GI SLIDE DECK 2016

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

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 **European Society of Medical Oncology 2016 Congress** and is available in English, French 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 which 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.

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

Yours sincerely,

Eric Van Cutsem
Wolff Schmiegel
Phillippe Rougier
Thomas Seufferlein

(ESDO Governing Board)

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european society of digestive oncology

ESDO Medical Oncology Slide Deck
Editors 2016

COLORECTAL CANCERS



Prof Eric Van Cutsem	Digestive Oncology Unit, University Hospital Gasthuisberg, Leuven, Belgium
Prof Wolff Schmiegel	Department of Medicine, Ruhr University, Bochum, Germany
Prof Thomas Gruenberger	Department of Surgery I, Rudolf Foundation Clinic, Vienna, Austria

PANCREATIC CANCER AND HEPATOBILIARY TUMOURS


Prof Jean-Luc Van Laetham	Department of Gastroenterology-GI Cancer Unit, Erasme University Hospital, Brussels, Belgium
Prof Thomas Seufferlein	Clinic of Internal Medicine I, University of Ulm, Ulm, Germany

GASTRO-OESOPHAGEAL AND NEUROENDOCRINE TUMOURS


Prof Philippe Rougier	Digestive Oncology Department, European Hospital Georges Pompidou, Paris, France
Prof Côme Lepage	University Hospital & INSERM, Dijon, France

BIOMARKERS


Prof Eric Van Cutsem	Digestive Oncology Unit, University Hospital Gasthuisberg, Leuven, Belgium
Prof Thomas Seufferlein	Clinic of Internal Medicine I, University of Ulm, Ulm, Germany

esdo

Glossary

1L	first line
2L	second line
5FU	5-fluorouracil
AE	adverse event
AMP	amplification
ATM	ataxia-telangiectasia mutated
BCLC	Barcelona Clinic Liver Cancer
BSA	body surface area
CA19-9	carbohydrate-associated antigen 19-9
(NCI)-CTCAE	(National Cancer Institute)-Common Terminology Criteria for Adverse Events
CI	confidence interval
CIN	chromosome instability
CIS	cisplatin
CR	complete response
CRT	chemoradiotherapy
CT	chemotherapy
DCF	docetaxel, cisplatin, 5FU
DCR	disease control rate
DMFS	distant metastasis-free survival
Doc	docetaxel
EAC	oesophageal adenocarcinoma
EBV	Epstein-Barr virus
EMR	early metabolic responder
ESCC	oesophageal squamous cell carcinoma
ECOG	Eastern Cooperative Oncology Group
ECX	epirubicin, cisplatin, capecitabine
EGFR	endothelial growth factor receptor
EOX	epirubicin, oxaliplatin, capecitabine
EQ-5D	EuroQol five dimension questionnaire
FACT(-Hep)	Functional Assessment of Cancer Therapy(-Hepatobiliary)
FAS	full analysis set
FISH	fluorescence in situ hybridisation
GC	gastric cancer
GEJ	gastroesophageal junction
HCC	hepatocellular carcinoma
HER2	human epidermal growth factor receptor 2
HR	hazard ratio
IGBC	incidental gallbladder cancer
IHC	immunohistochemistry
IRR	immediate radical re-resection
iv	intravenous
KPS	Karnofsky performance status
LAPC	locally advanced pancreatic cancer
LAR	long-acting release
LNR	lymph node ratio
LV	leucovorin
MSI	microsatellite instability
MST	median survival time
MUT	mutant
NE	not evaluable
NET	neuroendocrine tumour
NGS	next generation sequencing
NMR	non-metabolic responder
OGJ	oesophagogastric junction
OR	odds ratio
ORR	objective response rate
(m)OS	(median) overall survival
PARP	poly ADP ribose polymerase
PCI	peritoneal cancer index
PD	progressive disease
PET	positron emission tomography
(m)PFS	(median) progression-free survival
PR	partial response
PS	performance status
(HR)QoL	(health-related) quality of life
R	randomised
RECIST	Response Evaluation Criteria In Solid Tumors
RR	response rate
RT	radiotherapy
RTK	receptor tyrosine kinase
SAE	serious adverse event
SD	stable disease
SSA	somatostatin analogue
TCGA	The Cancer Genome Atlas
TEAE	treatment-emergent adverse event
TKI	tyrosine kinase inhibitor
TTP	time to progression
VAS	visual analogue scale
WBC	white blood cell
WRT	wedge resection rate

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CANCERS OF THE OESOPHAGUS AND STOMACH

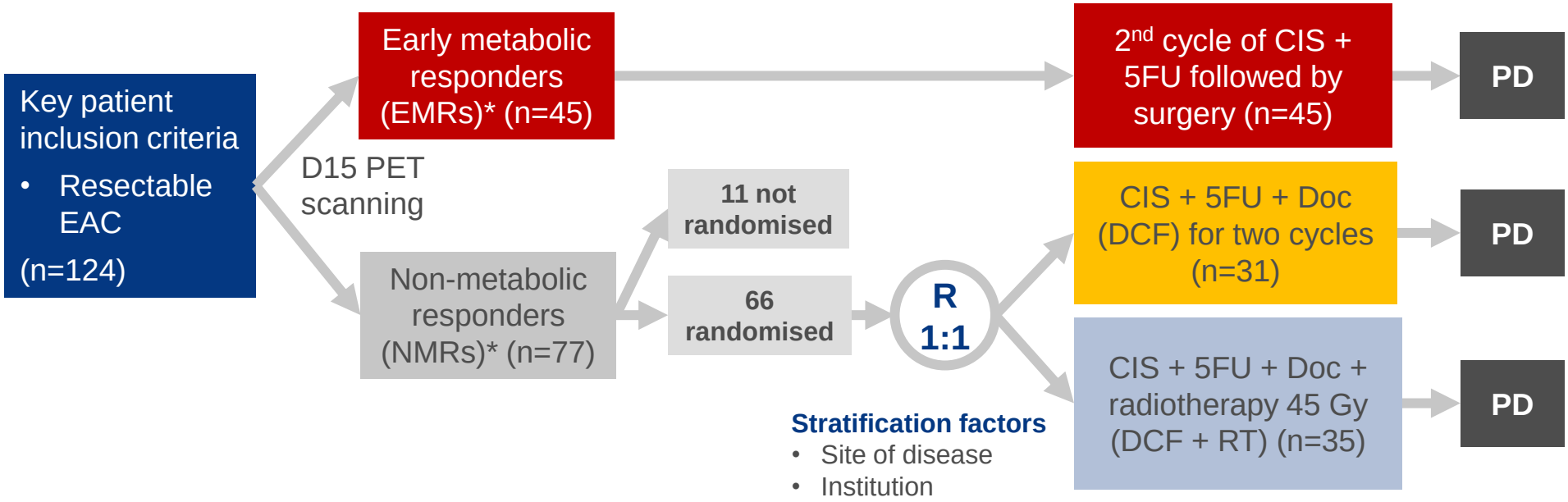
Cancers of the oesophagus and stomach

PREOPERATIVE

610O: An AGITG trial –A randomised phase II study of pre-operative cisplatin, fluorouracil and DOCetaxel +/-radioTherapy based on poOR early response to cisplatin and fluorouracil for resectable esophageal adenocarcinoma – Barbour et al

Study objective

- To investigate whether modifying neoadjuvant therapy improves histological response in patients not showing early metabolic response after first cycle of treatment



PRIMARY ENDPOINT(S)

- Histological response (<10% residual tumour)

SECONDARY ENDPOINTS

- PET response, toxicity, tumour down-staging, OS, DFS, QoL, translational sub-studies

*Based on PET scans at baseline and post-treatment (after receiving 1 cycle of CIS and 5FU on d15), if SUV_{max} decreased by ≥35%, patients were classed as EMR or otherwise as NMR.

Barbour A et al. Ann Oncol 2016; 27 (suppl 6): abstr 610O

610O: An AGITG trial –A randomised phase II study of pre-operative cisplatin, fluorouracil and DOCetaxel +/-radioTherapy based on poOR early response to cisplatin and fluorouracil for resectable esophageal adenocarcinoma – Barbour et al

Key results

Primary tumour response in all study groups

Study group	Complete/extensive histological response, n/N (%)	95% CI
EMR	3/45 (7)	2, 17
NMR (not randomised)	0/11 (0)	0, 26
All not randomised*	3/56 (5)	2, 14
CIS + 5FU + Doc†	6/31 (19)	9, 36
CIS + 5FU + Doc with RT†	22/35 (63)	46, 77

*Excludes 2 patients with no d15 PET (both with no histological response); †patients without surgery categorised as no histological response.

Barbour A et al. Ann Oncol 2016; 27 (suppl 6): abstr 610O

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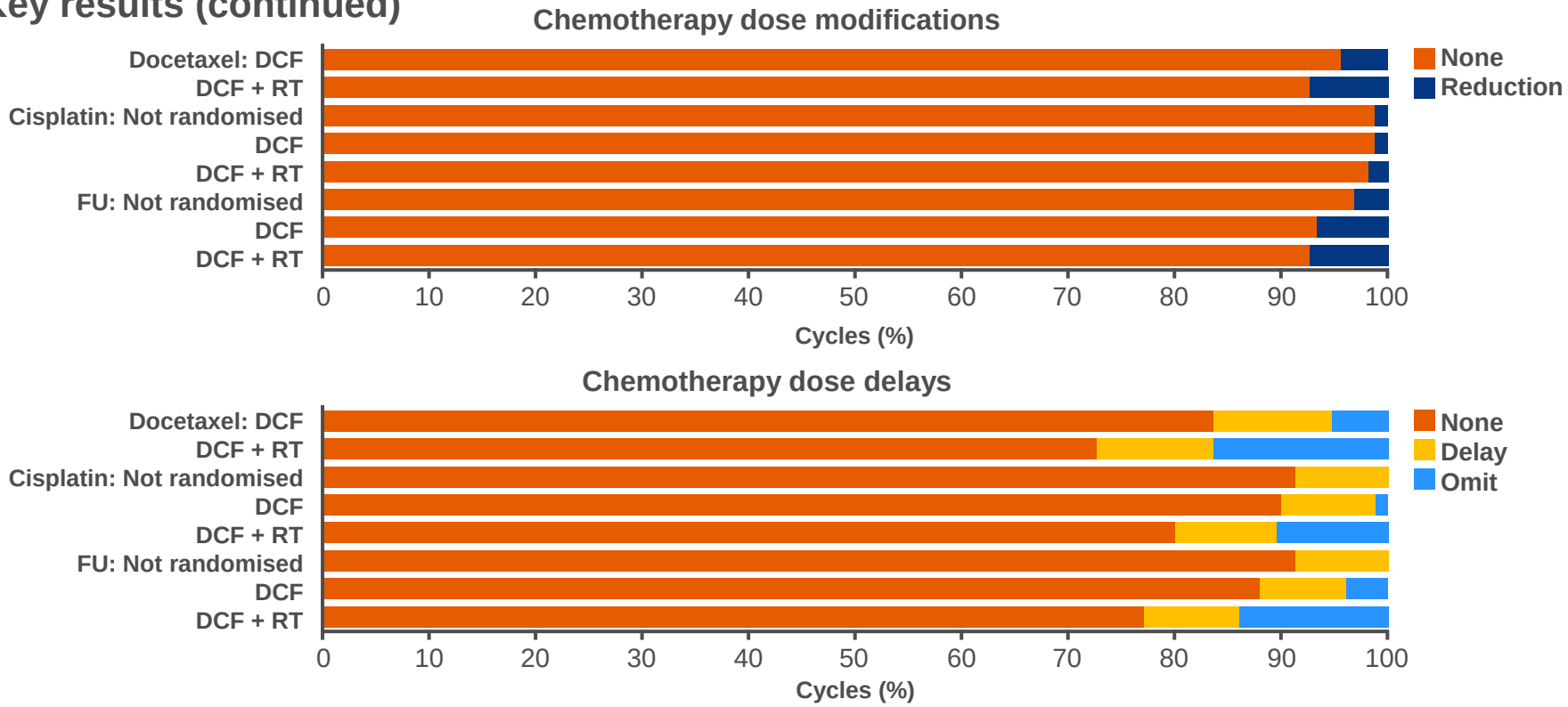
Key results (continued)

Clinical assessment,* n (%)		EMR (n=45)	CIS + 5FU + Doc (n=31)	CIS + 5FU + Doc + RT (n=35)	All patients (n=111)
Endoscopic tumour response	Extensive: >90 regression	6 (13)	2 (6)	7 (20)	15 (14)
	Partial: 50–90% regression	11 (24)	11 (35)	12 (34)	34 (31)
	Minor: <50% regression	25 (56)	11 (35)	6 (17)	42 (38)
	Unknown	3 (7)	7 (23)	10 (29)	20 (18)
CT – local disease response	CR	2 (4)	1 (3)		3 (3)
	Persistent local disease	38 (84)	25 (81)	33 (94)	96 (86)
	Local PD		1 (3)	2 (6)	3 (3)
	Unknown	5 (11)	4 (13)		9 (8)

*Table excludes 11 NMR not randomised and 2 with no d15 PET. Barbour A et al. Ann Oncol 2016; 27 (suppl 6): abstr 610O

610O: An AGITG trial –A randomised phase II study of pre-operative cisplatin, fluorouracil and DOCetaxel +/-radioTherapy based on poOR early response to cisplatin and fluorouracil for resectable esophageal adenocarcinoma – Barbour et al

Key results (continued)



- Grade 3/4 AEs were observed in:
  - 19/58 (33%) patients on CIS + 5FU and 13/45 (29%) EMRs on CIS + 5FU
  - 14/31 (45%) patients on CIS + 5FU + Doc and 25/35 (71%) patients on CIS + 5FU + Doc with RT

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Key results (continued)

- Oesophagectomy was performed in:
  - 45 (100%) EMR
  - 28/31 (90%) patients on CIS + 5FU + Doc
  - 33/35 (94%) patients on CIS + 5FU + Doc with RT (2 progressed)
- R0 (>1 mm margin) resection was achieved in:
  - 31/45 (69%) EMR
  - 18/28 (64%) patients on CIS + 5FU + Doc
  - 31/33 (94%) patients on CIS + 5FU + Doc with RT

Conclusions

- **Docetaxel added to a combination of CIS + 5FU, particularly CIS + 5FU + Doc with RT, can induce higher rates of histological responses in NMRs**
- **The results of this study, therefore, indicate that designing a multimodality therapy based on individual PET response is safe and feasible for patients with EAC although further investigations are required to study the impact of such therapy on survival**

Barbour A et al. Ann Oncol 2016; 27 (suppl 6): abstr 610O

Cancers of the oesophagus and stomach

PERIOPERATIVE

LBA26: A randomised phase II study of perioperative epirubicin, cisplatin and capecitabine (ECX) ± lapatinib for operable, HER-2 positive gastric, oesophagogastric junctional (OGJ) or lower oesophageal adenocarcinoma: Results from the UK MRC ST03 lapatinib feasibility study (ISRCTN 46020948) – Smyth et al

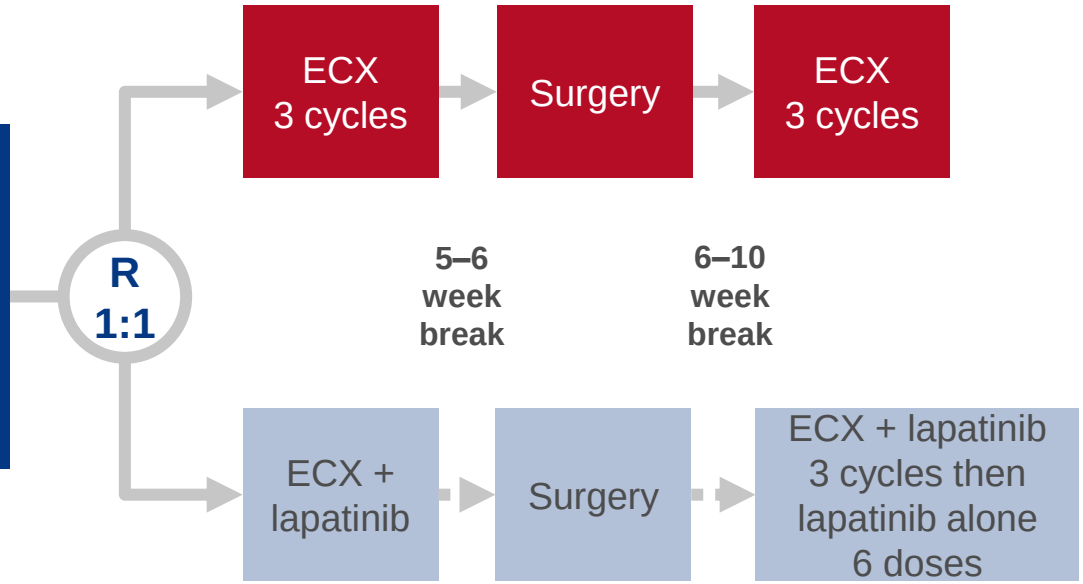
Study objective

- To assess the safety and feasibility of adding the TKI lapatinib to perioperative ECX

Key patient inclusion criteria

- HER2 positive operable, gastric/OGJ/lower oesophageal adenocarcinoma

(n=44)



PRIMARY ENDPOINT

- Determine recommended dosing regimen (grade 3/4 diarrhoea not exceed 20%)

ECX: Epirubicin 50 mg/m^2 iv d1; cisplatin 60 mg/m^2 iv d1; capecitabine 1250 mg/m^2 po daily

ECX + L: Epirubicin 50 mg/m^2 iv d1; cisplatin 60 mg/m^2 iv d1; capecitabine at a reduced 1000 mg/m^2 daily; lapatinib 1250 mg daily. Maintenance lapatinib at 1500 mg po daily.

Smyth E et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA26

LBA26: A randomised phase II study of perioperative epirubicin, cisplatin and capecitabine (ECX) ± lapatinib for operable, HER-2 positive gastric, oesophagogastric junctional (OGJ) or lower oesophageal adenocarcinoma: Results from the UK MRC ST03 lapatinib feasibility study (ISRCTN 46020948) – Smyth et al

Key results

Pre-operative chemotherapy and surgery

n (%)	ECX (n=24)	ECX + L (n=20)	Total (n=44)
Received all 3 cycles	23 (96)	16 (80)	39 (88)
Dose reduction	9 (38)	9 (45)	18 (41)
Lapatinib dose reduced	-	4 (20)	-
Surgery status, n			
Surgery not yet due	1	1	2
Unclear if performed	2	0	2
No resection*	5	3	8
Resection performed	16	16	32

*Reasons for no surgery: disease progression (4 patients; 2 ECX, 2 ECX + L); found to be inoperable (3 patients; 3 ECX); patient not fit enough (1 patient; 1 ECX + L).

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Key results (continued)

Grade ≥3 AEs during chemotherapy

Pre-operative, n (%)	ECX	ECX + L	Total
	n=24	n=19*	n=43
Neutropenia	5 (21)	8 (42)	13 (30)
Diarrhea	0 (0)	4 (21)	4 (9)
Lethargy	1 (4)	2 (11)	3 (7)
Vomiting	0 (0)	2 (11)	2 (5)
Infection with neutropenia	0 (0)	1 (5)	1 (2)
Post-operative, n (%)	**n=6**	**n=10**	**n=16**
Neutropenia	1 (17)	4 (40)	5 (31)
Lethargy	1 (17)	0 (0)	1 (6)
Infection with neutropenia	0 (0)	0 (0)	0 (0)

*20 ECX + L began chemotherapy; of these, 1 withdrew on day 1 and did not provide any toxicity information, so was not included.

Smyth E et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA26

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Key results (continued)

Post-operative complications

n (%)	ECX (n=15)	ECX + L (n=16)	Total (n=31)
Anastomotic leak	3 (20)	2 (13)	5 (16)
Wound healing	1 (7)	3 (19)	4 (13)
Superficial wound infection	1 (7)	3 (19)	4 (13)
Respiratory tract infection	2 (13)	2 (13)	4 (13)
Respiratory failure	1 (7)	2 (13)	3 (10)
Cardiac complications	2 (13)	0 (0)	2 (6)
Empyema	2 (13)	0 (0)	2 (6)

Smyth E et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA26

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Conclusions

- The addition of lapatinib to perioperative ECX chemotherapy, with a reduced capecitabine dose, is feasible
- There was a suggestion for an increase in diarrhoea and neutropenia, but this did not appear to compromise operative management

Smyth E et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA26

Cancers of the oesophagus and stomach

FIRST-LINE THERAPY

616PD: Phase III study comparing intraperitoneal paclitaxel plus S-1/paclitaxel with S-1/cisplatin in gastric cancer patients with peritoneal metastasis: PHOENIX-GC trial – Fujiwara et al

Study objective

- To evaluate the efficacy of intraperitoneal paclitaxel + S-1/paclitaxel vs. standard systemic chemotherapy in patients with pathologically confirmed gastric adenocarcinoma

Key patient inclusion criteria

- Pathologically confirmed GC
- Peritoneal metastasis (with no distant metastasis)
- No or <2 months prior CT
- ECOG PS 0–1
- 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

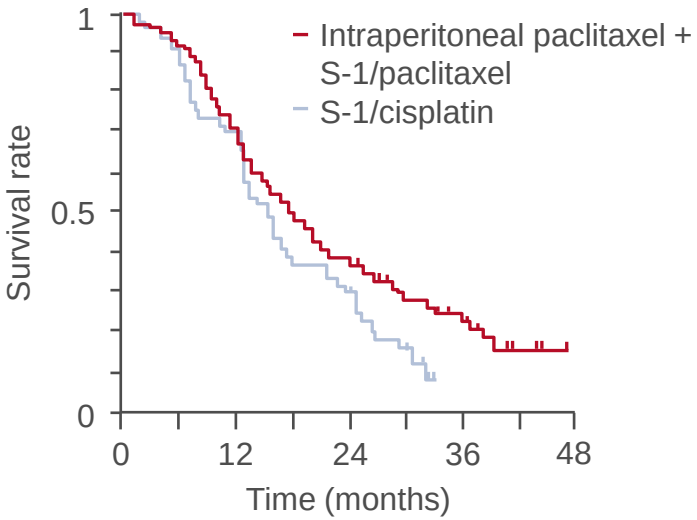
*Paclitaxel 50 mg/m^2 iv d1+8 + S-1 80 mg/m^2/d d1–14, q3w;
†Cisplatin 60 mg/m^2 iv d8 + S-1 80 mg/m^2/d d1–21, q5w.

Fujiwara Y et al. Ann Oncol 2016; 27 (suppl 6): abstr 616PD

616PD: Phase III study comparing intraperitoneal paclitaxel plus S-1/paclitaxel with S-1/cisplatin in gastric cancer patients with peritoneal metastasis: PHOENIX-GC trial – Fujiwara et al

Key results

OS: Primary analysis (FAS population)



n=164	MST, months (95% CI)	p-value
Intraperitoneal paclitaxel + S-1/paclitaxel	17.7 (14.7, 21.5)	0.080*
S-1/cisplatin	15.2 (12.8, 21.8)	

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	RR, %	Fischer's test
Intraperitoneal paclitaxel + S-1/paclitaxel (n=17)	0	9	4	4	0	53	p=1.0
S-1/cisplatin (n=5)	0	3	1	0	1	60	

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

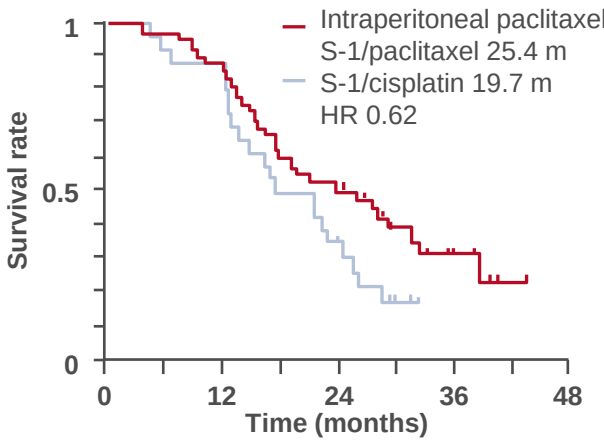
Fujiwara Y et al. Ann Oncol 2016; 27 (suppl 6): abstr 616PD

616PD: Phase III study comparing intraperitoneal paclitaxel plus S-1/paclitaxel with S-1/cisplatin in gastric cancer patients with peritoneal metastasis: PHOENIX-GC trial – Fujiwara et al

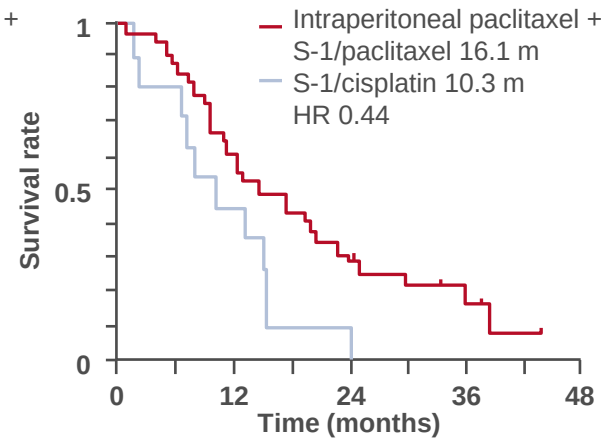
Key results (continued)

OS by ascites level (sensitivity analysis)

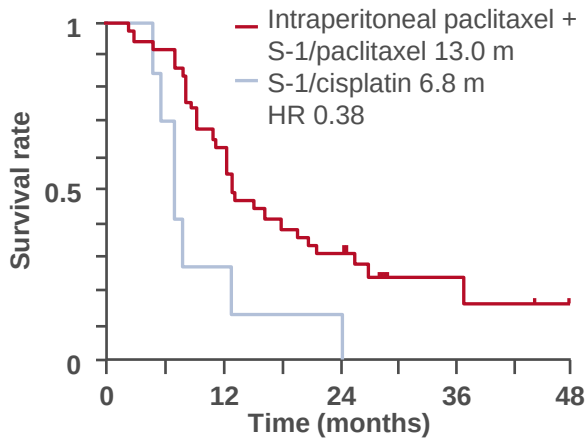
No ascites



Small amount (within pelvic cavity)



Moderate amount (beyond pelvic cavity)



*For the FAS population: HR 0.59 (95% CI 0.39, 0.87); p=0.0079
*For the PPS population: HR 0.48 (95% CI 0.32, 0.73); p=0.0008

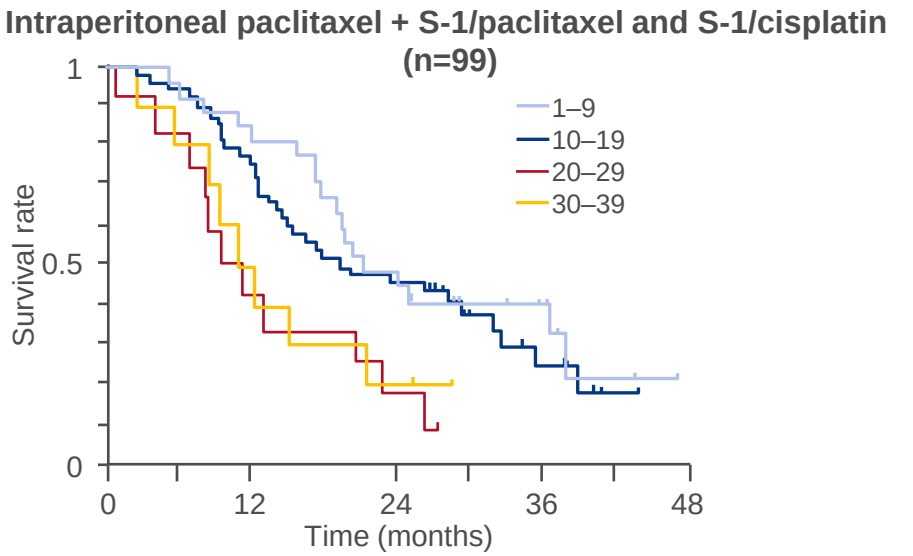
*Cox regression analysis.

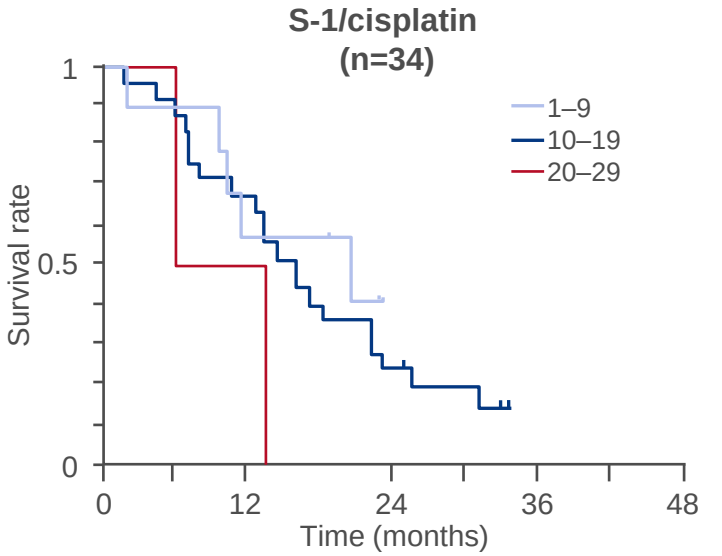
Fujiwara Y et al. Ann Oncol 2016; 27 (suppl 6): abstr 616PD

616PD: Phase III study comparing intraperitoneal paclitaxel plus S-1/paclitaxel with S-1/cisplatin in gastric cancer patients with peritoneal metastasis: PHOENIX-GC trial – Fujiwara et al

Key results (continued)

OS according to PCI level in patients successfully classified by laparoscopy (n=133)





PCI	1–9	10–19	20–29	30–39
n	50	27	12	10
MST, m	19.9	21.3	10.6	11.7

PCI	1–9	10–19	20–29
n	25	7	2
MST, m	15.6	14.8	9.4

Fujiwara Y et al. Ann Oncol 2016; 27 (suppl 6): abstr 616PD

616PD: Phase III study comparing intraperitoneal paclitaxel plus S-1/paclitaxel with S-1/cisplatin in gastric cancer patients with peritoneal metastasis: PHOENIX-GC trial – Fujiwara et al

Key results (continued)

Grade 3/4 AEs occurring in ≥1%, n (%)	Intraperitoneal paclitaxel + S-1/paclitaxel (n=116)	S-1/cisplatin (n=53)	Fisher's test, p-value
Leukopenia	29 (25)	5 (9)	0.023
Neutropenia	58 (50)	16 (30)	0.028
Anaemia	15 (13)	6 (11)	1.000
Thrombocytopenia	0 (0)	0 (0)	-
Febrile neutropenia	9 (8)	1 (2)	0.174
Creatinine increased	1 (1)	1 (2)	0.525
Nausea	8 (7)	5 (9)	0.549
Vomiting	4 (3)	2 (4)	1.000
Diarrhoea	10 (9)	3 (6)	0.757
Anorexia	12 (10)	7 (13)	0.605
Fatigue	9 (8)	4 (8)	1.000
Sensory neuropathy	2 (2)	0 (0)	1.000

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, sensitivity analyses regarding imbalance of ascites indicated clinical efficacy with intraperitoneal paclitaxel + S-1/paclitaxel in GC with peritoneal metastasis**

Fujiwara Y et al. Ann Oncol 2016; 27 (suppl 6): abstr 616PD

612O: Clinical next generation sequencing (NGS) of esophagogastric (EG) adenocarcinomas identifies distinct molecular signatures of response to HER2 inhibition, first-line 5FU/platinum and PD1/CTLA4 blockade – Janjigian et al

Objective

- To investigate TCGA-identified potential therapeutic targets, unique to oesophagogastric adenocarcinoma subtypes, including RTK alterations in CIN tumours and immunotherapy in EBV and MSI tumours

Methods

- Patients with stage IV oesophagogastric adenocarcinoma (n=319) were analysed using an NGS assay (MSK-IMPACT) capable of detecting somatic mutations (MUT), deletions and amplifications (AMP) with results correlated with clinical outcomes

Janjigian YY et al. Ann Oncol 2016; 27 (suppl 6): abstr 612O

612O: Clinical next generation sequencing (NGS) of esophagogastric (EG) adenocarcinomas identifies distinct molecular signatures of response to HER2 inhibition, first-line 5FU/platinum and PD1/CTLA4 blockade – Janjigian et al

Key results

Sample characteristics

HER2-positive cases	n=105
Pre-trastuzumab, n	88
Post-trastuzumab, n	49
Matched pre-/post-trastuzumab progression samples, n	33
Pre-trastuzumab HER2-positive[a], n (%) HER2 IHC 3+ HER2 IHC 2+/FISH >2.2 IMPACT only (insufficient sample for IHC)	 60 (57) 41 (39) 4(4)
Loss of HER2 in post-trastuzumab sample, n/N (%)	12/49[b] (24)

[a]11 patients HER2 IHC/FISH positive per outside report, no baseline sample for confirmation of status at MSK by IHC/FISH and IMPACT

[b]4 post-trastuzumab samples tested by IHC/FISH/IMPACT and 8 additional samples tested by IHC/FISH only (IMPACT not available on post-trastuzumab sample)

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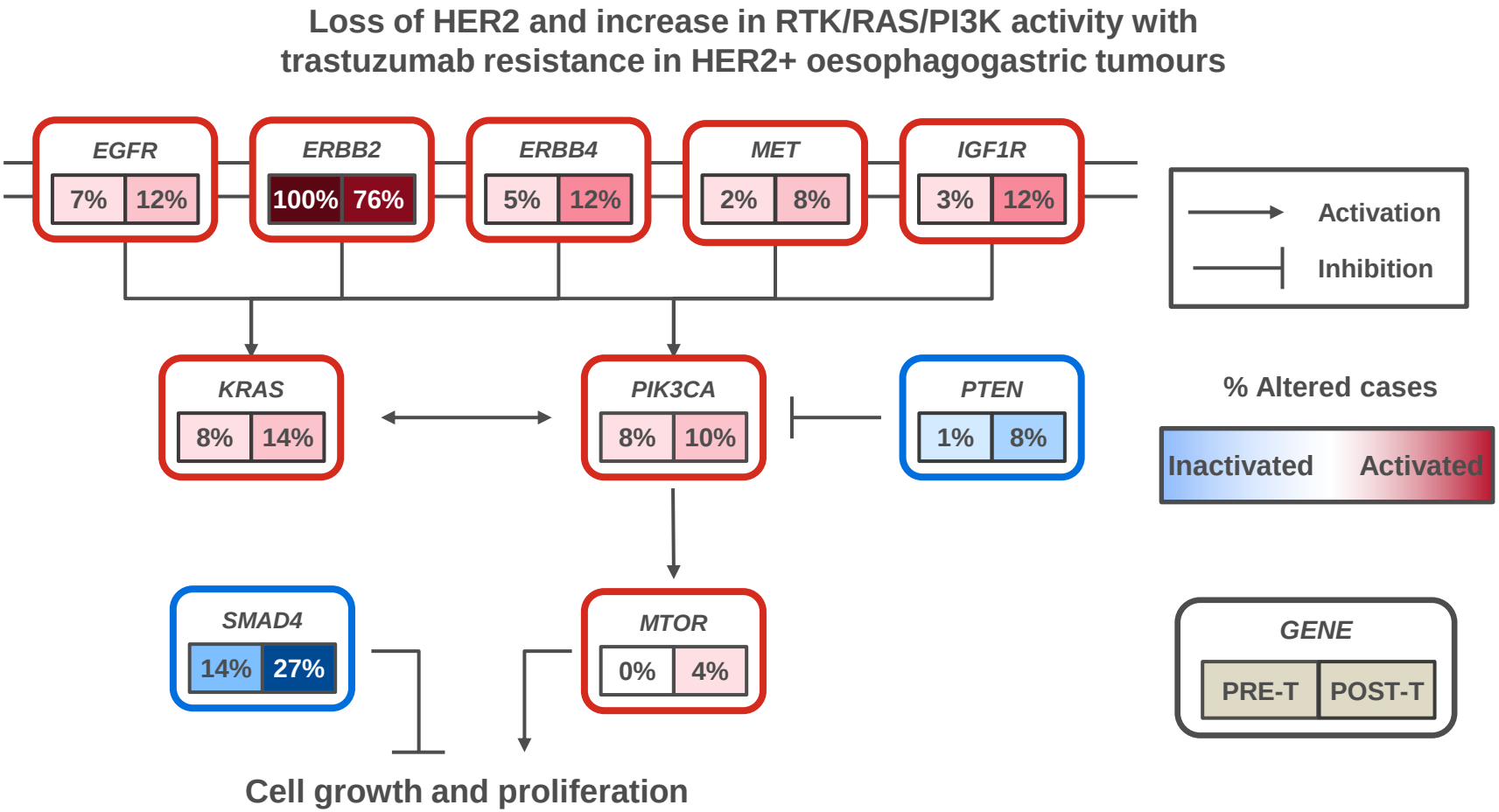
Key results (continued)



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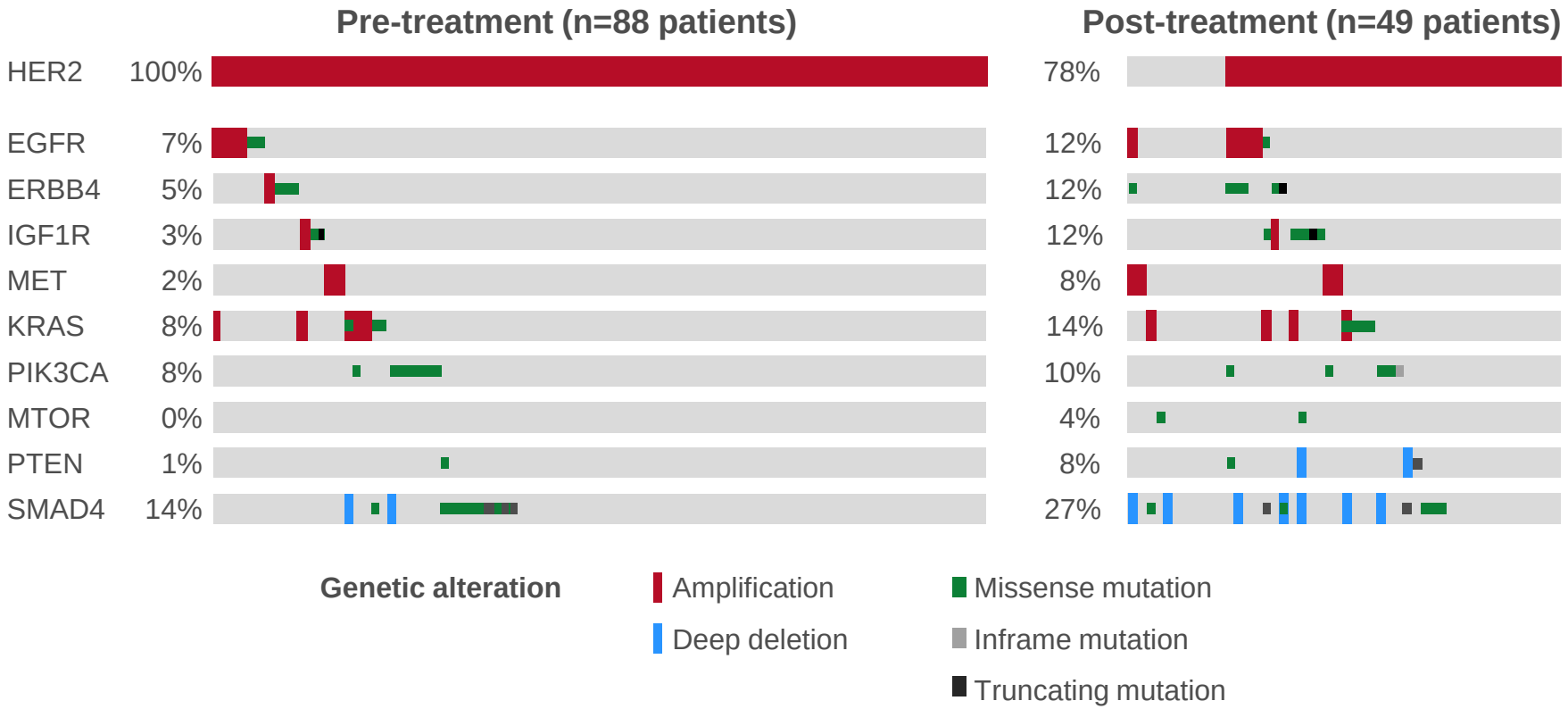
Key results (continued)



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Conclusions

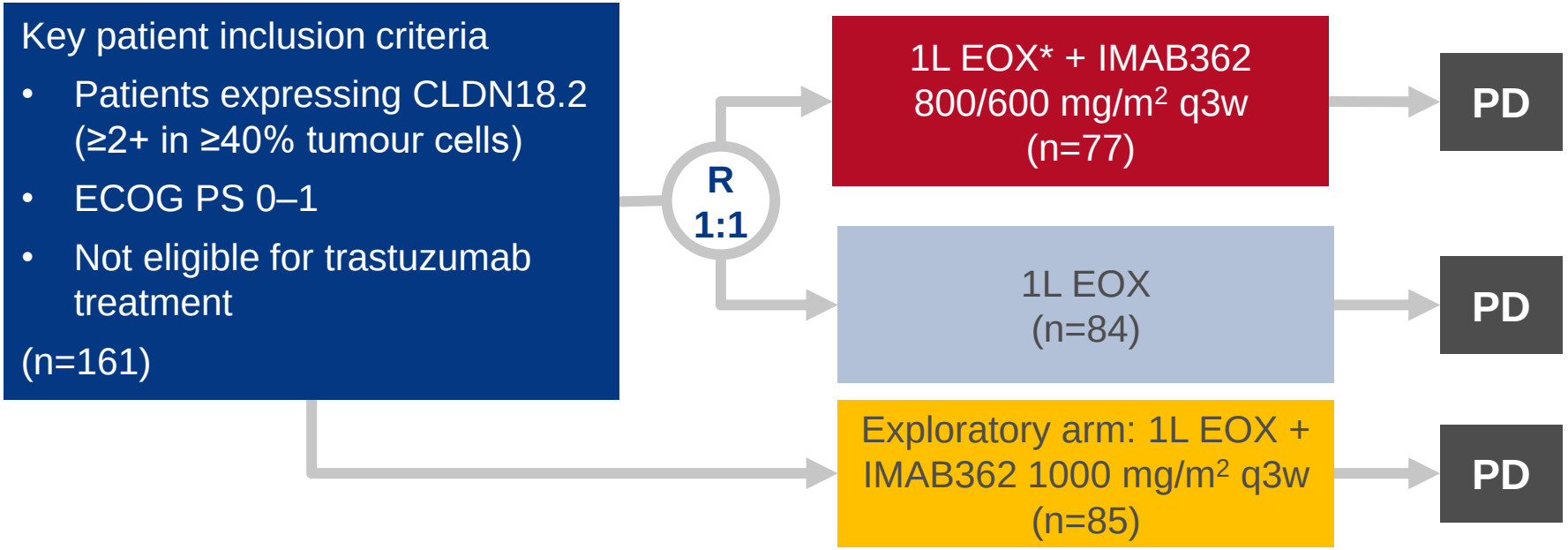
- These results indicate that patients with acquired trastuzumab resistance display HER2 loss and may also possess secondary alterations in the RTK/RAS/PI3K pathway
  - Frequent mutations such as SMAD4, KRAS and EGFR were identified
- These data are in line with the observed failure rate for TDM1 and lapatinib in 2L treatment
- The use of repeat biopsies is recommended so that appropriate 2L HER2-directed therapy may be selected
- This observed loss of heterozygosity in BRCA 1/2 may influence oesophagogastric cancer pathogenesis and therapy response
- It is important to identify MSI and EBV oesophagogastric adenocarcinoma subsets (unique subsets) so that they may be treated with immunotherapy

Janjigian YY et al. Ann Oncol 2016; 27 (suppl 6): abstr 612O

614O: Final results of the FAST study, an international, multicenter, randomized, phase II trial of epirubicin, oxaliplatin, and capecitabine (EOX) with or without the anti-CLDN18.2 antibody IMAB362 as first-line therapy in patients with advanced CLDN18.2+ gastric and gastroesophageal junction (GEJ) adenocarcinoma – Schuler et al

Study objective

- To evaluate the expression of Claudin18.2 (CLDN18.2), which mediates the anti-cancer activity of IMAB362 – in patients with advanced/recurrent gastric and GEJ cancer by using immunohistochemistry



PRIMARY ENDPOINT(S)

- PFS

SECONDARY ENDPOINTS

- OS

*Epirubicin 50 mg/m^2, oxaliplatin 130 mg/m^2 d1 and capecitabine 625 mg/m^2 bid, d1–21; q22d

Schuler M et al. Ann Oncol 2016; 27 (suppl 6): abstr 614O

614O: Final results of the FAST study, an international, multicenter, randomized, phase II trial of epirubicin, oxaliplatin, and capecitabine (EOX) with or without the anti-CLDN18.2 antibody IMAB362 as first-line therapy in patients with advanced CLDN18.2+ gastric and gastroesophageal junction (GEJ) adenocarcinoma – Schuler et al

Key results

PFS and OS

	EOX (n=84)	EOX + IMAB362 800/600 mg/m² (n=77)	EOX + IMAB362 1000 mg/m² (n=85)
mPFS, months	4.8	7.9	7.1
HR (95% CI)		0.47 (0.31, 0.70)	0.59
p-value		0.0001	0.003
mOS, months	8.4	13.2	9.7
HR (95% CI)		0.51 (0.36, 0.73)	0.76
p-value		0.0001	0.00498

- Common IMAB362-related AEs included vomiting, neutropenia and anaemia, which were mostly of NCI-CTCAE grade 1/2
- Grade 3/4 events were not significantly increased by IMAB362

Schuler M et al. Ann Oncol 2016; 27 (suppl 6): abstr 614O

614O: Final results of the FAST study, an international, multicenter, randomized, phase II trial of epirubicin, oxaliplatin, and capecitabine (EOX) with or without the anti-CLDN18.2 antibody IMAB362 as first-line therapy in patients with advanced CLDN18.2+ gastric and gastroesophageal junction (GEJ) adenocarcinoma – Schuler et al

Conclusions

- Combination therapy of IMAB362 and EOX is a viable and tolerable 1L treatment option for patients with advanced or metastatic oesophagogastric adenocarcinoma
- A significant improvement in PFS and OS was observed in the current study in patients subjected to combined IMAB362 + EOX therapy
- These results lay a strong basis for the phase 3 development of IMAB362

Schuler M et al. Ann Oncol 2016; 27 (suppl 6): abstr 614O

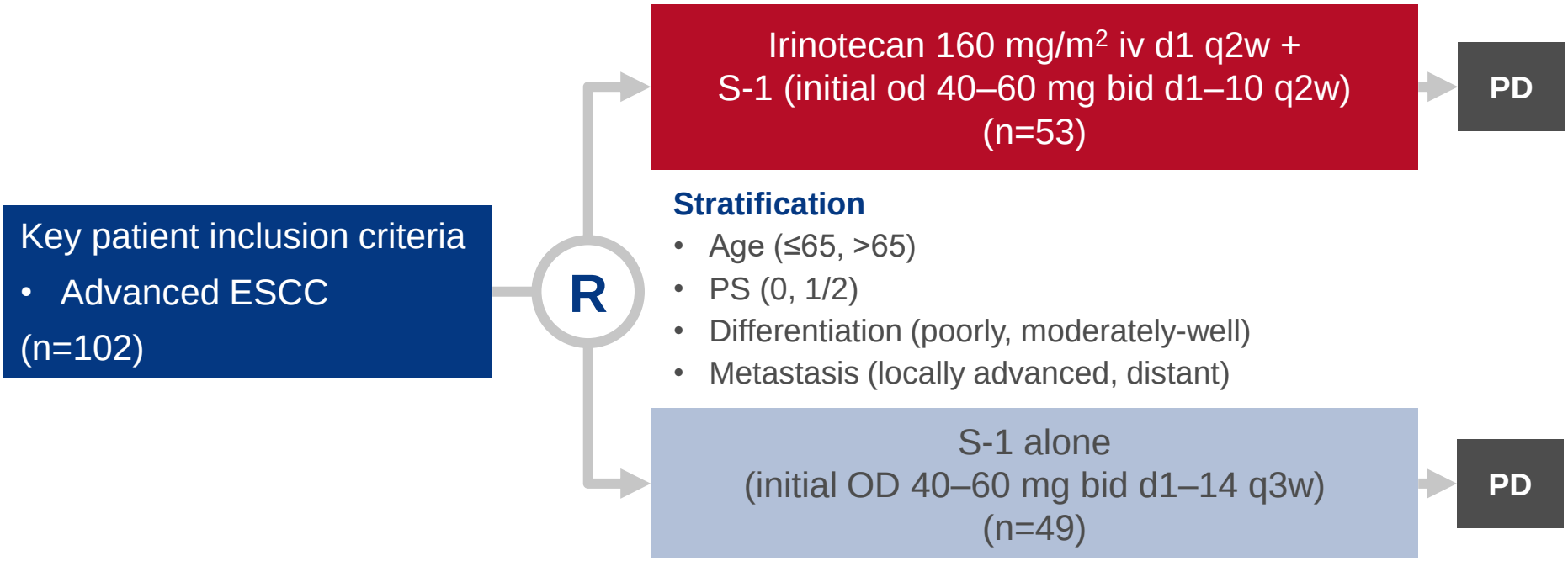
Cancers of the oesophagus and stomach

SECOND-LINE THERAPY

LBA27: Randomized, open-label, phase III study comparing irinotecan plus S-1 with S-1 alone in patients with advanced esophageal squamous cell carcinoma after failure of prior platinum- or taxane-based chemotherapy – Huang et al

Study objective

- To compare the efficacy and safety of irinotecan + S-1 with S-1 alone in patients with advanced ESCC refractory to platinum- or taxane-based 1L CT



PRIMARY ENDPOINT(S)

- PFS

SECONDARY ENDPOINTS

- RR, DCR, OS

Huang J et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA27

LBA27: Randomized, open-label, phase III study comparing irinotecan plus S-1 with S-1 alone in patients with advanced esophageal squamous cell carcinoma after failure of prior platinum- or taxane-based chemotherapy – Huang et al

Key results

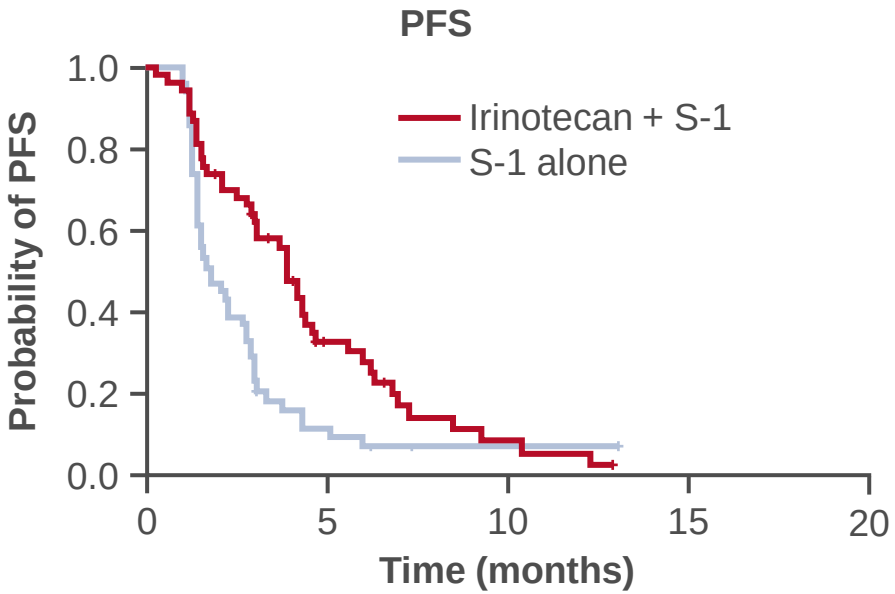
Patient entry characteristics, n (%)		Irinotecan + S-1 (n=53)	S-1 alone (n=49)	p-value
ECOG	0	21 (39.6)	17 (34.7)	0.79700[a]
	1	29 (54.7)	30 (61.2)	
	2	3 (5.7)	2 (4.1)	
Tumour grade	Poorly differentiated	23 (43.4)	23 (46.9)	0.73700[a]
	Moderately differentiated	27 (50.9)	25 (51.0)	
	Well differentiated	3 (5.7)	1 (2.0)	
Metastasis status	Local	2 (3.8)	1 (2.0)	
	Distal	51 (96.2)	48 (98.0)	
Previous surgery	No	30 (56.6)	35 (71.4)	0.12000[b]
	Yes	23 (43.4)	14 (28.6)	
Previous CT	1 regimen	44 (83.0)	38 (79.2)	0.62100[b]
	2 regimens	9 (17.0)	10 (20.8)	
Previous RT	No	26 (49.1)	24 (50.0)	0.92500[b]
	Yes	27 (50.9)	24 (50.0)	

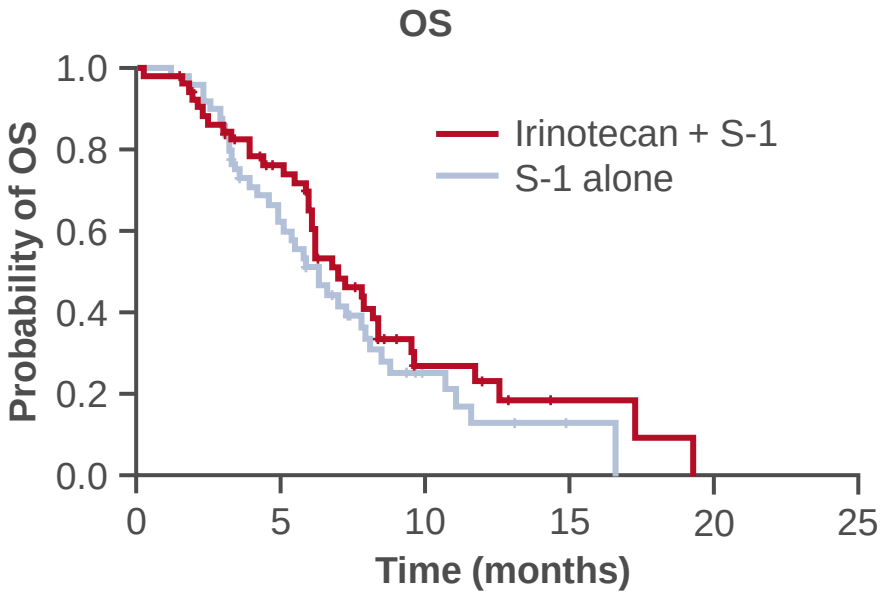
[a]Fisher's test; [b]Chi-squared test.

Huang J et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA27

LBA27: Randomized, open-label, phase III study comparing irinotecan plus S-1 with S-1 alone in patients with advanced esophageal squamous cell carcinoma after failure of prior platinum- or taxane-based chemotherapy – Huang et al

Key results (continued)





	Irinotecan + S-1 (n=53)	S-1 alone (n=49)
PFS, months	3.9	1.8
HR (95% CI); p-value	0.56 (0.37, 0.85); 0.0019	

	Irinotecan + S-1 (n=53)	S-1 alone (n=49)
PFS, months	7.0	6.3
HR (95% CI); p-value	0.77 (0.48, 1.22); 0.2622	

Huang J et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA27

LBA27: Randomized, open-label, phase III study comparing irinotecan plus S-1 with S-1 alone in patients with advanced esophageal squamous cell carcinoma after failure of prior platinum- or taxane-based chemotherapy – Huang et al

Key results (continued)

RR

Response, n (%)	Irinotecan + S-1	S-1 alone	Total	p-value
CR + PR	15 (28.3)	6 (12.2)	21 (20.6)	
SD + PD	38 (71.7)	43 (87.8)	81 (79.4)	0.04500[a]
Total	53	49	102	

Grade 3/4 AEs

AE, n (%)	Irinotecan + S-1	S-1 alone	p-value
Anaemia	2 (3.8)	1 (2.0)	3 (2.9)
Leukopenia	9 (17.0)	0 (0.0)	9 (8.8)
Neutropenia	6 (11.3)	0 (0.0)	6 (5.9)
Thrombocytopenia	2 (3.8)	0 (0.0)	2 (2.0)
Diarrhoea	2 (3.8)	1 (2.0)	3 (2.9)
Nausea	3 (5.7)	0 (0.0)	3 (2.9)
Vomiting	1 (1.9)	1 (2.0)	2 (2.0)
Fatigue	2 (3.8)	1 (2.0)	3 (2.9)
Bilirubin	1 (1.9)	0 (0.0)	1 (1.0)

[a]Chi-squared test.

Huang J et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA27

LBA27: Randomized, open-label, phase lll study comparing irinotecan plus S-1 with S-1 alone in patients with advanced esophageal squamous cell carcinoma after failure of prior platinum- or taxane-based chemotherapy – Huang et al

Conclusions

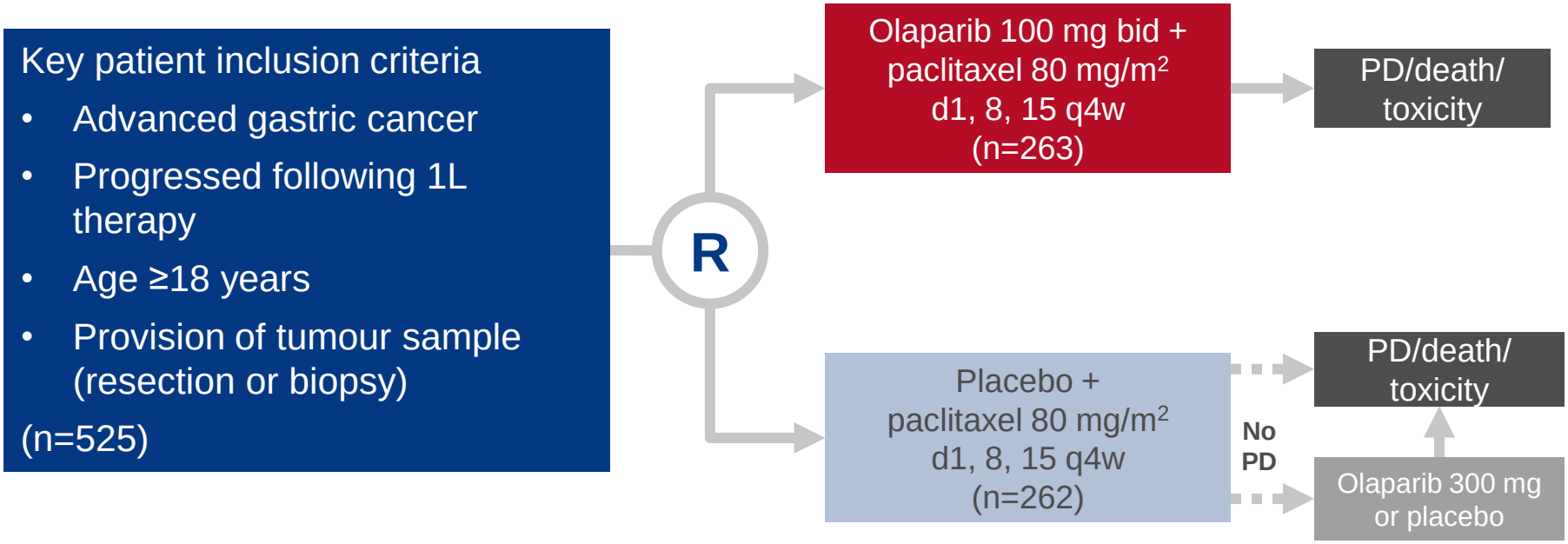
- **Compared with S-1 alone, irinotecan + S-1 regimen appears to show clinically meaningful PFS benefit; 44% risk reduction in PD or death was observed**
- **Irinotecan + S-1 regimen was feasible and well tolerated in patients with advanced ESCC**
- **Irinotecan + S-1 regimen is a suitable treatment option in patients with advanced oesophageal squamous cell carcinoma after failure of prior platinum- or taxane-based CT**

Huang J et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA27

LBA25: Olaparib in combination with paclitaxel in patients with advanced gastric cancer who have progressed following first-line therapy: Phase III GOLD study – Bang et al

Study objective

- To evaluate the efficacy and safety of olaparib (an oral PARP inhibitor) in combination with paclitaxel compared with placebo in combination with paclitaxel in patients with advanced gastric cancer



CO-PRIMARY ENDPOINTS

- OS for full analysis set (FAS) and ATM-negative patients

SECONDARY ENDPOINTS

- PFS, ORR, safety

Note: Based on data from abstract only

Bang Y et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA25

LBA25: Olaparib in combination with paclitaxel in patients with advanced gastric cancer who have progressed following first-line therapy: Phase III GOLD study – Bang et al

Key results

	Olaparib + paclitaxel (n=263)	Placebo + paclitaxel (n=262)	HR (97.5% CI); p-value
All patients (FAS; 72.6% OS maturity)			
mOS, months	8.8	6.9	0.79 (0.63, 1.00); 0.0262
mPFS, months	3.7	3.2	0.84 (0.67, 1.04); 0.0645
Adjusted ORR,* %	24.0	15.8	1.69 (0.92, 3.17); 0.0548
ATM− patients (68.1% OS maturity)			
mOS, months	12.0	10.0	0.73 (0.40, 1.34); 0.2458
mPFS, months	5.3	3.7	0.74 (0.45, 1.29); 0.2199
Adjusted ORR,* %	37.5	16.1	4.24 (0.95, 23.23); 0.0309

*Response rate in patients with measurable disease only

Note: Based on data from abstract only

Bang Y et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA25

LBA25: Olaparib in combination with paclitaxel in patients with advanced gastric cancer who have progressed following first-line therapy: Phase III GOLD study – Bang et al

Key results (continued)

	Olaparib + paclitaxel (n=263)	Placebo + paclitaxel (n=262)
Any grade ≥3 AEs, % Neutropenia	78 30	62 23
SAEs, %	35	25
AEs leading to discontinuation, %	16	10

Note: Based on data from abstract only

Bang Y et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA25

LBA25: Olaparib in combination with paclitaxel in patients with advanced gastric cancer who have progressed following first-line therapy: Phase III GOLD study – Bang et al

Conclusions

- With olaparib + paclitaxel there was a trend for OS benefit compared with placebo + paclitaxel in the FAS and ATM-negative patients
  - There was no statistically significant increase in OS, PFS or ORR with olaparib + paclitaxel
- There were no new safety signals for olaparib. Olaparib + paclitaxel followed by olaparib monotherapy was well tolerated

Note: Based on data from abstract only

Bang Y et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA25

CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

Cancers of the pancreas, small bowel and hepatobiliary tract

PANCREATIC CANCER

621PD: Randomized phase II study of S-1 and concurrent radiotherapy with versus without induction chemotherapy of gemcitabine for locally advanced pancreatic cancer (LAPC): Final analysis of JCOG1106 – Loka et al

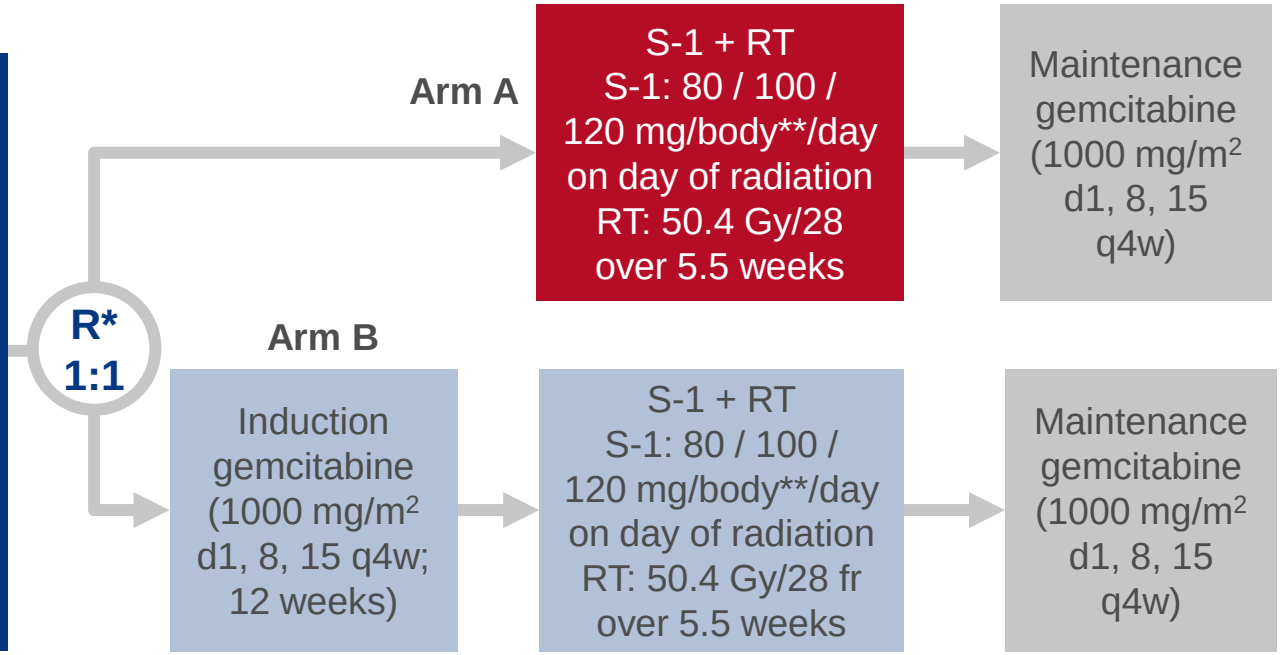
Study objective

- To evaluate the efficacy and safety of chemoradiotherapy (CRT) with/without induction chemotherapy

Key patient inclusion criteria

- LAPC (confirmed by imaging)
- Carcinoma confirmed by histology/cytology
- Treatment-naïve
- ECOG PS 0–1
- All lesions and metastases included in the radiation field

(n=102)



*Patients were stratified by institution and CA19-9 level (<1000 / ≥1000 IU/mL)
**According to body surface area (m^2; BSA < 1.25, 1.25 ≤ BSA <1.5, BSA ≥ 1.5)

PRIMARY ENDPOINT

- OS (1 year after accrual completion)

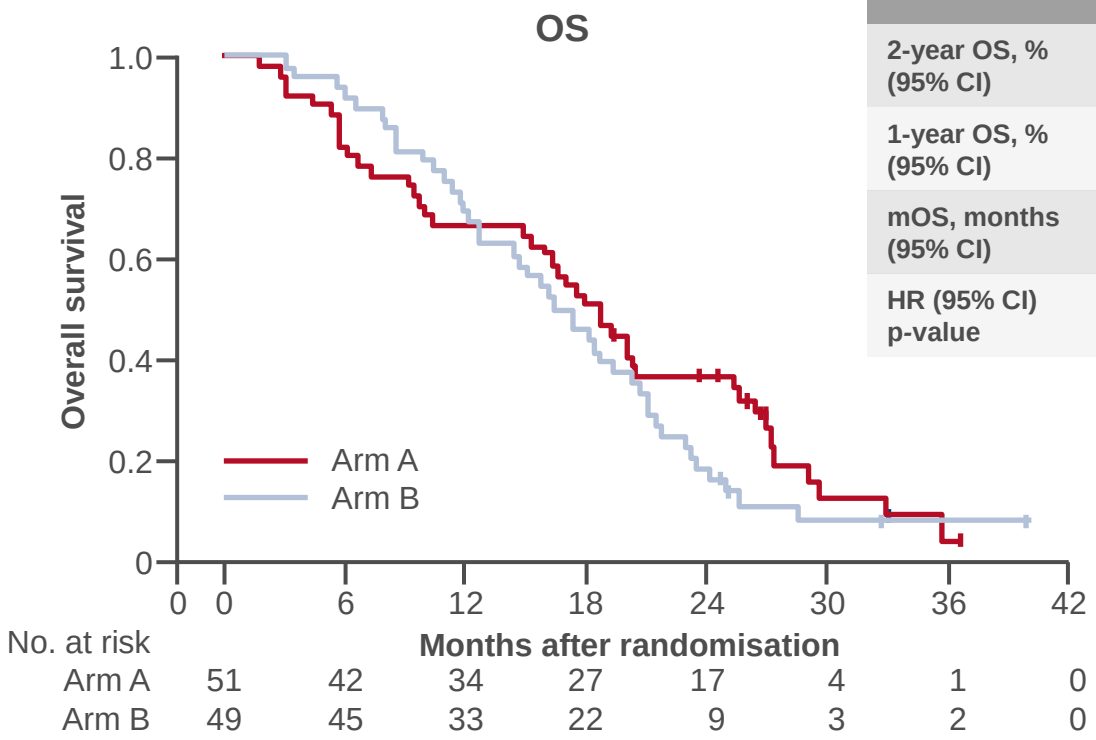
SECONDARY ENDPOINTS

- PFS, DMFS, CA19-9 response, safety

Loka T et al. Ann Oncol 2016; 27 (suppl 6): abstr 621PD

621PD: Randomized phase II study of S-1 and concurrent radiotherapy with versus without induction chemotherapy of gemcitabine for locally advanced pancreatic cancer (LAPC): Final analysis of JCOG1106 – Loka et al

Key results



	Arm A (42 events)	Arm B (43 events)
2-year OS, % (95% CI)	36.9 (23.9, 50.0)	18.9 (9.3, 31.0)
1-year OS, % (95% CI)	66.7 (52.0, 77.8)	69.3 54.3, 80.2)
mOS, months (95% CI)	19.0 (15.0, 20.6)	17.2 (12.6, 20.3)
HR (95% CI)	1.26 (0.82, 1.93)	
p-value	0.30	

- A total of 26 patients discontinued treatment (9 in Arm A, 17 in Arm B), with 76 patients still on treatment at the end of the study

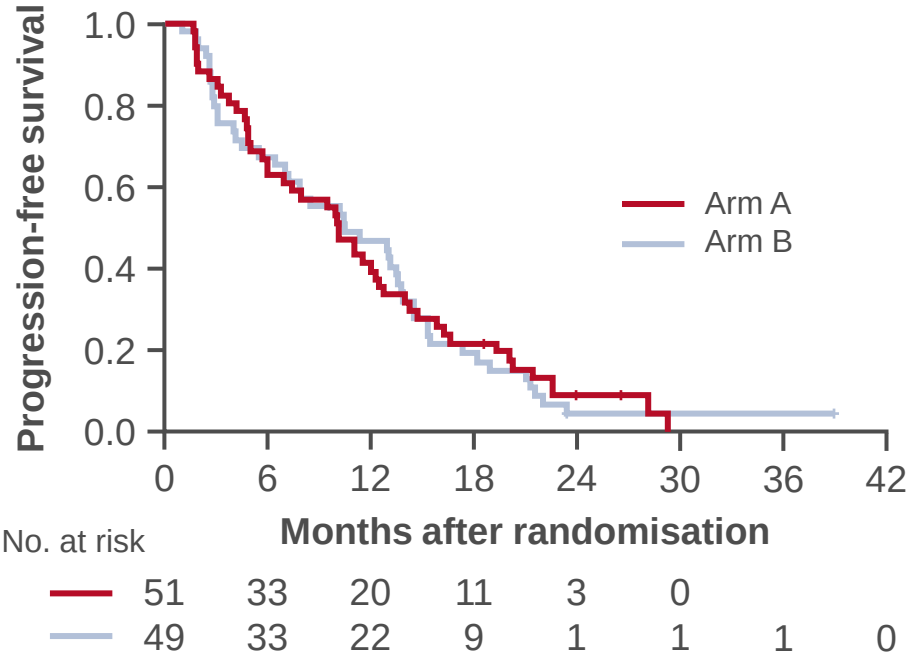
Loka T et al. Ann Oncol 2016; 27 (suppl 6): abstr 621PD

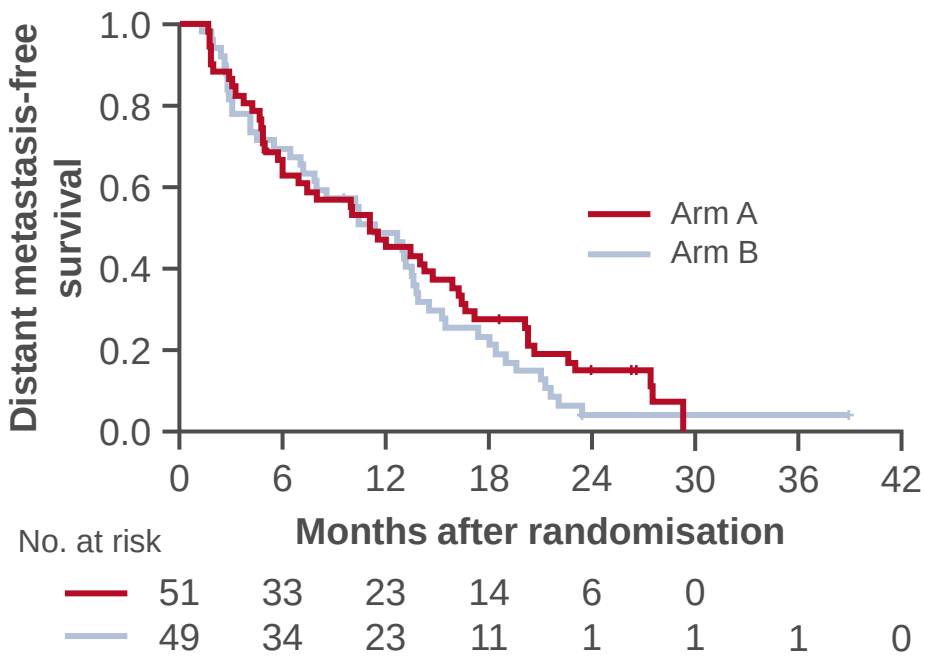
621PD: Randomized phase II study of S-1 and concurrent radiotherapy with versus without induction chemotherapy of gemcitabine for locally advanced pancreatic cancer (LAPC): Final analysis of JCOG1106 – Loka et al

Key results (continued)

	Arm A (48 events)	Arm B (46 events)
2-year PFS, % (95% CI)	8.6 (2.8, 18.6)	4.2 (0.8, 12.8)
1-year PFS, % (95% CI)	39.2 (26.0, 52.2)	46.6 (32.2, 59.8)
mPFS, months (95% CI)	10.1 (6.0, 12.5)	10.4 (7.0, 13.6)
HR (95% CI) **p-value**	1.03 (0.69, 1.55) 0.87	

	Arm A (47 events)	Arm B (46 events)
2-year DMFS, % (95% CI)	14.8 (6.6, 26.1)	4.2 (0.8, 12.7)
1-year DMFS, % (95% CI)	45.1 (31.2, 58.0)	48.7 (34.1, 61.8)
mDMFS, months (95% CI)	11.0 (6.0, 15.9)	11.4 (7.2, 13.6)
HR (95% CI) **p-value**	1.20 (0.79, 1.80) 0.37	





Loka T et al. Ann Oncol 2016; 27 (suppl 6): abstr 621PD

621PD: Randomized phase II study of S-1 and concurrent radiotherapy with versus without induction chemotherapy of gemcitabine for locally advanced pancreatic cancer (LAPC): Final analysis of JCOG1106 – Loka et al

Key results (continued)

CTCAE v4.0	Arm A (n=50), %		Arm B (n=49), %	
	Any	Grade 3–4	Any	Grade 3–4
Decreased WBC	94	62	94	61
Decreased neutrophils	92	54	96	57
Anaemia	100	18	98	12
Decreased platelet count	100	10	94	14
Anorexia	88	16	76	4
Fatigue	66	8	65	4
Nausea	80	8	63	2
Diarrhoea	46	6	37	4
Vomiting	50	2	33	4
Biliary infection	20	20*	27	27
Gastric/duodenal haemorrhage	10	10*	12	6
Gastric/duodenal ulcer	6	6	8	4
Pneumonitis	6	4*	4	2

*Treatment-related deaths occurred in 3 patients in Arm A (pneumonitis, duodenal haemorrhage and biliary infection)

Loka T et al. Ann Oncol 2016; 27 (suppl 6): abstr 621PD

621PD: Randomized phase II study of S-1 and concurrent radiotherapy with versus without induction chemotherapy of gemcitabine for locally advanced pancreatic cancer (LAPC): Final analysis of JCOG1106 – Loka et al

Conclusions

- **2-year OS was higher in Arm A than in Arm B, and the HR value exceeded 1.186 (the pre-specified decision rule value)**
- **Treatment was generally well tolerated, although the number of AEs was higher in Arm A and 3 treatment-related deaths occurred in this arm**
- **Compared with CRT alone, the addition of induction gemcitabine to CRT was less toxic in the short-term, but resulted in poorer long-term survival**

Loka T et al. Ann Oncol 2016; 27 (suppl 6): abstr 621PD

Cancers of the pancreas, small bowel and hepatobiliary tract

GALLBLADDER CANCER

619PD: Prognostic factors in curative treatment of gallbladder cancer - Data of 950 cases of “The German-Registry” – Goetze et al

Study objectives

- To assess
  - the dependency of treatment of incidental gallbladder carcinoma (IGBC) on the surgical or oncological expertise of the clinics
  - the techniques of liver resection in various stages of cancer
  - importance of lymph node ratio and
  - multimodal aspects

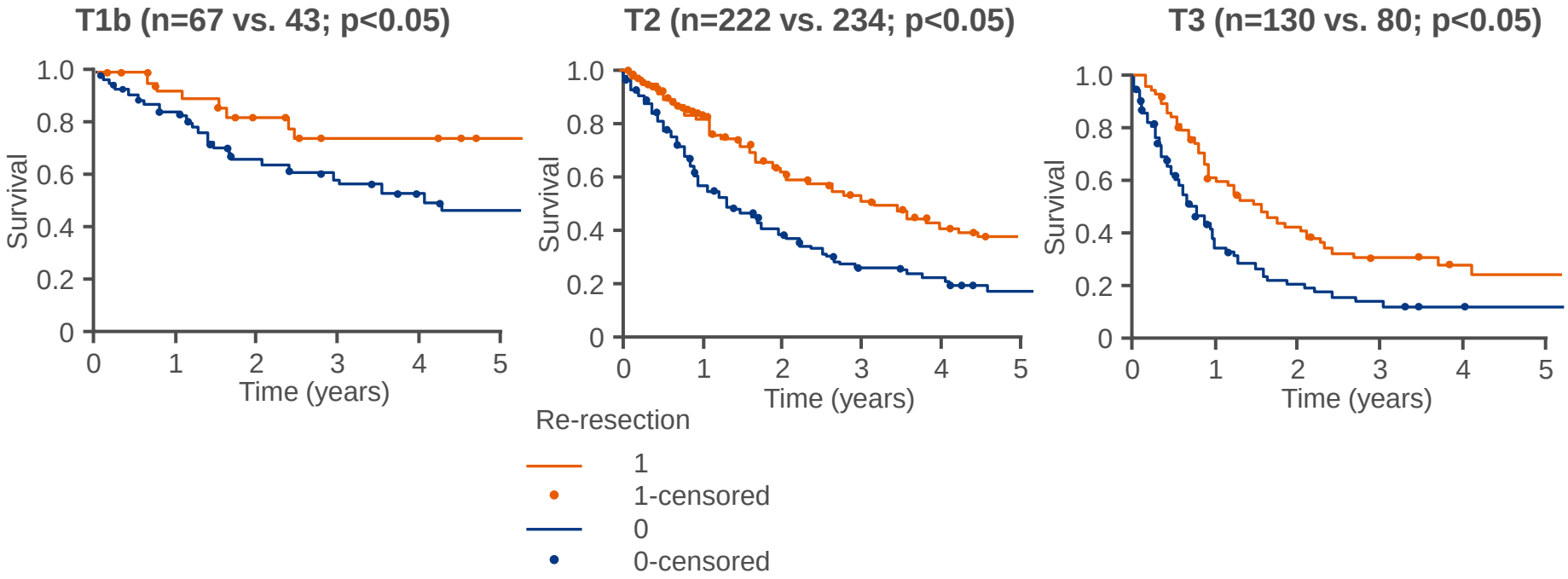
Methods

Goetze TO et al. Ann Oncol 2016; 27 (suppl 6): abstr 619PD

619PD: Prognostic factors in curative treatment of gallbladder cancer - Data of 950 cases of “The German-Registry” – Goetze et al

Key results

- To date, >950 cases of IGBC in the German Registry have been analysed
- There was an IRR in 42 of 113 T1b cases, with a significant survival benefit for T1b after IRR
- A significant survival benefit was also seen for the 228 T2 and 80 T3 with IRR of the 461 T2 and 215 T3 tumours

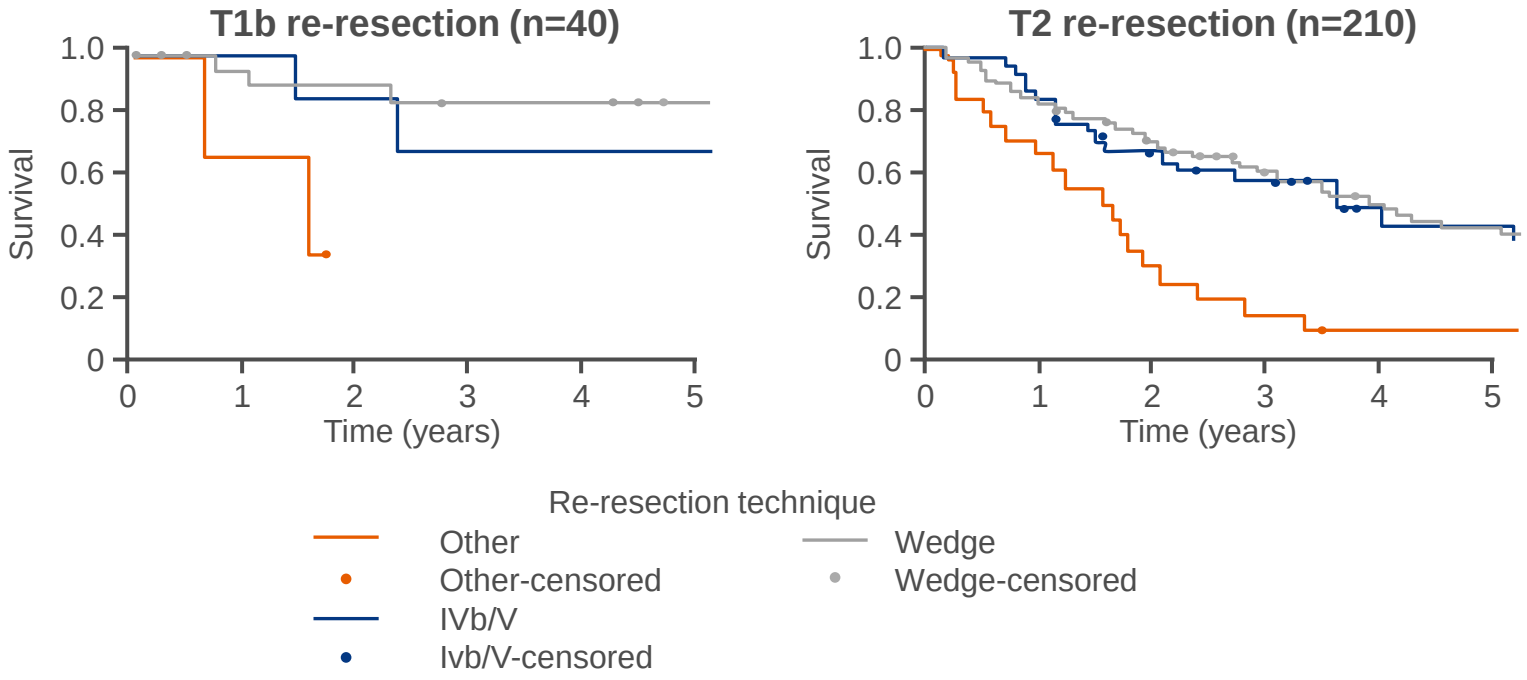


Goetze TO et al. Ann Oncol 2016; 27 (suppl 6): abstr 619PD

619PD: Prognostic factors in curative treatment of gallbladder cancer - Data of 950 cases of “The German-Registry” – Goetze et al

Key results (continued)

- Comparison of liver resection showed good results for the WRT in T1b and T2; more radical techniques showed better results for T3
- Re-resection was performed for <50% of T2–3 tumours in the registry
- Liver resection was performed significantly more often in clinics with high patient volume



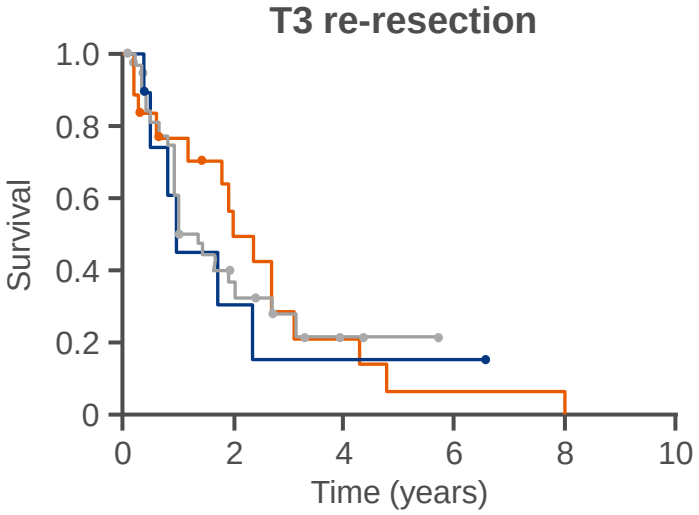
WRT, wedge resection rate

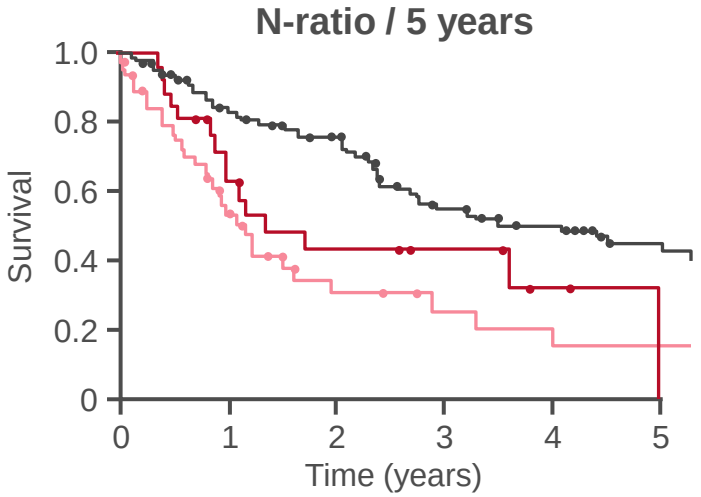
Goetze TO et al. Ann Oncol 2016; 27 (suppl 6): abstr 619PD

619PD: Prognostic factors in curative treatment of gallbladder cancer - Data of 950 cases of “The German-Registry” – Goetze et al

Key results (continued)

- Lymph node ratio (LNR) could be estimated in 212 patients, with statistics showing it to be a significant prognostic factor
  - Referral of patients from a low- to high- volume clinic has no practical relevance





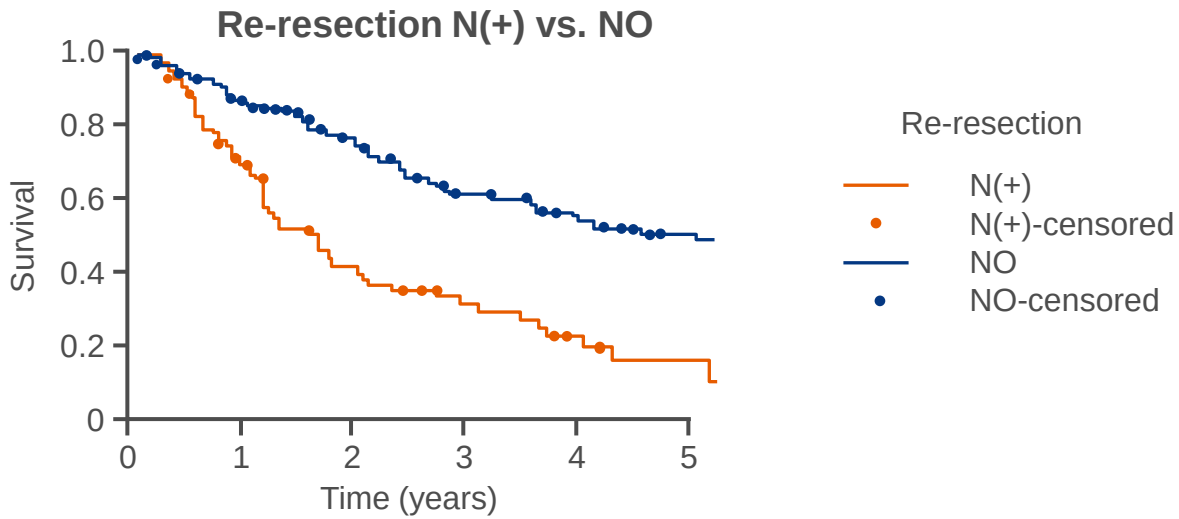
Re-resection technique

Other	0.5<LNR<1.0
Other-censored	0.5<LNR<1.0-censored
IVb/V	0<LNR<0.5
IVb/V-censored	0<LNR<0.5-censored
Wedge-resection	LNR=0
Wedge-censored	LNR=0-censored

Goetze TO et al. Ann Oncol 2016; 27 (suppl 6): abstr 619PD

619PD: Prognostic factors in curative treatment of gallbladder cancer - Data of 950 cases of “The German-Registry” – Goetze et al

Key results (continued)



Conclusions

- IGBCs up to T1b need radical surgery
- Wedge-resection is an efficient procedure for T1b / T2 IGBC as it is less invasive despite oncological adequacy; WRT implants can also be fitted in low-volume centres that have limited experience in liver surgery
- The number of retrieved lymph nodes is essential
- Adherence to correct decision processes benefits more patients
- For a further increase in cure rate in T2-3 IGBC patients, another multimodal therapy (GAIN) trial has already been planned

Goetze TO et al. Ann Oncol 2016; 27 (suppl 6): abstr 619PD

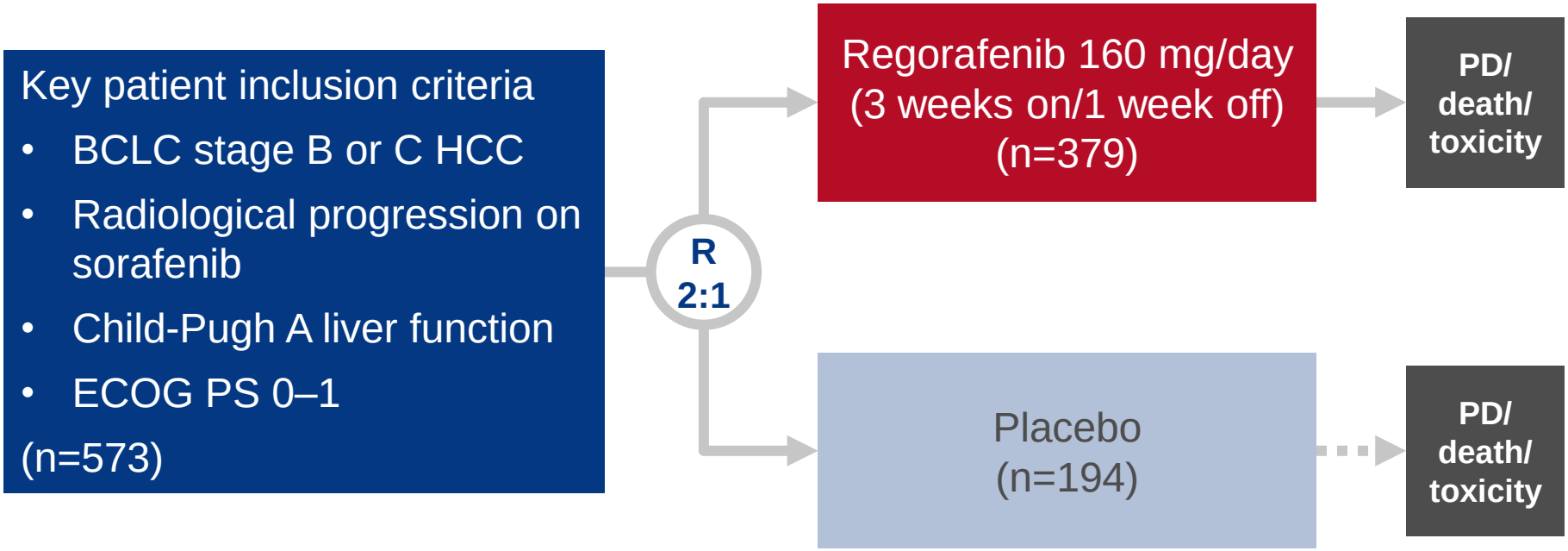
Cancers of the pancreas, small bowel and hepatobiliary tract

HEPATOCELLULAR CARCINOMA

LBA28: Efficacy, safety, and health-related quality of life (HRQoL) of regorafenib in patients with hepatocellular carcinoma (HCC) progressing on sorafenib: Results of the international, double-blind phase 3 RESORCE trial – Bruix et al

Study objective

- To evaluate the efficacy, safety and QoL of regorafenib in patients with HCC who had disease progression on sorafenib



PRIMARY ENDPOINT(S)

- OS

SECONDARY ENDPOINTS

- HRQoL (FACT-Hep, EQ-5D), OS, PFS, TTP, DCR

Note: Based on data from abstract only

Bruix J et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA28

LBA28: Efficacy, safety, and health-related quality of life (HRQoL) of regorafenib in patients with hepatocellular carcinoma (HCC) progressing on sorafenib: Results of the international, double-blind phase 3 RESORCE trial – Bruix et al

Key results (continued)

	Regorafenib (n=379)	Placebo (n=194)	HR (95% CI)	p-value
mOS, months	10.6	7.8	0.63 (0.50, 0.79)	<0.001
mPFS, months			0.46 (0.37, 0.56)	<0.001
Median TTP, months			0.44 (0.36, 0.55)	<0.001
DCR, %	65.2	36.1		<0.001

Least square mean time-adjusted AUC (95% CI)	Regorafenib (n=379)	Placebo (n=194)	p-value
EQ-5D	0.76 (0.75, 0.78)	0.77 (0.75, 0.79)	0.47
EQ-5D visual analogue scale (VAS)	71.68 (70.46, 72.90)	73.45 (71.84, 75.06)	0.06
FACT-General	75.14 (74.12, 76.16)	76.55 (75.20, 77.90)	0.07
FACT-Hep total	129.31 (127.84, 130.79)	133.17 (131.21, 135.12)	<0.001

Note: Based on data from abstract only

Bruix J et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA28

LBA28: Efficacy, safety, and health-related quality of life (HRQoL) of regorafenib in patients with hepatocellular carcinoma (HCC) progressing on sorafenib: Results of the international, double-blind phase 3 RESORCE trial – Bruix et al

Key results (continued)

	Regorafenib (n=379)	Placebo (n=194)
Any grade ≥3 AE, %	79.7	58.5
Grade ≥3 AEs occurring more frequently with regorafenib, %		
Hypertension	15.2	4.7
Hand–foot skin reaction	12.6	0.5
Fatigue	9.1	4.7
Diarrhoea	3.2	0

Note: Based on data from abstract only

Bruix J et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA28

LBA28: Efficacy, safety, and health-related quality of life (HRQoL) of regorafenib in patients with hepatocellular carcinoma (HCC) progressing on sorafenib: Results of the international, double-blind phase 3 RESORCE trial – Bruix et al

Conclusions

- Following regorafenib treatment, a statistically significant improvement in OS was observed for patients with HCC who progressed on prior sorafenib treatment
  - Risk of death was reduced by 37% (HR 0.63; 95% CI 0.50, 0.79; p<0.001)
  - mOS was 10.6 vs. 7.8 months
- Regorafenib treatment significantly improved PFS and TTP
- A significantly higher response rate and DCR (almost doubled) was observed in patients treated with regorafenib
- No new AEs related to regorafenib were seen in this study

Note: Based on data from abstract only

Bruix J et al. Ann Oncol 2016; 27 (suppl 6): abstr LBA28

Cancers of the pancreas, small bowel and hepatobiliary tract

NEUROENDOCRINE TUMOUR

420PD: NETTER-1 phase III in patients with midgut neuroendocrine tumors treated with 177Lu-dotatate: Efficacy, safety, QoL results and subgroup analysis – Strosberg et al

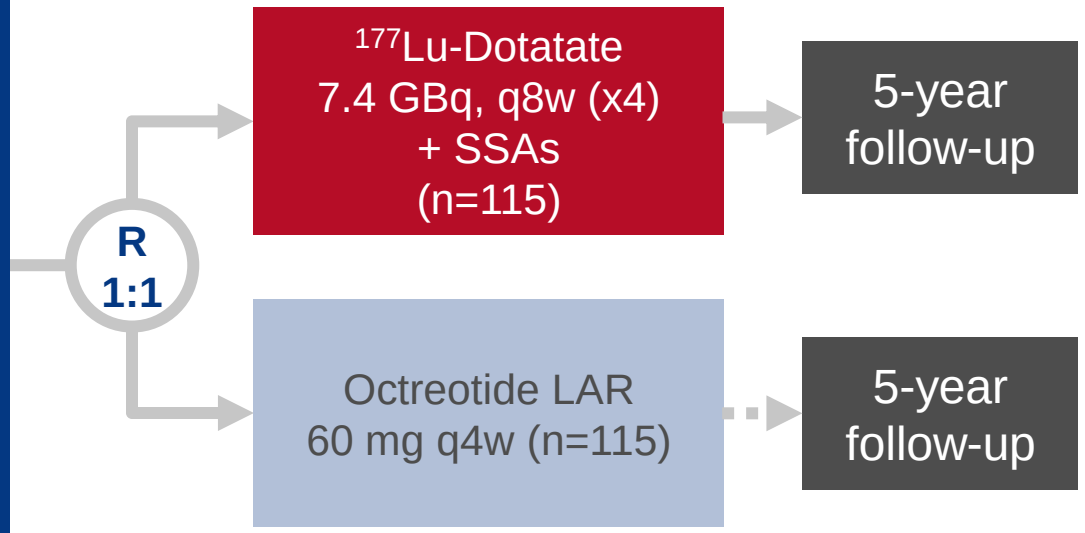
Study objective

- To evaluate the efficacy and safety of ^{177}Lu-Dotatate compared with octreotide LAR in patients with advanced, progressive somatostatin receptor positive midgut NETs

Key patient inclusion criteria

- Grade 1–2 metastatic or locally advanced, midgut NETs
- PD on octreotide LAR (20–30 mg q3/4w)
- Somatostatin receptor positive disease
- KPS ≥60

(n=230)



PRIMARY ENDPOINT

- PFS (RECIST 1.1)

SECONDARY ENDPOINTS

- ORR, OS, TTP, safety, QoL

Strosberg J et al. Ann Oncol 2016; 27 (suppl 6): abstr 420PD

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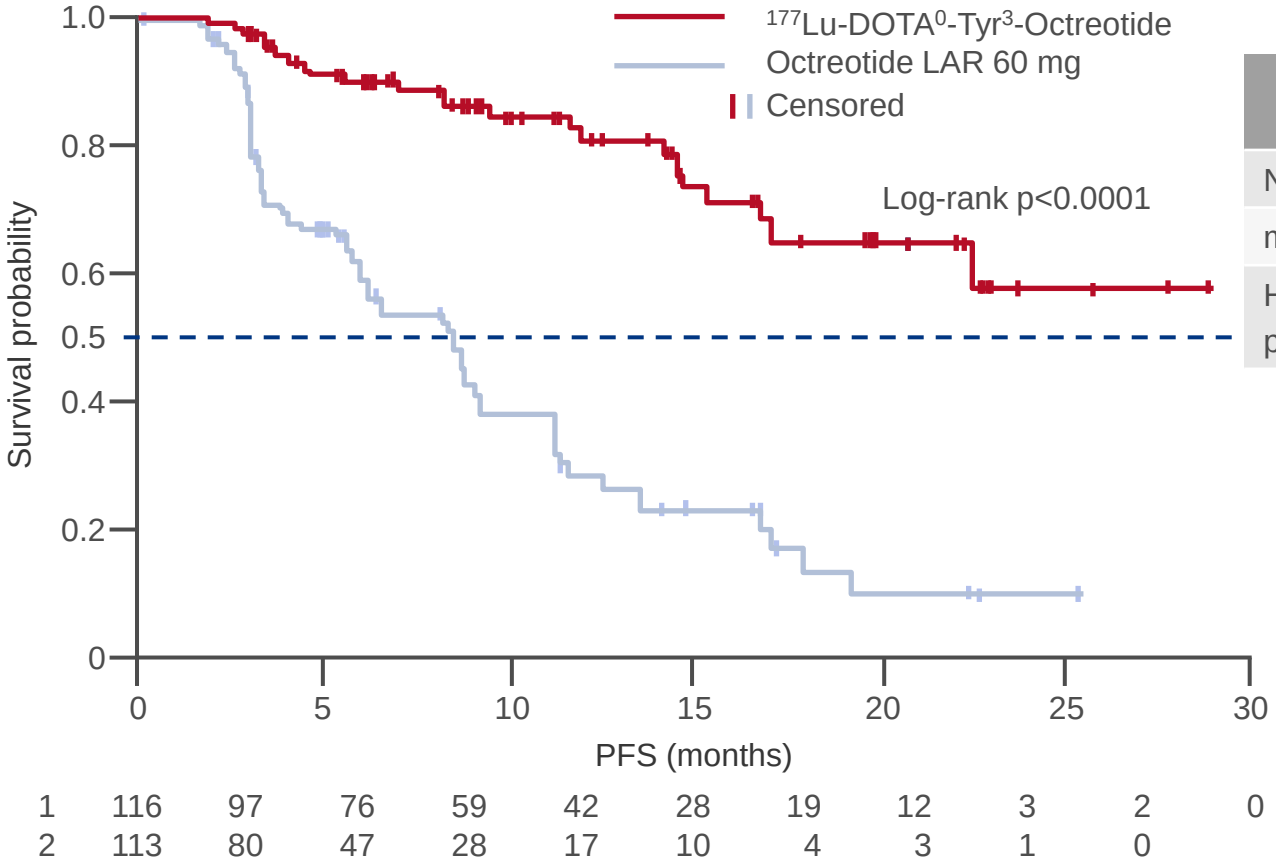
Key results



	^{177}Lu-Dotatate	Octreotide LAR
No. of events	23	68
mPFS, months	NR	8.4
HR (95% CI)	0.21 (0.13, 0.33)	
p-value	<0.0001	

↓

79% reduction in the risk of PD/death on ^{177}Lu-dotatate vs. octreotide LAR

↓

Estimated mPFS on ^{177}Lu-dotatate: 40 months

- Subgroup analyses for PFS confirmed consistent benefits of ^{177}Lu-Dotatate irrespective of stratification and prognostic factors including tumour grade, age, gender, tumour marker levels and levels of radiotracer uptake

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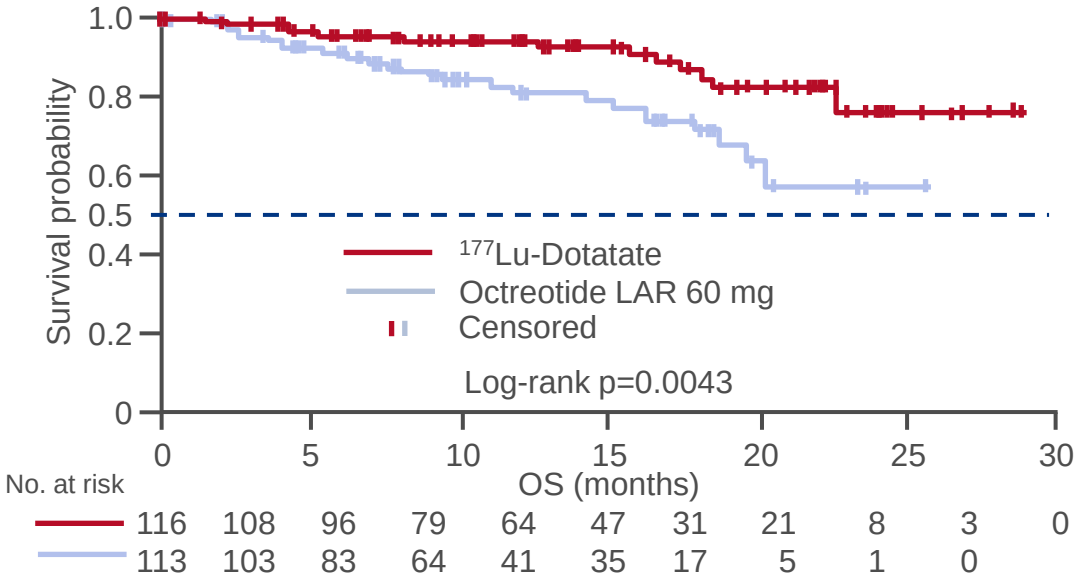
Key results (continued)



	177Lu-Dotatate	Octreotide LAR
No. of deaths	14	26
HR (95% CI)	0.398 (0.21, 0.77)	
p-value	0.0043	

Pre-specified interim analysis: p<0.000085

Stage	CR, n	PR, n	ORR,* %	95% CI	p-value
177Lu-Dotatate (n=101)*	1	17	18	10–15	0.0008
Octreotide LAR 60 mg (n=100)*	0	3	3	0–6	

*Excludes patients with no post-baseline scan or central response available.

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Key results (continued)

Treatment-related AEs, n (%)	^{177}Lu-Dotatate (n=111)	Octreotide LAR (n=110)
Treatment-related AEs	95 (86)	34 (31)
Treatment-related SAEs	10 (9)	1 (1)
Treatment-related withdrawal	5 (5)	0 (0)
Grade 3/4 AEs occurring in ≥1%, %		
Nausea	4	2
Vomiting	7	0
Diarrhoea	3	2
Abdominal pain	3	5
Fatigue/asthenia	2	2
Thrombocytopenia	2	0
Lymphocytopenia	9	0
Leukopenia	1	0
Neutropenia	1	0

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Conclusions

- **Clinically meaningful improvements were observed for ^{177}Lu-Dotatate vs. Octreotide LAR in PFS (p<0.0001) and ORR (18% vs. 3%; p=0.0008)**
- **Interim analysis suggests an increased OS (14 vs. 26 deaths), but to be confirmed in the final analysis**
- **A favourable safety profile was observed for ^{177}Lu-Dotatate, with no clinically relevant findings reported especially regarding haematological and renal and parameters**
- **Preliminary QoL analysis suggests benefit in key domains that are pertinent to midgut NETs, including global health and diarrhoea**
  - **No clear evidence of benefit in flushing/sweats vs. high-dose octreotide**

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