GI SLIDE DECK 2018

Selected abstracts from:

2018 Gastrointestinal Cancers Symposium

18–20 January 2018 | San Francisco, USA

esdo european society of digestive oncology

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Letter from ESDO

DEAR COLLEAGUES

It is our 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 2018. This slide set specifically focuses on the **2018 Gastrointestinal Cancers Symposium** 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.

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
Thomas Seufferlein
Côme Lepage
Wolff Schmiegel
Phillippe Rougier (hon.)

Ulrich Güller
Thomas Grünberger
Tamara Matysiak-Budnik
Jaroslaw Regula
Jean-Luc Van Laethem

(ESDO Governing Board)

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ESDO Medical Oncology Slide Deck
Editors 2018

COLORECTAL CANCERS




Prof Eric Van Cutsem	Digestive Oncology, University Hospitals, Leuven, Belgium
Prof Wolff Schmiegel	Department of Medicine, Ruhr University, Bochum, Germany
Prof Thomas Gruenberger	Department of Surgery I, Rudolf Foundation Clinic, Vienna, Austria
Prof Jaroslaw Regula	Department of Gastroenterology and Hepatology, Institute of Oncology, Warsaw, Poland

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
Prof Ulrich Güller	Medical Oncology & Hematology, Kantonsspital St Gallen, St Gallen, Switzerland

GASTRO-OESOPHAGEAL AND NEUROENDOCRINE TUMOURS


Prof Côme Lepage	University Hospital & INSERM, Dijon, France
Prof Tamara Matysiak	Hepato-Gastroenterology & Digestive Oncology, Institute of Digestive Diseases, Nantes, France

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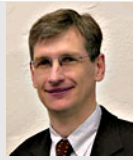

Prof Eric Van Cutsem	Digestive Oncology, University Hospitals, Leuven, Belgium
Prof Thomas Seufferlein	Clinic of Internal Medicine I, University of Ulm, Ulm, Germany

esdo

Glossary

1L	first-line
5FU	5-fluorouracil
AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BICR	blinded independent central review
bid	twice daily
BOR	best overall response
CAPOX	capecitabine + oxaliplatin
CI	confidence interval
CPK	creatinine phosphokinase
CR	complete response
(m)CRC	(metastatic) colorectal cancer
CRS	cytoreductive surgery
CT	chemotherapy
D	day
DCR	disease control rate
DFS	disease-free survival
dMMR	DNA mismatch repair deficient
DoR	duration of response
ECOG	Eastern Cooperative Oncology Group
EHS	extrahepatic spread
EIPL	extensive intraoperative peritoneal lavage
EpCAM	epithelial cell adhesion molecule
FFPE	formalin fixed paraffin-embedded
FLOT	docetaxel + 5-fluorouracil + leucovorin + oxaliplatin
FOLFOX	leucovorin + 5-fluorouracil + oxaliplatin
GEJ	gastro-oesophageal junction
GEM	gemcitabine
gGT	gamma-glutamyl transpeptidase
HBV	hepatitis B virus
HCV	hepatitis C virus
HCC	hepatocellular carcinoma
HER2	human epidermal growth factor receptor 2
HIPEC	hyperthermic intraperitoneal chemotherapy
HR	hazard ratio
HRQoL	health-related quality of life
IHC	immunohistochemistry
IV	intravenous
IP	intraperitoneal
LMWH	low-molecular-weight heparin
mAb	monoclonal antibody
MCDC	modified Clavien–Dindo classification
mFOLFIRINOX	modified leucovorin + 5-fluorouracil + irinotecan + oxaliplatin
MMR	mismatch repair
mRNA	messenger RNA
MSI-H	microsatellite instability-high
MSS	microsatellite stable
MVI	macroscopic vascular invasion
NE	not evaluable
ORR	objective response rate
(m)OS	(median) overall survival
OTE	open transthoracic oesophagectomy
PD	progressive disease
PD-1	programmed death-protein 1
PD-L1	programmed death-ligand 1
PK	pharmacokinetics
(m)PFS	(median) progression-free survival
PR	partial response
PS	performance status
q2/3w	every 2/3 weeks
QoL	quality of life
R	randomised
RAMIE	robot-assisted minimally invasive thoraco-laparoscopic oesophagectomy
RECIST	Response Evaluation Criteria In Solid Tumors
RFS	recurrence-free survival
RT	radiotherapy
RT-PCR	reverse transcription polymerase chain reaction
S-1	tegafur + gimeracil + oteracil
SAE	serious adverse event
SD	stable disease
SE	standard error
SoC	standard of care
SSI	surgical site infection
TCR	treatment completion rate
TIC	tumour-infiltrating immune cells
TRAE	treatment-related adverse event
VAS	visual analogue scale
WBC	white blood cell

Contents

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Note: To jump to a section, right click on the number and ‘Open Hyperlink’

CANCERS OF THE OESOPHAGUS AND STOMACH

1: Long-term outcome of a randomized phase III trial exploring the significance of extensive intraoperative peritoneal lavage in addition to standard treatment for ≥ T3 resectable gastric cancer: CCOG 1102 – Morimoto D, et al

Study objective

- To show superiority of extensive intraoperative peritoneal lavage (EIPL) over conventional irrigation in patients with ≥T3 gastric cancer

Key patient inclusion criteria

- Advanced gastric adenocarcinoma
- cT3(SS), T4a(SE) or T4b(SI)
- cH0 and M0
- R0 surgery possible
- Neoadjuvant CT allowed
- ECOG PS 0–1

(n=314)

R 1:1

EIPL
10,000 mL saline
(n=145)

Stratification

- Institution
- cT3 vs. cT4a vs. cT4b
- Neoadjuvant (yes vs. no)

Non-EIPL
3,000 mL saline
(n=150)

pStage I – no treatment

pStage II/III – S-1 for 12 months

p/cStage IV – physician's choice

PRIMARY ENDPOINT

- DFS

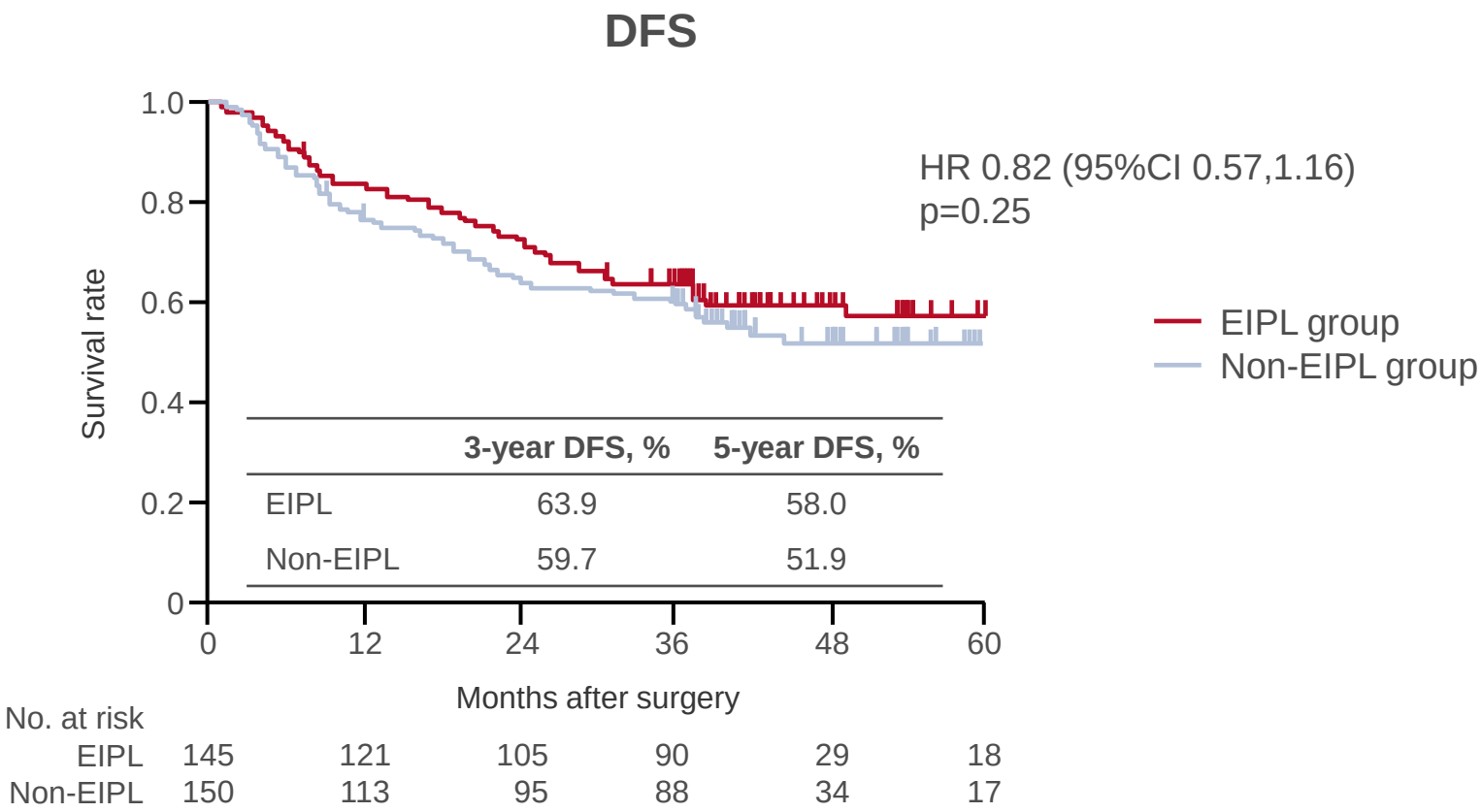
SECONDARY ENDPOINTS

- OS, peritoneal RFS, safety

Morimoto D, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 1

1: Long-term outcome of a randomized phase III trial exploring the significance of extensive intraoperative peritoneal lavage in addition to standard treatment for ≥ T3 resectable gastric cancer: CCOG 1102 – Morimoto D, et al

Key results



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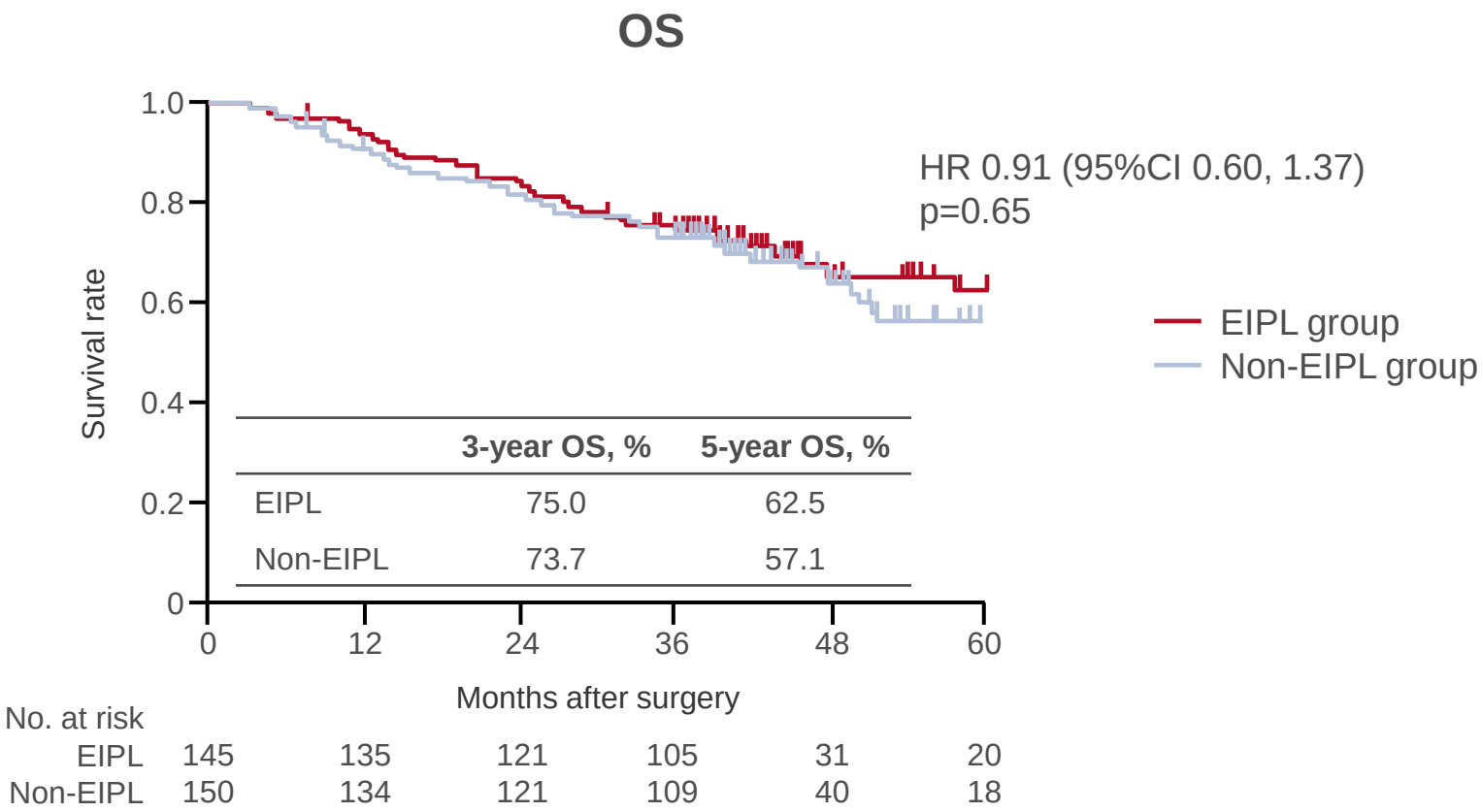
Key results (cont.)



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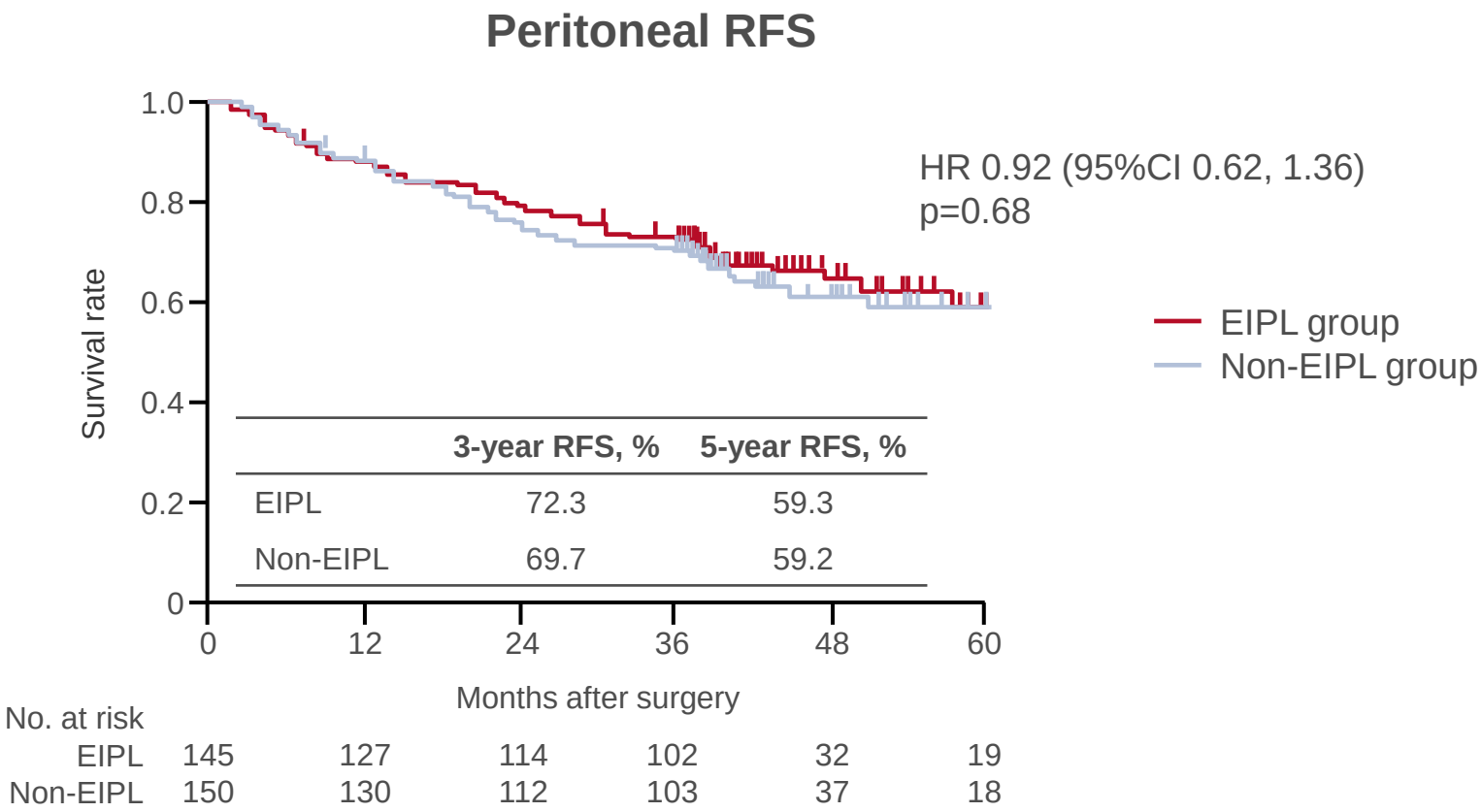
Key results (cont.)



Morimoto D, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 1

1: Long-term outcome of a randomized phase III trial exploring the significance of extensive intraoperative peritoneal lavage in addition to standard treatment for ≥ T3 resectable gastric cancer: CCOG 1102 – Morimoto D, et al

Key results (cont.)

Grade ≥2 surgical complications	EIPL (n=145)	Non-EIPL (n=150)	p-value
Overall, n (%)	29 (20.0)	41 (27.3)	0.17
Intra-abdominal SSI, n (%)	15 (10.3)	19 (12.7)	0.59
Leakage	3 (2.1)	3 (2.0)	0.97
Pancreatic fistula	7 (4.8)	14 (9.3)	0.13
Abscess	11 (7.6)	7 (4.7)	0.30

Conclusions

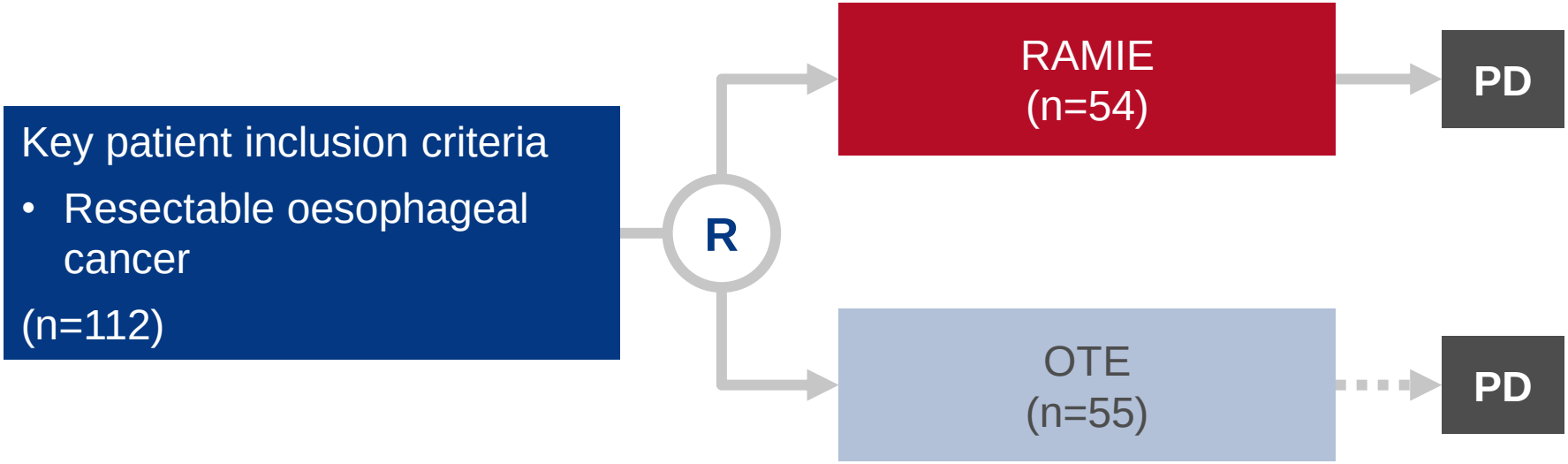
- **In patients with advanced gastric cancer, EIPL was tolerable, but was not found to be superior to conventional irrigation**
  - **In patients with intra-abdominal SSI, EIPL demonstrated a trend for decreasing recurrence**

Morimoto D, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 1

6: Robot-assisted minimally invasive thoraco-laparoscopic esophagectomy versus open transthoracic esophagectomy for resectable esophageal cancer: A randomized controlled trial – van der Sluis PC, et al

Study objective

- To compare the efficacy and safety of robot-assisted minimally invasive thoraco-laparoscopic oesophagectomy (RAMIE) vs. open transthoracic oesophagectomy (OTE) in patients with resectable intrathoracic oesophageal cancer



PRIMARY ENDPOINT

- Overall postoperative complications (MCDC grade 2–5)

SECONDARY ENDPOINTS

- Resource use, QoL, postoperative pain, OS, DFS

van der Sluis PC, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 6

6: Robot-assisted minimally invasive thoraco-laparoscopic esophagectomy versus open transthoracic esophagectomy for resectable esophageal cancer: A randomized controlled trial – van der Sluis PC, et al

Key results

Postoperative complications, n (%)	RAMIE (n=54)	OTE (n=55)	p-value
Overall (MCDC 2, 3, 4 and 5)	32 (59)	44 (80)	0.02
Pulmonary complications	17 (32)	32 (58)	0.005
Cardiac complications	12 (22)	26 (47)	0.006
Wound infections	2 (4)	8 (14)	0.09
Anastomotic leakage	13 (24)	11 (20)	0.57
Mediastinitis	12 (22)	11 (20)	0.42
Chylothorax	17 (32)	12 (22)	0.69
Recurrent laryngeal nerve injury	5 (9)	6 (11)	0.78

van der Sluis PC, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 6

6: Robot-assisted minimally invasive thoraco-laparoscopic esophagectomy versus open transthoracic esophagectomy for resectable esophageal cancer: A randomized controlled trial – van der Sluis PC, et al

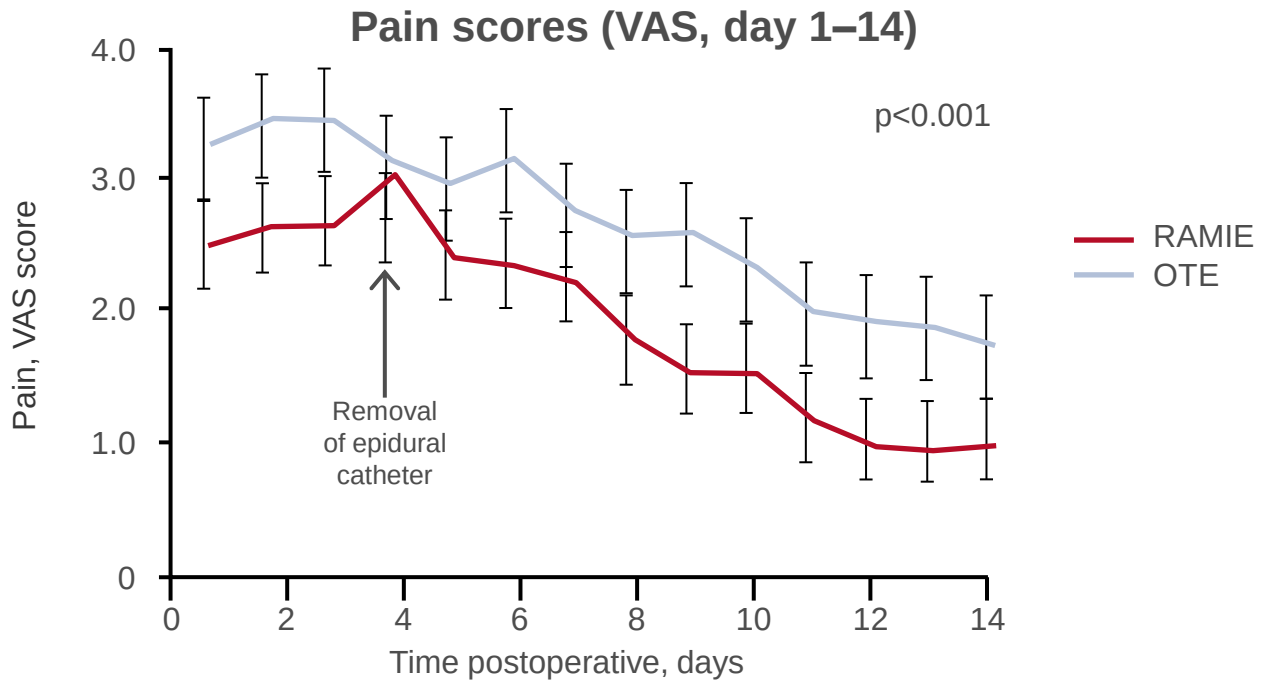
Key results (cont.)

	RAMIE (n=54)	OTE (n=55)	p-value
In-hospital mortality, n (%)	2 (4)	1 (2)	0.62
Functional recovery within 2 weeks, n (%)	38 (70)	28 (51)	0.04
Short-term QoL (QLQ-C30)			
HRQoL (discharge)	57.9 (49.9–66.1)	44.6 (36.7–52.5)	0.02
HRQoL (6 weeks)	68.7 (61.5–75.9)	57.6 (50.6–64.6)	0.03
Physical functioning (discharge)	54.5 (45.8–63.3)	41.0 (32.4–49.6)	0.03
Physical functioning (6 weeks)	69.3 (61.6–76.9)	58.6 (51.1–66.0)	0.049
Radicality of surgery, n (%)			
R0	50 (93)	53 (96)	0.35
R1	2 (4)	2 (4)	
Unresectable	2 (4)	0 (0)	

van der Sluis PC, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 6

6: Robot-assisted minimally invasive thoraco-laparoscopic esophagectomy versus open transthoracic esophagectomy for resectable esophageal cancer: A randomized controlled trial – van der Sluis PC, et al

Key results (cont.)

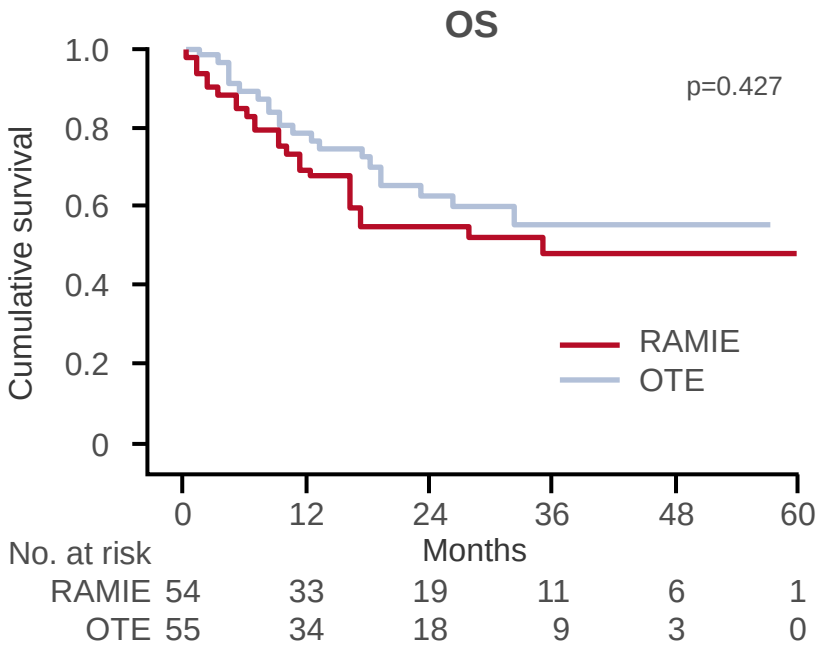


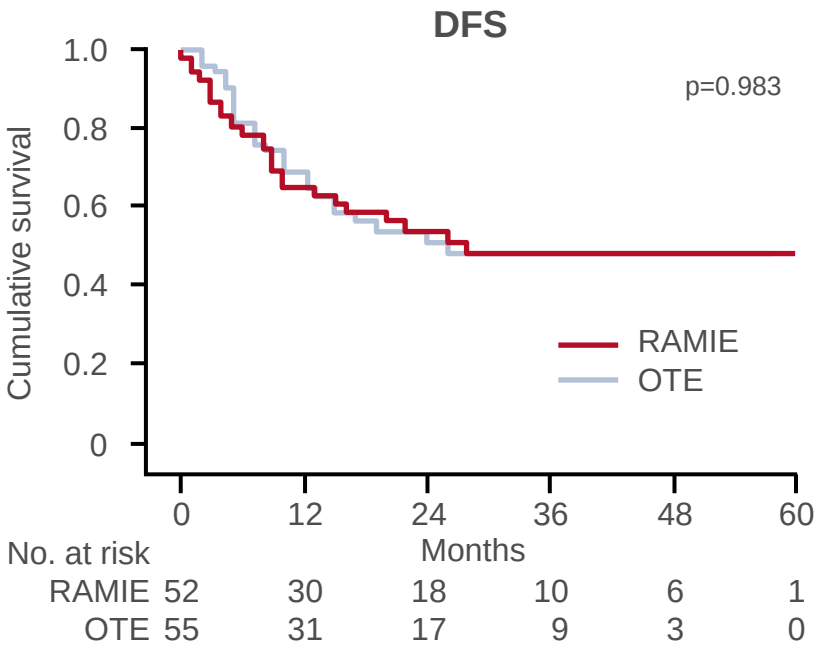
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Overall
RAMIE	2.45	2.58	2.58	2.97	2.38	2.29	2.18	1.73	1.48	1.48	1.13	0.95	0.89	0.93	1.86
OTE	3.22	3.39	3.41	3.09	2.91	3.13	2.71	2.51	2.58	2.31	1.97	1.88	1.85	1.72	2.62
SE	0.40	0.40	0.40	0.40	0.40	0.40	0.39	0.39	0.39	0.39	0.39	0.40	0.40	0.40	0.13
p-value	0.05	0.04	0.04	0.76	0.18	0.03	0.15	0.05	0.01	0.03	0.03	0.02	0.02	0.05	<0.001

van der Sluis PC, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 6

6: Robot-assisted minimally invasive thoraco-laparoscopic esophagectomy versus open transthoracic esophagectomy for resectable esophageal cancer: A randomized controlled trial – van der Sluis PC, et al

Key results (cont.)





Conclusions

- **In patients with resectable oesophageal cancer, compared with OTE, RAMIE resulted in fewer postoperative complications, with lower postoperative pain, better short-term QoL and a better short-term postoperative functional recovery**
- **There was no difference in oncological outcomes**

van der Sluis PC, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 6

8: CYTO-CHIP: Cytoreductive surgery versus cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for gastric cancer with peritoneal metastasis: A propensity-score analysis from BIG RENAPE and FREGAT working groups – Bonnot P-E, et al

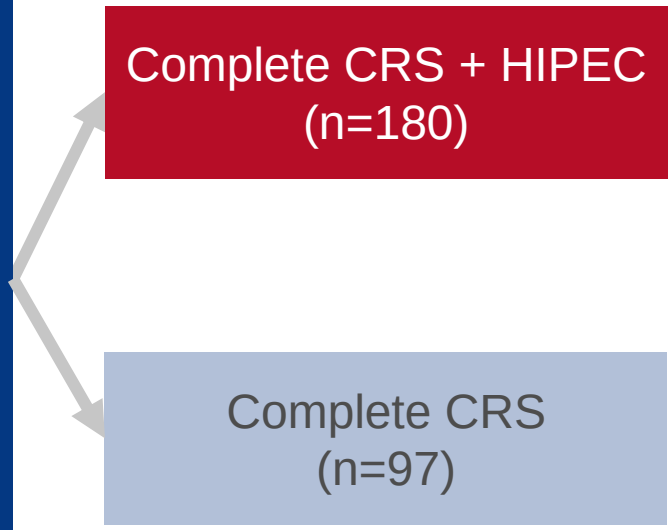
Study objective

- To evaluate the impact of hyperthermic intraperitoneal chemotherapy (HIPEC) after complete cytoreductive surgery (CRS) compared with CRS alone on survival and postoperative outcomes

Key patient inclusion criteria

- Peritoneal carcinomatosis histologically proven and/or positive cytology and/or ovarian metastasis from gastric adenocarcinoma
- Patients from 2 databases – BIG-RENAPE and FREGAT diagnosed between 1989 and 2014
- Propensity analysis included age, primary tumour, peritoneal disease extension and preoperative treatment

(n=277)



ENDPOINTS

- OS, postoperative outcomes

Bonnot P-E, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 8

8: CYTO-CHIP: Cytoreductive surgery versus cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for gastric cancer with peritoneal metastasis: A propensity-score analysis from BIG RENAPE and FREGAT working groups – Bonnot P-E, et al

Key results

- There were no significant differences between the two groups with regard to the quality of cytoreduction

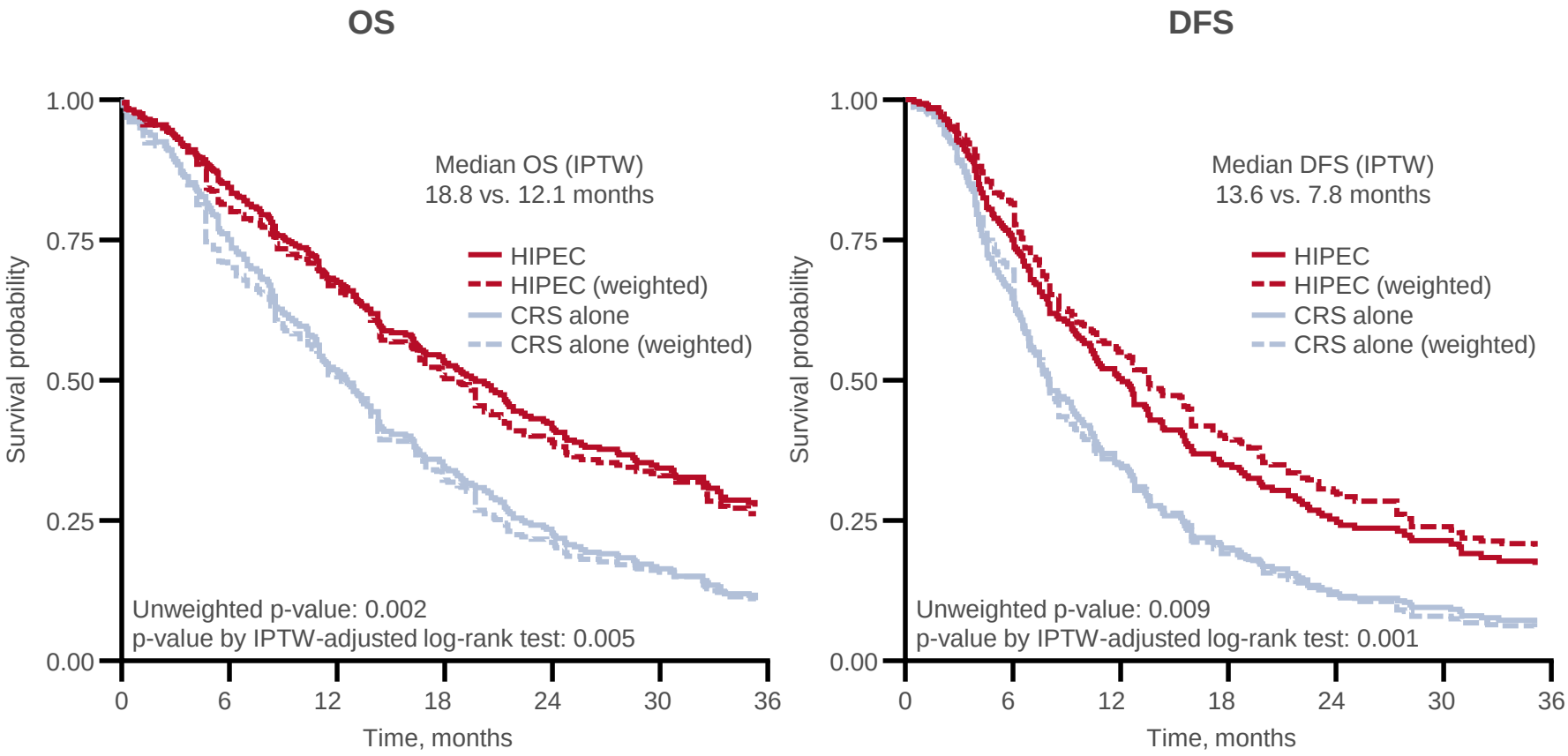
Variable	Modality	Overall (n=277)	HIPEC (n=180)	CRS alone (n=97)	p-value	Adjusted p-value on PS
Peritoneal cytology	Positive	100 (54.3)	69 (54.3)	31 (54.4)	0.994	0.807
Peritoneal Cancer Index*	Median (range)	3 (0–25)	6 (0–25)	2 (0–13)	<0.001	0.004
	Mean (SD)	5.42 (5.47)	7.2 (5.87)	2.11 (2.23)		
Completeness of cytoreduction score	CC-0	219 (79.1)	138 (76.7)	81 (83.5)	0.182	0.904
	CC-1	58 (20.9)	42 (23.3)	16 (16.5)		
Ovarian metastases	Yes	60 (22.5)	53 (30.8)	7 (7.4)	<0.001	0.604

*0 = isolated positive peritoneal cytology ± ovarian metastases ± microscopic peritoneal tumour deposit next to the primitive tumour on final pathological exam without macroscopic lesion during surgery; CC-0, no macroscopic residual cancer; CC-1, no residual nodules >2.5 mm at the end of surgery. PS, propensity score

Bonnot P-E, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 8

8: CYTO-CHIP: Cytoreductive surgery versus cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for gastric cancer with peritoneal metastasis: A propensity-score analysis from BIG RENAPE and FREGAT working groups – Bonnot P-E, et al

Key results (cont.)



IPTW, inverse probability of treatment weighting

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Key results (cont.)

	Before PS analyses		After PS and IPTW analyses	
	HIPEC	CRS alone	HIPEC	CRS alone
OS				
Median, months	18.6	11.4	18.8	12.1
HR (95%CI)	1.00	1.53 (1.16, 2.03)	1.00	1.66 (1.17, 2.37)
3-year survival rate, %	26.72	13.08	26.21	10.82
5-year survival rate, %	**19.92**	**7.36**	**19.87**	**6.43**
DFS				
Median, months	11.6	7.60	13.6	7.8
HR (95%CI)	1.00	1.46 (1.1, 1.94)	1.00	1.78 (1.26, 2.52)
3-year survival rate, %	16.52	5.85	20.40	5.87
5-year survival rate, %	**13.51**	**2.92**	**17.05**	**3.76**

Bonnot P-E, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 8

8: CYTO-CHIP: Cytoreductive surgery versus cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for gastric cancer with peritoneal metastasis: A propensity-score analysis from BIG RENAPE and FREGAT working groups – Bonnot P-E, et al

Key results (cont.)

Variable, n (%IPTW)	Overall (n=277)	HIPEC (n=180)	CRS alone (n=97)	Adjusted p-value on PS
Grade 3–4 overall complications	134 (54.3)	87 (53.7)	47 (55.3)	0.496
Surgical complications	92 (37.7)	59 (37.1)	33 (38.8)	0.922
Interventional radiology procedure	39 (15.8)	27 (16.9)	12 (13.8)	0.982
Re-operation	65 (26.1)	42 (25.9)	23 (26.4)	0.424
90 days mortality	21 (8.4)	12 (7.4)	9 (10.1)	0.820
30 days mortality	8 (3.2)	4 (2.5)	4 (4.1)	0.707
Median hospital stay, days (range)	19 (3–157)	20 (5–157)	19 (3–130)	0.911

Conclusions

- **HIPEC combined with CRS improved OS and DFS in patients with gastric cancer and localised or limited peritoneal metastasis**
- **HIPEC plus CRS did not increase postoperative mortality or morbidity**

Bonnot P-E, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 8

9: Associations of PD-1 and PD-L1 expression with mismatch repair status and prognosis in chemoradiotherapy-naïve esophageal and gastric adenocarcinoma – Svensson MC, et al

Objective

- To examine the expression of PD-L1 in tumour cells and TIC, and the receptor PD-1 in TIC, in patients with oesophageal and gastric adenocarcinoma

Methods

- Primary tumours from a retrospective consecutive cohort of 174 patients with chemoradiotherapy-naïve resected oesophageal and gastric adenocarcinoma had PD-L1 and PD-1 expression in tumour cells and/or TIC assessed by IHC on tissue microarrays
- IHC analysis was also used to determine MMR status, defined as loss of IHC expression of MLH1, PMS2, MSH2 or MSH6
- In addition, the prognostic value of PD-L1 and PD-1 was examined at the mRNA level in 354 cases of gastric adenocarcinoma in The Cancer Genome Atlas for validation purposes

Svensson MC, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 9

9: Associations of PD-1 and PD-L1 expression with mismatch repair status and prognosis in chemoradiotherapy-naïve esophageal and gastric adenocarcinoma – Svensson MC, et al

Key results

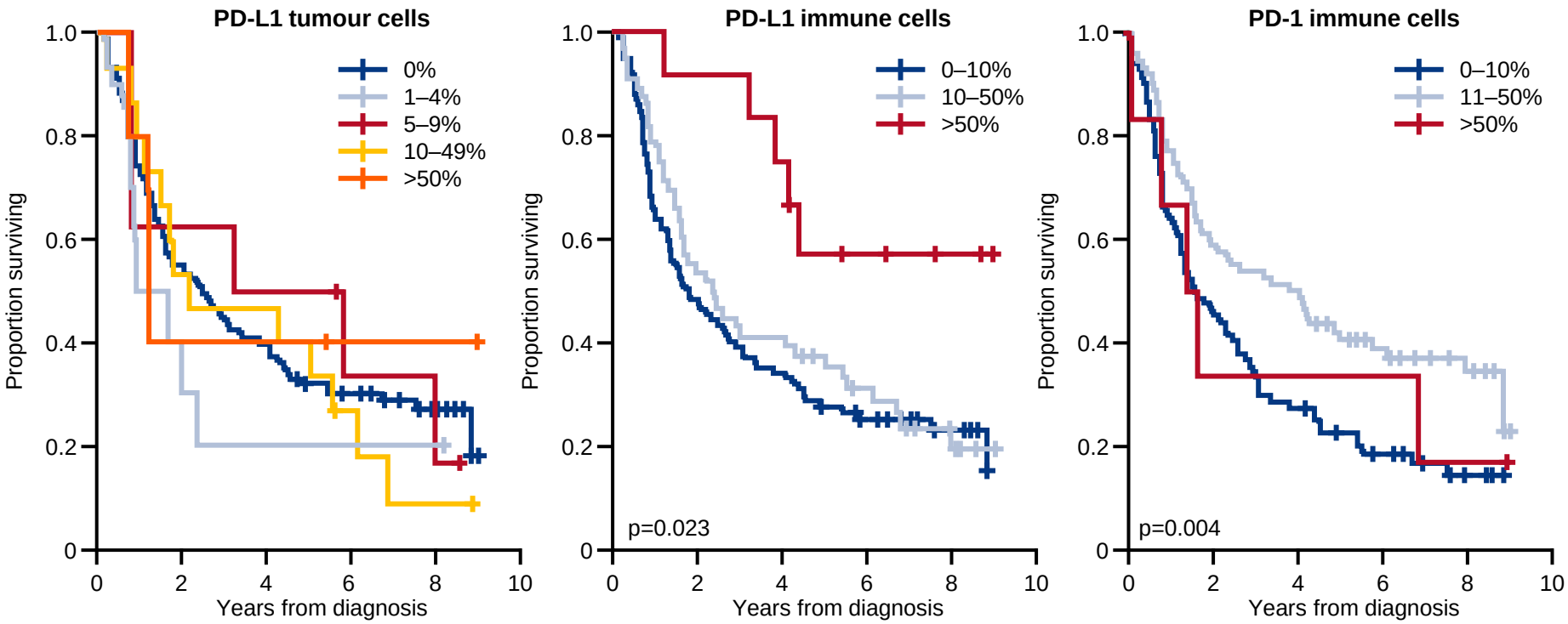
- High PD-1 (>10%) and PD-L1 (>50%) expression in TIC was significantly associated with a prolonged OS
- High PD-L1 expression remained an independent prognostic factor after adjustment for relevant clinicopathological factors and MMR status (HR 0.39; 95%CI 0.15, 0.99)
- Neither tumour cell PD-L1 nor MMR status was prognostic
- At the transcript level, PD-L1 expression in gastric adenocarcinoma was not prognostic, whereas high PD-1 expression was significantly associated with a prolonged OS (p=0.012)

Svensson MC, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 9

9: Associations of PD-1 and PD-L1 expression with mismatch repair status and prognosis in chemoradiotherapy-naïve esophageal and gastric adenocarcinoma – Svensson MC, et al

Key results (cont.)

OS in relation to expression of PD-L1 and PD-1

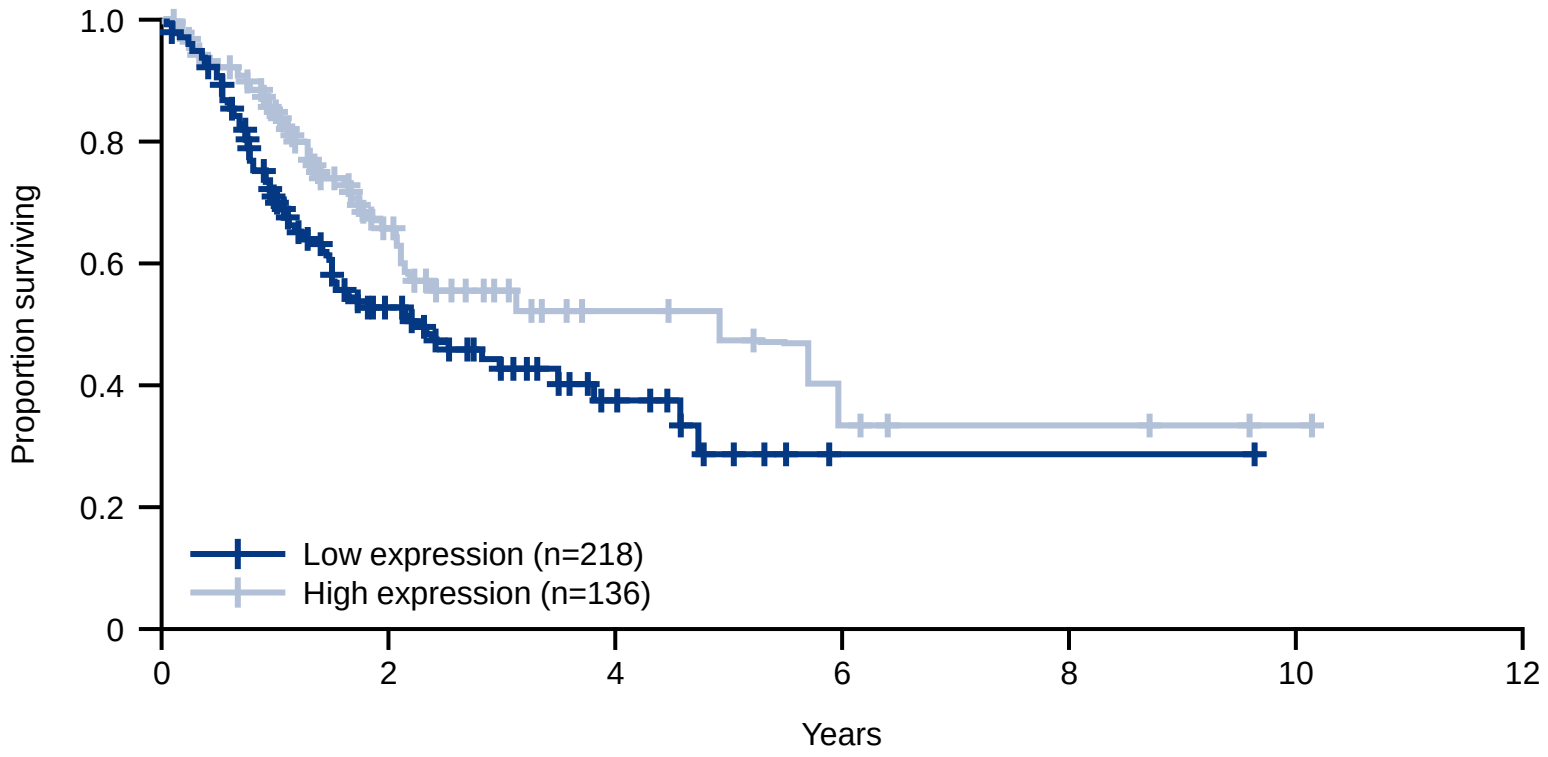


Svensson MC, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 9

9: Associations of PD-1 and PD-L1 expression with mismatch repair status and prognosis in chemoradiotherapy-naïve esophageal and gastric adenocarcinoma – Svensson MC, et al

Key results (cont.)

OS in relation to PD-L1 gene expression in gastric adenocarcinoma in The Cancer Genome Atlas



Svensson MC, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 9

9: Associations of PD-1 and PD-L1 expression with mismatch repair status and prognosis in chemoradiotherapy-naïve esophageal and gastric adenocarcinoma – Svensson MC, et al

Conclusions

- **In patients with oesophageal and gastric adenocarcinoma, there was a significant association between high expression of PD-L1 in tumour cells and TIC and MMR deficiency**
- **In TIC high expression of PD-1 was associated with prolonged survival**
- **In TIC, but not tumour cells, high PD-L1 expression was associated with prolonged survival independently of other prognostic factors and MMR status**
- **In gastric adenocarcinoma, PD-1 expression was significantly associated with a prolonged OS at the transcript level**

Svensson MC, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 9

91: A prospective multicenter trial of S-1 with lafutidine vs S-1 as adjuvant chemotherapy for gastric cancer in Japan: AEOLUS – Machida N, et al

Study objective

- To evaluate improvements in the completion rate of adjuvant S-1 therapy with the addition of lafutidine to reduce toxicity in Japanese patients with resected gastric cancer

Key patient inclusion criteria

- Histologically proven gastric carcinoma
- R0 resection with D≥2 lymph node dissection
- pStage II/III (Japanese classification)

(n=202)

R 1:1

S-1† + lafutidine‡ (n=101)

Stratification

- Institution
- pStage (II vs. IIIA vs. IIIB)
- Total vs. distal gastrectomy

S-1† alone (n=101)

PRIMARY ENDPOINT

- TCR of S-1#

SECONDARY ENDPOINTS

- Safety, relative total administration dose of S-1

†80–120 mg/day, 4 weeks administration with 2 weeks rest, repeated for 1 year; ‡20 mg/day for 1 year; #completion defined as S-1 continuation for 1 year with >70% planned dose

Machida N, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 91

91: A prospective multicenter trial of S-1 with lafutidine vs S-1 as adjuvant chemotherapy for gastric cancer in Japan: AEOLUS – Machida N, et al

Key results

Treatment completion rate

	S-1 + lafutidine (n=101)	S-1 alone (n=101)	p-value
No. completed	69	61	
Completion rate, %	68.3	60.4	0.072

Relative total administration dose

	S-1 + lafutidine (n=101)	S-1 alone (n=101)	p-value
Dose intensity, n (%)			
<70%	32 (31.7)	40 (39.6)	0.152
≥70%	69 (68.3)	61 (60.4)	

Machida N, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 91

91: A prospective multicenter trial of S-1 with lafutidine vs S-1 as adjuvant chemotherapy for gastric cancer in Japan: AEOLUS – Machida N, et al

Key results (cont.)

Adverse events, n (%)	S-1 + lafutidine (n=102)		S-1 alone (n=100)	
	All grades	Grade ≥3	All grades	Grade ≥3
All	99 (97.1)	31 (30.4)	97 (97.0)	36 (36.0)
Neutropenia	2 (2.0)	0 (0)	3 (3.0)	1 (1.0)
Thrombocytopenia	29 (28.4)	0 (0)	34 (34.0)	3 (3.0)
Total bilirubin increased	33 (32.4)	2 (2.0)	35 (35.0)	1 (1.0)
AST increased	24 (23.5)	2 (2.0)	38 (38.0)	0 (0)
Anorexia	74 (72.5)	15 (14.7)	70 (70.0)	17 (17.0)
Nausea	56 (54.9)	5 (4.9)	45 (45.0)	5 (5.0)
Stomatitis	49 (48.0)	3 (3.0)	43 (43.0)	0 (0)
Diarrhoea	67 (65.7)	2 (2.0)	63 (63.0)	6 (6.0)
Fatigue	71 (69.6)	11 (10.8)	72 (72.0)	8 (8.0)
Watering eyes	48 (47.1)	3 (2.9)	45 (45.0)	1 (1.0)

Machida N, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 91

91: A prospective multicenter trial of S-1 with lafutidine vs S-1 as adjuvant chemotherapy for gastric cancer in Japan: AEOLUS – Machida N, et al

Conclusions

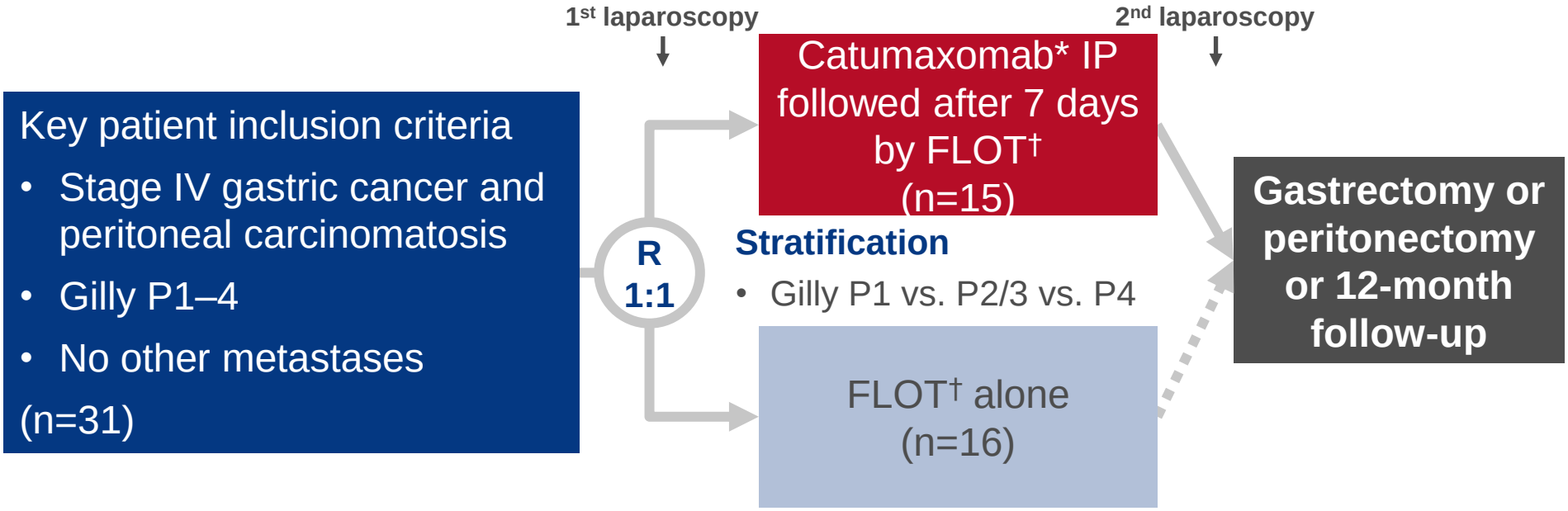
- In Japanese patients with stage II/III gastric cancer, lafutidine may increase the completion rate of adjuvant S-1
- There was no difference between the groups for relative dose intensity or AEs

Machida N, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 91

4: Intraperitoneal immunotherapy with the bispecific anti-EpCAM x anti-CD3 directed antibody catumaxomab for patients with peritoneal carcinomatosis from gastric cancer: Final results of a randomized phase II AIO trial – Lordick F, et al

Study objective

- To assess the efficacy and safety of the bispecific anti-EpCAM/CD3 mAb catumaxomab then FLOT vs. FLOT alone in patients with peritoneal carcinomatosis from gastric cancer



PRIMARY ENDPOINT

- Complete remission of peritoneal carcinomatosis at second laparoscopy

SECONDARY ENDPOINTS

- OS, PFS, safety

*10 µg D0, 20 µg D3, 50 µg D7, 150 µg D10; †Oxaliplatin 85 mg/m^2 D1, leucovorin 200 mg/m^2 D1, 5FU 2600 mg/m^2 (24-h infusion) D1, docetaxel 50 mg/m^2 D1 (6 cycles)

Lordick F, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 4

4: Intraperitoneal immunotherapy with the bispecific anti-EpCAM x anti-CD3 directed antibody catumaxomab for patients with peritoneal carcinomatosis from gastric cancer: Final results of a randomized phase II AIO trial – Lordick F, et al

Key results

Macroscopic complete remission of peritoneal carcinomatosis	Catumaxomab + FLOT (n=15)	FLOT alone (n=16)
Complete remission, n (%)	4 (27)	3 (19)
p-value	0.69	
Non-complete remission, n (%)	9 (60)	9 (56)
No data, n (%)	2 (13)	4 (25)

	Catumaxomab + FLOT (n=15)	FLOT alone (n=16)
Secondary resection rate, n (%)	8 (53)	5 (31)

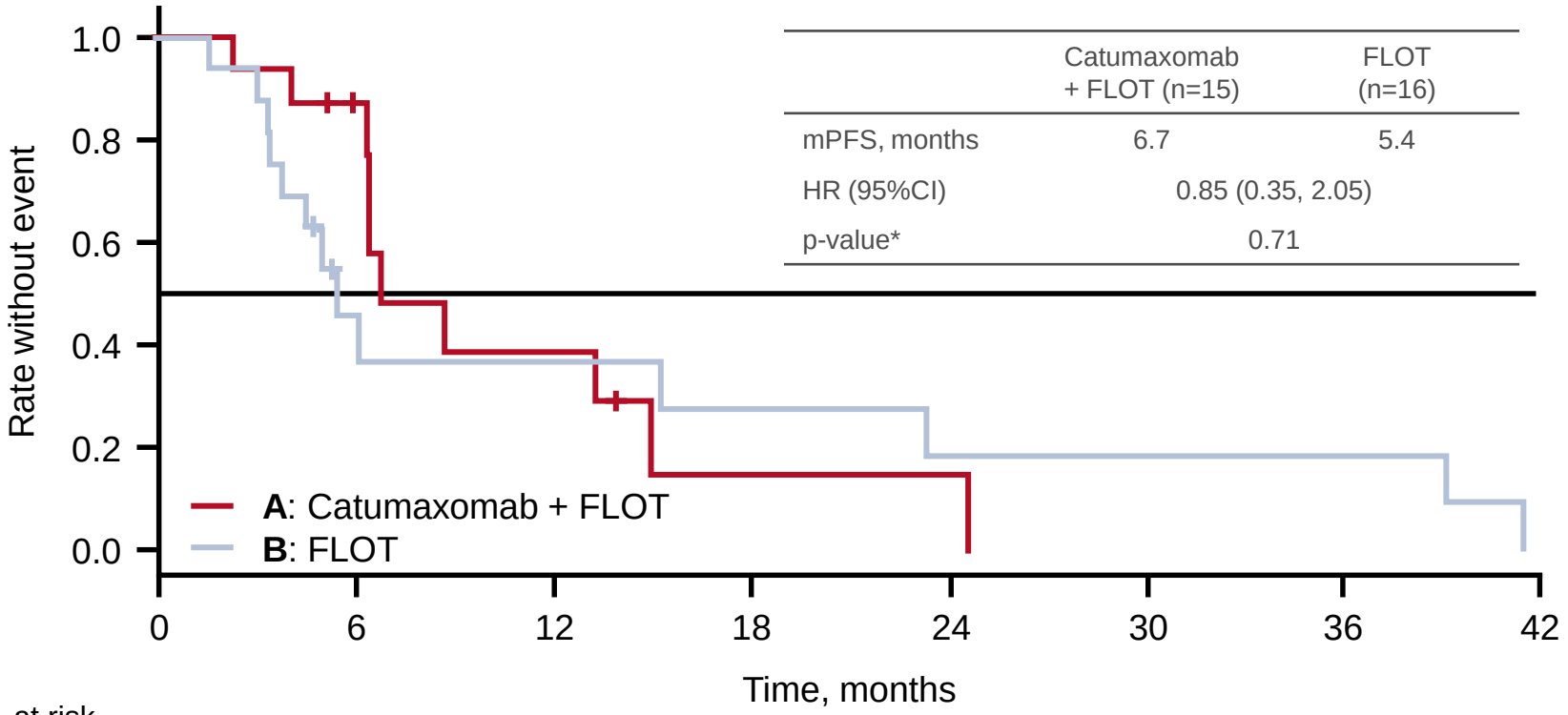
Lordick F, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 4

4: Intraperitoneal immunotherapy with the bispecific anti-EpCAM x anti-CD3 directed antibody catumaxomab for patients with peritoneal carcinomatosis from gastric cancer: Final results of a randomized phase II AIO trial – Lordick F, et al

Key results (cont.)

PFS

	Catumaxomab + FLOT (n=15)	FLOT (n=16)
mPFS, months	6.7	5.4
HR (95%CI)	0.85 (0.35, 2.05)	
p-value*	0.71	



No. at risk

A:	15	9	4	1	1	0	0
B:	16	5	4	3	2	2	2

*Log-rank t-test with FLOT as reference

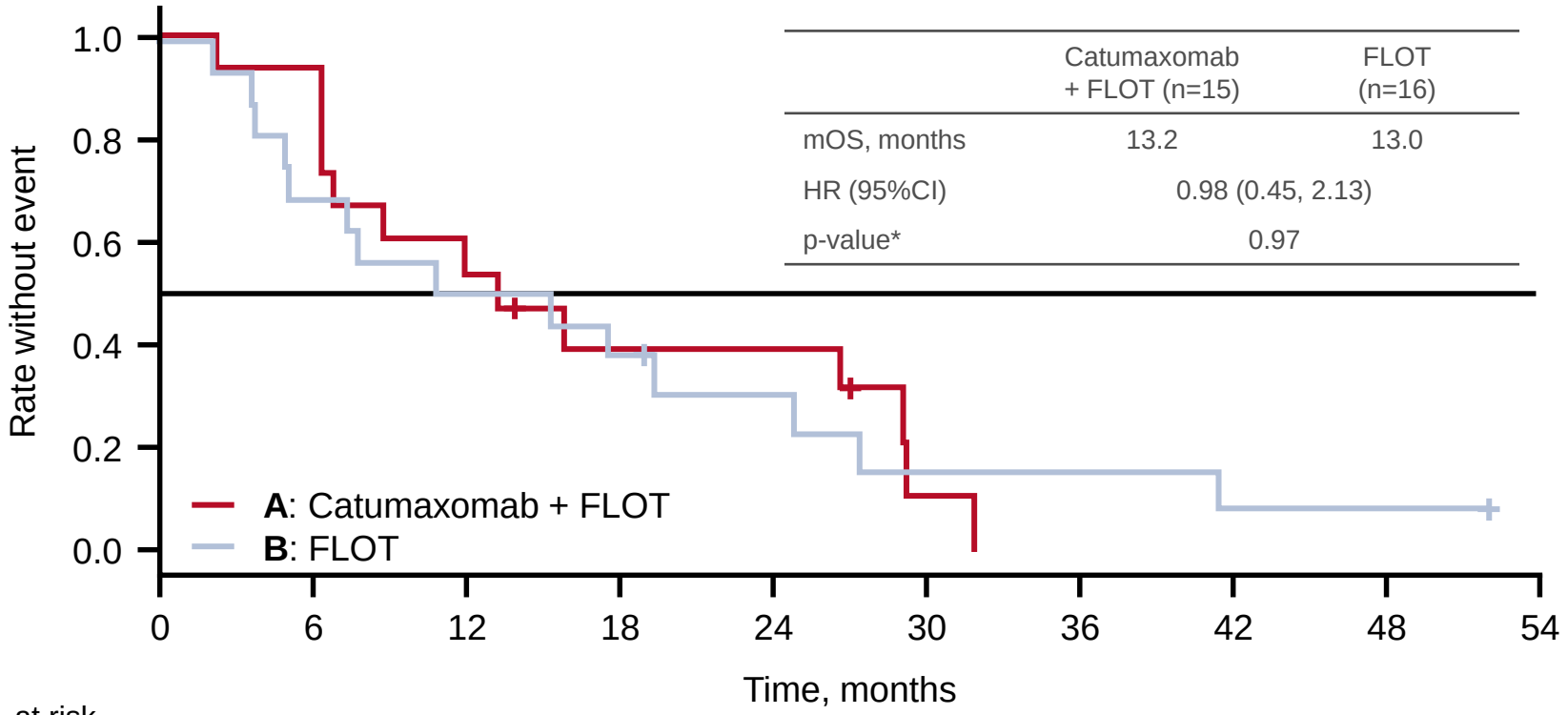
Lordick F, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 4

4: Intraperitoneal immunotherapy with the bispecific anti-EpCAM x anti-CD3 directed antibody catumaxomab for patients with peritoneal carcinomatosis from gastric cancer: Final results of a randomized phase II AIO trial – Lordick F, et al

Key results (cont.)

OS

	Catumaxomab + FLOT (n=15)	FLOT (n=16)
mOS, months	13.2	13.0
HR (95%CI)	0.98 (0.45, 2.13)	
p-value*	0.97	



No. at risk

A:	15	14	8	5	5	1	0	0	0
B:	16	11	8	6	4	2	2	1	1

*Log-rank t-test with FLOT as reference

Lordick F, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 4

4: Intraperitoneal immunotherapy with the bispecific anti-EpCAM x anti-CD3 directed antibody catumaxomab for patients with peritoneal carcinomatosis from gastric cancer: Final results of a randomized phase II AIO trial – Lordick F, et al

Key results (cont.)

- Grade 3/4 AEs occurring with catumaxomab included nausea (15%), fever (23%), abdominal pain (31%) and elevated liver enzymes – gGT (31%), bilirubin (23%)
- 4 (29%) patients experienced SAEs with catumaxomab
- 3 (23%) patients experienced SAEs with FLOT after catumaxomab and 5 (29%) with FLOT alone

Conclusions

- **In patients with peritoneal carcinomatosis from gastric cancer there was a trend towards superior complete remission rate with catumaxomab IP followed by FLOT vs. FLOT alone**
  - **However, the difference between the groups was not significant**
- **PFS and OS rates were similar between the groups and within the expected range for patients with Stage IV gastric cancer**
- **Catumaxomab followed by FLOT was tolerable in this patient population and FLOT after catumaxomab was equally tolerated as FLOT alone**

Lordick F, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 4

5: RAINFALL: A randomized, double-blind, placebo-controlled phase III study of cisplatin (Cis) plus capecitabine (Cape) or 5FU with or without ramucirumab (RAM) as first-line therapy in patients with metastatic gastric or gastroesophageal junction (G-GEJ) adenocarcinoma – Fuchs CS, et al

Study objective

- To investigate the efficacy and safety of ramucirumab + CT vs. placebo + CT as 1L therapy for patients with metastatic gastric/GEJ cancer

Key patient inclusion criteria

- Metastatic gastric/GEJ cancer
- No prior systemic therapy
- HER2 negative
- ECOG PS 0/1

(n=645)

R 1:1

Ramucirumab 8 mg/kg IV D1, D8 + cisplatin* + capecitabine† q3w (n=326) → PD/ toxicity

Placebo + cisplatin* + capecitabine† q3w (n=319) → PD/ toxicity

Stratification

- ECOG PS (0 vs. 1)
- Primary tumour location (gastric vs. GEJ)
- Disease measurability
- Geographical region (Japan vs. other countries)

PRIMARY ENDPOINT

- PFS (investigator assessed)

SECONDARY ENDPOINTS

- OS, ORR, DoR, safety, QoL, PK profile

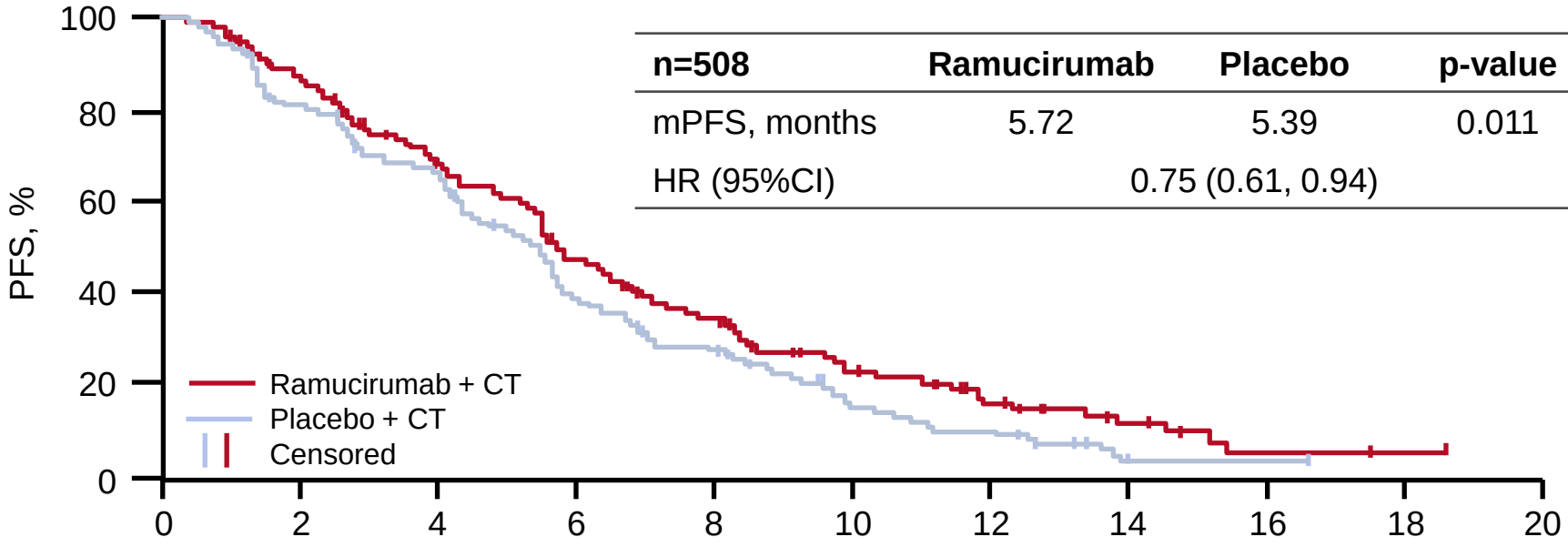
*Cisplatin 80 mg/m^2 IV D1 (6 cycles); †capecitabine 1000 mg/m^2 oral bid D1–14 or 5FU 800 mg/m^2/day IV D1–5 for patients unable to swallow capecitabine

Fuchs CS, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 5

5: RAINFALL: A randomized, double-blind, placebo-controlled phase III study of cisplatin (Cis) plus capecitabine (Cape) or 5FU with or without ramucirumab (RAM) as first-line therapy in patients with metastatic gastric or gastroesophageal junction (G-GEJ) adenocarcinoma – Fuchs CS, et al

Key results

PFS (investigator assessed)



n=508	Ramucirumab	Placebo	p-value
mPFS, months	5.72	5.39	0.011
HR (95%CI)		0.75 (0.61, 0.94)	

No. at risk

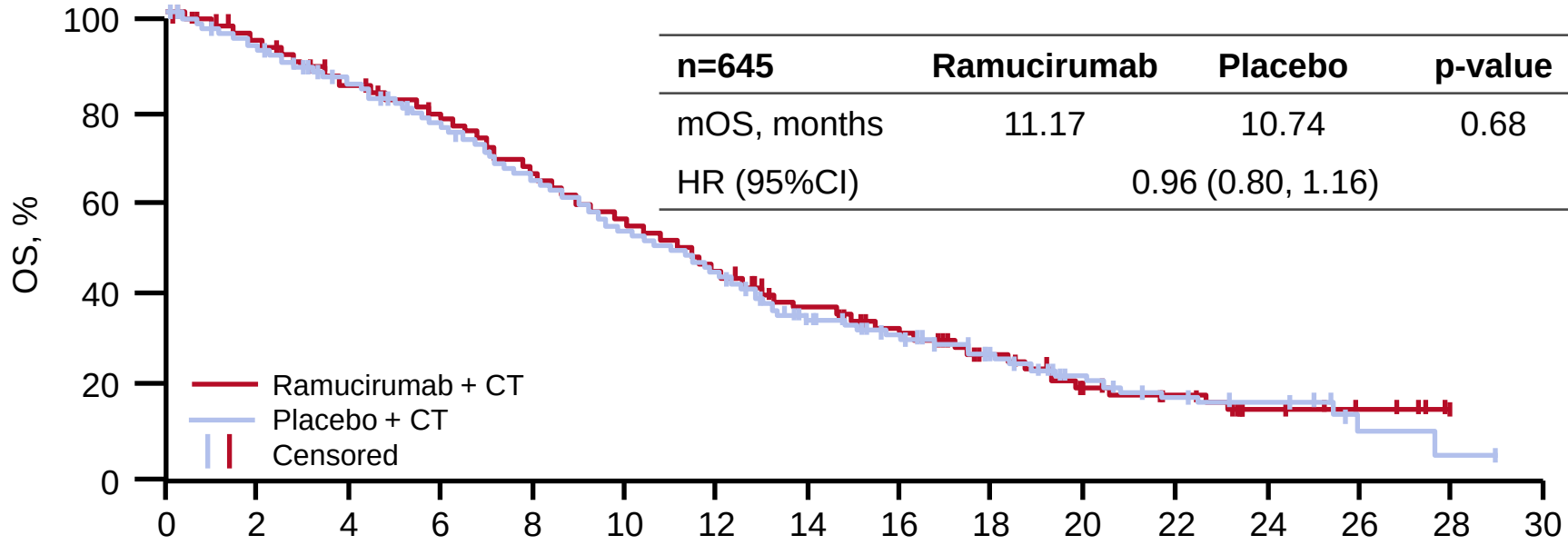
Ramucirumab	255	194	144	89	60	29	15	7	2	1	0
Placebo	253	179	141	78	51	21	12	1	1	0	0

Fuchs CS, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 5

5: RAINFALL: A randomized, double-blind, placebo-controlled phase III study of cisplatin (Cis) plus capecitabine (Cape) or 5FU with or without ramucirumab (RAM) as first-line therapy in patients with metastatic gastric or gastroesophageal junction (G-GEJ) adenocarcinoma – Fuchs CS, et al

Key results (cont.)

OS



n=645	Ramucirumab	Placebo	p-value
mOS, months	11.17	10.74	0.68
HR (95%CI)		0.96 (0.80, 1.16)	

No. at risk

Ramucirumab	326	301	267	237	198	166	127	99	75	54	31	21	10	8	1	0
Placebo	319	290	256	225	184	152	125	89	68	52	33	17	11	5	1	0

Fuchs CS, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 5

5: RAINFALL: A randomized, double-blind, placebo-controlled phase III study of cisplatin (Cis) plus capecitabine (Cape) or 5FU with or without ramucirumab (RAM) as first-line therapy in patients with metastatic gastric or gastroesophageal junction (G-GEJ) adenocarcinoma – Fuchs CS, et al

Key results (cont.)

Grade ≥3 TEAEs occurring in ≥5% of patients, %	Ramucirumab + CT (n=326)	Placebo + CT (n=319)
Neutropenia	26	27
Anaemia	12	14
Hypertension	9.9	1.6
Hand-foot syndrome	8.7	3.8
Fatigue	8.4	7.9
Thrombocytopenia	7.7	3.5
Nausea	6.8	8.3
Vomiting	6.5	9.8
Decreased appetite	6.5	3.2
Abdominal pain	5.6	3.5
Leukopenia	5.0	5.4
Diarrhoea	4.6	7.3
Febrile neutropenia	3.7	5.1

Fuchs CS, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 5

5: RAINFALL: A randomized, double-blind, placebo-controlled phase III study of cisplatin (Cis) plus capecitabine (Cape) or 5FU with or without ramucirumab (RAM) as first-line therapy in patients with metastatic gastric or gastroesophageal junction (G-GEJ) adenocarcinoma – Fuchs CS, et al

Key results (cont.)

Best overall response, %	Ramucirumab + CT (n=326)	Placebo + CT (n=319)	Stratified p-value
CR	1.2	1.6	
PR	40	35	
SD	41	40	
PD	7.1	12	
ORR (CR + PR)	41	36	0.17
DCR (CR + PR + SD)	82	77	0.10

Conclusions

- In patients with metastatic gastric/GEJ adenocarcinoma, the addition of ramucirumab to 1L CT reduced the risk of disease progression or death by 25%, but with no improvement in OS
- No new safety signals were observed

Fuchs CS, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 5

CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

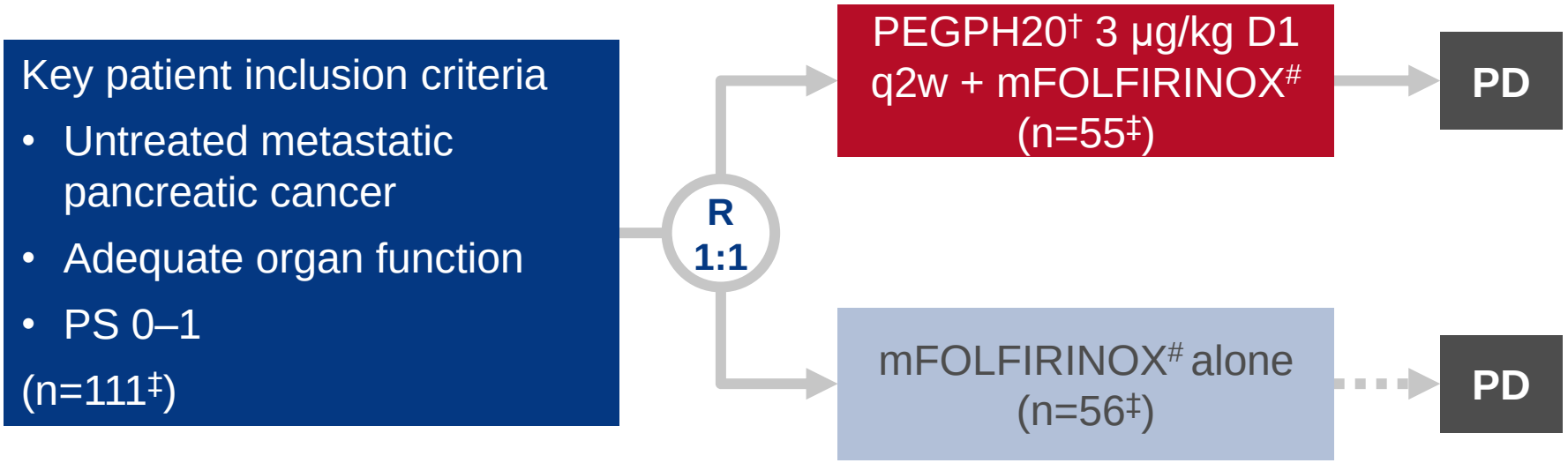
Cancers of the pancreas, small bowel and hepatobiliary tract

PANCREATIC CANCER

208: A phase IB/II randomized study of mFOLFIRINOX (mFFOX) + pegylated recombinant human hyaluronidase (PEGPH20) versus mFFOX alone in patients with good performance status metastatic pancreatic adenocarcinoma (mPC): SWOG S1313 (NCT #01959139) – Ramanathan R, et al

Study objective

- To assess the efficacy and safety of PEGH20* in combination with mFOLFIRINOX in patients with metastatic pancreatic cancer (planned interim analysis)



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

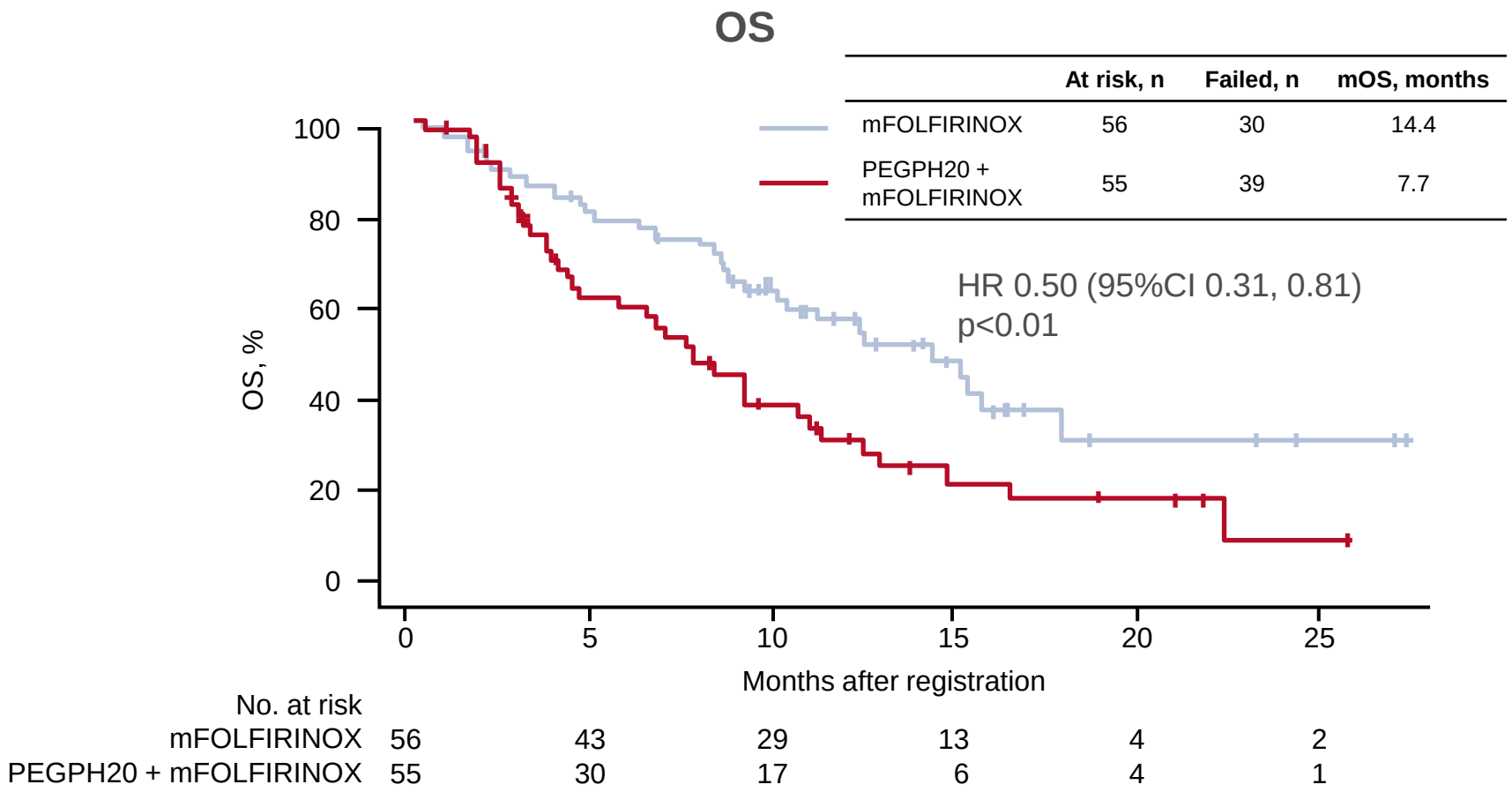
- PFS, response rate, treatment exposure, toxicity

*Pegylated recombinant human hyaluronidase that degrades hyaluronan; †a protocol amendment added LMWH prophylaxis to the PEGPH20 arm; ‡planned n=138 per arm (total n=276); #no bolus 5FU

Ramanathan R, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 208

208: A phase IB/II randomized study of mFOLFIRINOX (mFFOX) + pegylated recombinant human hyaluronidase (PEGPH20) versus mFFOX alone in patients with good performance status metastatic pancreatic adenocarcinoma (mPC): SWOG S1313 (NCT #01959139) – Ramanathan R, et al

Key results



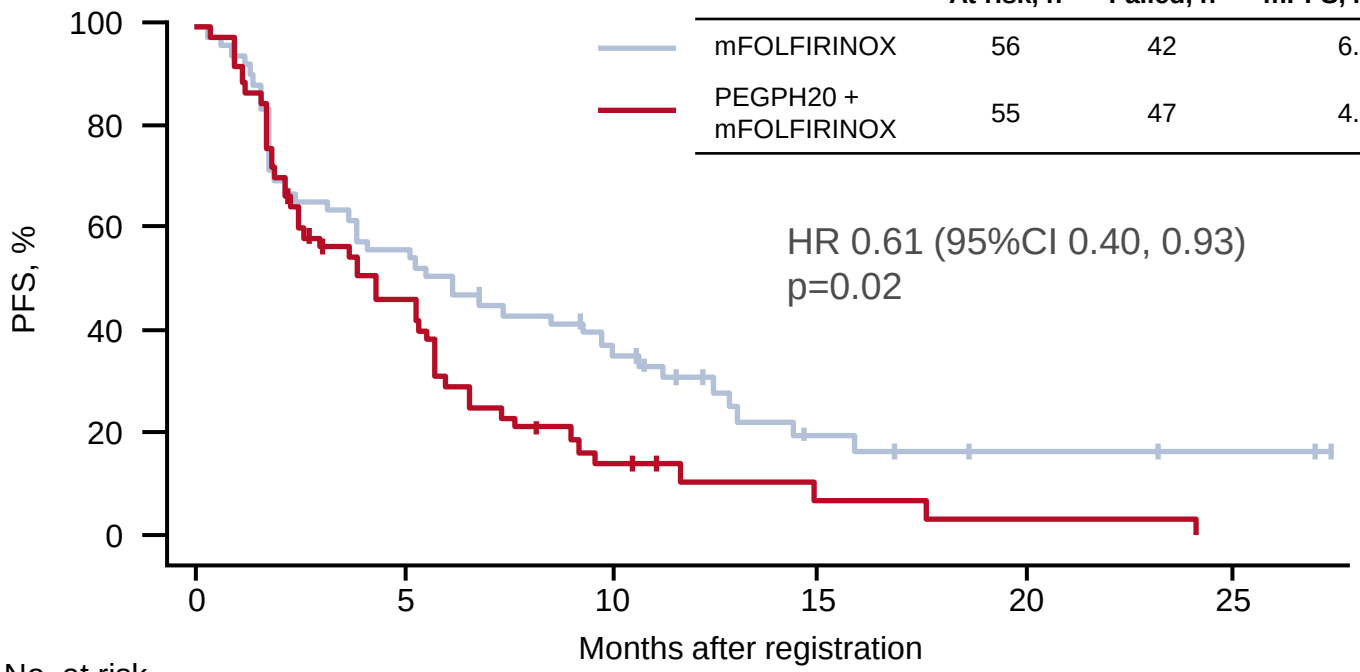
Ramanathan R, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 208

208: A phase IB/II randomized study of mFOLFIRINOX (mFFOX) + pegylated recombinant human hyaluronidase (PEGPH20) versus mFFOX alone in patients with good performance status metastatic pancreatic adenocarcinoma (mPC): SWOG S1313 (NCT #01959139) – Ramanathan R, et al

Key results (cont.)

PFS

	At risk, n	Failed, n	mPFS, months
mFOLFIRINOX	56	42	6.2
PEGPH20 + mFOLFIRINOX	55	47	4.3



No. at risk						
mFOLFIRINOX	56	31	19	6	3	2
PEGPH20 + mFOLFIRINOX	55	22	6	2	1	0

Ramanathan R, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 208

208: A phase IB/II randomized study of mFOLFIRINOX (mFFOX) + pegylated recombinant human hyaluronidase (PEGPH20) versus mFFOX alone in patients with good performance status metastatic pancreatic adenocarcinoma (mPC): SWOG S1313 (NCT #01959139) – Ramanathan R, et al

Key results (cont.)

	PEGPH20 + mFOLFIRINOX	mFOLFIRINOX alone
Response rate, % (95%CI)	33 (21, 47)	45 (31, 59)
Treatment exposure, median cycles (range)	4 (0–43)	8 (0–37)
p-value	p=0.05	

Selected AEs (grade 3–4 unless stated otherwise), %	PEGPH20 + mFOLFIRINOX (n=54)	mFOLFIRINOX alone (n=51)
Diarrhoea	24	19
Dehydration	8	13
Fatigue	20	11
Nausea	25	15
Vomiting	22	13
TE events (all grades)	18	4
TE events after LMWH	9	5

- One grade 5 AE occurred in the mFOLFIRINOX arm due to sepsis

Ramanathan R, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 208

208: A phase IB/II randomized study of mFOLFIRINOX (mFFOX) + pegylated recombinant human hyaluronidase (PEGPH20) versus mFFOX alone in patients with good performance status metastatic pancreatic adenocarcinoma (mPC): SWOG S1313 (NCT #01959139) – Ramanathan R, et al

Conclusions

- In patients with metastatic pancreatic cancer, survival with mFOLFIRINOX alone was superior to PEGPH20 + mFOLFIRINOX
  - Adding PEGPH20 to mFOLFIRINOX seems detrimental resulting in increased toxicity
  - There was less mFOLFIRINOX treatment exposure in the PEGPH20 arm
- In contrast, a previous study reported favourable results with PEGPH20 + nab-paclitaxel/gemcitabine[1]
- Preclinical studies are planned to analyse the hyaluronan content in tumour cells

[1]Hingorani SR, et al. J Clin Oncol 2017;[epub ahead of print].

Cancers of the pancreas, small bowel and hepatobiliary tract

HEPATOCELLULAR CARCINOMA

207: Cabozantinib (C) versus placebo (P) in patients (pts) with advanced hepatocellular carcinoma (HCC) who have received prior sorafenib: results from the randomized phase 3 CELESTIAL trial – Abou-Alfa G, et al

Study objective

- To assess the efficacy and safety of cabozantinib vs. placebo in patients with advanced HCC after prior systemic therapy

Key patient inclusion criteria

- Advanced HCC
- Child-Pugh score A
- Received prior sorafenib
- Progressed after ≥1 prior systemic treatment for HCC
- Received ≤2 prior systemic regimens for advanced HCC
- ECOG PS 0–1

(n=760)

R 2:1

Cabozantinib 60 mg/day (n=470) → **Loss of clinical benefit/ toxicity**

Stratification

- Disease aetiology (HBV, HCV, other)
- Geographic region (Asia, other)
- Presence of extrahepatic spread and/or macrovascular invasion (EHS/MVI)

Placebo (n=237) → **Loss of clinical benefit/ toxicity**

PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

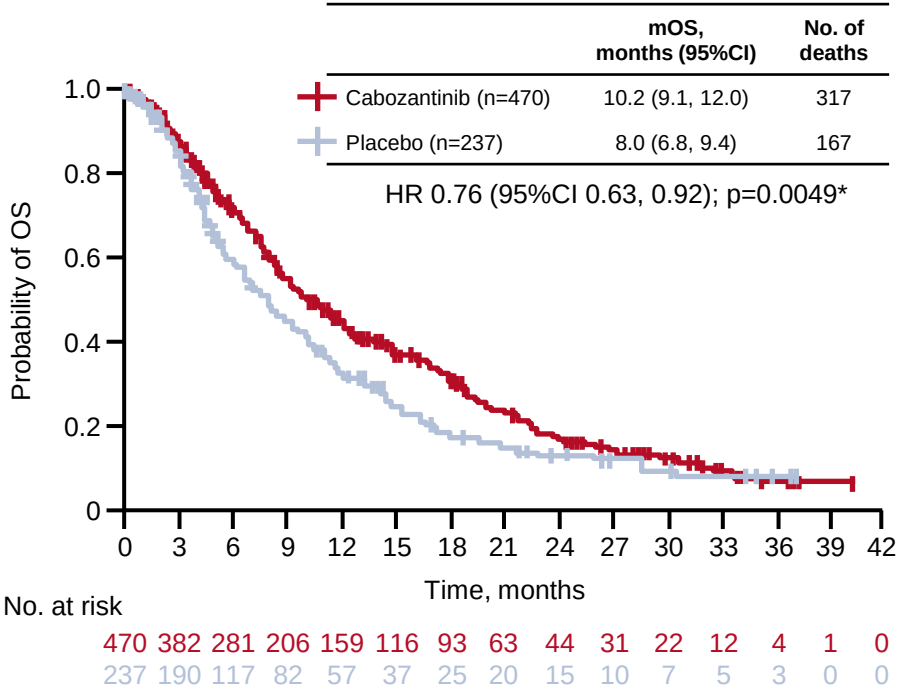
- PFS, ORR

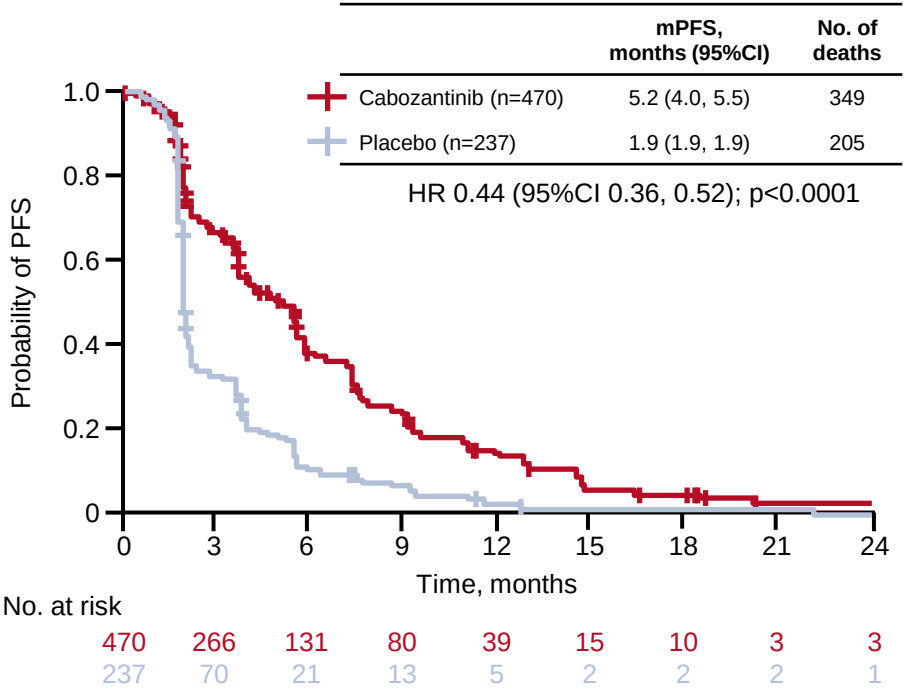
Abou-Alfa G, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 207

207: Cabozantinib (C) versus placebo (P) in patients (pts) with advanced hepatocellular carcinoma (HCC) who have received prior sorafenib: results from the randomized phase 3 CELESTIAL trial – Abou-Alfa G, et al

Key results

OS and PFS





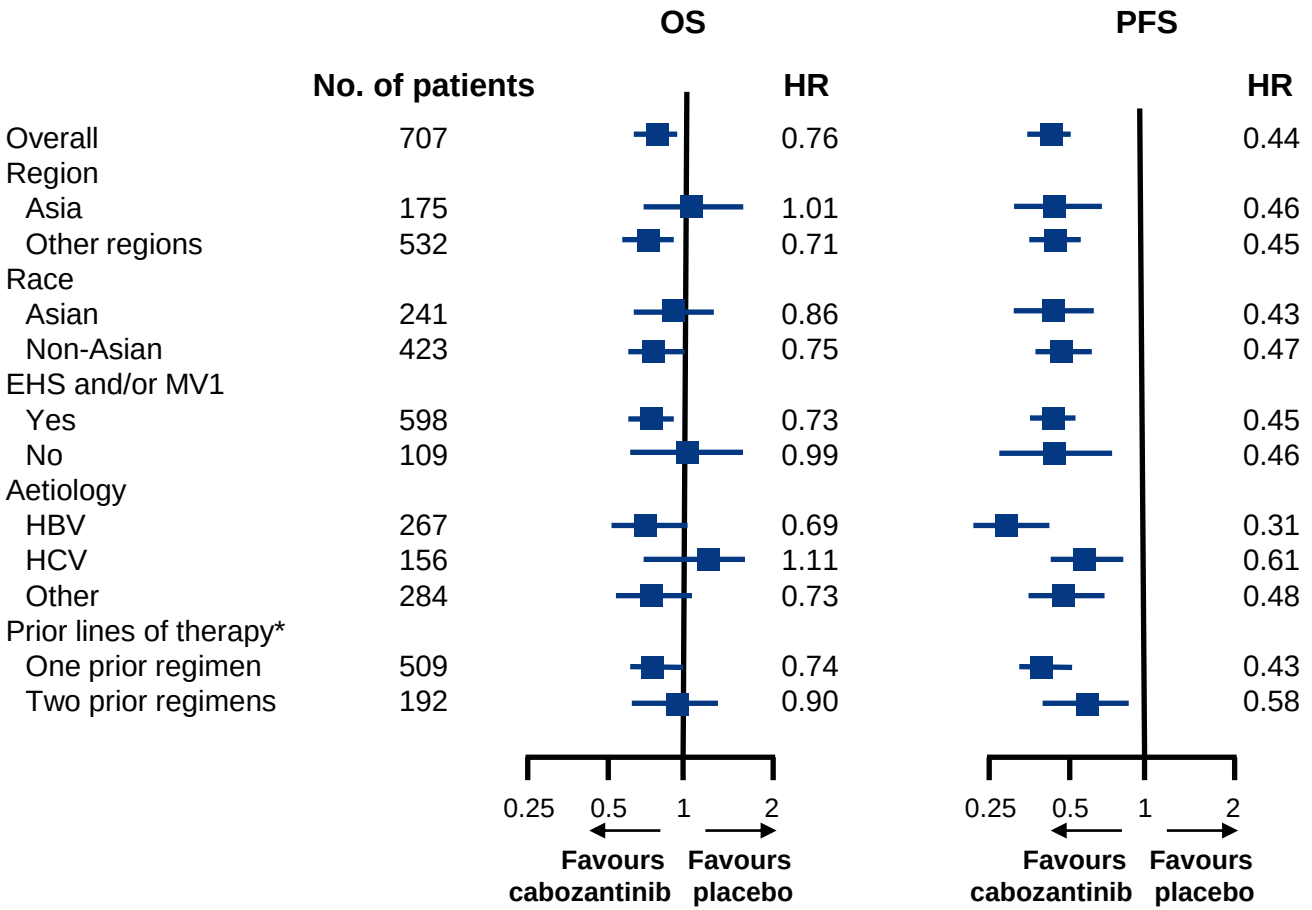
*Critical p-value ≤0.021 for second interim analysis

Abou-Alfa G, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 207

207: Cabozantinib (C) versus placebo (P) in patients (pts) with advanced hepatocellular carcinoma (HCC) who have received prior sorafenib: results from the randomized phase 3 CELESTIAL trial – Abou-Alfa G, et al

Key results (cont.)

OS and PFS in subgroups



*Prior systemic anticancer regimens for advanced HCC

Abou-Alfa G, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 207

207: Cabozantinib (C) versus placebo (P) in patients (pts) with advanced hepatocellular carcinoma (HCC) who have received prior sorafenib: results from the randomized phase 3 CELESTIAL trial – Abou-Alfa G, et al

Key results (cont.)

	Cabozantinib (n=467)	Placebo (n=237)
Median duration of exposure, months (range)	3.8 (0.1–37.3)	2.0 (0–27.2)
Median average daily dose, mg	35.8	58.9
Any dose reduction, %	62	13
Discontinuation due to TRAEs, %	16	3

Grade 3/4 AEs, %	Cabozantinib (n=467)	Placebo (n=237)
Any	68	36
Palmar-plantar erythrodysesthesia	17	0
Hypertension	16	2
AST increased	12	37
Fatigue	10	4
Diarrhoea	10	2
Asthenia	7	2
Decreased appetite	6	<1
Anaemia	4	5

Abou-Alfa G, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 207

207: Cabozantinib (C) versus placebo (P) in patients (pts) with advanced hepatocellular carcinoma (HCC) who have received prior sorafenib: results from the randomized phase 3 CELESTIAL trial – Abou-Alfa G, et al

Conclusions

- In patients with advanced HCC, cabozantinib significantly improved OS, PFS and ORR after prior systemic anticancer therapy
- The safety profile of cabozantinib was acceptable and rate of discontinuation due to TRAEs was low
- Cabozantinib may be a new treatment option for patients with advanced HCC after prior systemic anticancer therapy

Abou-Alfa G, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 207

Cancers of the pancreas, small bowel and hepatobiliary tract

BILIARY TRACT CANCER

205: Randomized phase III study of gemcitabine plus S-1 combination therapy versus gemcitabine plus cisplatin combination therapy in advanced biliary tract cancer: A Japan Clinical Oncology Group study (JCOG1113, FUGA-BT) – Morizane C, et al

Study objective

- To evaluate the non-inferiority of gemcitabine + S-1 vs. gemcitabine + cisplatin (SoC) in terms of OS, in patients with advanced biliary tract cancer

Key patient inclusion criteria

- Unresectable or recurrent biliary tract adenocarcinoma
- Treatment-naïve except surgery and biliary drainage
- No previous CT or RT
- Absence of watery diarrhoea
- ECOG PS 0–1

(n=354)

R

Gemcitabine† + S-1 (n=179) → PD

Stratification

- Primary tumour site (gall bladder vs. other)
- History of primary tumour resection (yes vs. no)
- Institution

Gemcitabine‡ + cisplatin (n=175) → PD

PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR, safety

†Gemcitabine 1000 mg/m^2 D1, D8 + S-1 60, 80 or 100 mg/body/day D1–14 q3w; ‡gemcitabine 1000 mg/m^2 + cisplatin 25 mg/m^2 D1, D8 q3w

Morizane C, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 205

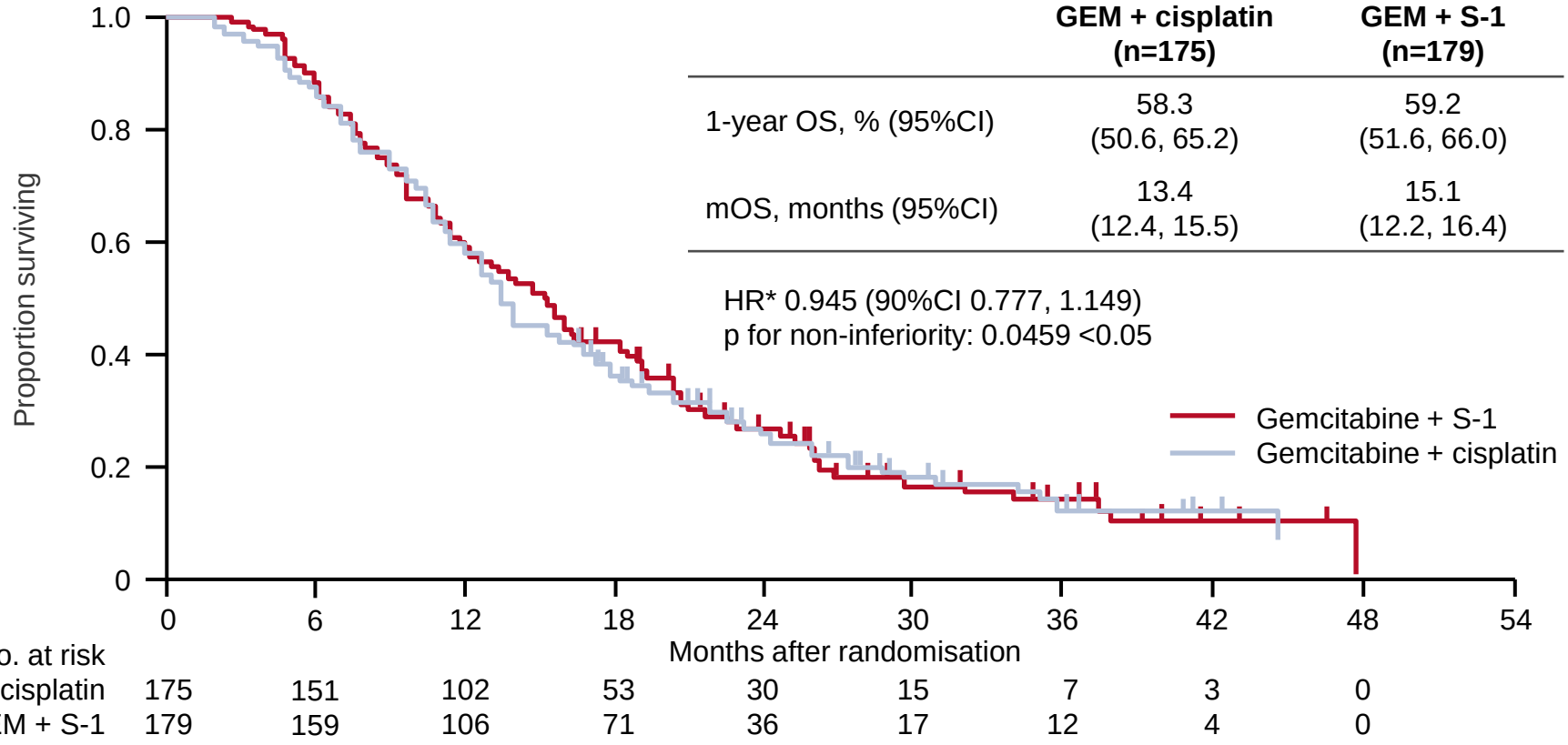
205: Randomized phase III study of gemcitabine plus S-1 combination therapy versus gemcitabine plus cisplatin combination therapy in advanced biliary tract cancer: A Japan Clinical Oncology Group study (JCOG1113, FUGA-BT) – Morizane C, et al

Key results

OS

	GEM + cisplatin (n=175)	GEM + S-1 (n=179)
1-year OS, % (95%CI)	58.3 (50.6, 65.2)	59.2 (51.6, 66.0)
mOS, months (95%CI)	13.4 (12.4, 15.5)	15.1 (12.2, 16.4)

HR* 0.945 (90%CI 0.777, 1.149)
p for non-inferiority: 0.0459 <0.05



No. at risk									
GEM + cisplatin	175	151	102	53	30	15	7	3	0
GEM + S-1	179	159	106	71	36	17	12	4	0

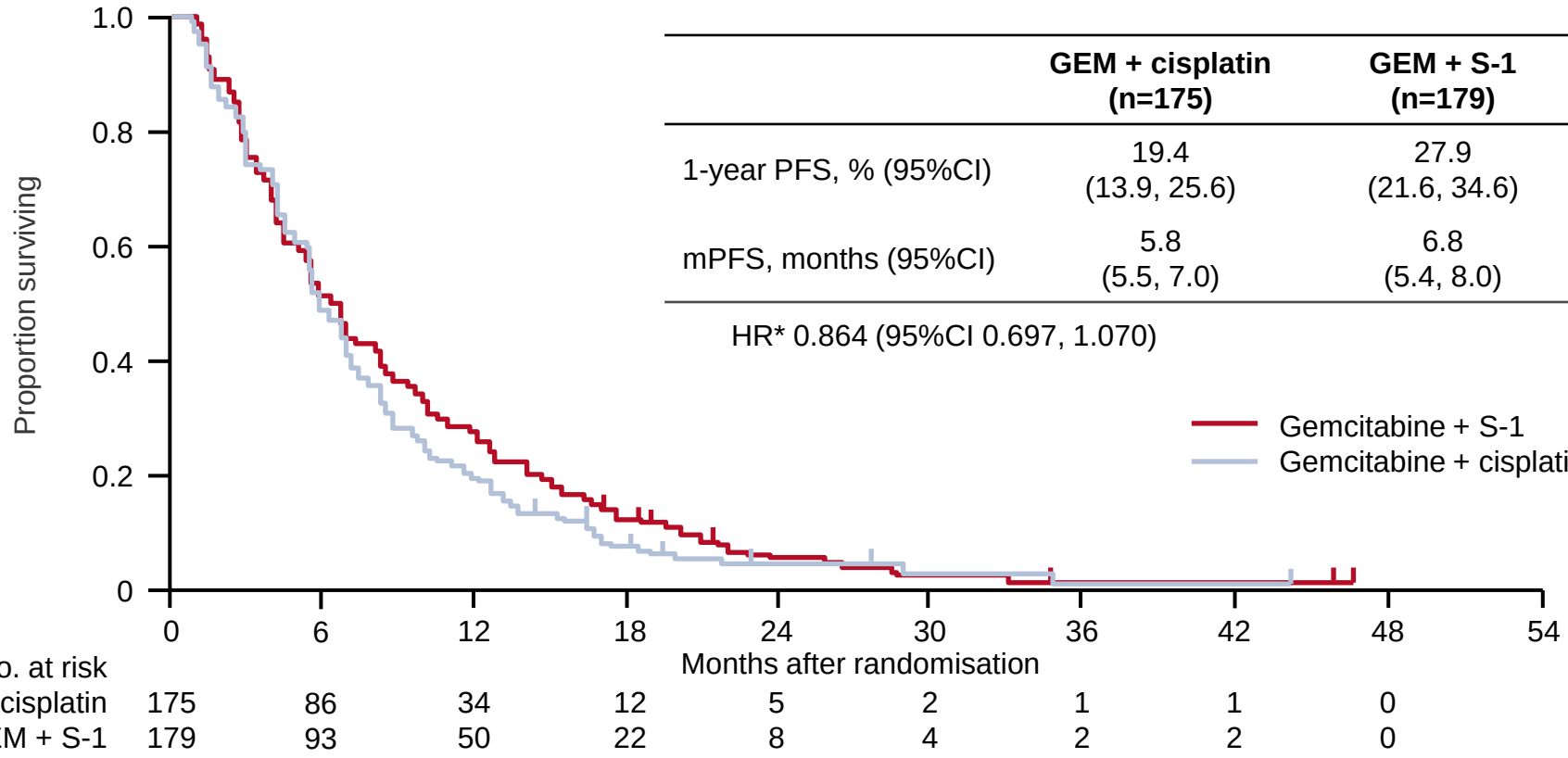
GEM, gemcitabine. *Cox proportional model stratified by primary tumour site and history of primary tumour resection

Morizane C, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 205

205: Randomized phase III study of gemcitabine plus S-1 combination therapy versus gemcitabine plus cisplatin combination therapy in advanced biliary tract cancer: A Japan Clinical Oncology Group study (JCOG1113, FUGA-BT) – Morizane C, et al

Key results (cont.)

PFS



	GEM + cisplatin (n=175)	GEM + S-1 (n=179)
1-year PFS, % (95%CI)	19.4 (13.9, 25.6)	27.9 (21.6, 34.6)
mPFS, months (95%CI)	5.8 (5.5, 7.0)	6.8 (5.4, 8.0)

HR* 0.864 (95%CI 0.697, 1.070)

No. at risk									
GEM + cisplatin	175	86	34	12	5	2	1	1	0
GEM + S-1	179	93	50	22	8	4	2	2	0

*Unstratified Cox proportional model

Morizane C, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 205

205: Randomized phase III study of gemcitabine plus S-1 combination therapy versus gemcitabine plus cisplatin combination therapy in advanced biliary tract cancer: A Japan Clinical Oncology Group study (JCOG1113, FUGA-BT) – Morizane C, et al

Key results (cont.)

	Gemcitabine + S-1 (n=141)	Gemcitabine + cisplatin (n=148)	p-value*
ORR, % (95%CI)	29.8 (22.4, 38.1)	32.4 (25.0, 40.6)	0.70
CR, n (%)	2 (1)	0 (0)	-
PR, n (%)	40 (28)	48 (32)	-
SD, n (%)	76 (54)	74 (50)	-
PD, n (%)	19 (13)	21 (14)	-
NE, n (%)	4 (3)	5 (3)	-

Grade 3–4 AEs (>5% patients), %	Gemcitabine + S-1 (n=177)	Gemcitabine + cisplatin (n=171)
WBC decrease	24.9	31.6
Anaemia	6.2	24.0
Platelet count decreased	7.3	16.4
Neutrophil count decreased	59.9	60.8
Rash maculopapular	6.2	0
Biliary tract infection	20.9	19.3
Fatigue	5.6	4.7
Anorexia	5.6	5.8

*Two-sided p-value by Fisher's exact test

Morizane C, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 205

205: Randomized phase III study of gemcitabine plus S-1 combination therapy versus gemcitabine plus cisplatin combination therapy in advanced biliary tract cancer: A Japan Clinical Oncology Group study (JCOG1113, FUGA-BT) – Morizane C, et al

Key results (cont.)

Clinically significant AEs*, n (%)	Gemcitabine + S-1 (n=177)	Gemcitabine + cisplatin (n=171)
Grade ≥2	**53 (29.9)**	**60 (35.1)**
Grade ≥3	19 (10.7)	14 (8.2)
Grade ≥4	1 (0.6)	0 (0)

Conclusions

- **In patients with advanced biliary tract cancer, gemcitabine + S-1 demonstrated non-inferiority in OS to gemcitabine + cisplatin**
- **Gemcitabine + S-1 had good tolerability and may be considered as a new convenient treatment option of SoC without hydration in this setting**

*Grade ≥2 AEs of fatigue, nausea, oral mucositis, anorexia, vomiting or diarrhoea

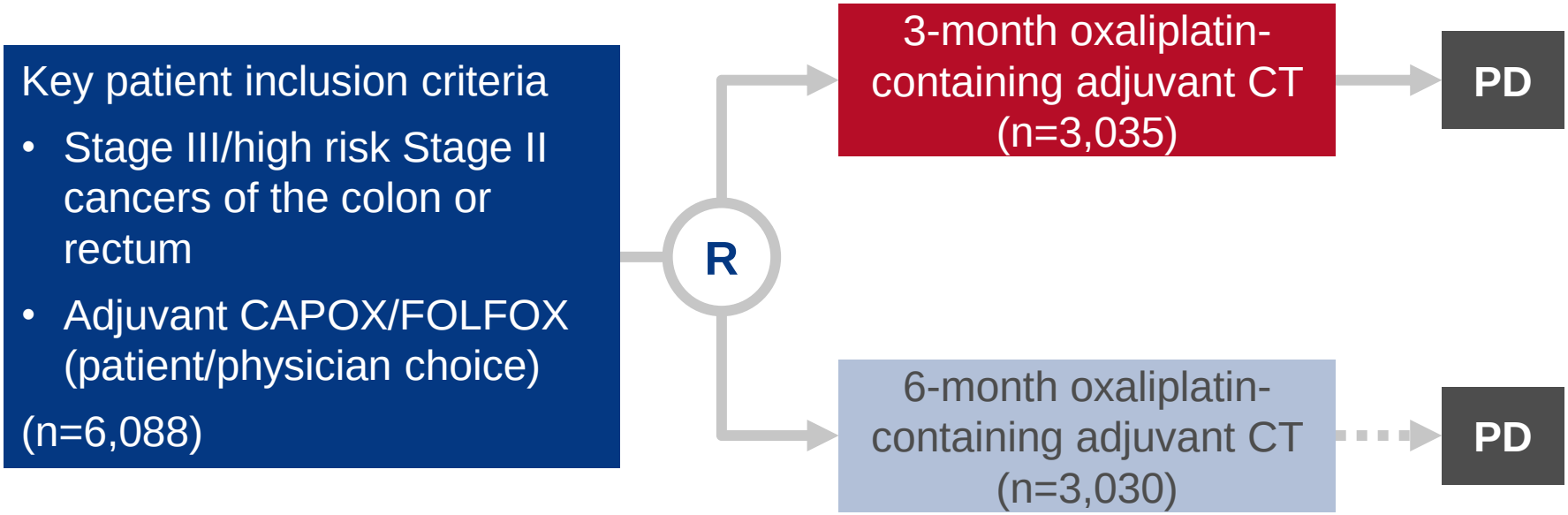
Morizane C, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 205

CANCERS OF THE COLON, RECTUM AND ANUS

558: SCOT: Tumor sidedness and the influence of chemotherapy duration on DFS – Saunders M, et al

Study objective

- To determine whether tumour sidedness had an impact on DFS in patients with CRC receiving 3- vs. 6-months of oxaliplatin-containing adjuvant CT (SCOT study sub-analysis)



PRIMARY ENDPOINT

- 3- year DFS
- Sidedness information was available for 3,219 patients (right n=1,207, left n=2,012)*

*Tumour locations were collated from pathological reports (information was not recorded at randomisation)

Saunders M, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 558

558: SCOT: Tumor sidedness and the influence of chemotherapy duration on DFS – Saunders M, et al

Key results

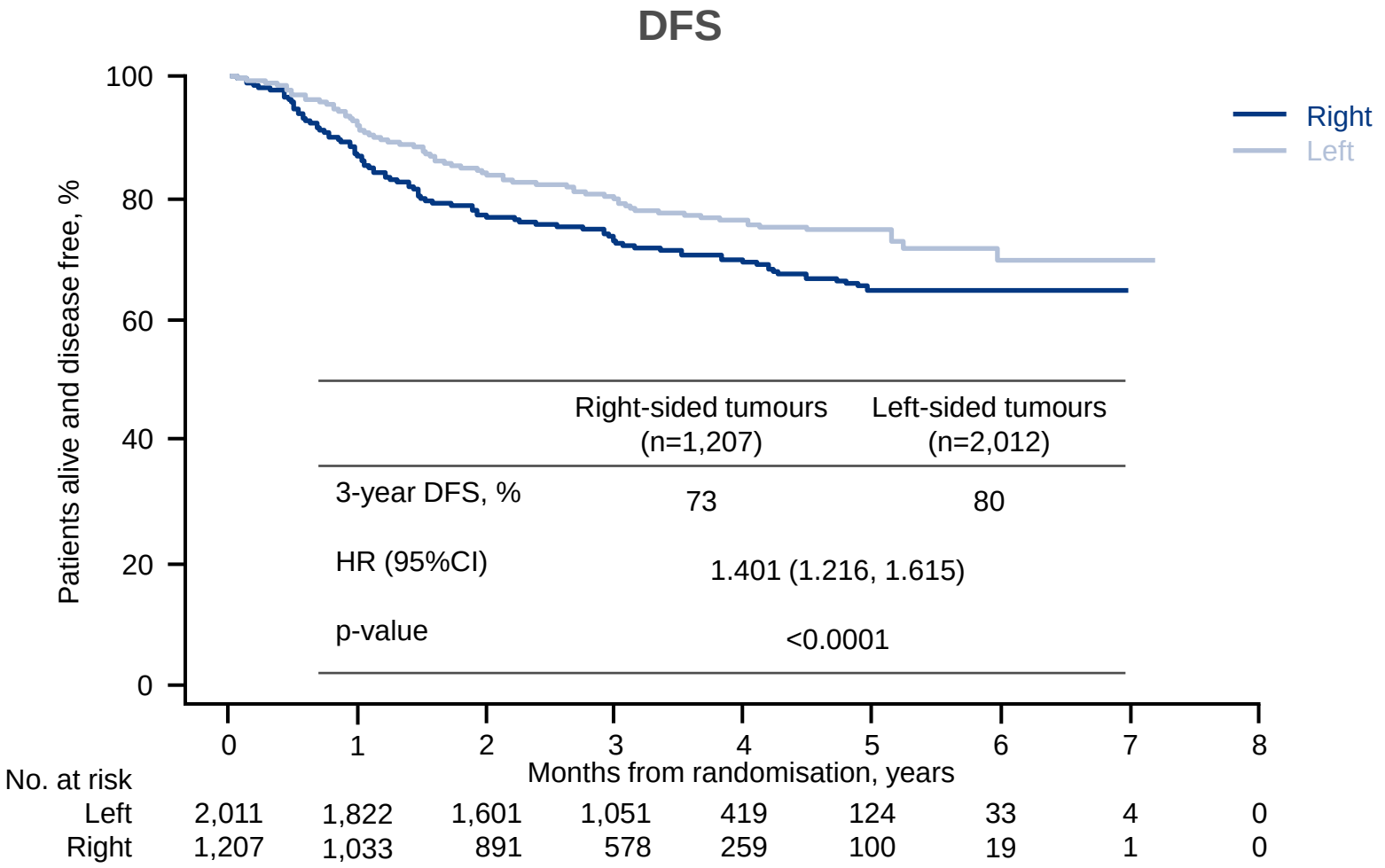
Patient information at 3-year follow-up	Right-sided tumours (n=1,207)	Left-sided tumours (n=2,012)	p-value*
Median age, years	66	64	<0.001
Male, %	53	66	<0.001
T2, %	41	24	<0.001
Stage II, %	17	21	0.001

*Left vs. right

Saunders M, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 558

558: SCOT: Tumor sidedness and the influence of chemotherapy duration on DFS – Saunders M, et al

Key results (cont.)



Saunders M, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 558

558: SCOT: Tumor sidedness and the influence of chemotherapy duration on DFS – Saunders M, et al

Key results (cont.)

	HR (95%CI)	p-value
3-year DFS by tumour sidedness*	1.401 (1.216, 1.615)	<0.0001
3-year DFS by tumour sidedness*, adjusting for T and N-stage	1.215 (1.051, 1.404)	0.009
3-year DFS by CT duration†		
Right-sided tumours	1.049 (0.849, 1.296)	0.327
Left-sided tumours	0.910 (0.753, 1.099)	

*Left- vs. right-sided tumours; †3 vs. 6 months

Saunders M, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 558

558: SCOT: Tumor sidedness and the influence of chemotherapy duration on DFS – Saunders M, et al

Conclusions

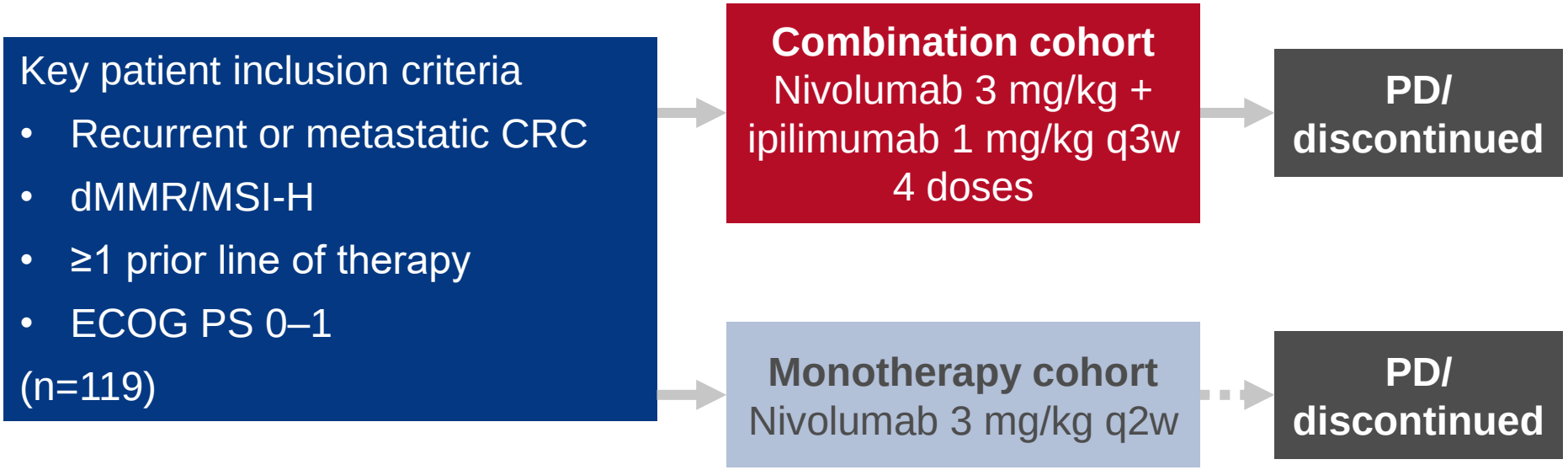
- **In patients with CRC receiving 3- vs. 6-months of adjuvant CT, those with right-sided tumours had significantly worse DFS than those with left-sided tumours**
  - **This is the first study to show that unselected patients with right- vs. left-sided tumours had a worse DFS**
- **This implies that prognosis is influenced primarily by greater recurrence rather than the contributing factors that influence OS**
- **Tumour sidedness did not affect the impact of CT duration (3- vs. 6-months) on DFS**

Saunders M, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 558

553: Nivolumab + ipilimumab combination in patients with DNA mismatch repair-deficient/microsatellite instability-high (dMMR/MSI-H) metastatic colorectal cancer (mCRC): First report of the full cohort from CheckMate-142 – André T, et al

Study objective

- To assess the efficacy and safety of nivolumab in combination with ipilimumab in patients with dMMR/MSI-H mCRC in CheckMate-142



PRIMARY ENDPOINT

- ORR RECIST v1.1 (investigator assessed)

SECONDARY ENDPOINTS

- ORR (BICR), DCR, DoR, PFS, OS, safety

André T, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 553

553: Nivolumab + ipilimumab combination in patients with DNA mismatch repair-deficient/microsatellite instability-high (dMMR/MSI-H) metastatic colorectal cancer (mCRC): First report of the full cohort from CheckMate-142 – André T, et al

Key results

	Nivolumab + ipilimumab (n=119)	Nivolumab (n=74)
ORR, % (95%CI)	55 (45.2, 63.8)	31 (20.8, 42.9)
BOR, %		
CR	3.4	0
PR	51.3	31.0
SD	31.0	38.0
PD	12.0	26.0
Unknown	9.0	5.0
DCR, % (95%CI)	80 (71.5, 86.6)	69 (57.1, 79.2)

- Median DoR was not reached in the nivolumab + ipilimumab cohort
- Durable responses were observed with 94% of responders having an ongoing response at data cut-off, and 83% had responses lasting ≥6 months

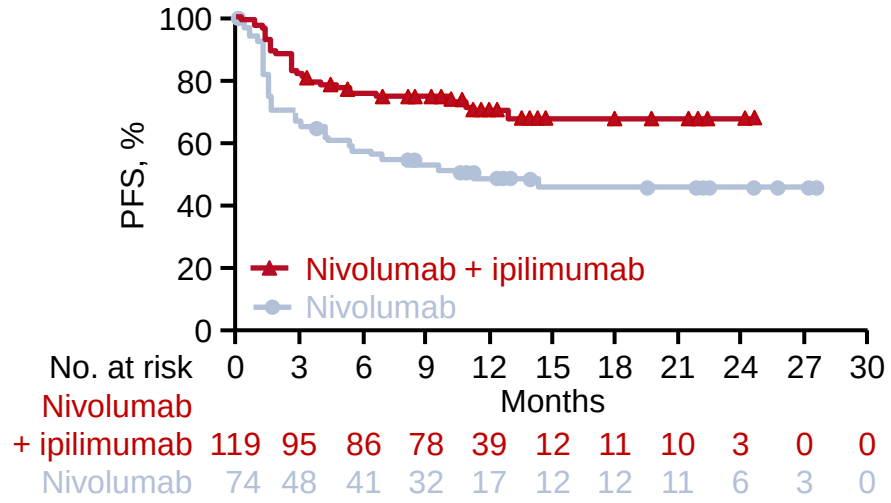
André T, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 553

553: Nivolumab + ipilimumab combination in patients with DNA mismatch repair-deficient/microsatellite instability-high (dMMR/MSI-H) metastatic colorectal cancer (mCRC): First report of the full cohort from CheckMate-142 – André T, et al

Key results (cont.)

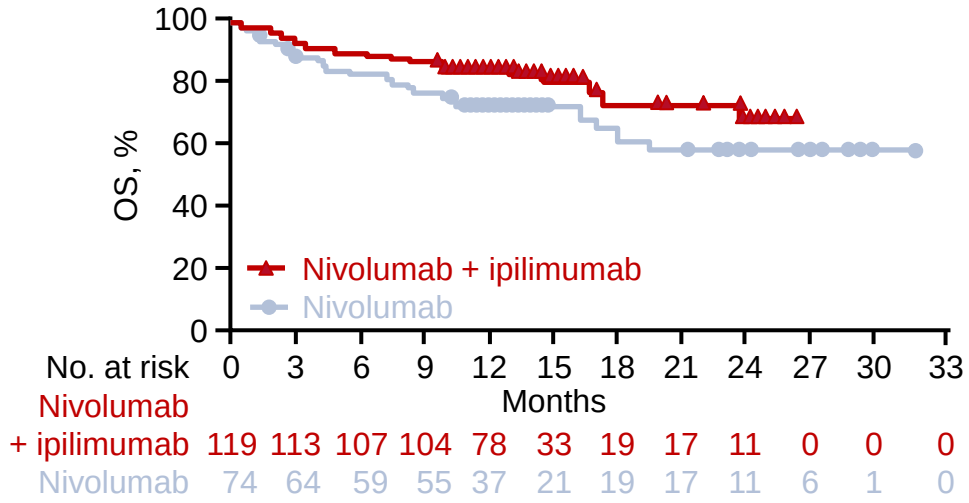
PFS

	Nivolumab + ipilimumab	Nivolumab
9-month rate, % (95%CI)	76 (67.0, 82.7)	54 (41.5, 64.5)
12-month rate, % (95%CI)	71 (61.4, 78.7)	50 (38.1, 61.4)



OS

	Nivolumab + ipilimumab	Nivolumab
9-month rate, % (95%CI)	87 (80.0, 92.2)	78 (66.2, 85.7)
12-month rate, % (95%CI)	85 (77.0, 90.2)	73 (61.5, 82.1)



André T, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 553

553: Nivolumab + ipilimumab combination in patients with DNA mismatch repair-deficient/microsatellite instability-high (dMMR/MSI-H) metastatic colorectal cancer (mCRC): First report of the full cohort from CheckMate-142 – André T, et al

Key results (cont.)

	Nivolumab + ipilimumab (n=119)[a]	
AEs, n (%)	Any grade	Grade 3–4
Any TRAE	87 (73)	38 (32)
Any serious TRAE	27 (23)	24 (20)
Any TRAE leading to discontinuation	15 (13)[b]	12 (10)
TRAE occurring in >10% of patients		
Diarrhea	26 (22)	2 (2)
Hypothyroidism	16 (13)	1 (1)
Nausea	15 (13)	1 (1)
Increased ALT	14 (12)	8 (7)
Rash	13 (11)	2 (2)
Hyperthyroidism	13 (11)	0

[a]Median follow-up 13.4 months (range 9–25); [b]Autoimmune hepatitis and acute kidney injury were the only TRAEs that led to discontinuation in >1 patient (2% each)

André T, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 553

553: Nivolumab + ipilimumab combination in patients with DNA mismatch repair-deficient/microsatellite instability-high (dMMR/MSI-H) metastatic colorectal cancer (mCRC): First report of the full cohort from CheckMate-142 – André T, et al

Conclusions

- In previously treated patients with dMMR/MSI-H mCRC, nivolumab + ipilimumab provided durable clinical benefit
- Nivolumab + ipilimumab had a manageable safety profile
- Nivolumab + ipilimumab may be a potential new treatment option for patients with previously treated dMMR/MSI-H mCRC

André T, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 553

560: A phase Ib study of safety and clinical activity of atezolizumab (A) and cobimetinib (C) in patients (pts) with metastatic colorectal cancer (mCRC) – Bendell JC, et al

Study objective

- To assess the safety and activity of atezolizumab + cobimetinib in patients with locally advanced or metastatic solid tumours, including CRC

Key patient inclusion criteria

- Chemotherapy refractory metastatic or locally advanced CRC
- PD-L1 status not an eligibility criterion
- ECOG PS 0–1

(n=84)

→ **Dose escalation**
Atezolizumab
800 mg q2w +
cobimetinib
20–60 mg/day
(21 days on/7 days off)

→ Dose expansion
Atezolizumab
800 mg q2w +
cobimetinib
60 mg/day
(21 days on/7 days off*)

→ PD

PRIMARY ENDPOINT

- Safety

SECONDARY ENDPOINTS

- ORR, DoR, PFS, OS

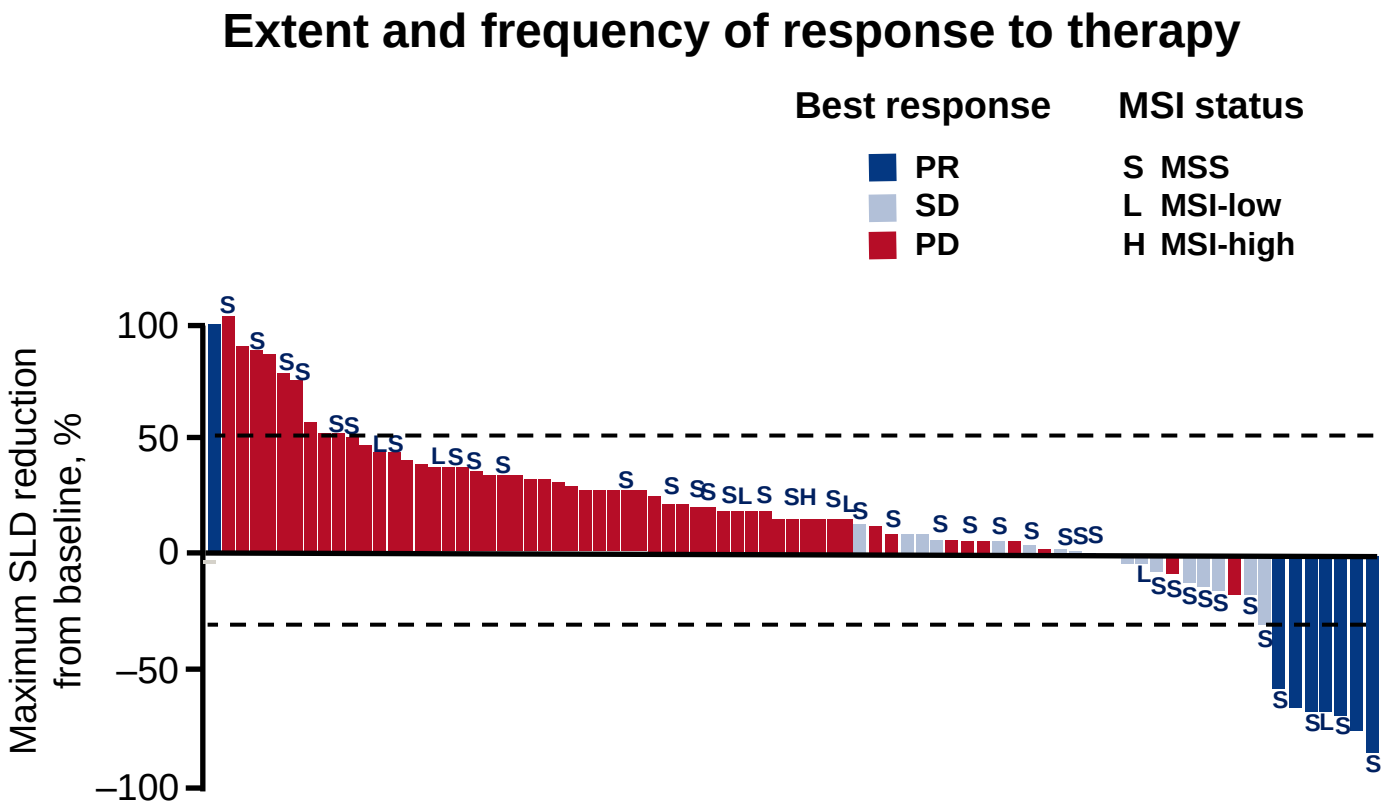
*14 days on/14 days off for patients in mCRC serial biopsy cohort (n=21)

Bendell JC, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 560

560: A phase Ib study of safety and clinical activity of atezolizumab (A) and cobimetinib (C) in patients (pts) with metastatic colorectal cancer (mCRC) – Bendell JC, et al

Key results

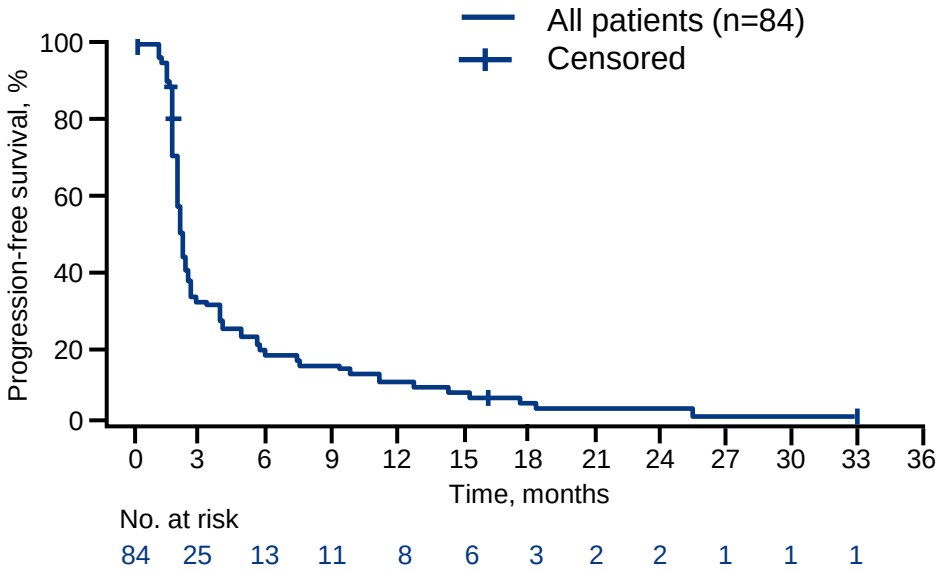
BOR, n (%)	n=84
ORR, n (%) [95%CI]	7 (8) [3, 16]
CR	0
PR	7 (8)
SD	19 (23)
DCR	36 (31)
PD	51 (61)

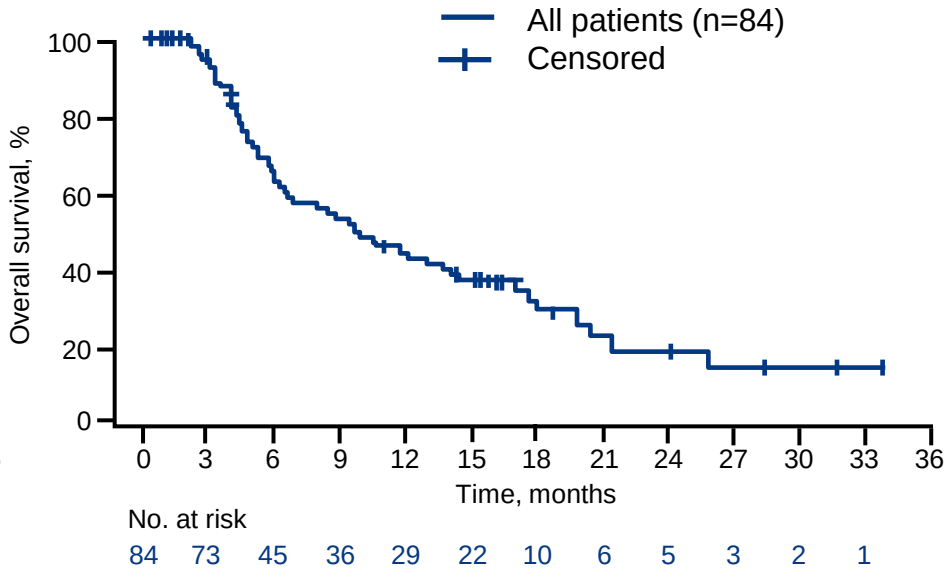


Bendell JC, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 560

560: A phase Ib study of safety and clinical activity of atezolizumab (A) and cobimetinib (C) in patients (pts) with metastatic colorectal cancer (mCRC) – Bendell JC, et al

Key results (cont.)





		All (n=84)	MSS (n=42)
PFS	Median, months (95%CI)	1.9 (1.8, 2.3)	2.5 (1.8, 3.7)
	6-month rate, %	18	27
OS	Median, months (95%CI)	9.8 (6.2, 14.1)	13.0 (6.0, 25.8)
	6-month rate, %	65	71
	12-month rate, %	43	51

Bendell JC, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 560

560: A phase Ib study of safety and clinical activity of atezolizumab (A) and cobimetinib (C) in patients (pts) with metastatic colorectal cancer (mCRC) – Bendell JC, et al

Key results (cont.)

AE, n (%)	n=84
All-cause, any grade	82 (98)
Treatment-related	
All grades	81 (96)
Grade 3–4	32 (38)
Grade 5	0
Serious	38 (45)
Treatment-related	10 (12)
Leading to withdrawal	20 (24)
Leading to withdrawal of atezolizumab	11 (13)
Leading withdrawal of cobimetinib	20 (24)

- Grade 3–4 TRAEs included diarrhea (5%), rash (5%), fatigue (5%), blood CPK increased (5%), maculopapular rash (2%), pruritus (1%) and nausea (1%)

Bendell JC, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 560

560: A phase Ib study of safety and clinical activity of atezolizumab (A) and cobimetinib (C) in patients (pts) with metastatic colorectal cancer (mCRC) – Bendell JC, et al

Conclusions

- **In heavily pre-treated patients with locally advanced or metastatic CRC atezolizumab combined with cobimetinib was tolerable**
  - **AEs were similar to those of atezolizumab and cobimetinib individually**
- **In patients with mCRC, the median OS was 9.8 months with a 12-month OS rate of 43% after a median follow-up of 17.0 months**
- **Atezolizumab combined with cobimetinib may be the first possible immune-modifying combination for patients with MSS mCRC**

Bendell JC, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 560

552: Age distribution of tumor gene expression in patients with stage II/III colon cancer – Hochster HS, et al

Study objective

- To examine differences in tumour gene expression between older vs. younger patients with Stage II/III colon cancer

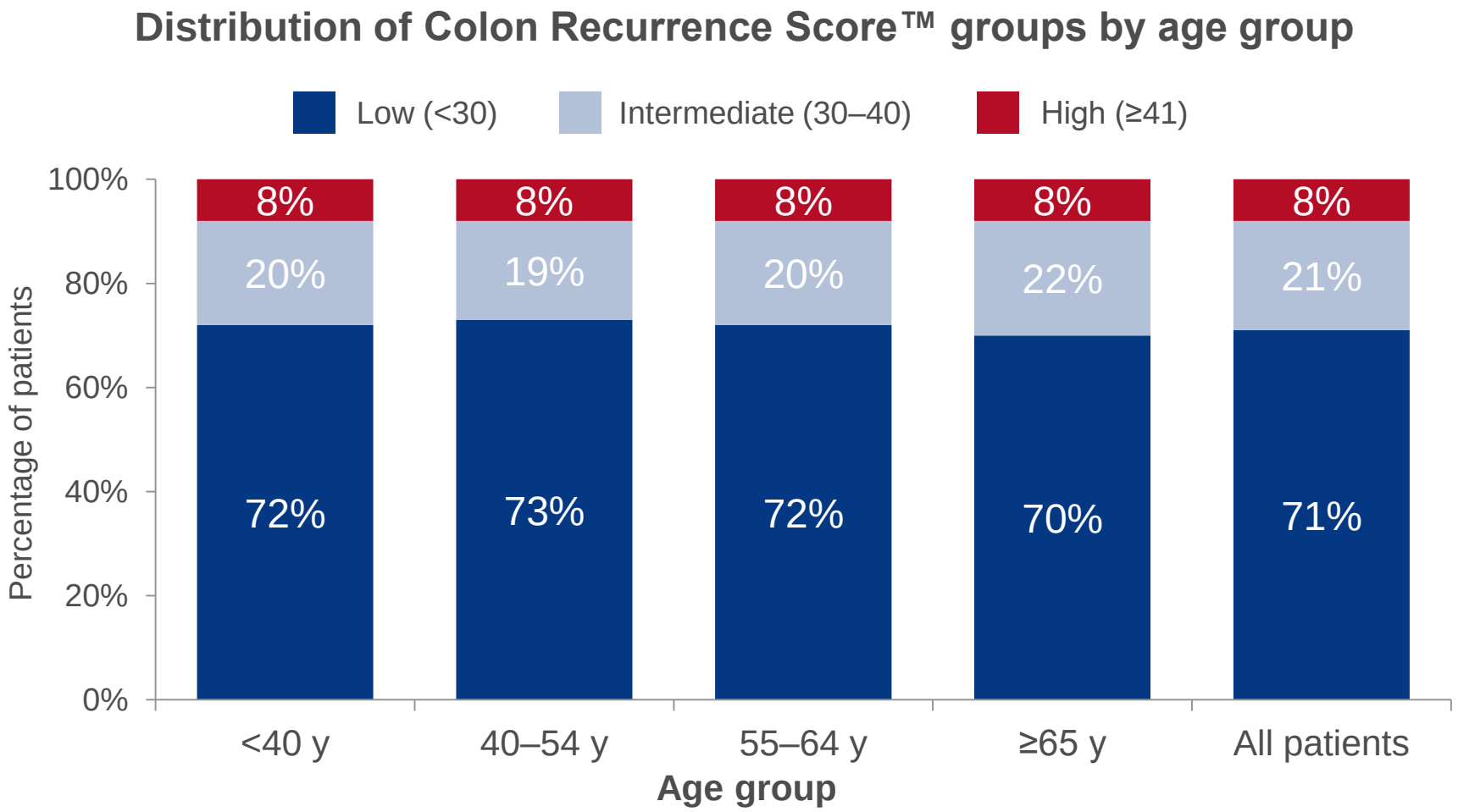
Methods

- The 12-gene Colon Recurrence Score™ test was used to predict the risk of recurrence in patients with Stage II/III colon cancer, using the following age categories:
  - <40 years, 40–54 years, 55–64 years and ≥65 years
  - Or <55 years and ≥55 years
- The Colon Recurrence Score™ assay measures the RNA expression of 12 genes (7 cancer-related genes and 5 reference genes), using RT-PCR in FFPE tumour tissue samples from 22,052 patients
- The Colon Recurrence Score™ test result was described according to patient risk group:
  - Low risk: score of <30
  - Intermediate risk: score of 30–40
  - High risk: score of ≥41

Hochster HS, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 552

552: Age distribution of tumor gene expression in patients with stage II/III colon cancer – Hochster HS, et al

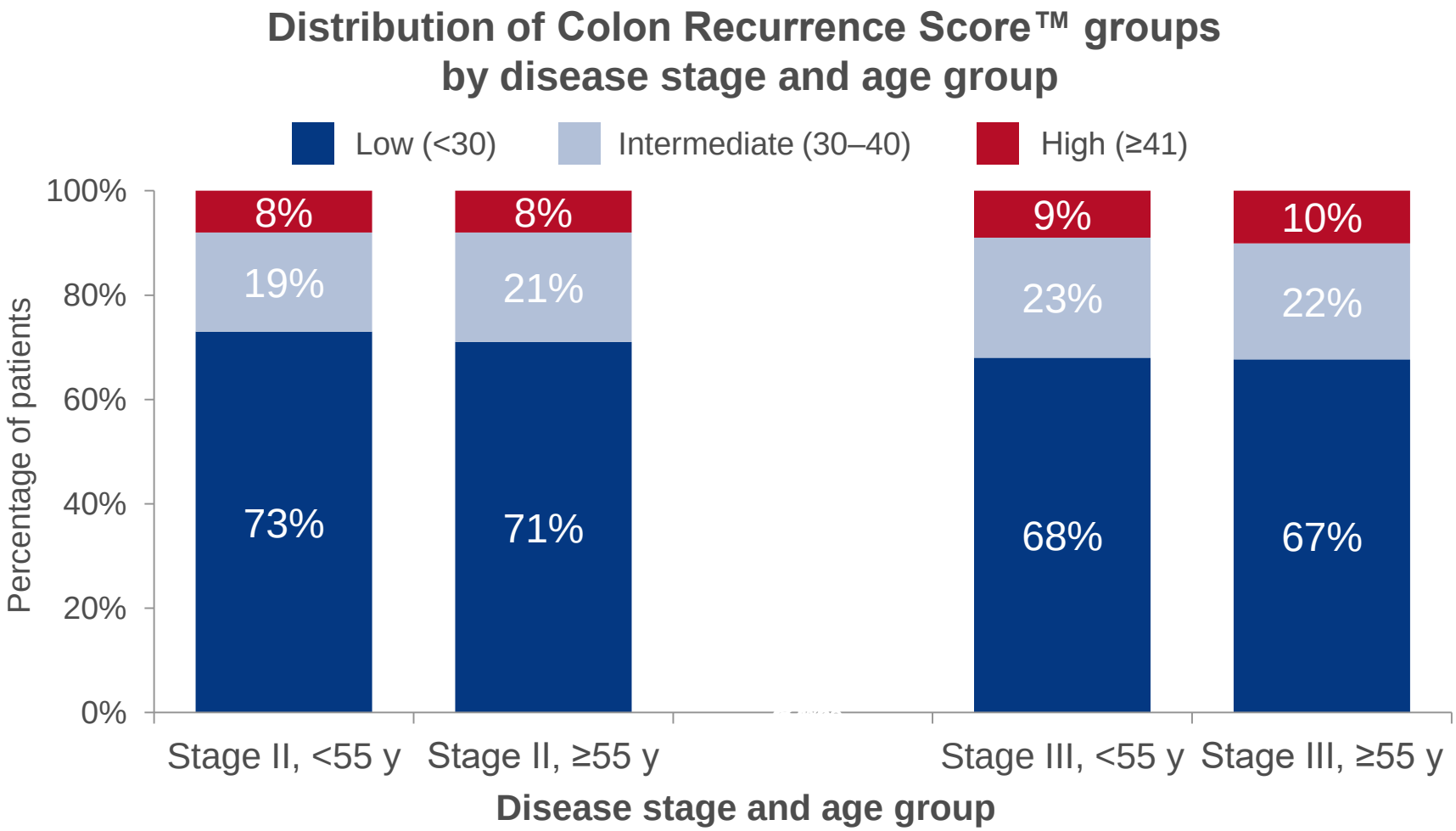
Key results



Hochster HS, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 552

552: Age distribution of tumor gene expression in patients with stage II/III colon cancer – Hochster HS, et al

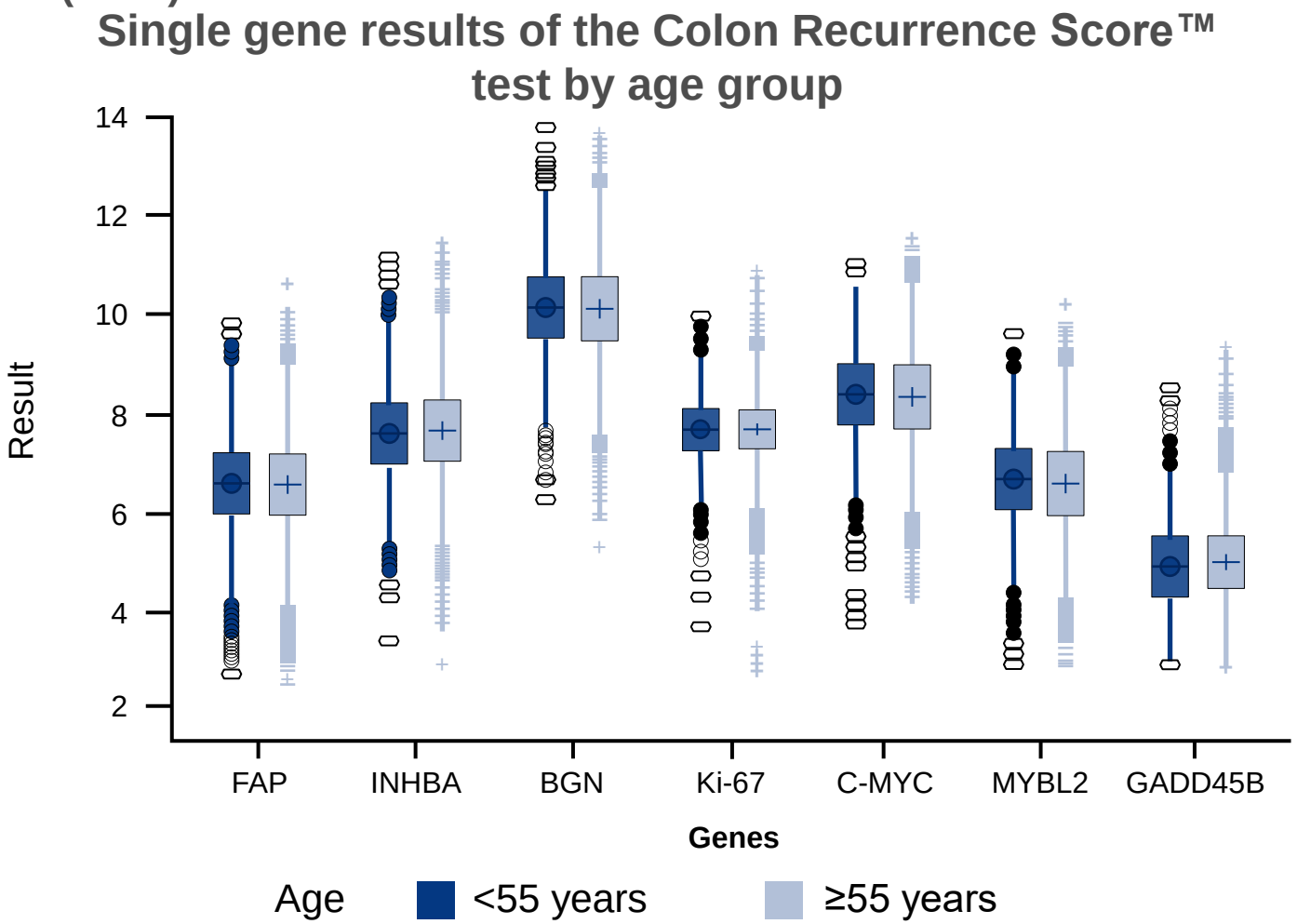
Key results (cont.)



Hochster HS, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 552

552: Age distribution of tumor gene expression in patients with stage II/III colon cancer – Hochster HS, et al

Key results (cont.)



Hochster HS, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 552

552: Age distribution of tumor gene expression in patients with stage II/III colon cancer – Hochster HS, et al

Conclusions

- **In patients with Stage II/III colon cancer, using the well-validated Colon Recurrence Score™ test in >22,000 patient samples, this study demonstrated similar gene expression across the age groups**
- **These results suggest that colon cancer in younger vs. older patients is not biologically different**
- **Most patients with Stage II/III colon cancer had low-risk disease, including younger patients (<55 years)**
- **The Colon Recurrence Score™ test is equally valid in identifying younger patients, for whom adjuvant CT may not be necessary**

Hochster HS, et al. J Clin Oncol 2018;36(Suppl 4S):Abstr 552