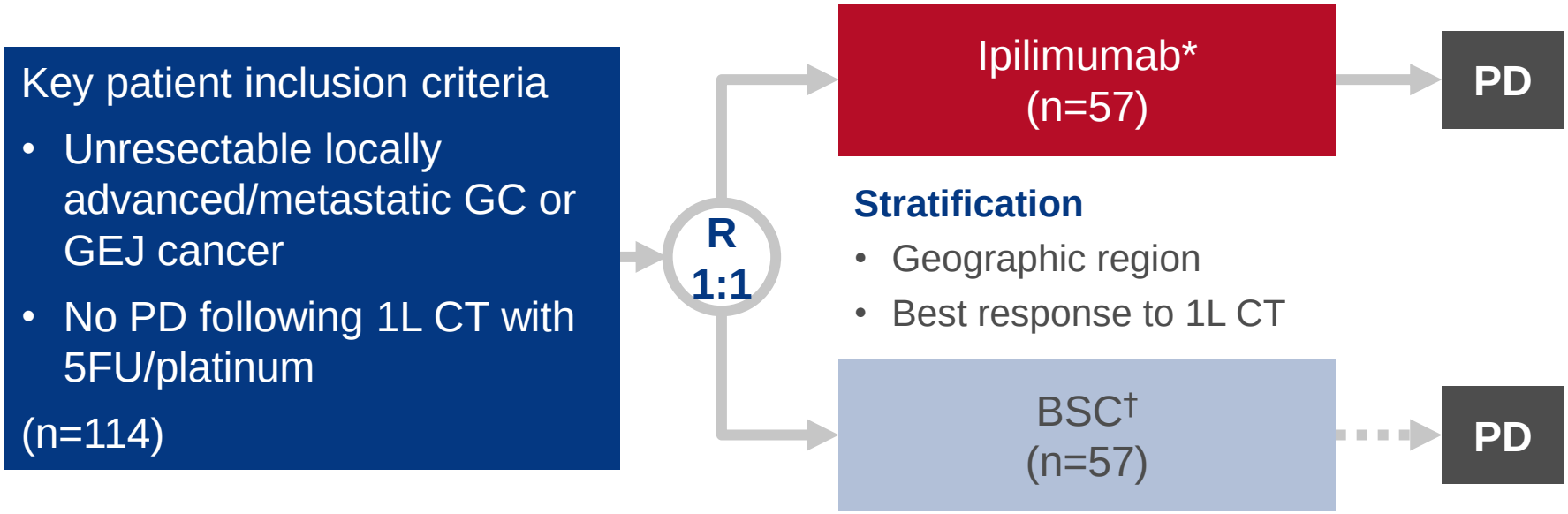
IPI, ipilimumab; NIVO, nivolumab.

Janjigian et al. J Clin Oncol 2016; 34 (suppl): abstr 4010

4011: A randomized, open-label, two-arm phase II trial comparing the efficacy of sequential ipilimumab (ipi) versus best supportive care (BSC) following first-line (1L) chemotherapy in patients with unresectable, locally advanced/metastatic (A/M) gastric or gastro-esophageal junction (G/GEJ) cancer – Moehler MH, et al

Study objective

- To assess the efficacy and safety of ipilimumab (anti-CTLA-4 mAb) vs BSC as sequential/ maintenance therapy in patients with unresectable locally advanced GC following 1L CT



PRIMARY ENDPOINT(S)

- Immune-related (ir) PFS

SECONDARY ENDPOINTS

- OS, irORR, irTTP

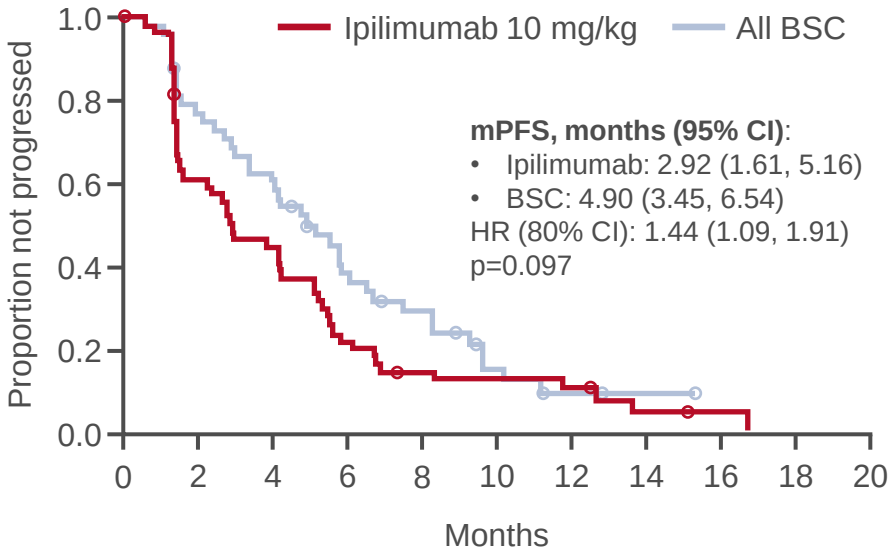
*10 mg/kg q3w for 4 doses, then 10 mg/kg q12w for ≤3 years;
†Maintenance CT (5FU/platinum) or no active treatment.

Moehler et al. J Clin Oncol 2016; 34 (suppl): abstr 4011

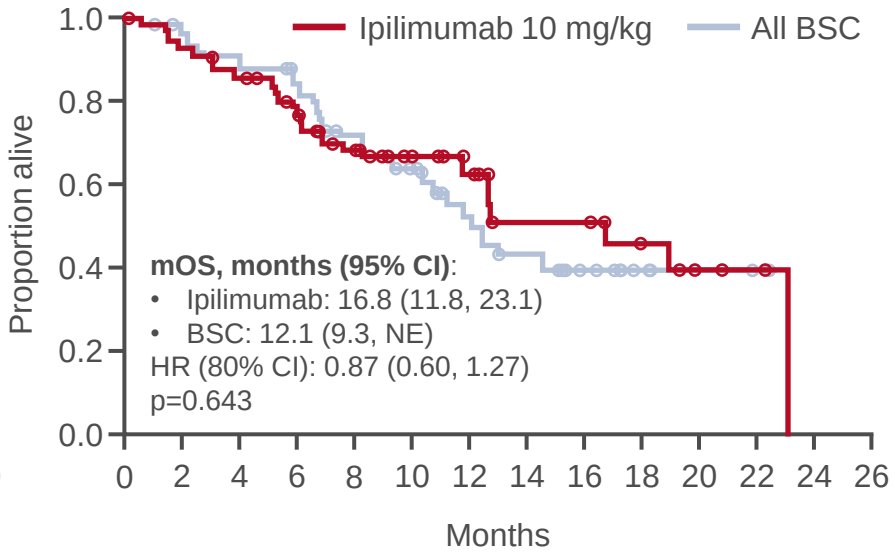
4011: A randomized, open-label, two-arm phase II trial comparing the efficacy of sequential ipilimumab (ipi) versus best supportive care (BSC) following first-line (1L) chemotherapy in patients with unresectable, locally advanced/metastatic (A/M) gastric or gastro-esophageal junction (G/GEJ) cancer – Moehler MH, et al

Key results

irPFS



OS



	Ipilimumab (n=57)	All BSC (n=57)
irORR, % (95% CI)	1.8 (0.91, 1.00)	7.0 (0.83, 0.98)
irTTP, median months (95% CI)	2.86 (1.41, 4.24)	5.19 (4.07, 9.69)

NE, not estimable; ir, immune-related.

Moehler et al. J Clin Oncol 2016; 34 (suppl): abstr 4011

4011: A randomized, open-label, two-arm phase II trial comparing the efficacy of sequential ipilimumab (ipi) versus best supportive care (BSC) following first-line (1L) chemotherapy in patients with unresectable, locally advanced/metastatic (A/M) gastric or gastro-esophageal junction (G/GEJ) cancer – Moehler MH, et al

Key results (continued)

TRAEs in ≥12% of patients, %	Ipilimumab (n=57)		Active BSC* (n=45)	
	Any grade	Grade 3–4	Any grade	Grade 3–4
Pruritus	31.6	0	2.2	0
Diarrhoea	24.6	8.8	6.7	0
Fatigue	22.8	5.3	6.7	0
Rash	17.5	0	4.4	0
Nausea	12.3	0	17.8	0

Conclusions

- **This was the first trial of ipilimumab and the first RCT of an immune checkpoint inhibitor in patients with GC/GEJ**
- **TRAE frequencies were consistent with ipilimumab trials in other patient populations**
- **Although this trial did not achieve its primary endpoint, its safety profile suggests ipilimumab warrants further study in patients with GC**

*Patients on maintenance CT (5FU/platinum).

Moehler et al. J Clin Oncol 2016; 34 (suppl): abstr 4011

4013: Efficacy of combined endoscopic resection and chemoradiotherapy for clinical stage I esophageal squamous cell carcinoma (ESCC): A single-arm confirmatory study (JCOG0508) – Muto M, et al

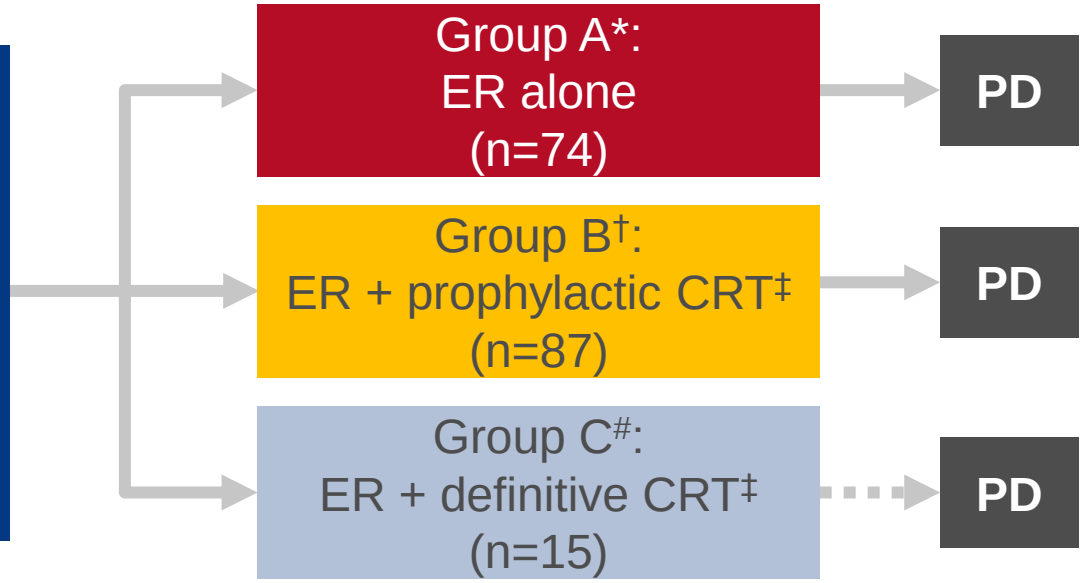
Study objective

- To evaluate the efficacy and safety of combined endoscopic resection (ER) + CRT in patients with clinical Stage 1 submucosal (cT1b) ESCC

Key patient inclusion criteria

- Histologically diagnosed thoracic ESCC
- T1b, cN0M0
- Tumour size ≤5 cm and ≤3/4 circumference

(n=176)



PRIMARY ENDPOINT

- 3-year OS (Group B)

SECONDARY ENDPOINTS

- 3-year OS, PFS (all patients)
- Safety

*__Group A__: pT1a with negative resection margin + no vascular invasion;

†__Group B__: pT1b with negative resection margin, and pT1a with vascular invasion;

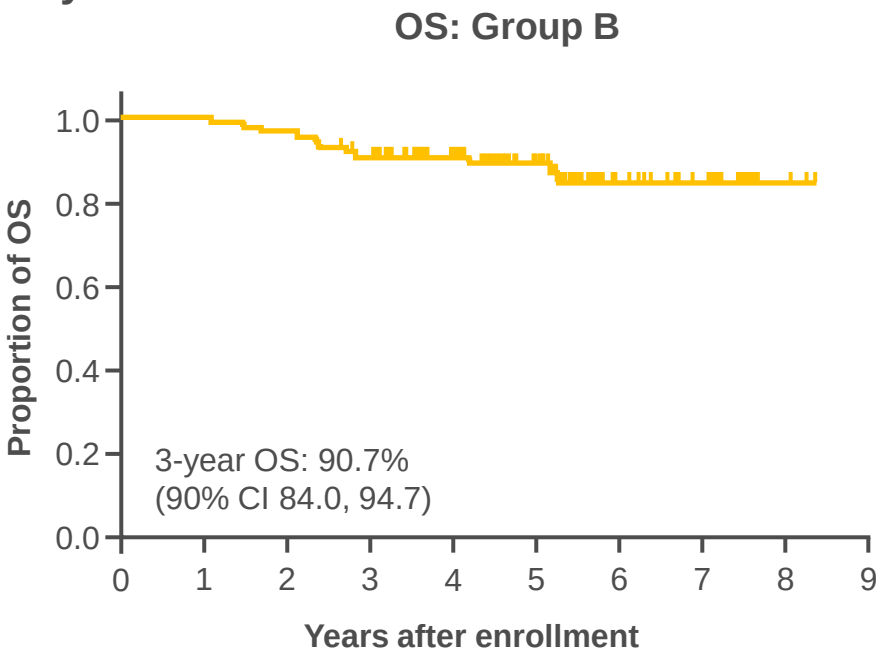
#__Group C__: pT1b with positive resection margin;

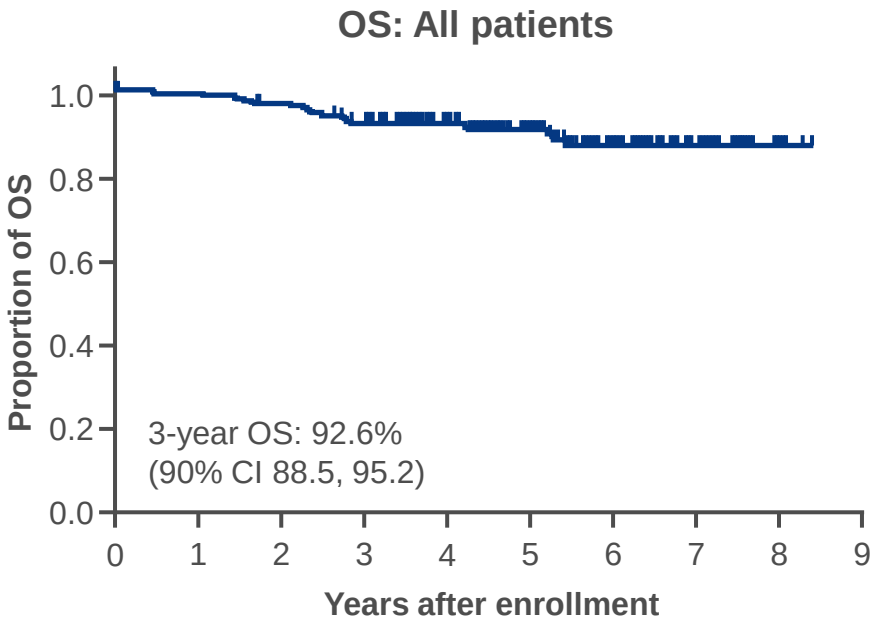
‡5FU (700 mg/m^2/d, d1–4 + d29–32, CIV) + cisplatin (70 mg/m^2/d, d1+29) + 41.4 Gy/23 fr to locoregional lymph-node [Group B] or 50.4 Gy/28 fr with a 9-Gy boost to the primary site [Group C].

Muto et al. J Clin Oncol 2016; 34 (suppl): abstr 4013

4013: Efficacy of combined endoscopic resection and chemoradiotherapy for clinical stage I esophageal squamous cell carcinoma (ESCC): A single-arm confirmatory study (JCOG0508) – Muto M, et al

Key results





Complication of ER (n=176)	Grade ≥3 (%)
Perforation-oesophagus	0
Haemorrhage-oesophagus	0
Stricture/stenosis-oesophagus	0.6

ER, endoscopic resection.

Muto et al. J Clin Oncol 2016; 34 (suppl): abstr 4013

4013: Efficacy of combined endoscopic resection and chemoradiotherapy for clinical stage I esophageal squamous cell carcinoma (ESCC): A single-arm confirmatory study (JCOG0508) – Muto M, et al

Key results (continued)

Toxicities of CRT (n=96)	Grade ≥3 (%)
Neutrophils	22.9
Hyponatraemia	7.3
Anorexia	7.3
Platelets	4.2
Oesophagitis	4.2
Dysphagia	2.1
Cardiac ischaemia/infarction	2.1
Pneumonitis	1
Pericardial effusion	0
Pleural effusion	0

Conclusion

- **In patients with cT1b ESCC, combined ER + CRT in addition to local excision gives comparable results to surgery alone in Stage pT1a in terms of efficacy and may be a new minimally invasive treatment option for cT1b ESCC**

ER, endoscopic resection.

Muto et al. J Clin Oncol 2016; 34 (suppl): abstr 4013

4014: Phase III study of intraperitoneal paclitaxel plus S-1/paclitaxel compared with S-1/cisplatin in gastric cancer patients with peritoneal metastasis: PHOENIX-GC trial – Ishigami H, et al

Study objective

- To investigate the efficacy and safety of intraperitoneal paclitaxel + S-1/paclitaxel vs S-1/cisplatin in patients with GC and peritoneal metastasis

Key patient inclusion criteria

- Pathologically confirmed GC
- Peritoneal metastasis (with no other distant metastasis)
- No or <2 months prior CT
- No prior gastrectomy
- No frequent ascites

(n=183)

R 2:1

Intraperitoneal paclitaxel 20 mg/m^2 + S-1/paclitaxel* (n=122) → PD

Stratification

- Centre
- Prior CT (yes/no)
- Extent of peritoneal disease (P1/P2–3)

S-1/cisplatin† (n=61) → PD

PRIMARY ENDPOINT(S)

- OS

SECONDARY ENDPOINTS

- ORR
- Safety

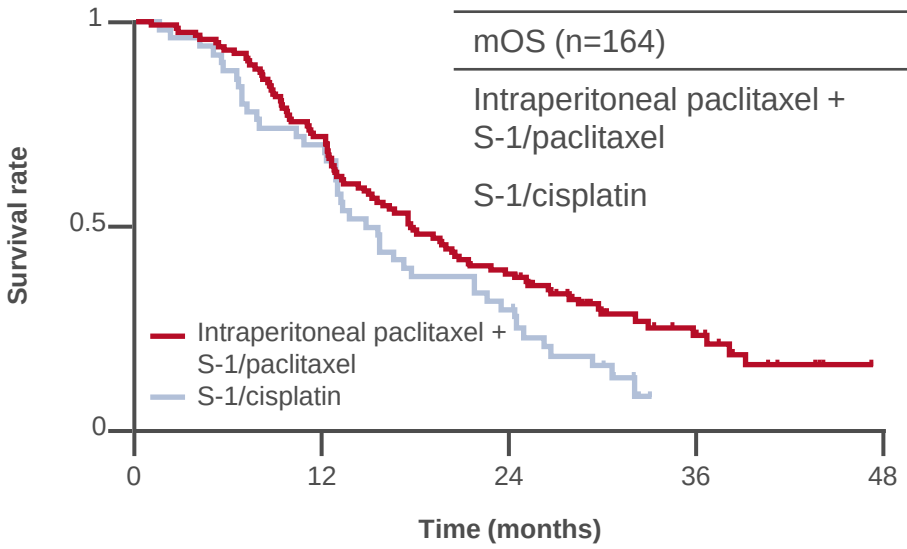
*Paclitaxel 50 mg/m^2 IV d1+8 + S-1 80 mg/m^2/d d1–14, q3w;
†Cisplatin 60 mg/m^2 IV d8 + S-1 80 mg/m^2/d d1–21, q5w.

Ishigami et al. J Clin Oncol 2016; 34 (suppl): abstr 4014

4014: Phase III study of intraperitoneal paclitaxel plus S-1/paclitaxel compared with S-1/cisplatin in gastric cancer patients with peritoneal metastasis: PHOENIX-GC trial – Ishigami H, et al

Key results

OS



mOS (n=164)	Time (months)	95% CI
Intraperitoneal paclitaxel + S-1/paclitaxel	17.7	14.7, 21.5
S-1/cisplatin	15.2	12.8, 21.8

*p=0.080

†HR: 0.72 (95% CI 0.49, 1.04); p=0.081

Best response (RECIST v1.1) (in patients with target lesions)	CR	PR	SD	PD	NE	Response rate	Fisher's test
Intraperitoneal paclitaxel + S-1/paclitaxel (n=17)	0	9	4	4	0	53%	p=0.001
S-1/cisplatin (n=5)	0	3	1	0	1	60%	

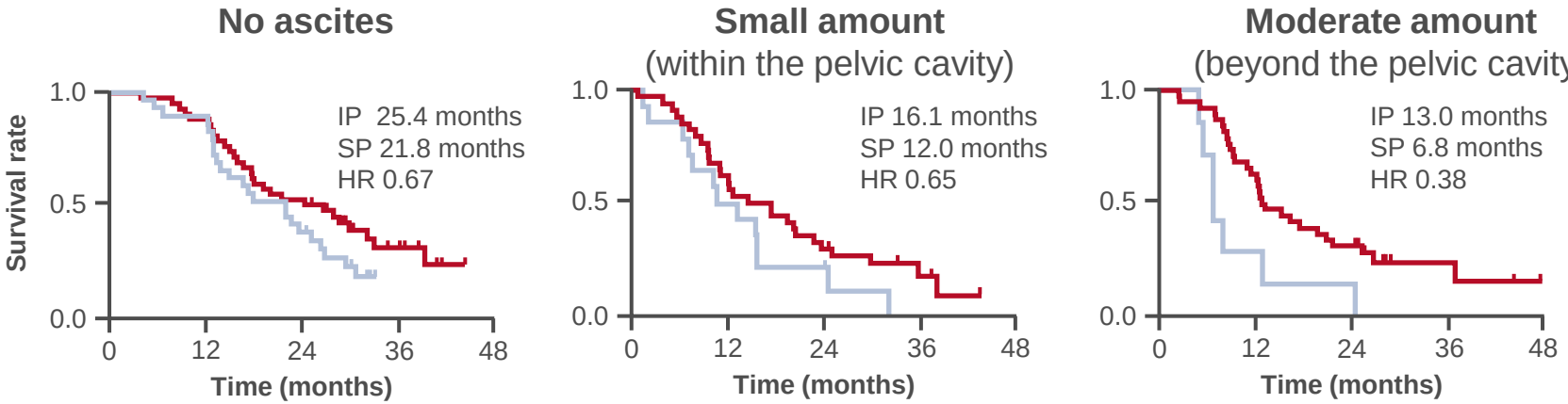
*Stratified log-rank test; †Cox regression analysis.

Ishigami et al. J Clin Oncol 2016; 34 (suppl): abstr 4014

4014: Phase III study of intraperitoneal paclitaxel plus S-1/paclitaxel compared with S-1/cisplatin in gastric cancer patients with peritoneal metastasis: PHOENIX-GC trial – Ishigami H, et al

Key results

OS by ascites level (sensitivity analysis)



*HR: 0.59 (95% CI 0.39, 0.87); p=0.0079

- AEs: Both regimens were tolerable and there were no treatment-related deaths

Conclusions

- **The primary analysis did not show statistical superiority with intraperitoneal paclitaxel + S-1/paclitaxel vs S-1/cisplatin alone in patients with GC and peritoneal metastasis**
- **However, the sensitivity analysis, which considered the imbalance of ascites, suggested clinical efficacy with intraperitoneal paclitaxel + S-1/paclitaxel**

*Cox regression analysis.

Ishigami et al. J Clin Oncol 2016; 34 (suppl): abstr 4014

4015: Phase III trial of s-1 plus oxaliplatin (SOX) vs s-1 plus cisplatin (SP) combination chemotherapy for first-line treatment of advanced gastric cancer (AGC): SOPP study – Ryu M-H, et al

Study objective

- To assess the efficacy and safety of S-1 + oxaliplatin vs S-1 + cisplatin in patients with previously untreated advanced GC

Key patient inclusion criteria

- Adults with histologically proven metastatic or recurrent GC or GEJ ADC
- ECOG PS ≤2
- ≥1 measurable disease by RECIST v1.1
- No prior CT*

(n=338)

R 1:1

S-1† + Oxaliplatin‡ q3w (n=173) → PD

S-1† + Cisplatin¥ q3w (n=164) → PD

Stratification

- Disease status (initially metastatic/recurrent/resected metastatic)
- Measurable disease (yes/no)
- Institution

PRIMARY ENDPOINT(S)

- PFS (RECIST v1.1)

SECONDARY ENDPOINTS

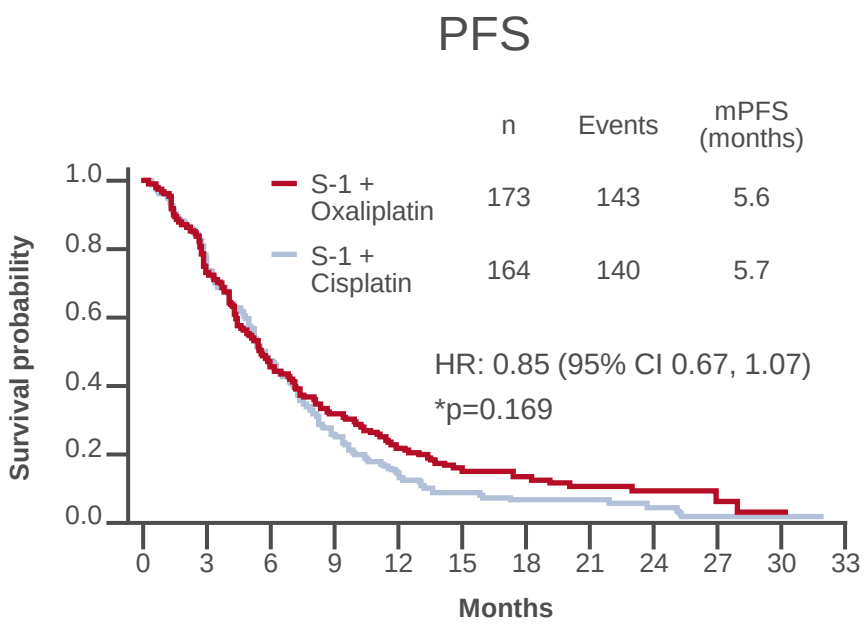
- OS and ORR
- Safety

*Apart from 5FU/cisplatin ≥6 months of study;
†80 mg/m^2/d d1–14 PO; ‡130 mg/m^2 d1 IV; ¥60 mg/m^2 d1 IV.

Ryu et al. J Clin Oncol 2016; 34 (suppl): abstr 4015

4015: Phase III trial of s-1 plus oxaliplatin (SOX) vs s-1 plus cisplatin (SP) combination chemotherapy for first-line treatment of advanced gastric cancer (AGC): SOPP study – Ryu M-H, et al

Key results



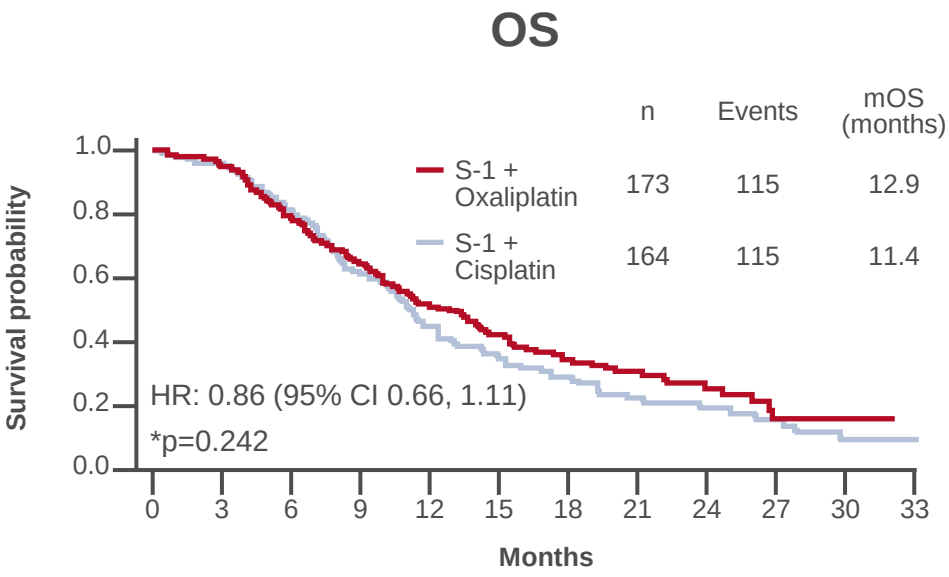
AEs, n (%)	S-1 + Oxaliplatin	S-1 + Cisplatin
WBC decreased	4 (2.3)	17 (10.42)
Neutropenia	28 (16.2)	65 (35.6)
Thrombocytopenia	13 (7.5)	8 (4.9)
Anaemia	9 (5.2)	18 (11)
Febrile neutropenia	7 (8)	7 (9)
Anorexia	15 (8.7)	11 (6.7)
Nausea	6 (3.5)	4 (2.4)
Vomiting	2 (1.2)	3 (1.8)
Diarrhoea	7 (4.0)	6 (3.7)
Fatigue	11 (6.4)	14 (8.5)
Peripheral neuropathy	15 (8.7)	6 (3.7)
Abdominal pain	4 (2.3)	3 (1.8)
Thromboembolic event	3 (1.8)	4 (2.3)
Creatinine increased	0 (0)	0 (0)

*Log-rank test.

Ryu et al. J Clin Oncol 2016; 34 (suppl): abstr 4015

4015: Phase III trial of s-1 plus oxaliplatin (SOX) vs s-1 plus cisplatin (SP) combination chemotherapy for first-line treatment of advanced gastric cancer (AGC): SOPP study – Ryu M-H, et al

Key results (continued)



Response rate, n (%)	S-1 + Oxaliplatin (n=92)	S-1 + Cisplatin (n=81)
CR	5 (5)	2 (2)
PR	48 (52)	47 (58)
SD	20 (22)	17 (21)
PD	12 (13)	8 (10)
NE	7 (8)	7 (9)
p=0.700 for ORR		

Conclusions

- S-1 + oxaliplatin was non-inferior to S-1 + cisplatin in terms of PFS, ORR and OS in patients with previously untreated advanced GC
- The two regimens were well tolerated with different toxicity profiles
- S-1 + oxaliplatin can be recommended as 1L treatment of advanced GC

*Log-rank test. NE, not estimable.

Ryu et al. J Clin Oncol 2016; 34 (suppl): abstr 4015

4016: Efficacy and safety findings from DREAM: A phase III study of DHP107 (oral paclitaxel) vs IV paclitaxel in patients with gastric cancer after failure of first-line chemotherapy – Kang Y-K, et al

Study objective

- To evaluate the efficacy and safety of oral paclitaxel (DHP107) vs paclitaxel IV in patients with advanced GC following failure of first-line CT

Key patient inclusion criteria

- Histologically or cytologically confirmed, unresectable recurrent/advanced GC
- Failure of 1L CT*
- ECOG PS ≤2
- Measurable lesion according to RECIST v1.1

(n=236)

R 1:1

DHP107 200 mg/m^2 PO bid d1,8,15 q4w (n=118) → PD

Stratification

- ECOG PS
- Disease status
- Prior treatment

Paclitaxel IV 175 mg/m^2 infused d1 q3w (n=118) → PD

PRIMARY ENDPOINT(S)

- Non-inferiority PFS

SECONDARY ENDPOINTS

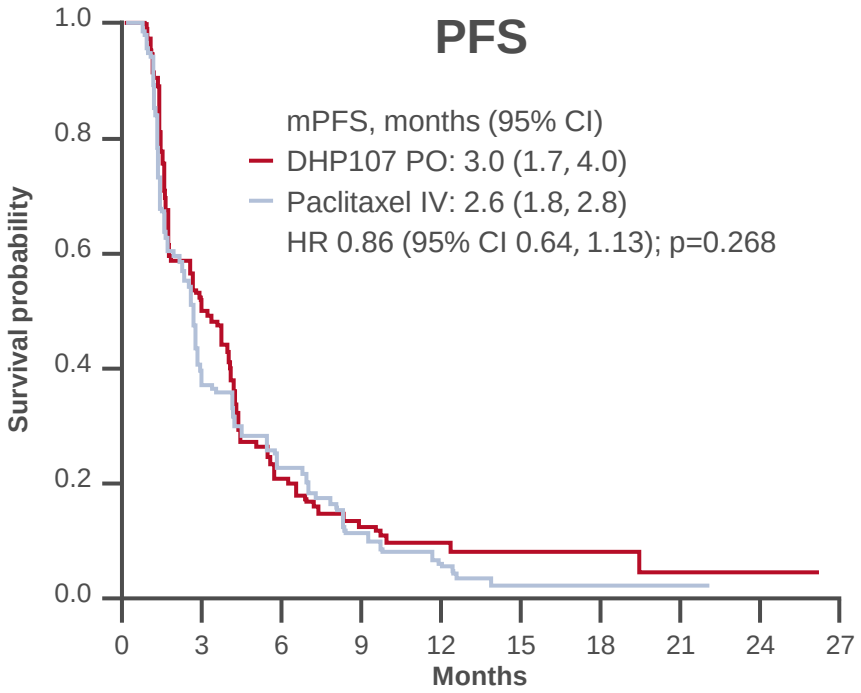
- OS; ORR
- Safety

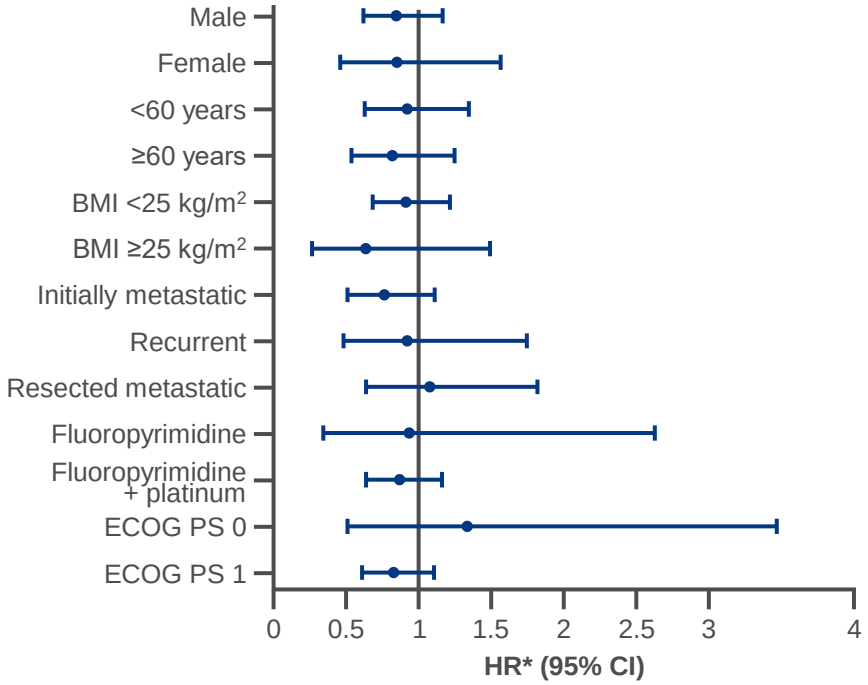
*Fluoropyrimidine ± platinum for metastatic or recurrent disease.

Kang et al. J Clin Oncol 2016; 34 (suppl): abstr 4016

4016: Efficacy and safety findings from DREAM: A phase III study of DHP107 (oral paclitaxel) vs IV paclitaxel in patients with gastric cancer after failure of first-line chemotherapy – Kang Y-K, et al

Key results





	DHP107 PO (n=118)	Paclitaxel IV (n=118)
mOS, months (95% CI)	9.7 (7.1, 11.5)	8.9 (7.1, 12.2)
HR (95% CI)	1.04 (0.76, 1.41)	
p-value	0.824	

*Reference: paclitaxel IV.

Kang et al. J Clin Oncol 2016; 34 (suppl): abstr 4016

4016: Efficacy and safety findings from DREAM: A phase III study of DHP107 (oral paclitaxel) vs IV paclitaxel in patients with gastric cancer after failure of first-line chemotherapy – Kang Y-K, et al

Key results (continued)

	DHP107 PO (n=118)	Paclitaxel IV (n=118)	p-value
ORR, %	17.8	25.4	0.155
CR	4.2	3.4	-
PR	13.6	22.0	-

Grade ≥3 AEs in ≥8% of patients, n %	DHP107 PO (n=118)	Paclitaxel IV (n=118)	p-value
Neutropenia	50 (42.4)	63 (53.4)	0.185
Febrile	7 (5.9)	3 (2.5)	0.333
Leukopenia	22 (18.6)	20 (16.9)	0.103
Anaemia	17 (14.4)	18 (15.3)	0.268
Peripheral sensory neuropathy	3 (2.5)	10 (8.5)	<0.001

Conclusions

- **PFS was non-inferior with oral DHP107 vs paclitaxel IV in patients with advanced GC**
- **OS, response rates and DCR* were comparable between treatment groups**
- **Both treatments were well tolerated**
- **DHP107 is the first oral paclitaxel with proven efficacy and safety in advanced GC**

*Data not presented at ASCO.

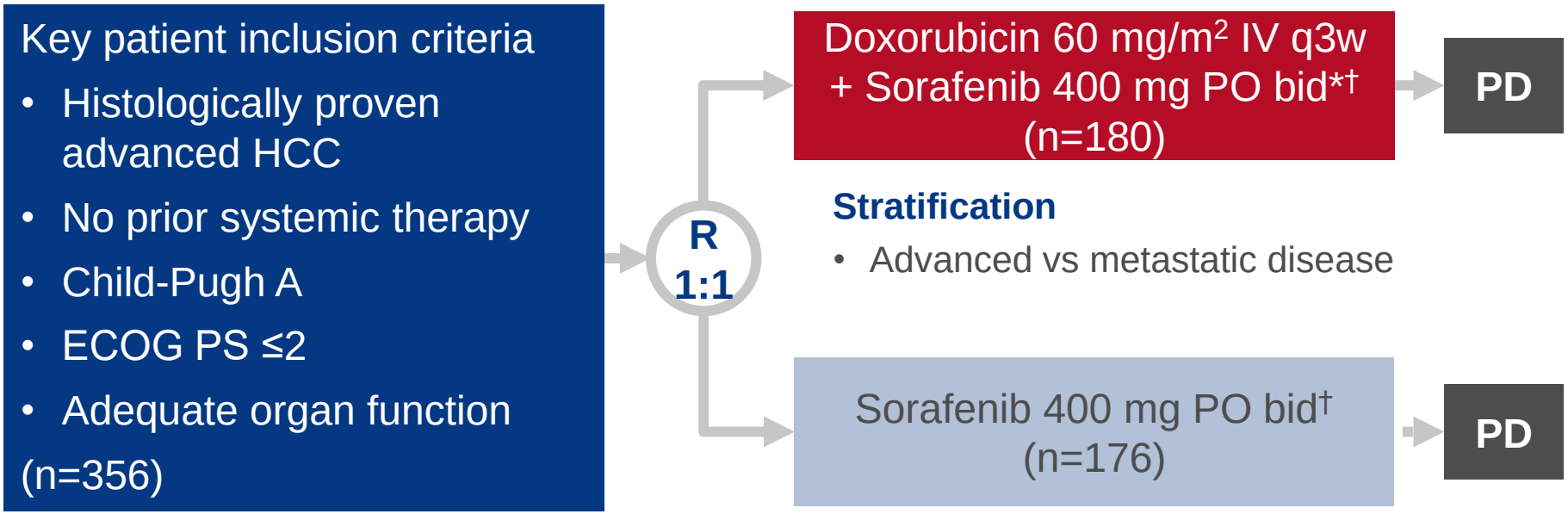
Kang et al. J Clin Oncol 2016; 34 (suppl): abstr 4016

HEPATOCELLULAR CARCINOMA

4003: Phase III randomized study of sorafenib plus doxorubicin versus sorafenib in patients with advanced hepatocellular carcinoma (HCC): CALGB 80802 (Alliance) – Abou-Alfa GK, et al

Study objective

- To investigate whether sorafenib + doxorubicin improved survival compared with sorafenib alone in patients with advanced HCC



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

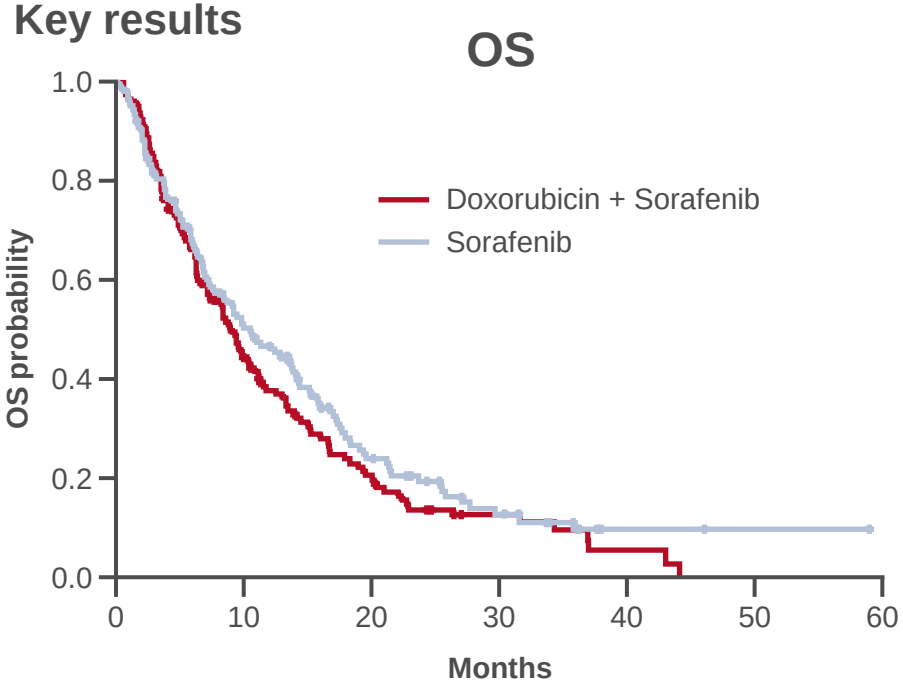
- PFS, TTP, tumour response (RECIST v1.1)
- Safety

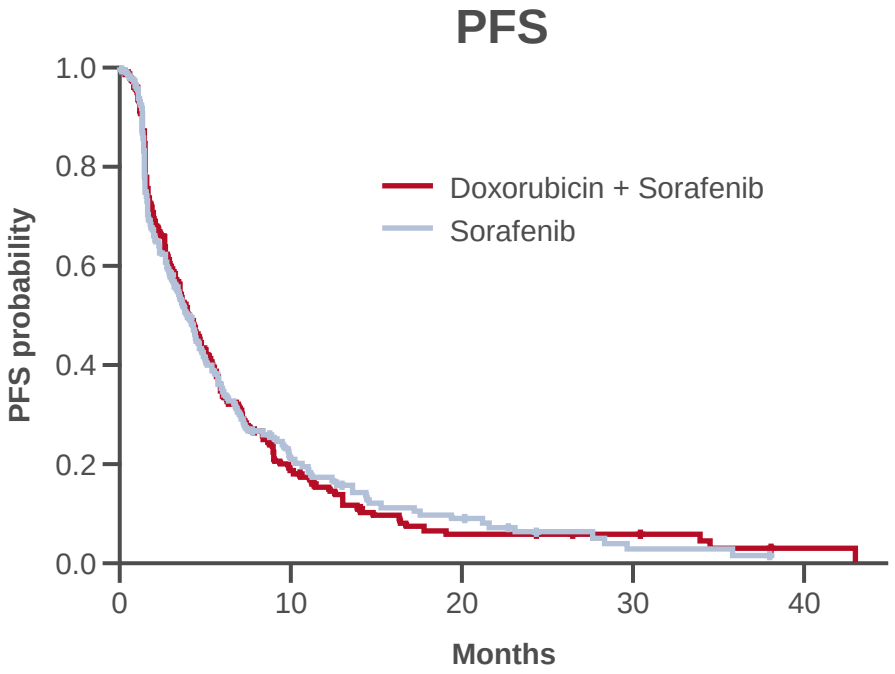
*After 6 cycles patients received sorafenib 400 mg PO bid alone;
†Half doses offered to patients with baseline bilirubin of >1.2.

Abou-Alfa et al. J Clin Oncol 2016; 34 (suppl): abstr 4003

4003: Phase III randomized study of sorafenib plus doxorubicin versus sorafenib in patients with advanced hepatocellular carcinoma (HCC): CALGB 80802 (Alliance) – Abou-Alfa GK, et al

Key results





	Doxorubicin + Sorafenib (n=180)	Sorafenib (n=176)	HR (95% CI); p-value
mOS, months	8.9	10.5	1.1 (0.8. 1.4); 0.24
mPFS, months	4.0	3.9	0.9 (0.7, 1.2); 0.98

Abou-Alfa et al. J Clin Oncol 2016; 34 (suppl): abstr 4003

4003: Phase III randomized study of sorafenib plus doxorubicin versus sorafenib in patients with advanced hepatocellular carcinoma (HCC): CALGB 80802 (Alliance) – Abou-Alfa GK, et al

Key results (results)

Grade 3–4 AEs in ≥10% of patients, %	Doxorubicin + Sorafenib (n=180)	Sorafenib (n=176)
Fatigue	10	7
Hypertension	3	13
WBC	11	0
Neutrophils	33	0
Platelets	14	1
Hand foot syndrome	10	14

Conclusions

- **In patients with advanced HCC, 1L doxorubicin + sorafenib did not improve survival vs sorafenib alone**
- **Additional toxicity was observed in the doxorubicin + sorafenib arm**
- **The results of planned correlative studies are currently awaited**

Abou-Alfa et al. J Clin Oncol 2016; 34 (suppl): abstr 4003

4017: Phase III randomized study of second line ADI-peg 20 (A) plus best supportive care versus placebo (P) plus best supportive care in patients (pts) with advanced hepatocellular carcinoma (HCC) – Abou-Alfa G, et al

Study objective

- To investigate the efficacy and safety of the arginine deiminase ADI-PEG 20 + BSC vs placebo + BSC in patients with refractory advanced HCC

Key inclusion criteria

- Histologically proven advanced HCC
- Child-Pugh ≤B7
- ECOG PS ≤2
- Failed/intolerant to prior systemic therapy

(n=635)

R 2:1

ADI-PEG 20 (18 mg/m^2 IM q1w) + BSC (n=424) → PD

Placebo (IM q1w) + BSC (n=211) → PD

Stratification

- Geographic location (Asia vs non-Asia)
- Prior sorafenib (yes vs no)

PRIMARY ENDPOINT(S)

- OS

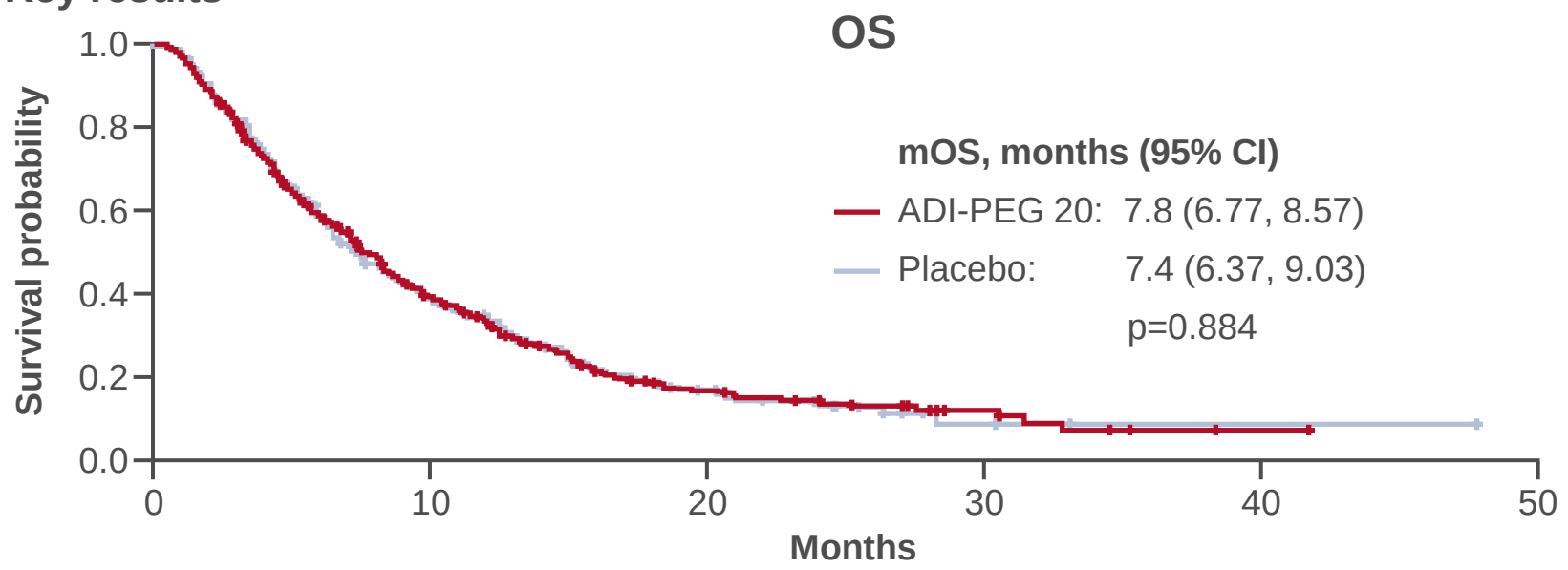
SECONDARY ENDPOINTS

- Response rates
- Safety

Abou-Alfa et al. J Clin Oncol 2016; 34 (suppl): abstr 4017

4017: Phase III randomized study of second line ADI-peg 20 (A) plus best supportive care versus placebo (P) plus best supportive care in patients (pts) with advanced hepatocellular carcinoma (HCC) – Abou-Alfa G, et al

Key results



n (%)	ADI-PEG 20 + BSC (n=424)	Placebo + BSC (n=211)
CR	0	0
PR	3 (1)	6 (3)
SD	102 (24)	60 (28)
PD	227 (53)	100 (47)
Missing	92 (22)	45 (21)

Abou-Alfa et al. J Clin Oncol 2016; 34 (suppl): abstr 4017

4017: Phase III randomized study of second line ADI-peg 20 (A) plus best supportive care versus placebo (P) plus best supportive care in patients (pts) with advanced hepatocellular carcinoma (HCC) – Abou-Alfa G, et al

Key results (continued)

mOS, months (95% CI)	>7 weeks	≤7 weeks	p-value
Arginine depletion	12.5 (10, 16.3)	6.3 (5.3, 7.4)	<0.0001
Citrulline increase	13 (10.9, 16.1)	5.6 (4.7, 7.1)	<0.0001

AEs, n (%)	ADI-PEG 20 + BSC (n=424)	Placebo + BSC (n=211)
Grade 3–4 AEs in ≥5% of patients		
Haematology: Anaemia	19 (4)	12 (6)
Liver: AST	42 (10)	18 (9)
Skin: Pruritus and rash		
Grade 1–2	142 (34)	52 (25)
Grade 3	5 (1)	2 (1)
Deaths on study	68 (16)	36 (17)

Conclusions

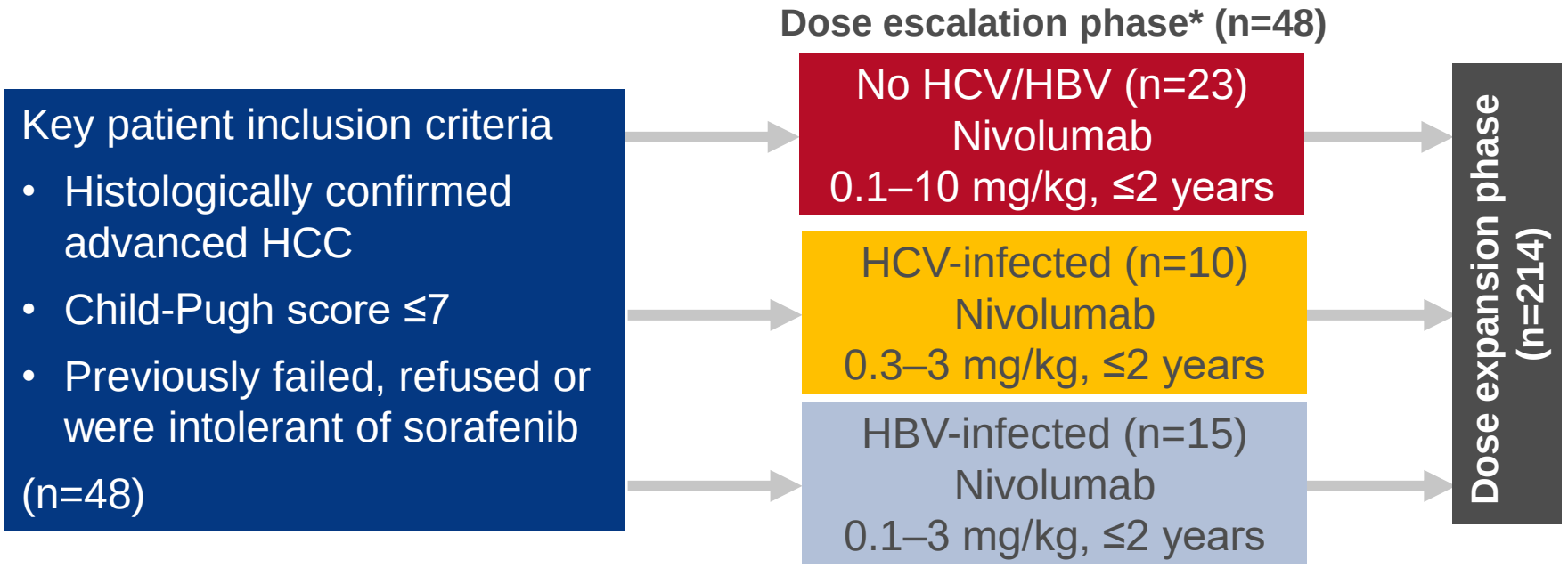
- **ADI-PEG monotherapy did not improve survival vs placebo in patients with advanced HCC who had failed or were intolerant to prior systemic therapy**
- **ADI-PEG was well tolerated**

Abou-Alfa et al. J Clin Oncol 2016; 34 (suppl): abstr 4017

4012: Phase I/II safety and antitumor activity of nivolumab (nivo) in patients (pts) with advanced hepatocellular carcinoma (HCC): Interim analysis of the CheckMate-040 dose escalation study – El-Khoueiry AB, et al

Study objective

- To investigate the efficacy and safety of escalating doses of nivolumab in patients with advanced HCC



PRIMARY ENDPOINT(S)

- Safety

SECONDARY ENDPOINTS

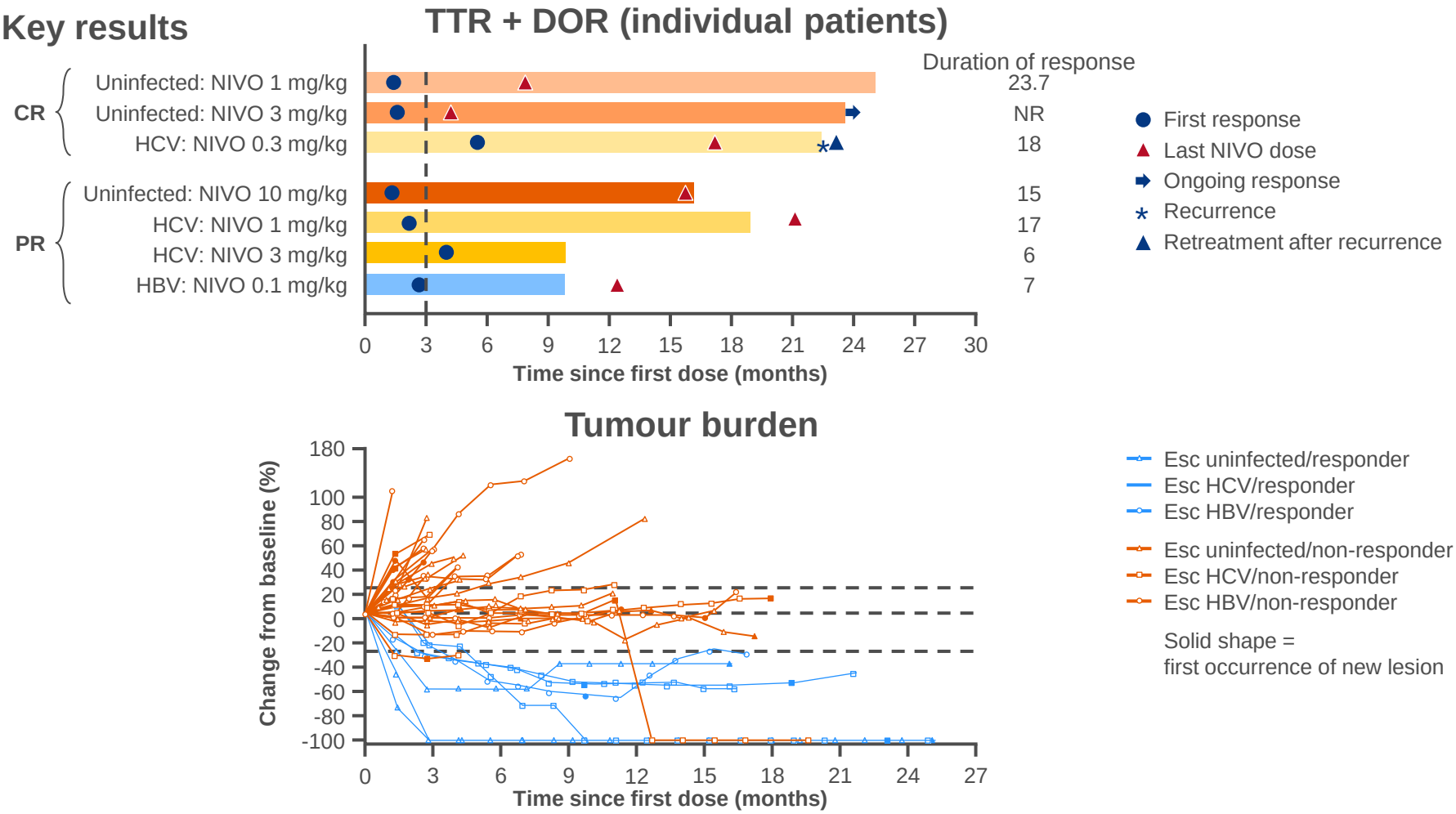
- Antitumor activity by RECIST 1.1
- DOR

*Reported in the current analysis.

El-Khoueiry et al. J Clin Oncol 2016; 34 (suppl): abstr 4012

4012: Phase I/II safety and antitumor activity of nivolumab (nivo) in patients (pts) with advanced hepatocellular carcinoma (HCC): Interim analysis of the CheckMate-040 dose escalation study – El-Khoueiry AB, et al

Key results



- mOS: 15.1 months (95% CI 9.6, 28.6)

NIVO, nivolumab.

El-Khoueiry et al. J Clin Oncol 2016; 34 (suppl): abstr 4012

4012: Phase I/II safety and antitumor activity of nivolumab (nivo) in patients (pts) with advanced hepatocellular carcinoma (HCC): Interim analysis of the CheckMate-040 dose escalation study – El-Khoueiry AB, et al

Key results (continued)

TRAEs in ≥10% of patients	All patients (n=48)	
	Any grade	Grade 3–4
Rash	11 (23)	0
Pruritus	7 (15)	0
AST increased	10 (21)	5 (10)
Lipase increased	10 (21)	6 (13)
Amylase increased	9 (19)	1 (2)
ALT increased	7 (15)	3 (6)

Conclusions

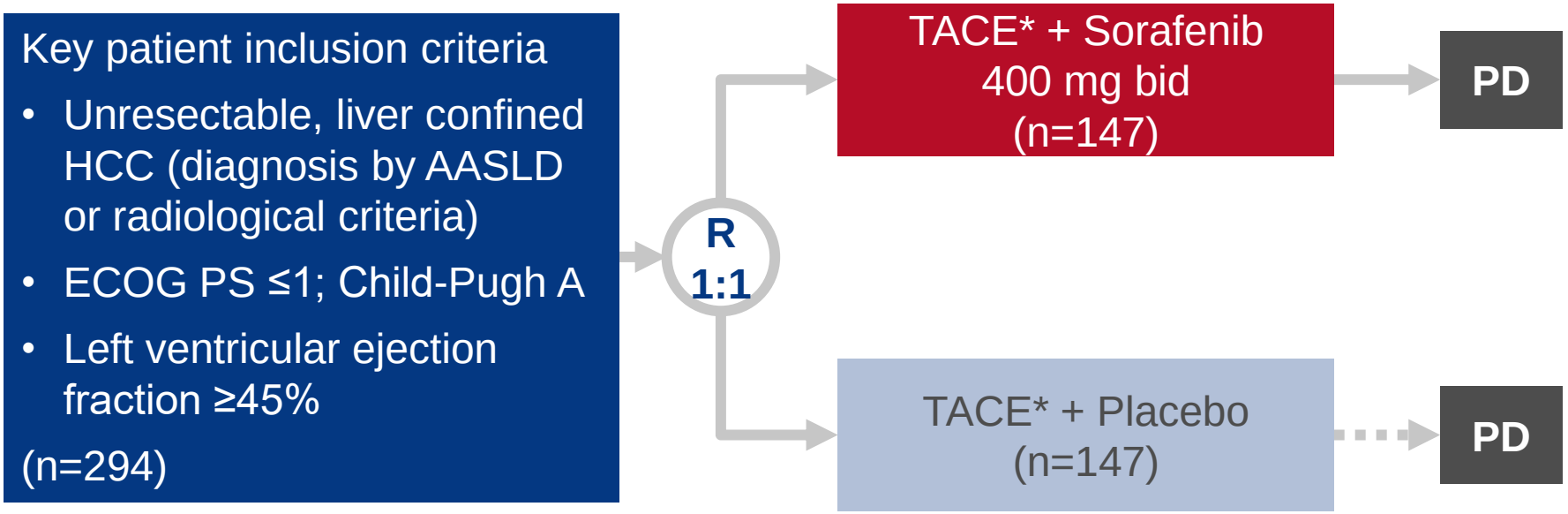
- **mOS with nivolumab was highly encouraging in patients with HCC**
- **Nivolumab had a manageable safety profile, including in patients with HBC or HCV**
  - **Apart from a higher frequency of AST/ALT, the safety profile was similar to that observed in other tumours**
- **The dose-escalation phase of this study supports the continued exploration of nivolumab 3 mg/kg in patients with HCC during an expansion phase**

El-Khoueiry et al. J Clin Oncol 2016; 34 (suppl): abstr 4012

4018: TACE 2: A randomized placebo-controlled, double-blinded, phase III trial evaluating sorafenib in combination with transarterial chemoembolisation (TACE) in patients with unresectable hepatocellular carcinoma (HCC) – Meyer T, et al

Study objective

- To assess the efficacy and safety of TACE + sorafenib vs TACE + placebo in patients with unresectable HCC



PRIMARY ENDPOINT(S)

- PFS

SECONDARY ENDPOINTS

- OS, TCC, disease control
- Safety, QoL

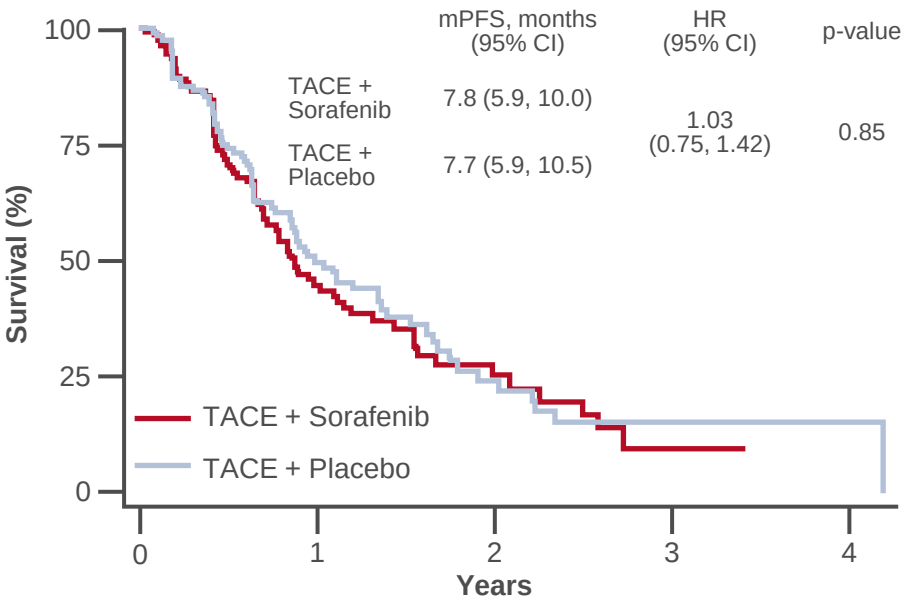
*Performed at 2–5 weeks using drug eluting beads loaded with 150 mg doxorubicin, then performed according to radiological response and patient tolerance.

Meyer et al. J Clin Oncol 2016; 34 (suppl): abstr 4018

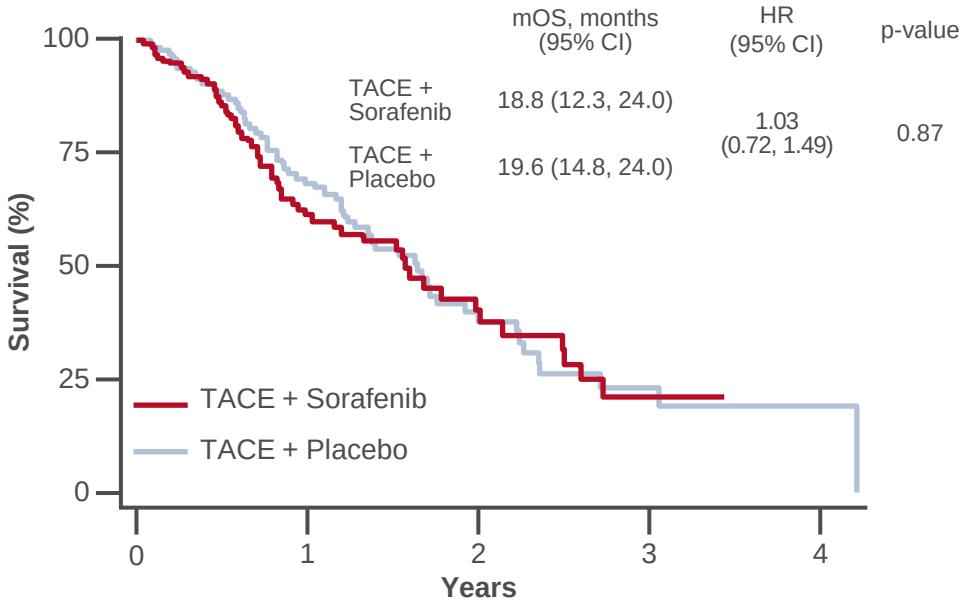
4018: TACE 2: A randomized placebo-controlled, double-blinded, phase III trial evaluating sorafenib in combination with transarterial chemoembolisation (TACE) in patients with unresectable hepatocellular carcinoma (HCC) – Meyer T, et al

Key results

PFS



OS



Best response (RECIST)	TACE + Sorafenib (n=147)	TACE + Placebo (n=147)	Overall (n=294)
CR, n (%)	5 (3.4)	5 (3.4)	10 (3.4)
PR, n (%)	46 (31.3)	41 (27.9)	87 (29.6)
SD, n (%)	76 (51.7)	77 (52.4)	153(52.0)
PD, n (%)	10 (6.8)	12 (8.2)	22 (7.5)

Meyer et al. J Clin Oncol 2016; 34 (suppl): abstr 4018

4018: TACE 2: A randomized placebo-controlled, double-blinded, phase III trial evaluating sorafenib in combination with transarterial chemoembolisation (TACE) in patients with unresectable hepatocellular carcinoma (HCC) – Meyer T, et al

Key results (continued)

	TACE + Sorafenib (n=77)	TACE + Placebo (n=78)	Overall (n=155)
Unrelated SAE, n (%)	50 (64.9)	66 (84.6)	116 (74.8)
SAR, n (%)	22 (28.6)	10 (12.8)	32 (20.6)
SUSAR, n (%)	5 (6.5)	2 (2.6)	7 (4.5)
Total, n (%)	77 (100.0)	78 (100.0)	155 (100.0)

Conclusions

- **There was no evidence that the addition of sorafenib to drug-eluting bead TACE improves PFS and OS in patients with intermediate HCC**
- **Alternative systemic therapies need to be evaluated in combination with TACE to improve outcomes for this patient population**

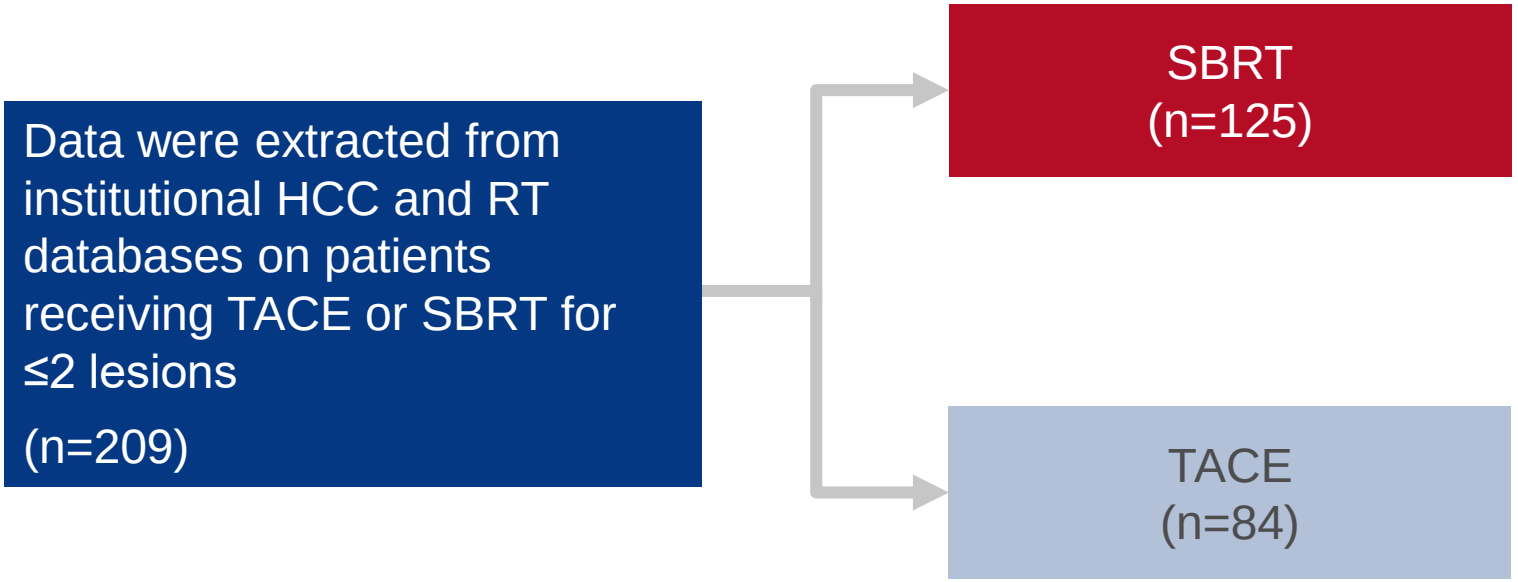
SAR, serious adverse reaction; SUSAR, suspected unexpected serious adverse reaction.

Meyer et al. J Clin Oncol 2016; 34 (suppl): abstr 4018

4087: Stereotactic body radiotherapy (SBRT) as an alternative to transarterial chemoembolization (TACE) for hepatocellular carcinoma (HCC) – Sapir E, et al

Study objective

- To investigate the efficacy and safety of SBRT vs TACE in patients with HCC



ENDPOINTS

- Local control*
- OS
- Safety

*No tumour growth within or immediately adjacent to the TACE cavity or original tumour.

Based on data from abstract only

Sapir et al. J Clin Oncol 2016; 34 (suppl): abstr 4087

4087: Stereotactic body radiotherapy (SBRT) as an alternative to transarterial chemoembolization (TACE) for hepatocellular carcinoma (HCC) – Sapir E, et al

Key results

	SBRT (n=125)	TACE (n=84)	HR (95% CI); p-value
Local control, %			18.8 (6.7, 52.7); <0.001
Year 1	97	41	
Year 2	91	18	
Predictors of worse local control*			
Increasing tumour size	-	-	1.2† (1.05, 1.23); <0.001
Partial portal venous tumour thrombus	-	-	7.0 (2.73, 15.2); <0.001

	SBRT (n=125)	TACE (n=84)	p-value
Grade ≥3 AEs, %	14	7	0.05

*Predicted worse local control with TACE but not with SBRT;
†Per cm.

Based on data from abstract only

Sapir et al. J Clin Oncol 2016; 34 (suppl): abstr 4087

4087: Stereotactic body radiotherapy (SBRT) as an alternative to transarterial chemoembolization (TACE) for hepatocellular carcinoma (HCC) – Sapir E, et al

Key results (continued)

- SBRT was initiated a mean of 9 months later than TACE; p<0.001
- Liver transplantation: 8% with SBRT vs 18% with TACE; p=0.01
- OS: HR* 0.73 (95% CI 0.48, 1.12); p=0.15

Conclusions

- **In patients with HCC, SBRT is an acceptable alternative to TACE for 1–2 tumours**
  - **SBRT provides superior local control, with no difference in OS**
- **Prospective comparative trials of TACE, SBRT and other ablative therapies are warranted**

Based on data from abstract only

*Adjusted for baseline liver function and transplantation.

Sapir et al. J Clin Oncol 2016; 34 (suppl): abstr 4087

PANCREATIC CANCER

LBA4006: ESPAC-4: A multicenter, international, open-label randomized controlled phase III trial of adjuvant combination chemotherapy of gemcitabine and capecitabine versus monotherapy gemcitabine in patients with resected pancreatic ductal adenocarcinoma – Neoptolemos J, et al

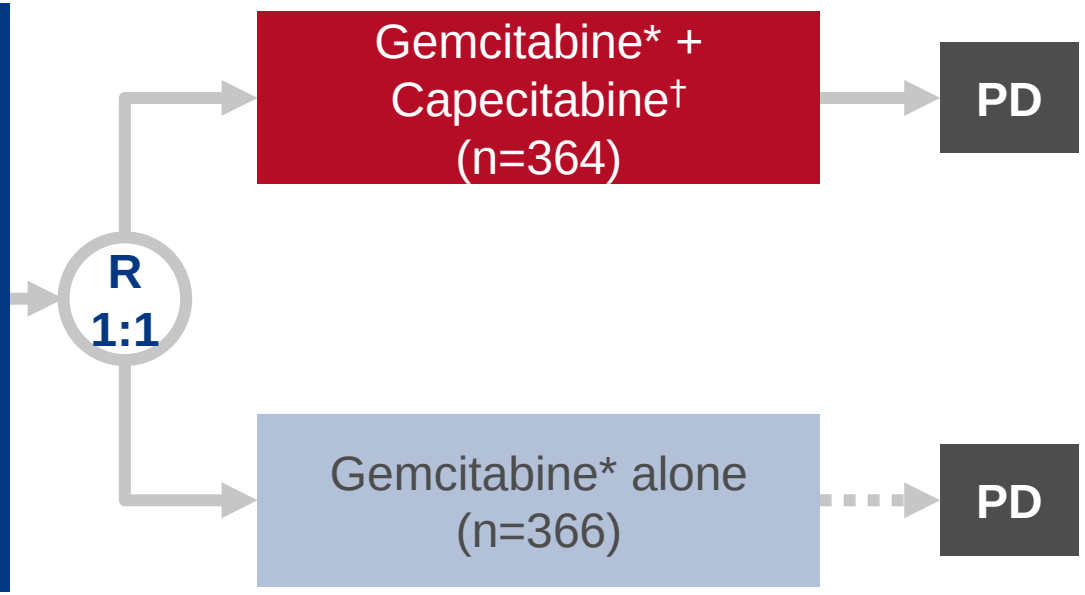
Study objective

- To investigate the efficacy and safety of gemcitabine + capecitabine vs gemcitabine alone as adjuvant therapy in patients with resected pancreatic cancer

Key patient inclusion criteria

- Pancreatic ductal ADC
- R0 or R1 resection
- No ascites, liver or peritoneal metastases
- WHO PS ≤2
- No malignancy diagnoses

(n=730)



PRIMARY ENDPOINT(S)

- OS

SECONDARY ENDPOINTS

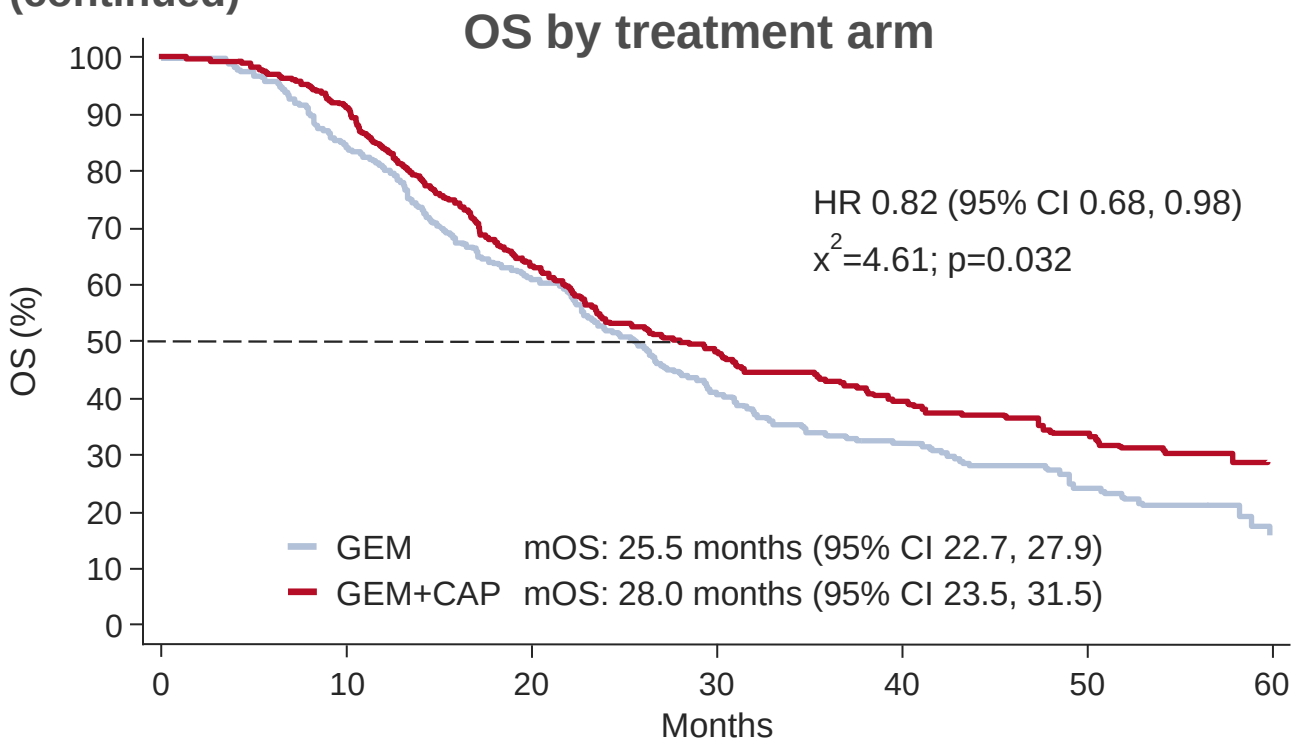
- Safety

*1000 mg/m^2 d1,8,16 (6 cycles); †1660 mg/m^2 21/28d.

Neoptolemos et al. J Clin Oncol 2016; 34 (suppl): abstr LBA4006

LBA4006: ESPAC-4: A multicenter, international, open-label randomized controlled phase III trial of adjuvant combination chemotherapy of gemcitabine and capecitabine versus monotherapy gemcitabine in patients with resected pancreatic ductal adenocarcinoma – Neoptolemos J, et al

Key results (continued)



	Gemcitabine + Capecitabine (n=366)	Gemcitabine (n=364)
5-year OS, % (95% CI)	28.8 (22.9, 35.2)	16.3 (10.2, 23.7)
χ^2; p-value*	4.61; 0.032	

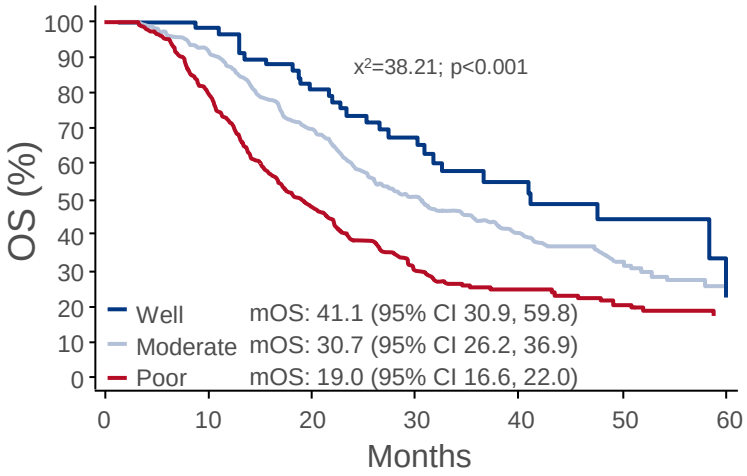
*Stratified by resection margin status and country.
CAP, capecitabine; GEM, gemcitabine.

Neoptolemos et al. J Clin Oncol 2016; 34 (suppl): abstr LBA4006

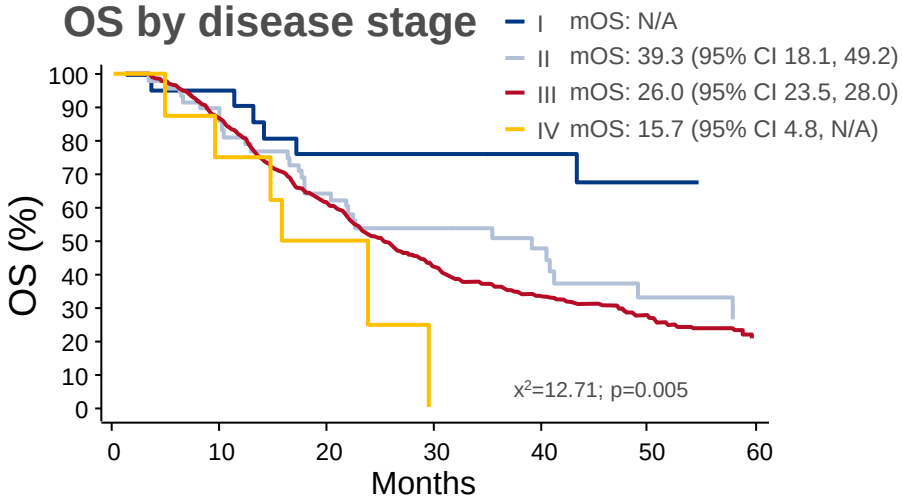
LBA4006: ESPAC-4: A multicenter, international, open-label randomized controlled phase III trial of adjuvant combination chemotherapy of gemcitabine and capecitabine versus monotherapy gemcitabine in patients with resected pancreatic ductal adenocarcinoma – Neoptolemos J, et al

Key results

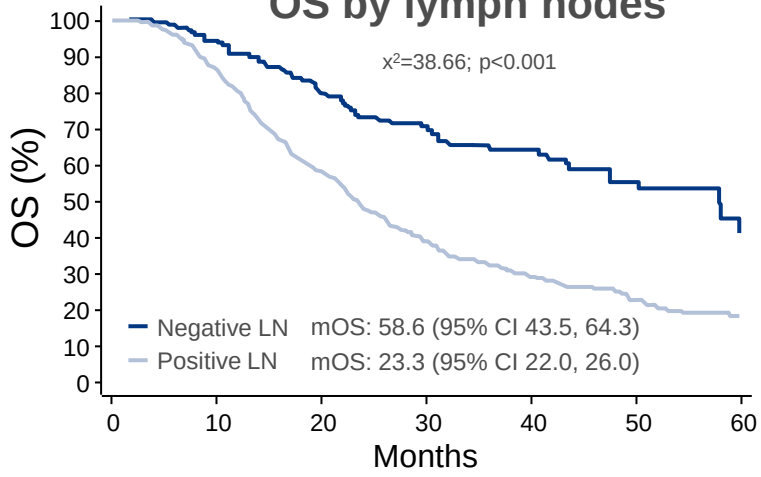
OS by disease grade



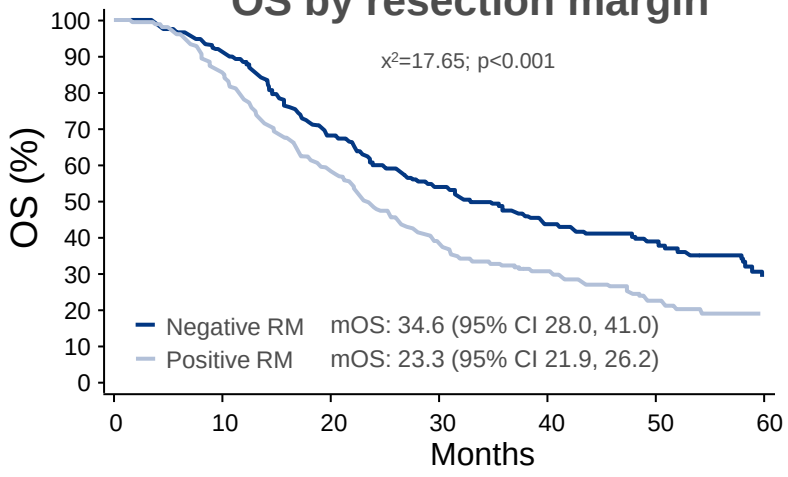
OS by disease stage



OS by lymph nodes



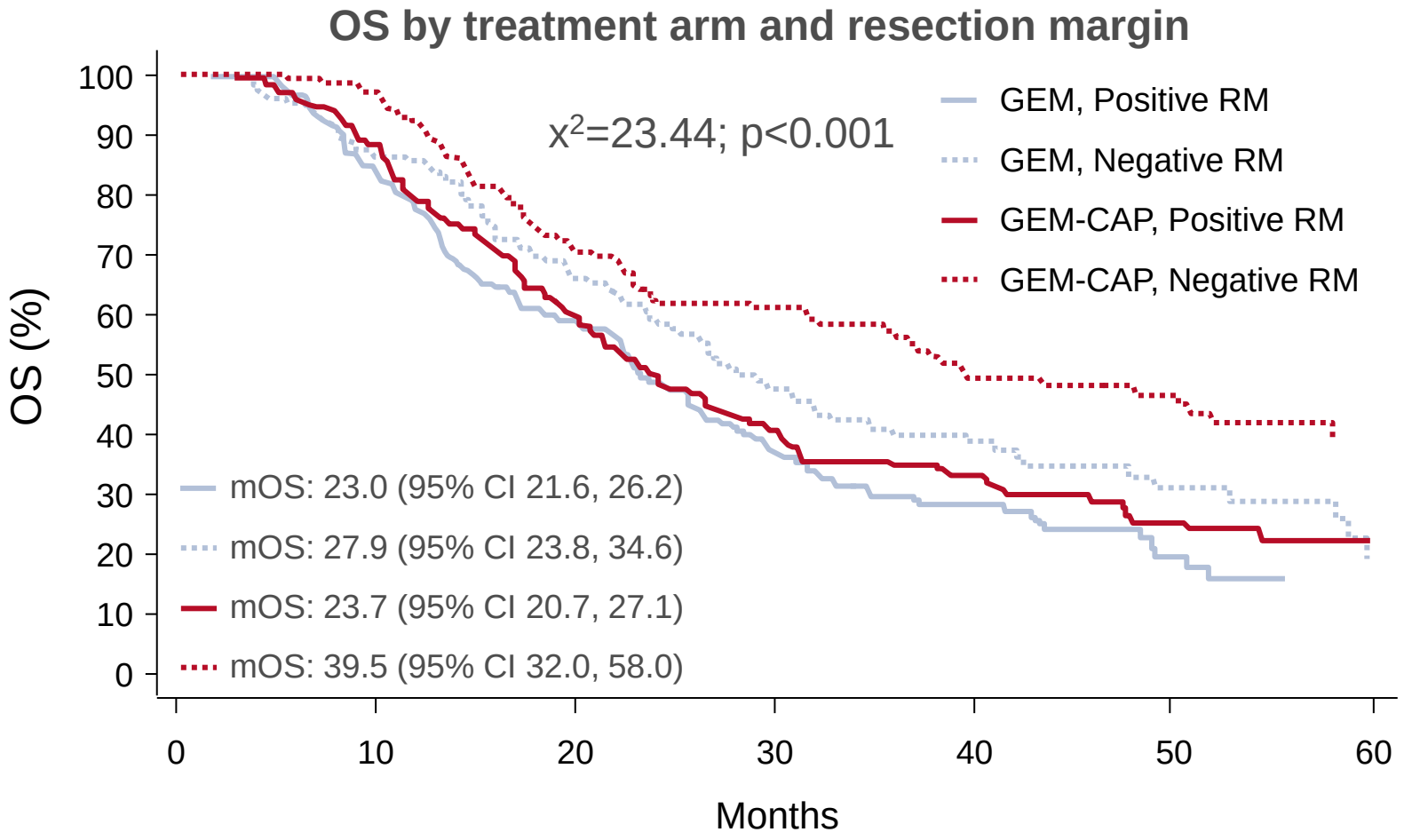
OS by resection margin



LN, lymph nodes; N/A, not available; RM, resection margin. Neoptolemos et al. J Clin Oncol 2016; 34 (suppl): abstr LBA4006

LBA4006: ESPAC-4: A multicenter, international, open-label randomized controlled phase III trial of adjuvant combination chemotherapy of gemcitabine and capecitabine versus monotherapy gemcitabine in patients with resected pancreatic ductal adenocarcinoma – Neoptolemos J, et al

Key results (continued)



CAP, capecitabine; GEM, gemcitabine; RM, resection margin.

Neoptolemos et al. J Clin Oncol 2016; 34 (suppl): abstr LBA4006

LBA4006: ESPAC-4: A multicenter, international, open-label randomized controlled phase III trial of adjuvant combination chemotherapy of gemcitabine and capecitabine versus monotherapy gemcitabine in patients with resected pancreatic ductal adenocarcinoma – Neoptolemos J, et al

Key results (continued)

AEs Grade 3–4 in ≥5% of patients, n (%)	Gemcitabine + Capecitabine (n=359)	Gemcitabine (n=366)	p-value*
Diarrhoea	19 (5)	6 (2)	0.008
Fatigue	20 (6)	19 (5)	0.870
Infection/infestation	9 (3)	24 (7)	0.012
Neutrophils	137 (38)	89 (24)	<0.001
Hand-foot syndrome	26 (7)	0	<0.001
WBC	37 (10)	28 (8)	0.242

- Treatment related SAEs: 24% gemcitabine + capecitabine vs 26% gemcitabine alone

Conclusions

- **Adjuvant gemcitabine + capecitabine demonstrated significant improvements in OS vs gemcitabine alone in patients with resected pancreatic cancer**
- **Toxicities were slightly more frequent with gemcitabine + capecitabine vs gemcitabine monotherapy, but overall these were manageable**
- **The 5-year OS survival rate was superior to previous ESPAC trials**
- **Adjuvant gemcitabine + capecitabine is the new SoC in this setting**

*Exploratory analysis: Fisher's exact test.

Neoptolemos et al. J Clin Oncol 2016; 34 (suppl): abstr LBA4006

4007: MAESTRO: A randomized, double-blind phase III study of evofosfamide in combination with gemcitabine in previously untreated patients with metastatic or locally advanced unresectable pancreatic ductal adenocarcinoma – Van Cutsem E, et al

Study objective

- To evaluate the efficacy and safety of 1L evofosfamide + gemcitabine in patients with advanced pancreatic cancer

Key inclusion criteria

- Unresectable, locally advanced or metastatic pancreatic ductal ADC
- ECOG PS ≤1
- No prior CT or systemic therapy*
- No neoadjuvant or adjuvant CT <6 months prior

(n=693)

R 1:1

Evofosfamide 340 mg/m^2 + Gemcitabine† (n=346) → PD

Stratification

- Extent of disease
- ECOG PS
- Geographic region

Placebo + Gemcitabine† (n=347) → PD

PRIMARY ENDPOINT

- Overall survival (OS)

SECONDARY ENDPOINTS

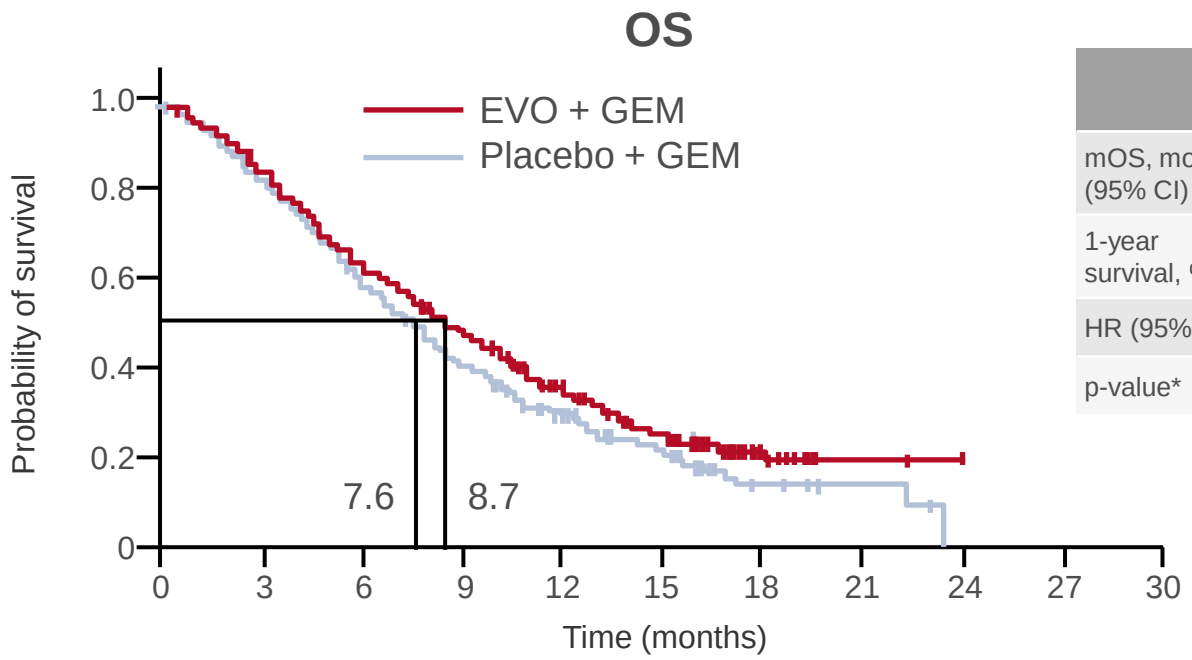
- PFS, ORR
- Safety, QoL

*Apart from radiosensitising doses of 5FU or gemcitabine (if relapse was ≥6 months after completion of gemcitabine); †1000 mg/m^2 d1,8,15 q28d.

Van Cutsem et al. J Clin Oncol 2016; 34 (suppl): abstr 4007

4007: MAESTRO: A randomized, double-blind phase III study of evofosfamide in combination with gemcitabine in previously untreated patients with metastatic or locally advanced unresectable pancreatic ductal adenocarcinoma – Van Cutsem E, et al

Key results



	EVO + GEM (n=346)	Placebo + GEM (n=347)
mOS, months (95% CI)	8.7 (7.6, 9.9)	7.6 (6.7, 8.3)
1-year survival, %	34.2	29.8
HR (95% CI)	0.84 (0.71, 1.01)	
p-value*	0.059	

	Placebo + GEM vs EVO + GEM	p-value*
PFS, HR (95% CI)	0.75 (0.63, 0.90)	0.002
Best response, OR (95% CI)	1.26 (0.83, 1.90)	0.227
Confirmed response, OR (95% CI)	1.79 (1.09, 2.96)	0.009

*Log-rank (stratified).
EVO, evofosfamide; GEM, gemcitabine.

Van Cutsem et al. J Clin Oncol 2016; 34 (suppl): abstr 4007

4007: MAESTRO: A randomized, double-blind phase III study of evofosfamide in combination with gemcitabine in previously untreated patients with metastatic or locally advanced unresectable pancreatic ductal adenocarcinoma – Van Cutsem E, et al

Key results (continued)

Grade 3–4 haematological AEs, n (%)	Evofosfamide + Gemcitabine (n=338)	Placebo + Gemcitabine (n=341)
Neutropenia	152 (45.0)	88 (25.8)
Febrile neutropenia	7 (2.1)	2 (0.6)
Thrombocytopenia	160 (47.3)	26 (7.6)
Anaemia	75 (22.2)	41 (12.0)

Conclusions

- **The trial did not meet its primary endpoint**
- **Evofosfamide + gemcitabine showed signs of antitumor activity (OS, PFS, ORR) vs placebo + gemcitabine in patients with advanced pancreatic cancer**
- **Haematological AEs were slightly more common with evofosfamide + gemcitabine**
  - **No new safety signals were identified**
- **Further analyses are ongoing**

Van Cutsem et al. J Clin Oncol 2016; 34 (suppl): abstr 4007

4008: PET-PANC: Multi-centre prospective diagnostic accuracy and clinical value trial of FDG PET/CT in the diagnosis and management of suspected pancreatic cancer – Ghaneh P, et al

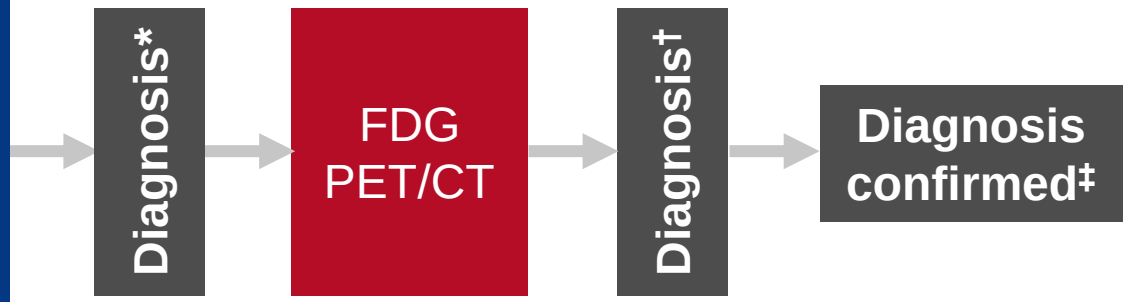
Study objective

- To investigate the impact of FDG PET-CT in addition to standard diagnostic workup in patients with suspected pancreatic cancer

Key patient inclusion criteria

- Suspected pancreatic cancer
- Able to attend for PET-CT + MDCT scan

(n=550)



PRIMARY ENDPOINT

- Incremental diagnostic value of FDG PET-CT in addition to MDCT

SECONDARY ENDPOINTS

- Changes in diagnosis, staging and patient management
- Costing

*Unblinded based on first MDT outcome; †Unblinded to PET/CT scan based on second MDT outcome, followed by actual diagnosis and management; ‡Reference standard: diagnosis made by an independent panel blinded to previous diagnoses/scans.

Ghaneh et al. J Clin Oncol 2016; 34 (suppl): abstr 4008

4008: PET-PANC: Multi-centre prospective diagnostic accuracy and clinical value trial of FDG PET/CT in the diagnosis and management of suspected pancreatic cancer – Ghaneh P, et al

Key results

Diagnostic accuracy	MDCT , % (95% CI)	PET-CT, % (95% CI)	Relative	p-value
Sensitivity	88.5 (84.6, 92.4)	92.7 (89.6 , 95.9)	1.05 (1.01, 1.09)	0.010
Specificity	70.6 (65.3 , 75.8)	75.8 (70.8 , 80.7)	1.07 (1.01, 1.14)	0.023
Positive predictive value	73.1 (68.2 , 78.0)	77.6 (72.9 , 82.2)	1.06 (1.00, 1.13)	0.062
Negative predictive value	87.1 (82.9 , 91.5)	92.0 (88.6 , 95.5)	1.06 (1.00, 1.11)	0.031

Change in patient management			
Pre-PET-CT	Post-PET-CT	Number of patients, n (%)	Number of patients due to PET-CT, n (%)
Resection*	No resection	61 (21)	58 (20)†
No resection	Resection	34 (13)	19 (7)
CT	No CT	8 (10)	1 (1)
No CT	CT	41 (9)	24 (5)
No further investigation	Further investigation	58 (13)	31 (7)
PET-CT identified second primary	–	5 (NA)	5 (NA)

- 56 (14%) of patients were changed from an incorrect to a correct stage with PET-CT

*290 patients planned for resection; †41 metastases, 17 benign.

Ghaneh et al. J Clin Oncol 2016; 34 (suppl): abstr 4008

4008: PET-PANC: Multi-centre prospective diagnostic accuracy and clinical value trial of FDG PET/CT in the diagnosis and management of suspected pancreatic cancer – Ghaneh P, et al

Key results (continued)

	All patients		PDAC		PDAC + resection	
	Nuclear medicine	Clinical oncology	Nuclear medicine	Clinical oncology	Nuclear medicine	Clinical oncology
Incremental costs, £	−645	−912	−639	−906	−1275	−1542
Incremental QALYs	0.0157		0.0119		0.0175	
ICER cost/QALY gained	PET-CT dominates					

Conclusions

- **FDG PET/CT provided significant benefit in the diagnosis of pancreatic cancer**
- **FDG PET/CT influenced the staging and management of patients, and prevented resection in patients scheduled for surgery**
- **FDG PET/CT was cost effective at current reimbursement rates to the UK NHS**

Ghaneh et al. J Clin Oncol 2016; 34 (suppl): abstr 4008

4019: A phase II, double-blind study of galunisertib+gemcitabine (GG) vs gemcitabine+placebo (GP) in patients (pts) with unresectable pancreatic cancer (PC) – Melisi D, et al

Study objective

- To evaluate the efficacy and safety of galunisertib + gemcitabine vs placebo + gemcitabine in patients with unresectable pancreatic cancer

Key patient inclusion criteria

- Pancreatic ADC with measurable disease (RECIST v1.1); ECOG PS ≤2
- Locally advanced (Stage II–III) or metastatic (Stage IV)
- Not amenable to resection with curative intent

(n=156)

R 2:1

Galunisertib* PO 150 mg bid + Gemcitabine† (n=104) → PD

Stratification

- ECOG PS (0 vs 1 vs 2)
- Disease stage (II–III vs IV)
- Previous gemcitabine (adjuvant/neoadjuvant vs no treatment)
- Centre

Placebo + Gemcitabine† (n=52) → PD

PRMARY ENDPOINT(S)

- OS

SECONDARY ENDPOINTS

- PFS, ORR, PK
- Safety, biomarkers

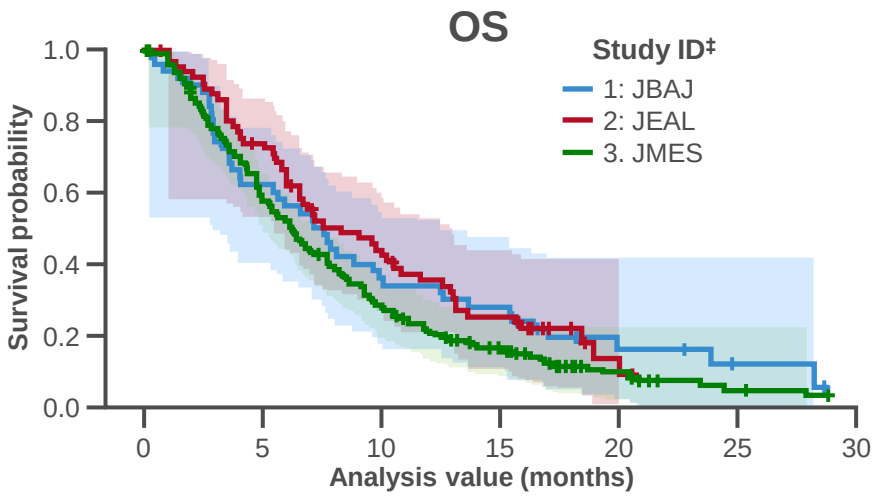
*14d on/14d off per cycle for a total of 3 cycles;
†Administered per label.

Melisi et al. J Clin Oncol 2016; 34 (suppl): abstr 4019

4019: A phase II, double-blind study of galunisertib+gemcitabine (GG) vs gemcitabine+placebo (GP) in patients (pts) with unresectable pancreatic cancer (PC) – Melisi D, et al

Key results

STRONG, borrowing from historical data*	ITT patients	Deaths	HR	Median survival, months	HR (95% CI)	Probability (of HR <1)†
Galunisertib + Gemcitabine	104	78	0.018	8.9	0.80 (0.60, 1.09)	0.92
Gemcitabine + Placebo	52	43	0.023	7.1	-	-



Study ID‡	N	Events	Censored	mOS (95% CI)
JBAJ	52	43	9	7.6 (4.0, 9.9)
JEAL	67	52	15	8.3 (6.1, 10.8)
JMES	282	245	37	6.3 (5.4, 7.0)

*The number of events borrowed from historical data was ~50;
†A positive outcome required ≥0.85 probability of HR <1;
‡Control arm was supplemented with data from these historical studies.

Melisi et al. J Clin Oncol 2016; 34 (suppl): abstr 4019

4019: A phase II, double-blind study of galunisertib+gemcitabine (GG) vs gemcitabine+placebo (GP) in patients (pts) with unresectable pancreatic cancer (PC) – Melisi D, et al

Key results (continued)

- HR (95% CI) for adjusted PFS was 0.78 (0.54, 1.13).
- The most frequent Grade 3/4 AEs possibly related to study treatment (galunisertib + gemcitabine vs gemcitabine + placebo) were anaemia (7.8 vs 13.5%), neutropenia (32.0 vs 26.9%) and thrombocytopenia (7.8 vs 9.6%)
- A decrease of >50% in CA19-9 was observed in 46% of patients in the galunisertib + gemcitabine group vs 43% of patients in gemcitabine + placebo group
  - 43% vs 41% had a >50% decrease in TGFβ1
- A reduction in TGFβ1 and CA19-9 correlated with improved OS

Conclusions

- **In patients with pancreatic cancer, galunisertib + gemcitabine improved OS and PFS vs gemcitabine + placebo, and had a manageable toxicity profile**
- **Based on augmenting the current control survival data with historical information, this is a positive trial per protocol**
- **Patients with lower TGFβ1 levels may have greater benefit from galunisertib therapy**

Melisi et al. J Clin Oncol 2016; 34 (suppl): abstr 4019

NEUROENDOCRINE TUMOUR

4005: NETTER-1 phase III: Efficacy and safety results in patients with midgut neuroendocrine tumors treated with ^{177}Lu-DOTATATE – Strosberg J, et al

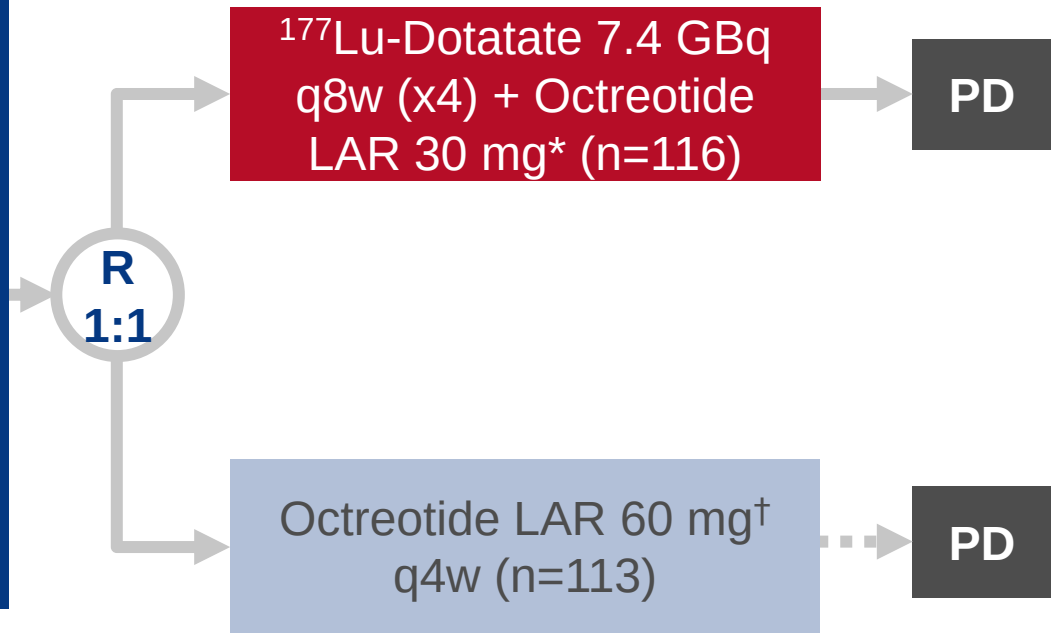
Study objective

- To evaluate the efficacy and safety of ^{177}Lu-Dotatate + octreotide LAR 30 mg vs octreotide LAR 60 mg in patients with advanced midgut NETs

Key inclusion criteria

- Metastatic/locally advanced, inoperable, histologically proven, SSTR+, midgut NET
- Ki67 index ≤20% (Grade 1–2)
- PD on Octreotide LAR 20–30mg q3–4w*
- Karnofsky PS ≥60

(n=230)



PRIMARY ENDPOINT(S)

- PFS (RECIST 1.1)

SECONDARY ENDPOINTS

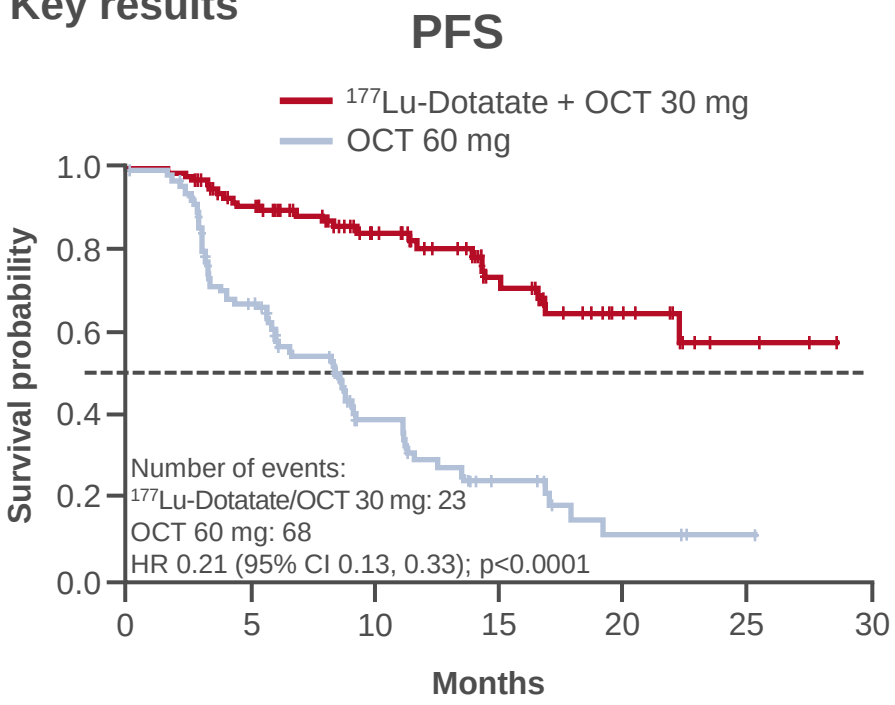
- ORR, OS, TTP
- Safety, QoL

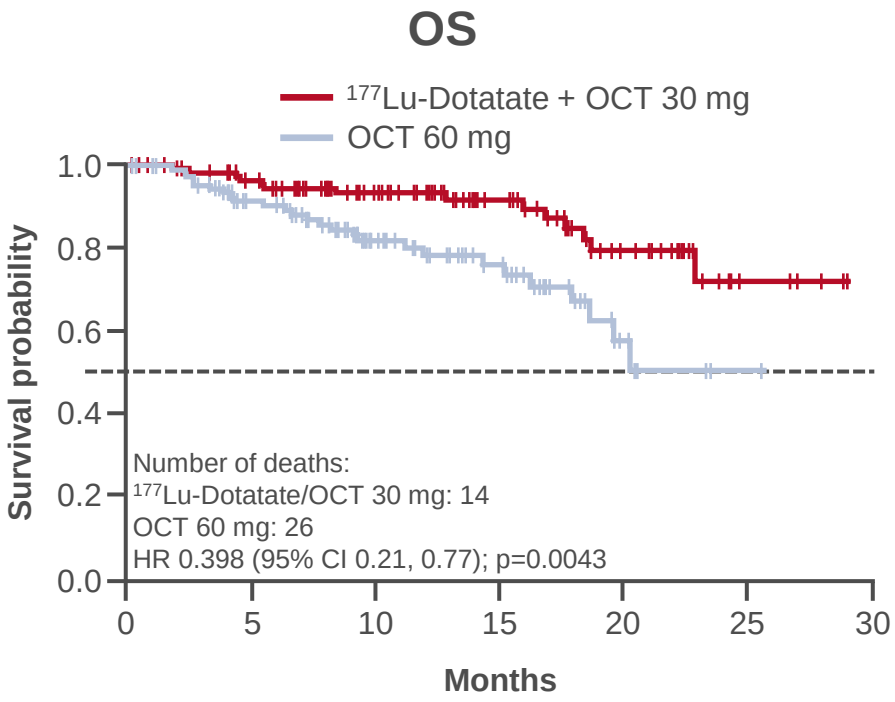
*Label use; †High dose (off label).

Strosberg et al. J Clin Oncol 2016; 34 (suppl): abstr 4005

4005: NETTER-1 phase III: Efficacy and safety results in patients with midgut neuroendocrine tumors treated with ^{177}Lu-DOTATATE – Strosberg J, et al

Key results





	177-Lu-Dotatate + OCT 30 mg (n=101)	OCT 60 mg (n=100)
ORR, % (95% CI)	18 (10, 25)	3 (0, 6)
p-value	0.0008	

OCT, Octreotide LAR.

Strosberg et al. J Clin Oncol 2016; 34 (suppl): abstr 4005

4005: NETTER-1 phase III: Efficacy and safety results in patients with midgut neuroendocrine tumors treated with ^{177}Lu-DOTATATE – Strosberg J, et al

Key results (continued)

Haematological AEs, %	^{177}Lu-Dotatate + OCT 30 mg (n=111)		OCT 60 mg (n=110)	
	Any grade	Grade 3–4	Any grade	Grade 3–4
Thrombocytopenia	25	2	1	0
Lymphopenia	18	9	2	0
Anaemia	14	0	5	0
Leukopenia	10	1	1	0
Neutropenia	5	1	1	0

Conclusions

- **^{177}Lu-Dotatate + octreotide LAR 30 mg significantly improved PFS and ORR vs octreotide LAR 60 mg alone, in patients with advanced midgut NETs**
- **^{177}Lu-Dotatate had a favourable safety profile, with no clinically relevant findings**
- **^{177}Lu-Dotatate provides a major therapeutic benefit for patients progressing on SSAs, for whom few treatment options are available**

OCT, Octreotide LAR.

Strosberg et al. J Clin Oncol 2016; 34 (suppl): abstr 4005

4020: Genomic profiling to distinguish poorly differentiated neuroendocrine carcinomas arising in different sites – Bergsland EK, et al

Study objective

- To examine genomic alterations in extrapulmonary poorly differentiated NET (GEP-NET) of different sites in comparison to SCLC

Study design

- Genomic profiling of 976 NETs identified in Foundation Medicine Database (February 2012 to November 2011)
- Hybridisation-captured, adaptor ligation based libraries were used for a mean coverage of 600X for 92 cancer-related genes between two different assays
- All classes of genomic alternations identified
- Group 1 (n=274): Pathologist #1 analysed data from 274 of 368 GEP-NET:
  - 123 pancreas, 92 colon, 59 “other GI” (oesophageal, stomach, small intestine) and compared with 593 SCLC
- Group 2 (n=159): Pathologist #2 subsequently reviewed 159 samples
  - 91 pancreas, 51 colorectal, 17 “other GI”
  - Stricter criteria used and distinguished large vs small cell NEC
- Analysis restricted to n>30

Bergsland et al. J Clin Oncol 2016; 34 (suppl): abstr 4020

4020: Genomic profiling to distinguish poorly differentiated neuroendocrine carcinomas arising in different sites – Bergsland EK, et al

Key results

	SCLC	Pancreas		CRC		Other GI
%	(n=593)	Group 1 (n=123)	Group 2 (n=91)	Group 1 (n=92)	Group 2 (n=51)	Group 1 (n=59)
TP53	90	18 S*, C*, O*	15 S*, C*	59 S*, P*	67 S*, P*	49 S*, P*
RB1	67	10 S*, C*	11 S*, C*	34 S*, P*	47 P*	29 S*
APC	2	3 C*	2 C*	47 S*, P*, O*	45 S*, P*	8 C*
CDKN2A	3	21 S, C*	22 S*, C*	5 P*, O*	2 P*	25 S*, C*
KRAS	4	7 C*	7 C*	37 S*, P*, O*	39 S*, P*	3 C*
MEN1	1	33 S*, C*, O*	29 S*, C*	3 P*	0 P*	2 P*
CDKN2B	1	16 S*, C*	18 S*	1 P*, O*	2	19 S*, C*
CCNE1	4	2 O*	2	1 O*	2	17 S*, P*, C*
DAXX	0	20 S*, C*, O*	14 S*	0 P*	0	0 P*
FBXW7	3	1 C*	0 C*	14 S*, P*	16 S*, P*	5

*Statistical significance vs SCLC (S), pancreas (P), colorectal (C) and other GI (O).

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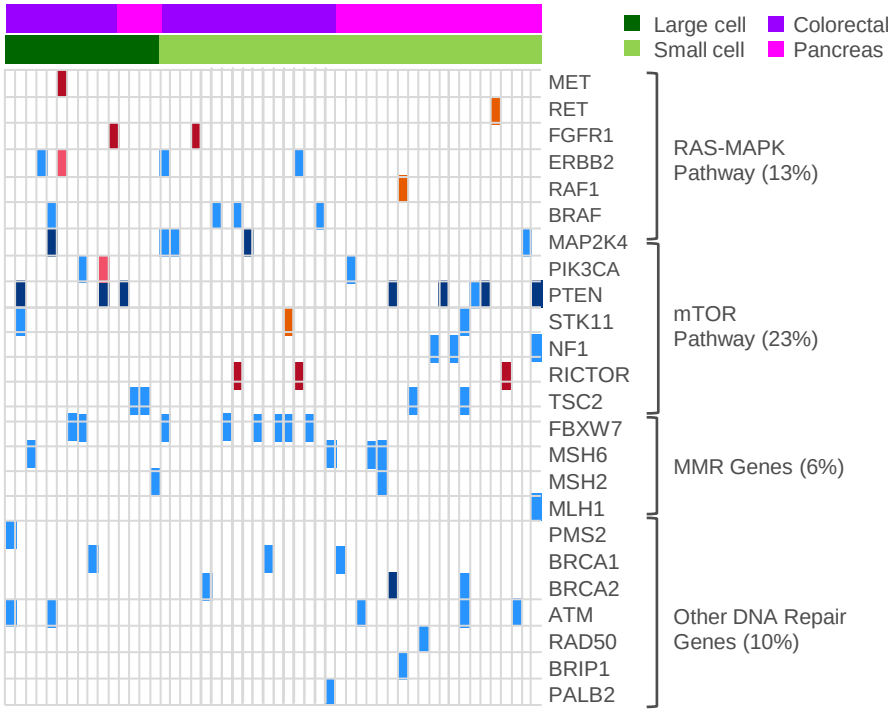
4020: Genomic profiling to distinguish poorly differentiated neuroendocrine carcinomas arising in different sites – Bergsland EK, et al

Key results (continued)



Conclusions

- Genetic alterations in GEP-NET differ from SCLC and from each other
  - GEP-NET therapy may be site-specific and different to that for SCLC
- A significant number of patients with GEP-NET had “actionable” alterations, with the possibility of germ line testing

Bergsland et al. J Clin Oncol 2016; 34 (suppl): abstr 4020