GI SLIDE DECK 2016

Selected abstracts from:

2016 Gastrointestinal Cancers Symposium

21–23 January 2016 | San Francisco, USA

esdo european society of digestive oncology

Supported by Eli Lilly and Company.
Eli Lilly and Company has not influenced the content of this publication

Lilly

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 **2016 Gastrointestinal Cancers Symposium** and is available in English and Japanese.

The area of clinical research in oncology is a challenging and ever changing environment. Within this environment, we all value access to scientific data and research 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)

esdo

european society of digestive oncology

ESDO Medical Oncology Slide Deck
Editors 2016

COLORECTAL CANCERS



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

PANCREATIC CANCER AND HEPATOBILIARY TUMOURS


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

GASTRO-OESOPHAGEAL AND NEUROENDOCRINE TUMOURS


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

BIOMARKERS


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

esdo

Glossary

1L	first-line
2L	second-line
5-FU	5-fluorouracil
ADC	adenocarcinoma
AE	adverse event
AFP	alpha-fetoprotein
AST	aspartate aminotransferase
ATP	adenosine triphosphate
AUC	area under the curve
bid	twice daily
CarPac	carboplatin/paclitaxel
CA 19-9	carbohydrate antigen 19-9
CEA	carcinoembryonic antigen
CI	confidence interval
CNS	central nervous system
CR	complete response
CRC	colorectal cancer
CRT	chemoradiotherapy
CT	chemotherapy
CyFra21-1	cytokeratin 19 fragment
DCR	disease control rate
DFS	disease-free survival
ECOG	Eastern Cooperative Oncology Group
ELISA	enzyme-linked immunosorbent assay
EORTC	European Organisation for Research and Treatment of Cancer
ERCC1	excision repair cross-complementation group 1
(m)FOLFIRI	(modified) leucovorin + 5-fluorouracil + irinotecan
(m)FOLFOX	(modified) leucovorin + 5-fluorouracil + oxaliplatin
FOLFOXIRI	leucovorin + 5-fluorouracil + oxaliplatin + irinotecan
GC	gastric cancer
GEC	gastro-oesophageal adenocarcinoma
GEJ	gastro-oesophageal junction
GI	gastrointestinal
Gy	Gray
HCC	hepatocellular carcinoma
HER2	human epidermal growth factor receptor 2
HGF	hepatocyte growth factor
HR	hazard ratio
HR-QoL	health-related quality of life
CRP	High-sensitivity C-reactive protein
IHC	immunohistochemistry
IR	incidence ratio
ITT	intent-to-treat
iv	intravenous
^{177}Lu-Dotatate	^{177}Lu-[DOTA^{0},Tyr^{3}]octreotate
LAR	long-acting release
mAb	monoclonal antibody
mCRC	metastatic colorectal cancer
MET	mesenchymal epithelial transition factor
MMR	mismatch repair
n/a	not available
NET	neuroendocrine tumour
NS	non-significant
OR	odds ratio
ORR	overall/objective response rate
(m)OS	(median) overall survival
OxCap	oxaliplatin/capecitabine
pCR	pathological complete response
PD	progressive disease
PDAC	pancreatic ductal adenocarcinoma
PD-L1	programmed death-ligand 1
(m)PFS	(median) progression-free survival
PK	pharmacokinetic
po	orally
PR	partial response
PS	performance status
q(2/3/4/8)w	every (2/3/4/8) week(s)
QoL	quality of life
RECIST	Response Evaluation Criteria In Solid Tumors
RT	radiotherapy
SAE	serious adverse event
SCC	squamous cell carcinoma
SD	stable disease
SEER	Surveillance, Epidemiology, and End Results
SLD	sum of longest diameters
SSA	somatostatin analogue
SSTR	somatostatin receptor
TEAE	treatment-emergent adverse event
TIMP1	TIMP metallopeptidase inhibitor 1
TNM	Tumour, Node, Metastasis
TTP	time to progression
(p)VEGF	(plasma) vascular endothelial growth factor

Contents

- Cancers of the oesophagus and stomach 6
- Cancers of the pancreas, small bowel and hepatobiliary tract 42
  - Pancreatic cancer 43
  - Hepatocellular carcinoma 53
  - Neuroendocrine tumour 61
  - General 67
- Cancers of the colon, rectum and anus 73
  - Colorectal cancer 74
  - Rectal cancer 89

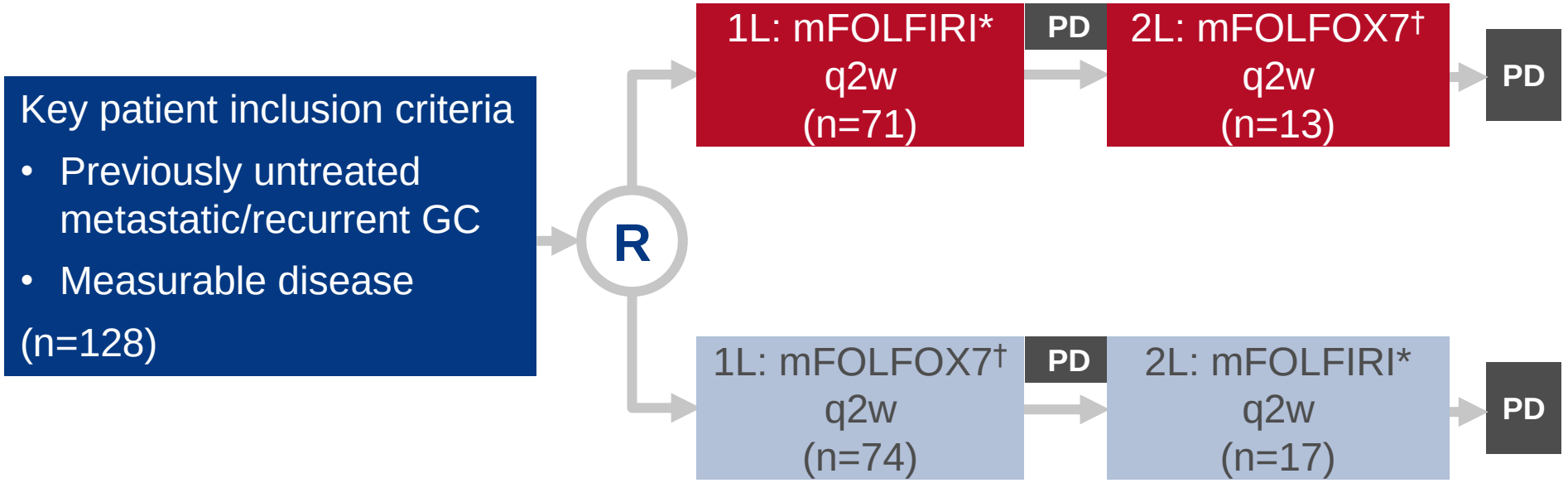
Note: To jump to a section, right click on the number and ‘Open Hyperlink’

CANCERS OF THE OESOPHAGUS AND STOMACH

1: Prospective randomized phase II study of FOLFIRI versus FOLFOX7 in advanced gastric adenocarcinoma: A Chinese Western Cooperative Gastrointestinal Oncology Group study – Bi F, et al

Study objective

- To assess the efficacy and safety of mFOLFIRI vs. mFOLFOX7 as 1L treatments in patients with locally advanced GC



PRIMARY ENDPOINT(S)

- PFS

SECONDARY ENDPOINTS

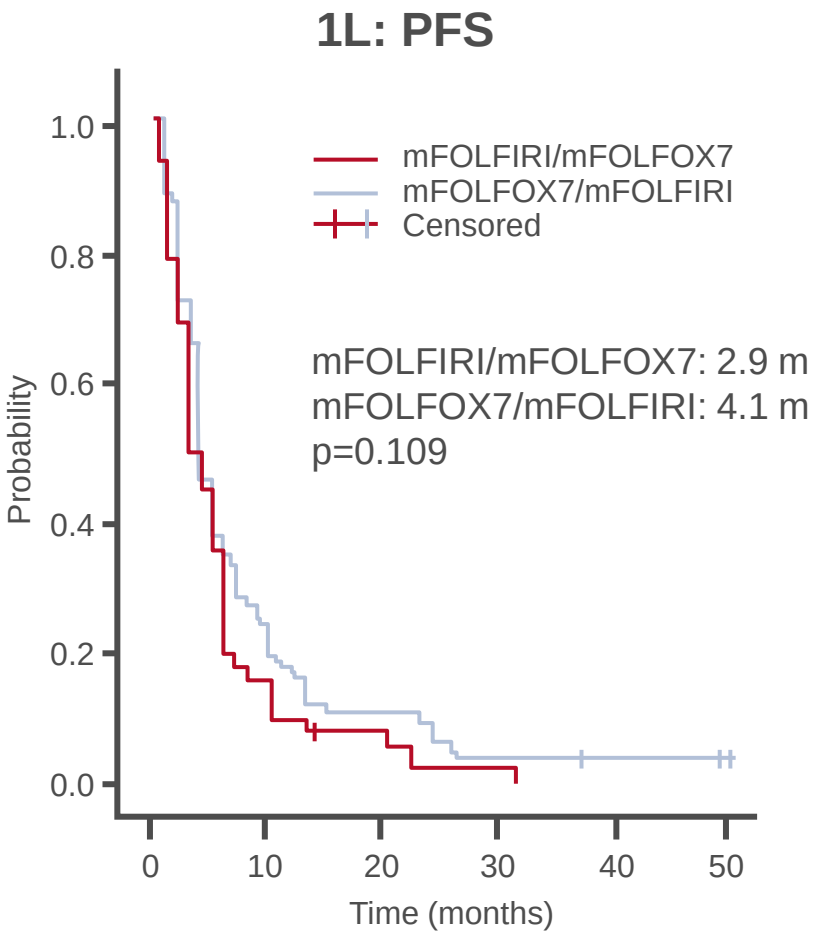
- OS, DCR
- Toxicity

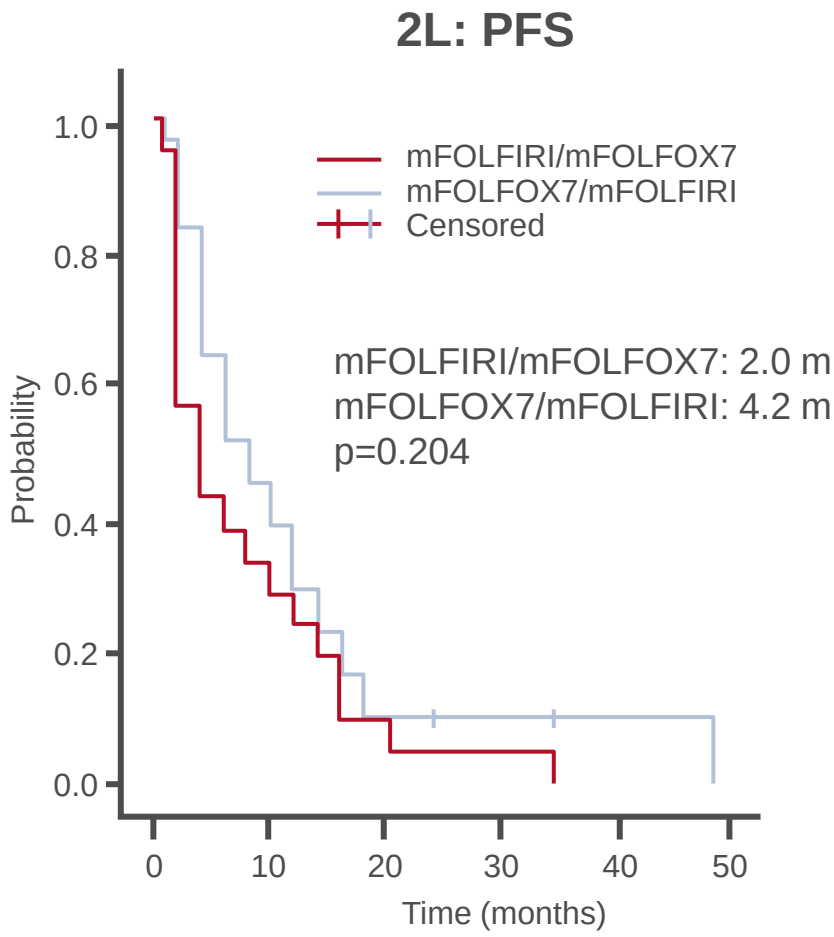
*Irinotecan 150 mg/m^2 iv 90 min d1, leucovorin 200 mg/m^2 iv 2 h d1, 5-FU 2400 mg/m^2 iv 46 h d1; †oxaliplatin 85 mg/m^2 2 h d1, leucovorin 200 mg/m^2 2 h d1, 5-FU 2400 mg/m^2 iv 46 h d1

Bi et al. J Clin Oncol 2016; 34 (suppl): abstr 1

1: Prospective randomized phase II study of FOLFIRI versus FOLFOX7 in advanced gastric adenocarcinoma: A Chinese Western Cooperative Gastrointestinal Oncology Group study – Bi F, et al

Key results

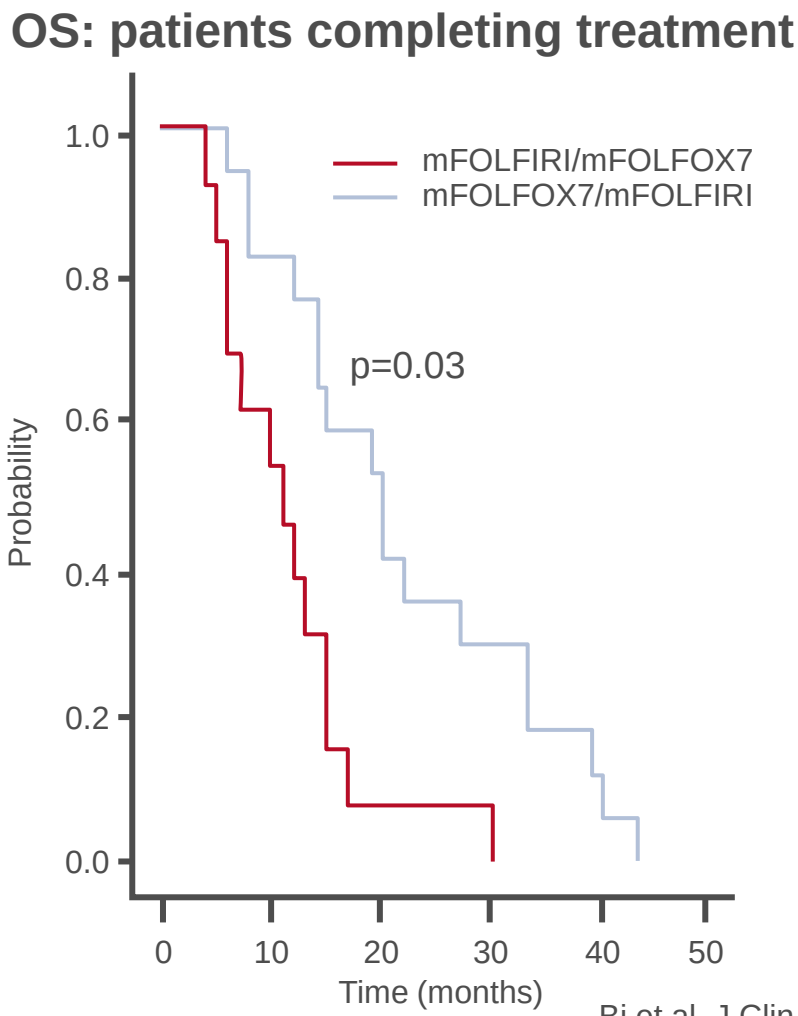




Bi et al. J Clin Oncol 2016; 34 (suppl): abstr 1

1: Prospective randomized phase II study of FOLFIRI versus FOLFOX7 in advanced gastric adenocarcinoma: A Chinese Western Cooperative Gastrointestinal Oncology Group study – Bi F, et al

Key results (continued)



Bi et al. J Clin Oncol 2016; 34 (suppl): abstr 1

1: Prospective randomized phase II study of FOLFIRI versus FOLFOX7 in advanced gastric adenocarcinoma: A Chinese Western Cooperative Gastrointestinal Oncology Group study – Bi F, et al

Key results (continued)

Patients completing treatment, months (95% CI)	mFOLFIRI/mFOLFOX7 (n=13)	mFOLFOX7/mFOLFIRI (n=17)	p-value
1L PFS	2.1 (0.6, 3.4)	8.0 (4.0, 12.0)	0.053
2L PFS	1.2 (n/a)	5.1 (1.9, 8.1)	0.287
Total PFS	8.1 (4.6, 11.4)	12.2 (6.1, 17.9)	0.008
OS	11.0 (5.1, 16.9)	20.2 (13.4, 26.6)	0.030

Event rate, n (%)	1L: mFOLFIRI (n=54)	1L: mFOLFOX7 (n=74)	2L: mFOLFIRI (n=13)	2L: mFOLFOX7 (n=17)
DCR	32 (59.3)	49 (66.3)	3 (23.1)	11 (64.7)
CR	1 (1.9)	2 (2.7)	0	0
PR	5 (9.3)	5 (6.8)	1 (7.7)	0
SD	26 (48.1)	42 (56.8)	2 (15.4)	11 (64.7)
PD	17 (31.5)	18 (24.3)	9 (69.2)	6 (35.3)
Not assessable	5 (9.3)	7 (9.5)	1 (7.7)	0

Bi et al. J Clin Oncol 2016; 34 (suppl): abstr 1

1: Prospective randomized phase II study of FOLFIRI versus FOLFOX7 in advanced gastric adenocarcinoma: A Chinese Western Cooperative Gastrointestinal Oncology Group study – Bi F, et al

Key results (continued)

Grade 3 / 4 AEs, %	1L: mFOLFIRI (n=71)	1L: mFOLFOX7 (n=74)	2L: mFOLFIRI (n=21)	2L: mFOLFOX7 (n=31)
Neutropenia	21.0 / 4.0	27.0 / 7.0	0.0 / 9.5	3.2 / 0.0
Sensory neuropathy	0.0 / 0.0	12.0 / 0.0	9.6 / 0.0	0.0 / 0.0
Delayed diarrhoea	6.0 / 0.0	1.0 / 0.0	4.8 / 0.0	0.0 / 0.0
Nausea	5.6 / 0.0	2.8 / 0.0	0.0 / 0.0	6.5 / 0.0
Vomiting	5.6 / 0.0	2.8 / 0.0	0.0 / 0.0	6.5 / 0.0
Alopecia	0.0 / 0.0	0.0 / 0.0	4.8 / 0.0	0.0 / 0.0
Hand-foot syndrome	0.0 / 0.0	0.0 / 0.0	14.3 / 0.0	0.0 / 0.0
Thrombocytopenia	5.6 / 0.0	2.8 / 0.0	14.3 / 0.0	0.0 / 0.0

Conclusions

- **There was no meaningful difference in the PFS or DCR with mFOLFIRI vs. mFOLFOX7 as 1L treatments in patients with locally advanced GC**
  - **OS may be improved with 1L mFOLFOX7 followed by 2L mFOLFIRI but this needs to be validated**
- **AEs were manageable in both treatment arms**

Bi et al. J Clin Oncol 2016; 34 (suppl): abstr 1

2: A western validation of a novel gastric cancer prognostic model using American data – Goldner BS, et al

Study objective

- To predict 5-year OS in an American cohort of patients with GC

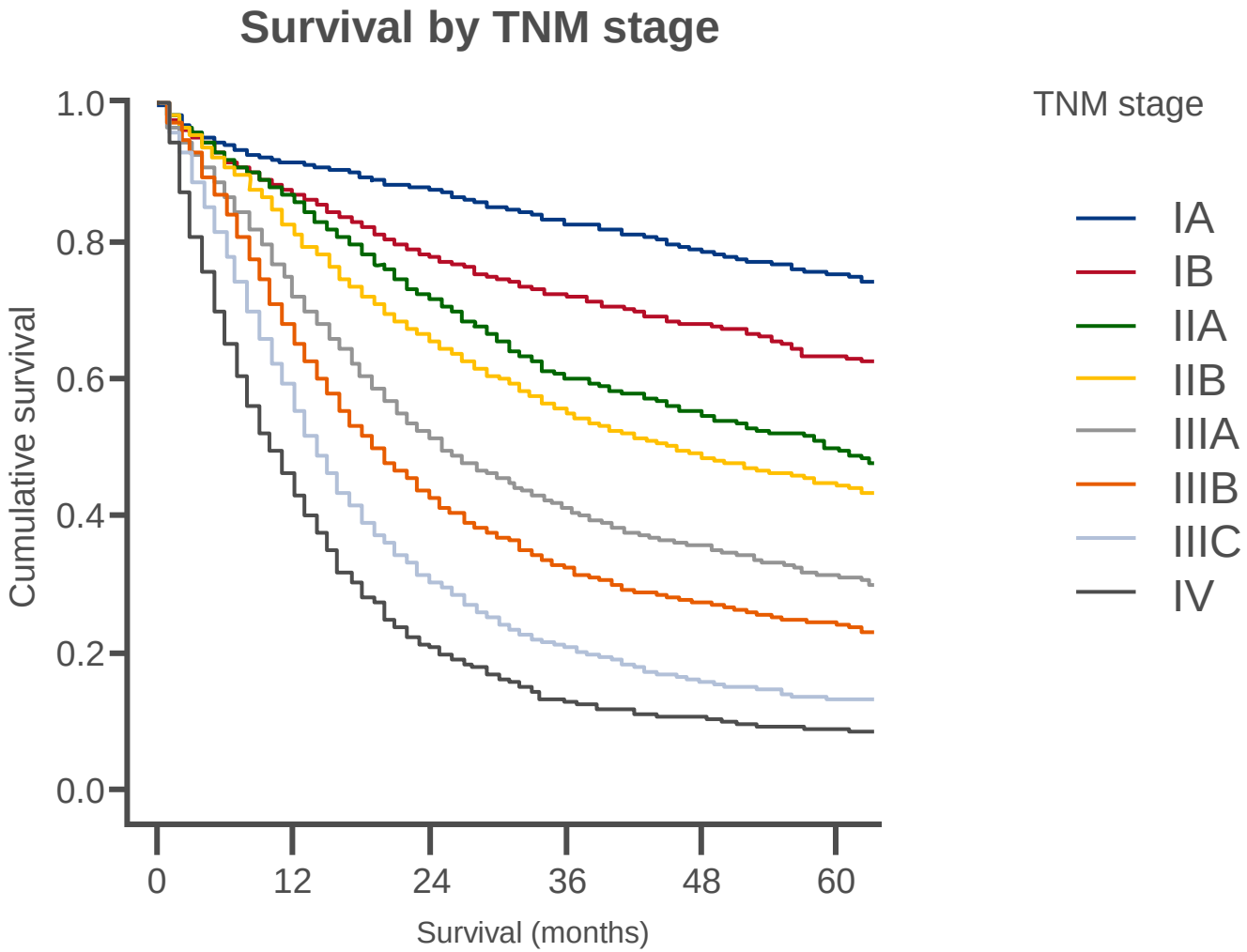
Study design

- The Yonsei University Gastric Cancer Prediction Model was developed using a prospectively maintained single institution database of 12,399 patients
  - The prediction model was validated using external data sets from Asia
- The prediction model was applied to an American population using the SEER 2014 dataset
  - All patients diagnosed with GEC between 2002–2012 who underwent resection were included (n=15,483)
  - The following characteristics were selected for analysis:
    - Age, gender, histology/grade, T-stage, M-stage, extent of resection, lymph nodes, vital status, survival
  - Kaplan–Meier estimates were plotted against predicted survival
  - The predicted probability of the model was compared with the 7th edition of the TNM staging system

Goldner et al. J Clin Oncol 2016; 34 (suppl): abstr 2

2: A western validation of a novel gastric cancer prognostic model using American data – Goldner BS, et al

Key results



Goldner et al. J Clin Oncol 2016; 34 (suppl): abstr 2

2: A western validation of a novel gastric cancer prognostic model using American data – Goldner BS, et al

Key results (continued)

Surgery		n	%	Mean	Yonsei (%)	Yonsei (mean)
Type of resection	Subtotal	11,424	74		27	
	Total	4059	26		73	
Nodes retrieved, n				16.6		40
Positive nodes, n				4.9		4.4
Adequacy of nodal dissection	<16 nodes	8645	55.8		3.2	
	≥16 nodes	6838	44.2		96.8	

Goldner et al. J Clin Oncol 2016; 34 (suppl): abstr 2

2: A western validation of a novel gastric cancer prognostic model using American data – Goldner BS, et al

Key results (continued)

Stage	Frequency	%	Yonsei (%)
IA	2074	13.4	37.2
IB	1405	9.1	9.9
IIA	1560	10.1	8.3
IIB	2112	14.6	9.7
IIIA	1896	12.2	7.5
IIIB	2373	15.3	9.6
IIIC	2512	16.2	13.4
IV	1551	10	4.2

Goldner et al. J Clin Oncol 2016; 34 (suppl): abstr 2

2: A western validation of a novel gastric cancer prognostic model using American data – Goldner BS, et al

Key results (continued)

C-Statistics: SEER database	Prognostic indices (95% CI)
Yonsei University Prediction Model	0.762 (0.754, 0.769)
7th TNM staging model	0.683 (0.677, 0.689)
p-value	<0.001

Conclusions

- **This is the first study to validate the Yonsei University Prediction Model in an American cohort of patients with GC**
- **The model had superior prognostic accuracy for 5-year survival**
- **The model accounts for both lymphadenectomy and non-curative resection**

Goldner et al. J Clin Oncol 2016; 34 (suppl): abstr 2

3: NEOSCOPE: A randomised Phase II study of induction chemotherapy followed by either oxaliplatin/capecitabine or paclitaxel/carboplatin based chemoradiation as pre-operative regimen for resectable oesophageal adenocarcinoma – Mukherjee S, et al

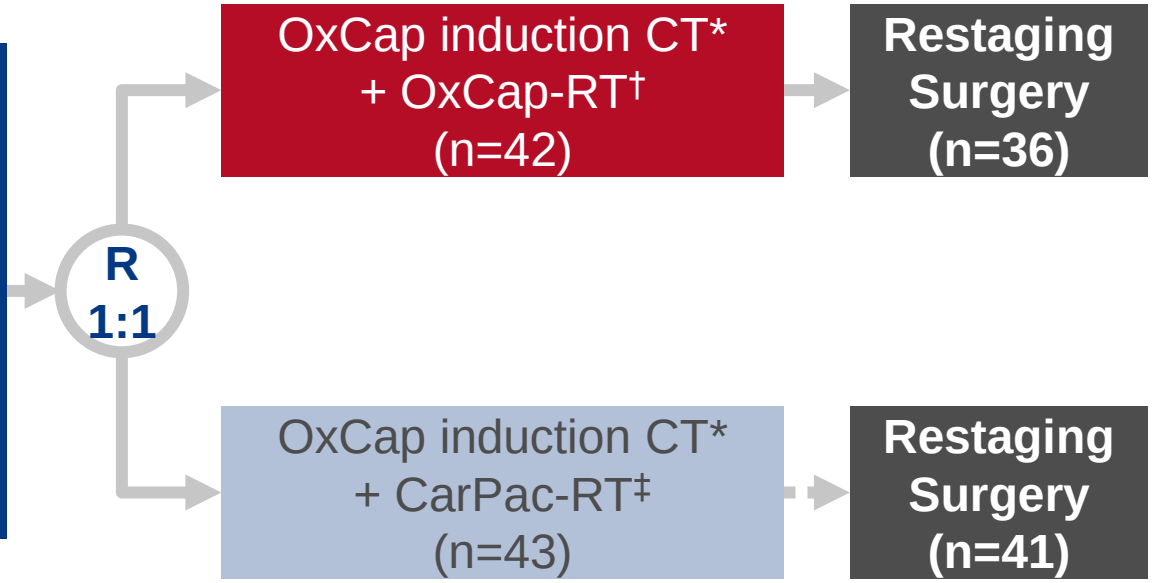
Study objective

- To evaluate the efficacy and safety of CarPac-RT vs. OxCap-RT in patients with resectable oesophageal ADC

Key patient inclusion criteria

- Resectable ADC of the oesophagus/GEJ
- Total disease length (T+N) <8 cm
- ECOG PS 0–1

(n=85)



PRIMARY ENDPOINT(S)

- pCR

SECONDARY ENDPOINTS

- R1 rate, resection rate, OS
- Safety, post-operative morbidity/mortality

*2 cycles oxaliplatin 130 mg/m^2 d1, capecitabine 625 mg/m^2 d1–21, q3w; †oxaliplatin 85 mg/m^2 d1,15, 29; capecitabine 625 mg/m^2 bid on days of RT + 45 Gy/25 fractions/5 weeks; ‡carboplatin AUC2; paclitaxel 50 mg/m^2 d1, 8, 15, 22, 29 + 45 Gy/25 fractions/5 weeks

Mukherjee et al. J Clin Oncol 2016; 34 (suppl): abstr 3

3: NEOSCOPE: A randomised Phase II study of induction chemotherapy followed by either oxaliplatin/capecitabine or paclitaxel/carboplatin based chemoradiation as pre-operative regimen for resectable oesophageal adenocarcinoma – Mukherjee S, et al

Key results

Mandard tumour regression grade (TRG)	OxCap-RT (n=42)		CarPac-RT (n=43)	
	n	%	n	%
1 (pCR)	5	11.9*	12	27.9*
2	13	31.0	16	37.2
3	13	31.0	10	23.3
4	4	9.5	3	7.0
5	0	0.0	0	0.0
Missing TRG data	1	2.4	0	0.0
No surgery	6	14.3	2	4.7

- 10 of the first 38 patients in the CarPacRT arm attained pCR, thereby meeting pre-specified criteria of success

*13.9% and 29.3%, respectively, of those undergoing surgery

Mukherjee et al. J Clin Oncol 2016; 34 (suppl): abstr 3

3: NEOSCOPE: A randomised Phase II study of induction chemotherapy followed by either oxaliplatin/capecitabine or paclitaxel/carboplatin based chemoradiation as pre-operative regimen for resectable oesophageal adenocarcinoma – Mukherjee S, et al

Key results (continued)

30-day post-operative complications		OxCap-RT (n=36)		CarPac-RT (n=41)	
		n	%	n	%
30-day post-operative mortality		1	2.8	1	2.4
Any 30-day post-operative complications	Yes	19	52.8	21	51.2
	Missing data	1	2.8	0	0.0
Cardiac complications		9	25.0	4	9.8
Respiratory complications		14	38.9	15	36.6
Chylothorax requiring treatment		1	2.8	2	4.9
Wound infection		3	8.3	5	12.2
Anastomotic leak	Radiological/endoscopic	0	0.0	3	7.3
	Missing data	4	11.1	3	7.3

Mukherjee et al. J Clin Oncol 2016; 34 (suppl): abstr 3

3: NEOSCOPE: A randomised Phase II study of induction chemotherapy followed by either oxaliplatin/capecitabine or paclitaxel/carboplatin based chemoradiation as pre-operative regimen for resectable oesophageal adenocarcinoma – Mukherjee S, et al

Key results (continued)

Selected grade 3–5 AEs, %	Induction OxCap (n=85)	OxCap-RT (n=38)	CarPac-RT (n=42)	p-value
Any toxicity	31.8	42.1	52.4	0.358
Toxic death	3.5	0.0	0.0	
Haematological	2.4	15.8	28.6	0.172
Febrile neutropenia	0.0	0.0	2.4	
Neutropenia	0.0	2.6	21.4	0.011 (post-hoc)
Diarrhoea	8.2	0.0	2.4	
Nausea/vomiting	7.1	0.0	2.4	
Oesophagitis	1.2	5.3	4.8	
Fatigue	10.6	10.5	14.3	
Neurological	7.1	0.0	0.0	
Thromboembolic	1.2	2.6	2.4	

Mukherjee et al. J Clin Oncol 2016; 34 (suppl): abstr 3

3: NEOSCOPE: A randomised Phase II study of induction chemotherapy followed by either oxaliplatin/capecitabine or paclitaxel/carboplatin based chemoradiation as pre-operative regimen for resectable oesophageal adenocarcinoma – Mukherjee S, et al

Key results (continued)

R0 resection	OxCap-RT (n=36)		CarPac-RT (n=41)	
	n	%	n	%
R0	26	72.2	33	80.5
R1	10	27.8	8	19.5

Conclusions

- Post-operative mortality was low and post-operative complications were as expected with CarPac-RT and OxCap-RT in patients with resectable oesophageal ADC
- Both regimens were well tolerated
  - Induction CT may have contributed to the high frequency of grade 3/4 neutropenia seen in the CarPac-RT arm
- CarPac-RT passed the pre-specified criteria to progress to a phase III study but OxCap-RT did not

Mukherjee et al. J Clin Oncol 2016; 34 (suppl): abstr 3

4: Multicenter double-blind randomized phase II: FOLFOX + ziv-aflibercept/ placebo for patients (pts) with chemo-naive metastatic esophagogastric adenocarcinoma (MEGA) – Enzinger PC, et al

Study objective

- To investigate efficacy and safety of FOLFOX + ziv-aflibercept (VEGF inhibitor) vs. FOLFOX + placebo in patients with CT-naïve metastatic GEC

Key patient inclusion criteria

- Histologically confirmed unresectable oesophageal, GEJ or gastric ADC
- CT-naïve
- ECOG PS ≤1
- Measurable disease not required

(n=64)

R 2:1

FOLFOX* q2w + ziv-aflibercept 4 mg/kg d1 (n=43) → PD

Stratification

- PS 1 vs. 2
- Oesophageal/GEJ vs. GC

FOLFOX* q2w + placebo (n=21) → PD

PRIMARY ENDPOINT(S)

- PFS (6 months)

SECONDARY ENDPOINTS

- OS, response (RECIST v1.1)
- TEAEs

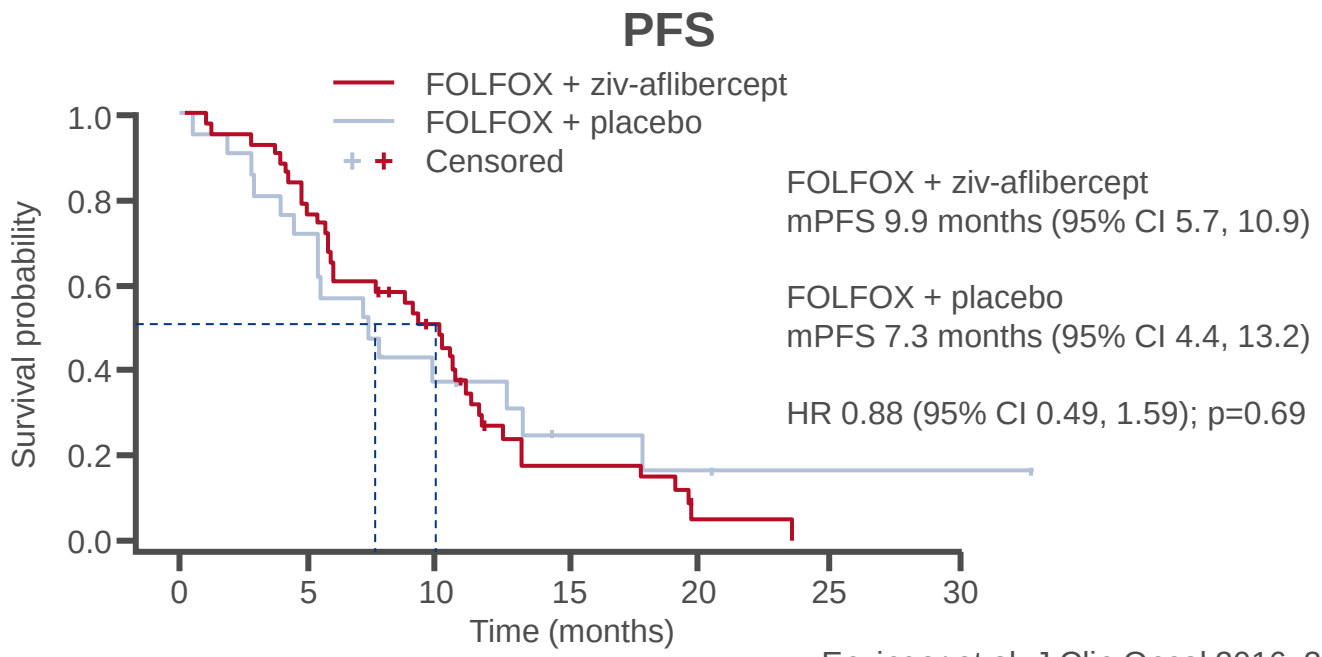
*Oxaliplatin 85 mg/m^2, 5-FU 400 mg/m^2 bolus then continuous 2400 mg/m^2, and leucovorin, 400 mg/m^2

Enzinger et al. J Clin Oncol 2016; 34 (suppl): abstr 4

4: Multicenter double-blind randomized phase II: FOLFOX + ziv-aflibercept/ placebo for patients (pts) with chemo-naive metastatic esophagogastric adenocarcinoma (MEGA) – Enzinger PC, et al

Key results

	Ziv-aflibercept (n=43)	Placebo (n=21)	p-value
6-month PFS, %	60.5	57.1	0.8
1-year OS, %	58.7	55.1	0.79
Major response rate, n/N (%)	22/36 (61.1)	12/16 (75.0)	0.33

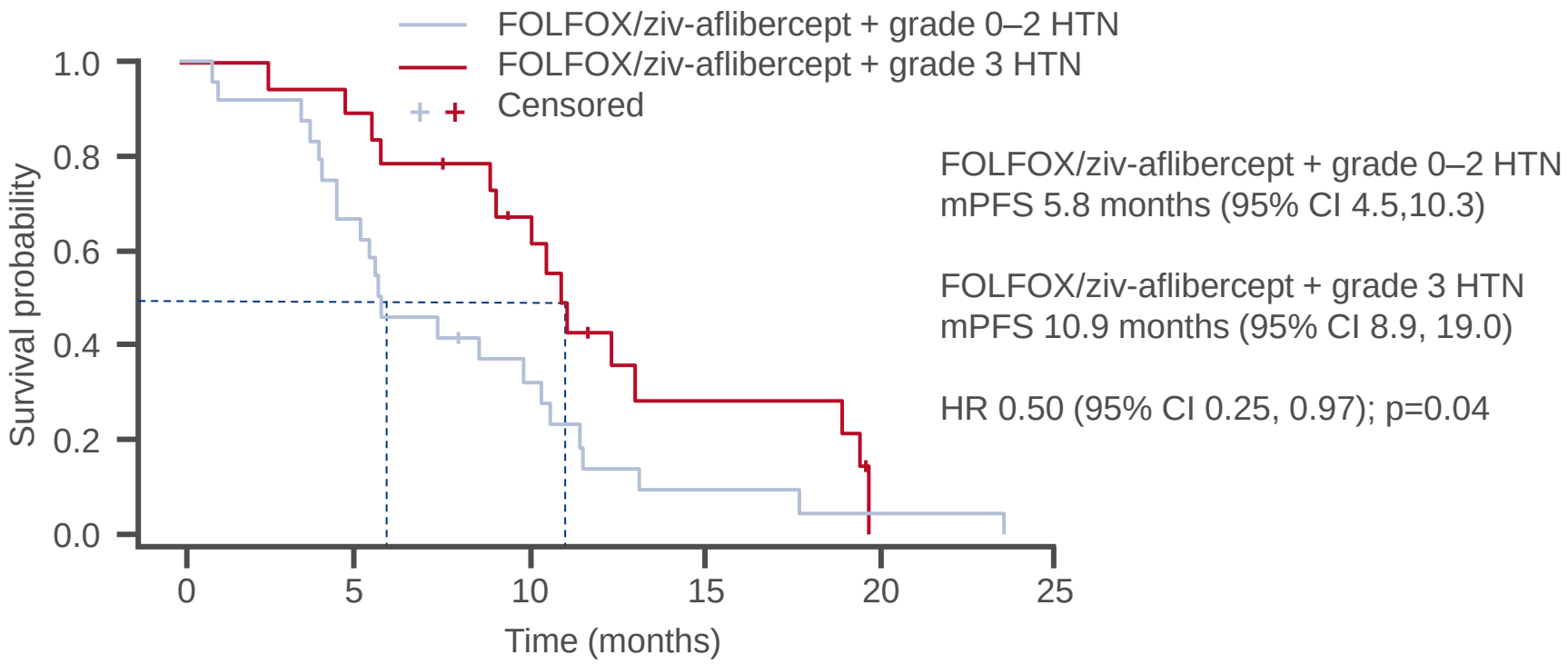


Enzinger et al. J Clin Oncol 2016; 34 (suppl): abstr 4

4: Multicenter double-blind randomized phase II: FOLFOX + ziv-aflibercept/ placebo for patients (pts) with chemo-naive metastatic esophagogastric adenocarcinoma (MEGA) – Enzinger PC, et al

Key results (continued)

PFS by hypertension grade



HTN, hypertension

Enzinger et al. J Clin Oncol 2016; 34 (suppl): abstr 4

4: Multicenter double-blind randomized phase II: FOLFOX + ziv-aflibercept/ placebo for patients (pts) with chemo-naive metastatic esophagogastric adenocarcinoma (MEGA) – Enzinger PC, et al

Key results (continued)

Grade 3–4 TEAEs occurring in ≥5% of patients, n (%)	Ziv-aflibercept (n=43)	Placebo (n=21)	p-value
Hypertension	20 (47)	1 (5)	0.0006
Absolute neutrophil count	12 (28)	4 (19)	0.55
Fatigue	5 (12)	1 (5)	0.65
Thromboembolic	4 (9)	1 (5)	0.66
Mucositis	3 (7)	0	0.54
Peripheral sensory neuropathy	2 (5)	2 (10)	0.59
Upper GI bleeding	2 (5)	1 (5)	1.00
Death on treatment	3 (7)	1 (5)	1.00

Enzinger et al. J Clin Oncol 2016; 34 (suppl): abstr 4

4: Multicenter double-blind randomized phase II: FOLFOX + ziv-aflibercept/ placebo for patients (pts) with chemo-naive metastatic esophagogastric adenocarcinoma (MEGA) – Enzinger PC, et al

Conclusions

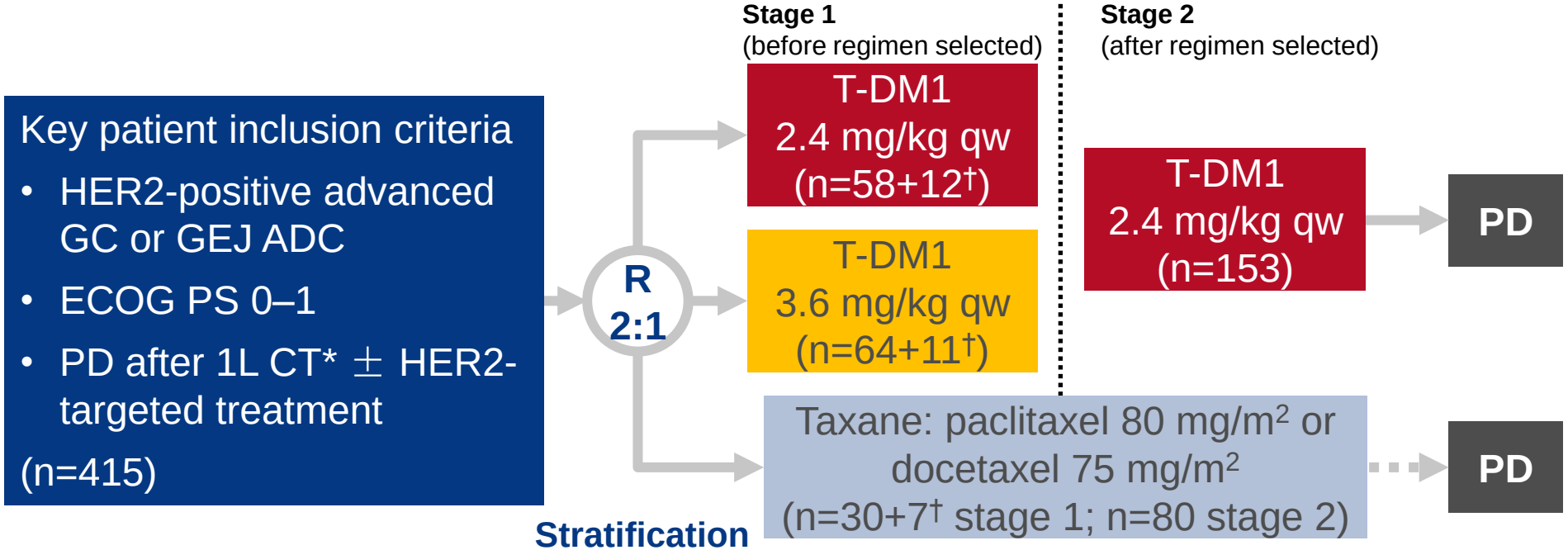
- **Ziv-aflibercept added to FOLFOX did not significantly improve efficacy vs. FOLFOX alone in patients with CT-naïve metastatic GEC**
- **Both regimens were well tolerated with an expected increase in hypertension in patients receiving ziv-aflibercept**
- **The potential improved efficacy with ziv-aflibercept in patients with grade 3 hypertension should be examined further**

Enzinger et al. J Clin Oncol 2016; 34 (suppl): abstr 4

5: A randomized, open-label, multicenter, adaptive phase 2/3 study of trastuzumab emtansine (T-DM1) versus a taxane (TAX) in patients (pts) with previously treated HER2-positive locally advanced or metastatic gastric/gastroesophageal junction adenocarcinoma (LA/MGC/GEJC) – Kang Y-K, et al

Study objective

- To assess the efficacy and safety of 2L trastuzumab emtansine vs. a taxane in patients with HER2-positive unresectable, locally advanced or metastatic GC



Stratification
- Geographical region
- Prior HER2-targeted therapy
- Prior gastrectomy

PRIMARY ENDPOINT(S)
- OS

SECONDARY ENDPOINTS
- PFS, ORR

*5-FU + platinum; †n, time until clinical cut-off for regimen selection analysis + interim regimen selection analysis. T-DM1, trastuzumab emtansine

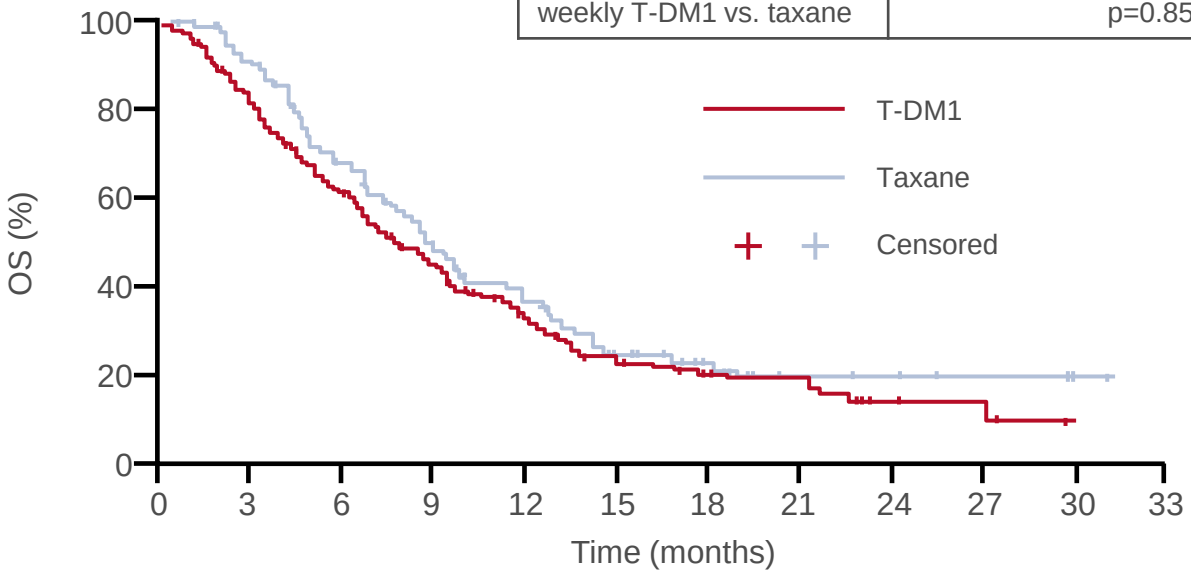
Kang et al. J Clin Oncol 2016; 34 (suppl): abstr 5

5: A randomized, open-label, multicenter, adaptive phase 2/3 study of trastuzumab emtansine (T-DM1) versus a taxane (TAX) in patients (pts) with previously treated HER2-positive locally advanced or metastatic gastric/gastroesophageal junction adenocarcinoma (LA/MGC/GEJC) – Kang Y-K, et al

Results

OS

	T-DM1 2.4 mg/kg (n=228)	Taxane (n=117)
Median OS, months	7.9	8.6
Number of events, n (%)	164 (71.9)	71 (60.7)
Unstratified HR (95% CI) weekly T-DM1 vs. taxane	1.15 (0.87, 1.51) p=0.8589	



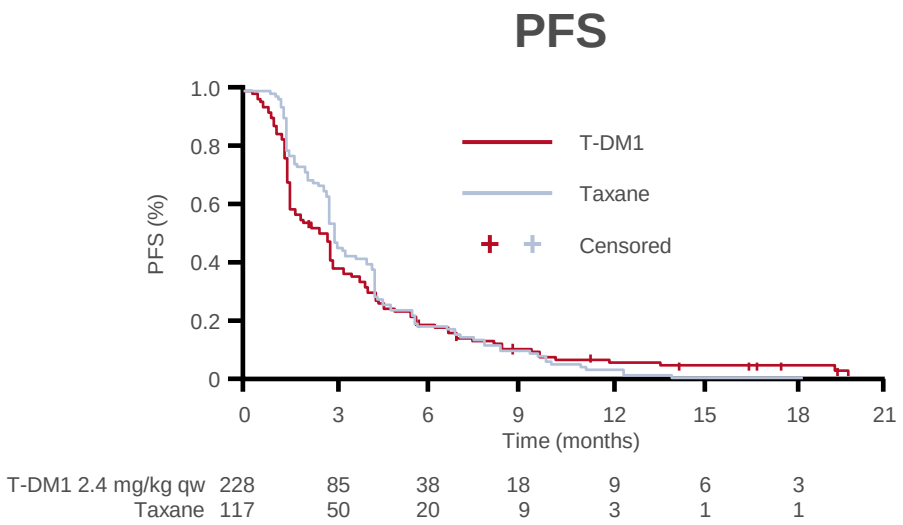
T-DM1 2.4 mg/kg qw	228	181	134	92	57	30	21	12	4	3	1
Taxane	117	96	68	43	26	16	8	6	5	3	2

T-DM1, trastuzumab emtansine

Kang et al. J Clin Oncol 2016; 34 (suppl): abstr 5

5: A randomized, open-label, multicenter, adaptive phase 2/3 study of trastuzumab emtansine (T-DM1) versus a taxane (TAX) in patients (pts) with previously treated HER2-positive locally advanced or metastatic gastric/gastroesophageal junction adenocarcinoma (LA/MGC/GEJC) – Kang Y-K, et al

Results (continued)



	T-DM1 2.4 mg/kg (n=228)	Taxane (n=117)
mPFS, months	2.7	2.9
Number of events, n (%)	212 (93.0)	104 (88.9)
Unstratified HR (95% CI) T-DM1 vs. taxane	1.13 (0.89, 1.43) p=0.3080 (two-sided)	

ORR and DoR	T-DM1 2.4 mg/kg (n=204)	Taxane (n=102)
ORR, n (%)	42 (20.6)	20 (19.6)
Difference, % (95% CI)	0.98 (−9.04, 11.00)	
p-value (Chi-square)	0.8406 (two-sided)	
Median duration of ORR, months (95% CI)	4.27 (3.02, 6.83)	3.65 (2.76, 5.55)

T-DM1, trastuzumab emtansine

5: A randomized, open-label, multicenter, adaptive phase 2/3 study of trastuzumab emtansine (T-DM1) versus a taxane (TAX) in patients (pts) with previously treated HER2-positive locally advanced or metastatic gastric/gastroesophageal junction adenocarcinoma (LA/MGC/GEJC) – Kang Y-K, et al

Results (continued)

Drug exposure	T-DM1 2.4 mg/kg qw* (n=224)	Docetaxel† (n=69)	Paclitaxel‡ (n=42)
Treatment duration [months], median (range)	1.8 (0, 19)	2.0 (0, 9)	2.8 (0, 11)
Dose intensity [%], median (range)	95.9 (33, 105)	98.0 (55, 109)	84.9 (50, 117)
Any dose reduction, n (%)	26 (11.6)	17 (24.6)	10 (24.4)
1st level dose reduction, n (%)	19 (8.5)	11 (15.9)	7 (16.7)
2nd level dose reduction, n (%)	7 (3.1)	6 (8.7)	3 (7.1)
Dose delay ≥7 days, n (%)	100 (44.6)	15 (21.7)	28 (66.7)

*Reduced to 2.0 mg/kg (dose level −1), 1.6 mg/kg (dose level −2);

†Reduced to 60 mg/m^2 (dose level −1), 50 mg/m^2 (dose level −2);

‡Reduced to 65 mg/m^2 (dose level −1), 50 mg/m^2 (dose level −2);

T-DM1, trastuzumab emtansine

Kang et al. J Clin Oncol 2016; 34 (suppl): abstr 5

5: A randomized, open-label, multicenter, adaptive phase 2/3 study of trastuzumab emtansine (T-DM1) versus a taxane (TAX) in patients (pts) with previously treated HER2-positive locally advanced or metastatic gastric/gastroesophageal junction adenocarcinoma (LA/MGC/GEJC) – Kang Y-K, et al

Results (continued)

AEs, n (%)	T-DM1 2.4 mg/kg qw (n=224)	Taxane (n=111)
Any AE	218 (97.3)	108 (97.3)
Grade ≥3 AE	134 (59.8)	78 (70.3)
SAE	65 (29.0)	31 (27.9)
AE leading to death	8 (3.6)	4 (3.6)
AEs leading to treatment discontinuation	31 (13.8)	15 (13.5)

Conclusions

- **Trastuzumab emtansine did not improve efficacy compared with taxane in patients with HER-positive locally advanced or metastatic GC**
- **Trastuzumab emtansine was well tolerated, with fewer grade ≥3 AEs than taxane**
  - **The overall frequency of AEs, SAEs, fatal AEs and discontinuations due to AEs were similar between the groups**

T-DM1, trastuzumab emtansine

Kang et al. J Clin Oncol 2016; 34 (suppl): abstr 5

6: Safety and activity of nivolumab monotherapy in advanced and metastatic (A/M) gastric or gastroesophageal junction cancer (GC/GEC): Results from the CheckMate-032 study – Le DT, et al

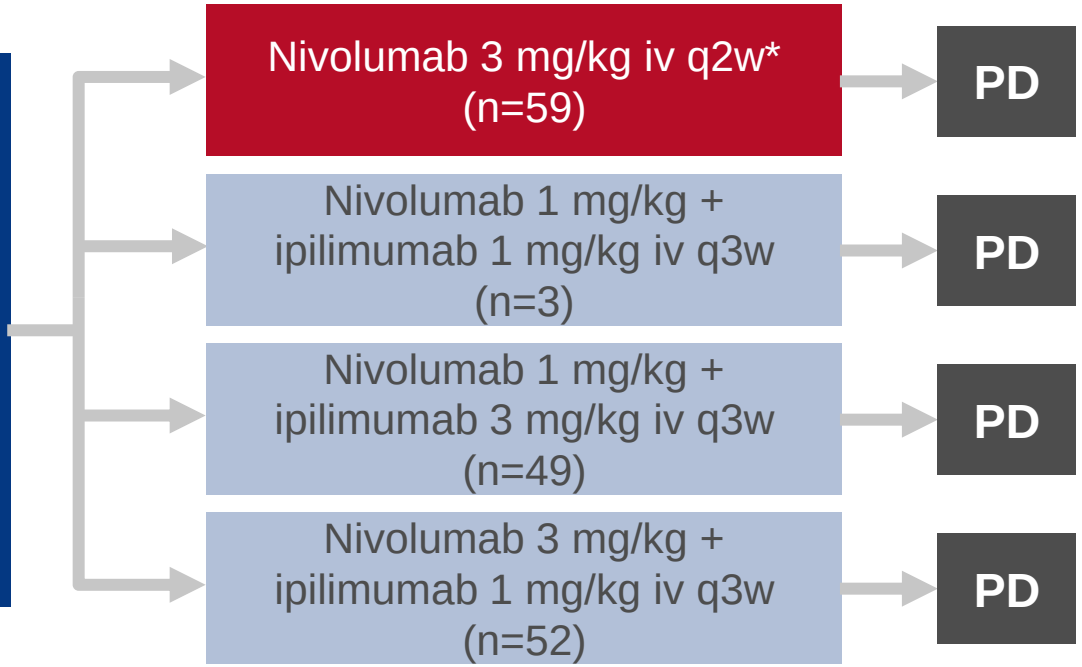
Study objective

- To investigate the efficacy and safety of nivolumab (anti-PD-1 IgG4 mAb) monotherapy in patients with advanced or metastatic gastric or GEJ cancer

Key patient inclusion criteria

- Tumour of lower oesophagus, GEJ or stomach, regardless of PD-L1 status
- Progressive or CT-refractory disease; ≥1 prior therapy
- ECOG PS 0–1

(n=59)



PRIMARY ENDPOINT(S)

- ORR

SECONDARY ENDPOINTS

- OS, PFS, duration of response
- Safety, PK/PD, biomarker status

*Data only presented for this arm of the study

Le et al. J Clin Oncol 2016; 34 (suppl): abstr 6

6: Safety and activity of nivolumab monotherapy in advanced and metastatic (A/M) gastric or gastroesophageal junction cancer (GC/GEC): Results from the CheckMate-032 study – Le DT, et al

Key results

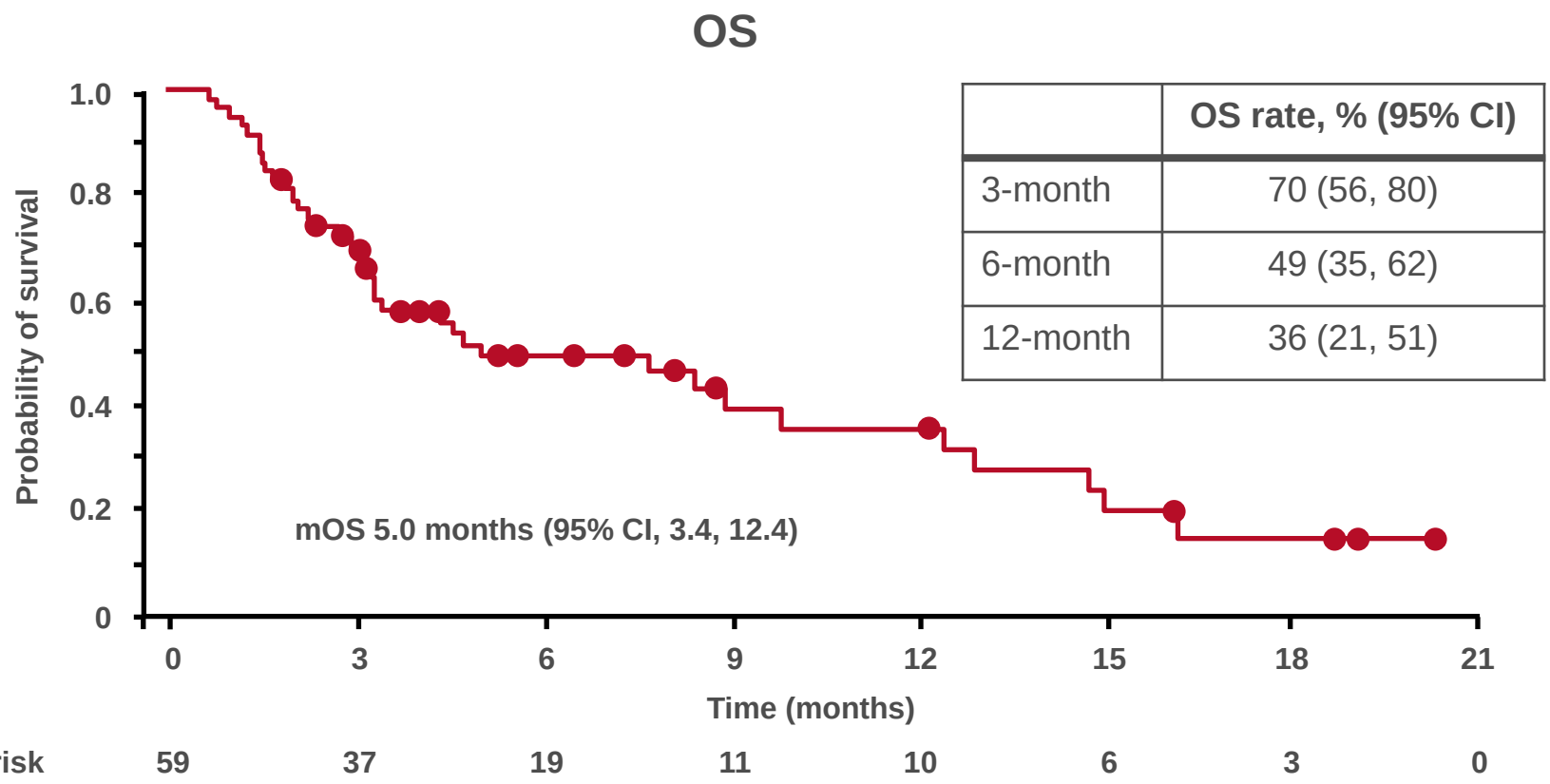
Best overall response	Nivolumab 3 mg/kg (N=59)
ORR, % (95% CI)	14 (6, 25)
CR, n (%)	1 (2)
PR, n (%)	7 (12)
SD, n (%)	11 (19)
PD, n (%)	34 (58)
Unknown, n (%)	6 (10)
DCR, n (%)	19 (32)

PD-L1 expression cut-off		ORR, n/N (%)	95% CI
1% expression	<1%	3/25 (12)	3, 31
	≥1%	4/15 (27)	8, 55
5% expression	<5%	5/34 (15)	5, 31
	≥5%	2/6 (33)	4, 78

Le et al. J Clin Oncol 2016; 34 (suppl): abstr 6

6: Safety and activity of nivolumab monotherapy in advanced and metastatic (A/M) gastric or gastroesophageal junction cancer (GC/GEC): Results from the CheckMate-032 study – Le DT, et al

Key results (continued)

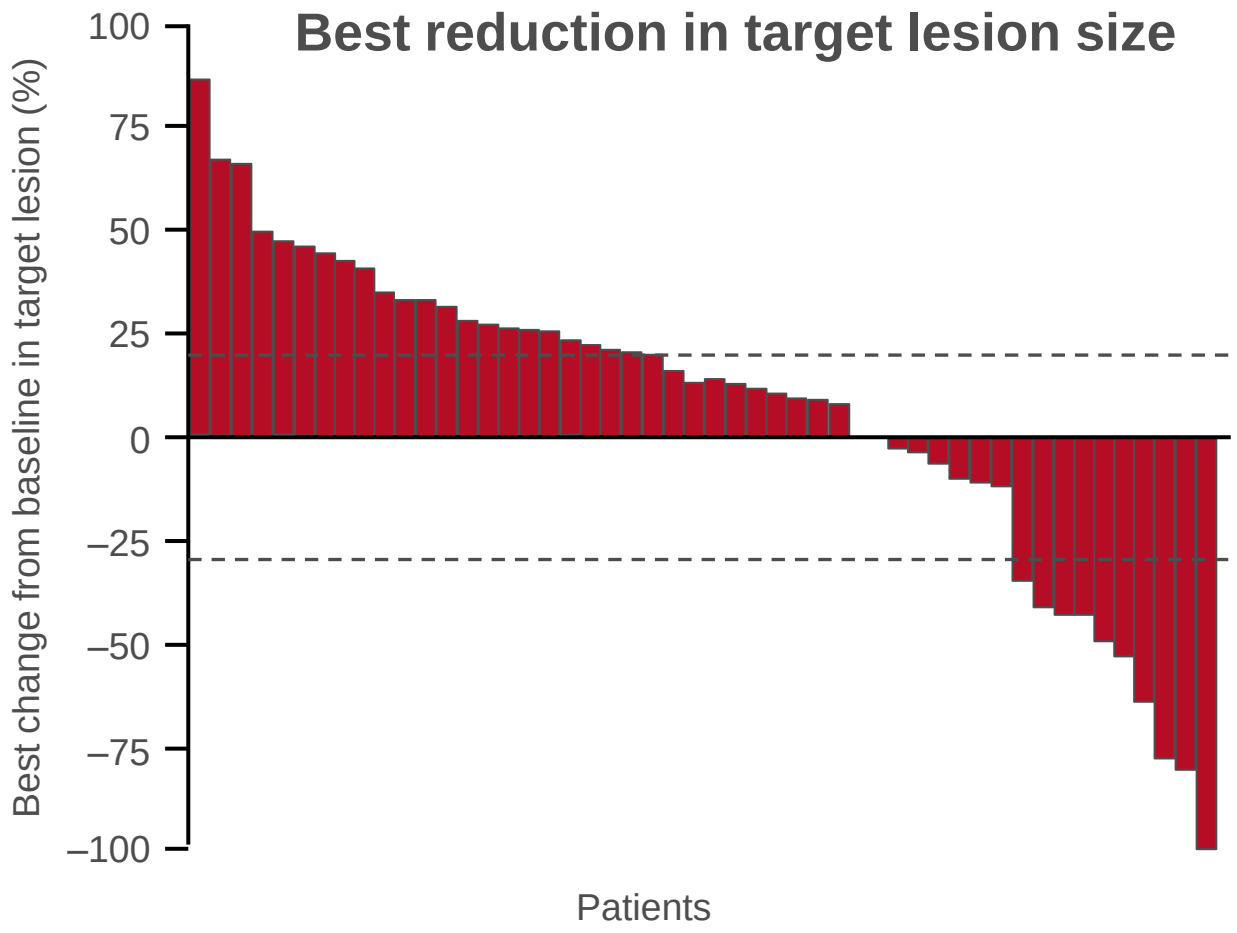


	OS rate, % (95% CI)
3-month	70 (56, 80)
6-month	49 (35, 62)
12-month	36 (21, 51)

Le et al. J Clin Oncol 2016; 34 (suppl): abstr 6

6: Safety and activity of nivolumab monotherapy in advanced and metastatic (A/M) gastric or gastroesophageal junction cancer (GC/GEC): Results from the CheckMate-032 study – Le DT, et al

Key results (continued)



Le et al. J Clin Oncol 2016; 34 (suppl): abstr 6

6: Safety and activity of nivolumab monotherapy in advanced and metastatic (A/M) gastric or gastroesophageal junction cancer (GC/GEC): Results from the CheckMate-032 study – Le DT, et al

Key results (continued)

TEAE in ≥10% patients, n (%)	Any grade	Grade ≥3
Any event	41 (69)	10 (17)
Fatigue	19 (32)	1 (2)
Pruritus	10 (17)	0
Decreased appetite	9 (15)	0
Diarrhoea	9 (15)	1 (2)
Nausea	8 (14)	0
AST increased	7 (12)	3 (5)
Pyrexia	6 (10)	0
Vomiting	6 (10)	1 (2)

Conclusions

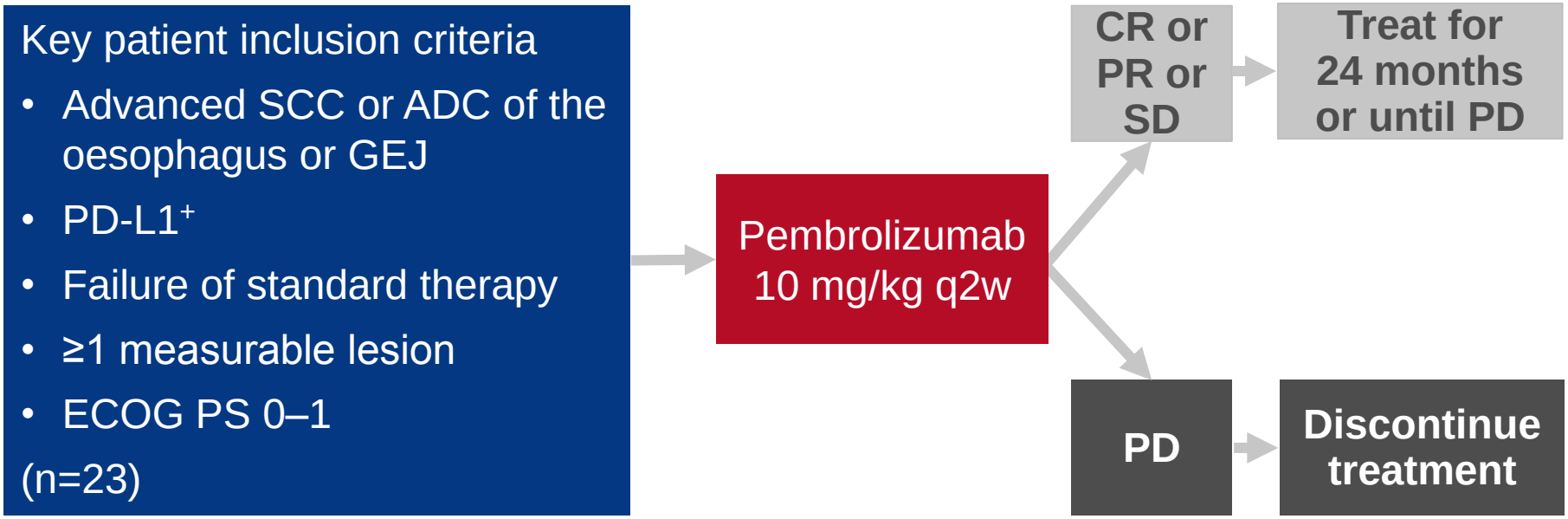
- **Nivolumab monotherapy had encouraging antitumor activity and was well tolerated in heavily pre-treated patients with advanced or metastatic GC/GEC**
- **49% of patients were still alive at 6 months and 36% at 12 months**
- **The AE profile was similar to other tumour types**

Le et al. J Clin Oncol 2016; 34 (suppl): abstr 6

7: Updated results for the advanced esophageal carcinoma cohort of the phase Ib KEYNOTE-028 study of pembrolizumab (MK-3475) – Doi T, et al

Study objective

- To evaluate the efficacy and safety of pembrolizumab in patients with PD-L1^{+} advanced GEC*



PRIMARY ENDPOINT(S)

- ORR (RECIST v1.1)

SECONDARY ENDPOINTS

- PFS, OS, duration of response
- Safety

*A cohort of the Phase Ib KEYNOTE-28 study

Doi et al. J Clin Oncol 2016; 34 (suppl): abstr 7

7: Updated results for the advanced esophageal carcinoma cohort of the phase Ib KEYNOTE-028 study of pembrolizumab (MK-3475) – Doi T, et al

Key results

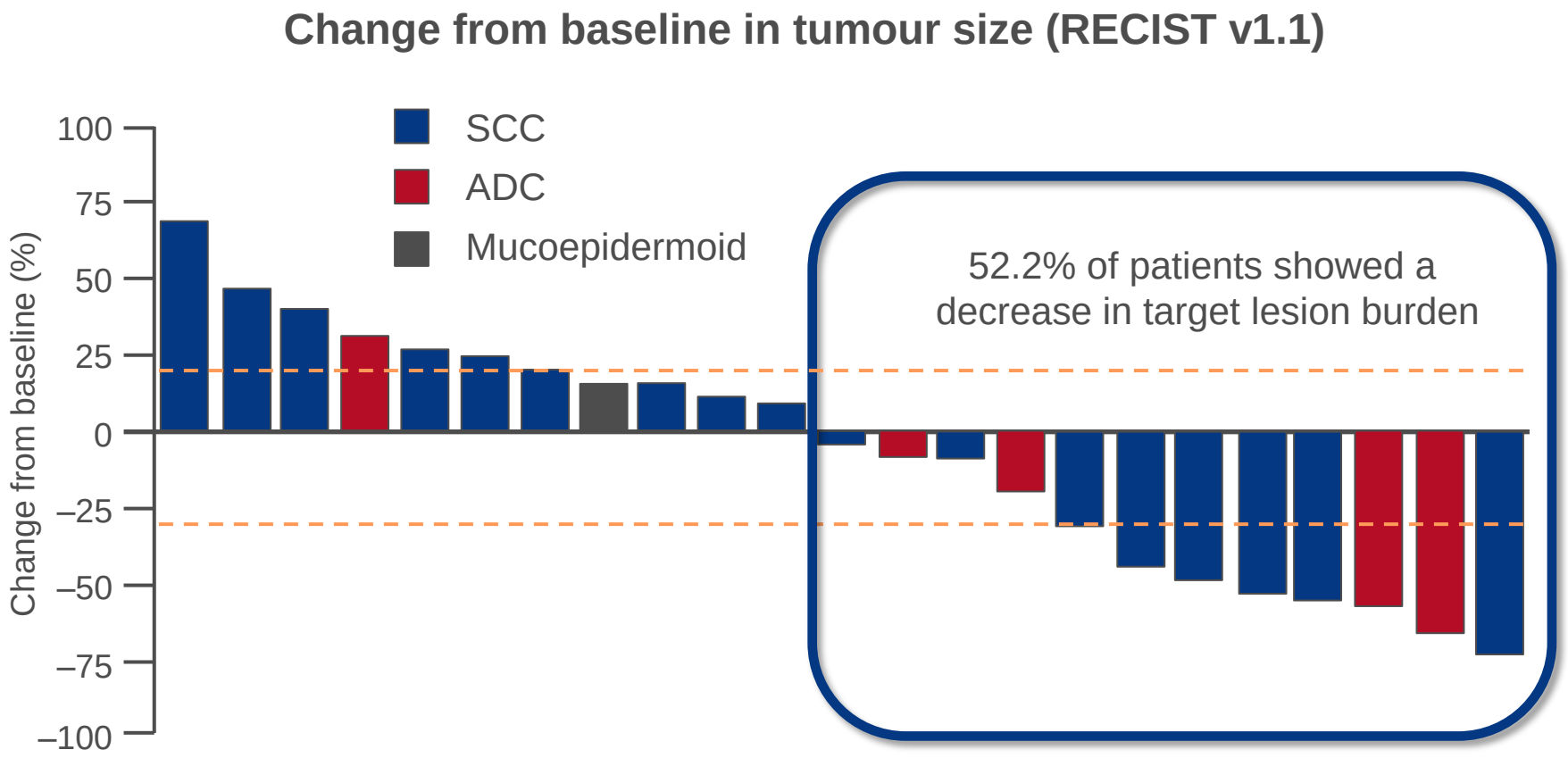
Best overall response	Pembrolizumab (n=23)	
	n (%)	95% CI
ORR	7 (30)	13, 53
CR	0	0, 15
PR	7 (30)	13, 53
SD	2 (9)	1, 28
PD	13 (56)	34, 77

- ORR: 29% (5/17) for SCC, 40% (2/5) for ADC

Doi et al. J Clin Oncol 2016; 34 (suppl): abstr 7

7: Updated results for the advanced esophageal carcinoma cohort of the phase Ib KEYNOTE-028 study of pembrolizumab (MK-3475) – Doi T, et al

Key results (continued)

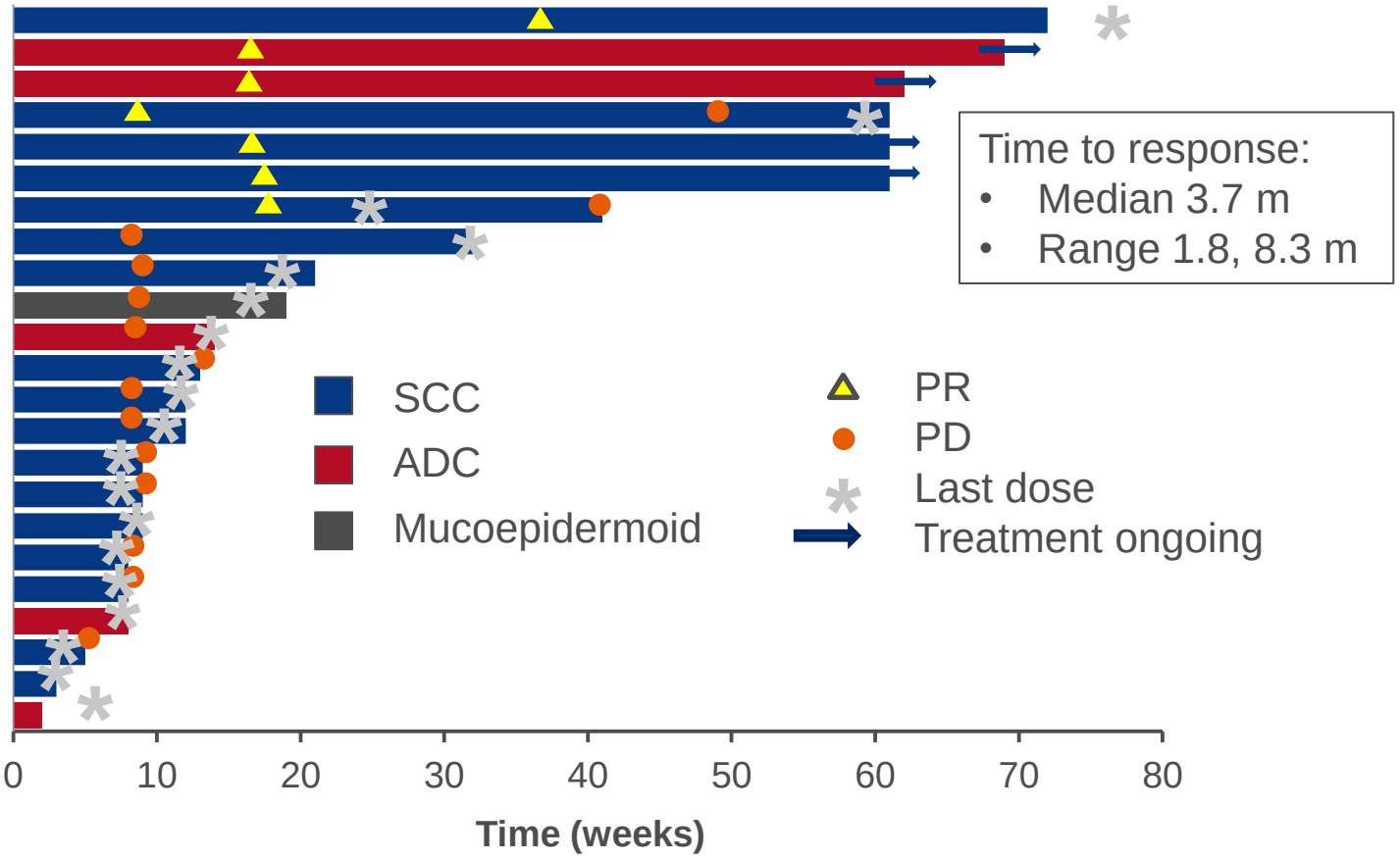


Doi et al. J Clin Oncol 2016; 34 (suppl): abstr 7

7: Updated results for the advanced esophageal carcinoma cohort of the phase Ib KEYNOTE-028 study of pembrolizumab (MK-3475) – Doi T, et al

Key results (continued)

Treatment exposure and response duration



Doi et al. J Clin Oncol 2016; 34 (suppl): abstr 7

7: Updated results for the advanced esophageal carcinoma cohort of the phase Ib KEYNOTE-028 study of pembrolizumab (MK-3475) – Doi T, et al

Key results (continued)

TEAEs	Pembrolizumab (n=23)
Any	9 (39)
Grade 3	4 (17)
Decreased appetite	
Grade 1–2	2 (9)
Grade 3	1 (4)
Decreased lymphocytes, grade 3	2 (9)
Rash, grade 1–2	2 (9)
Liver disorder, grade 3	1 (4)
Pruritic rash, grade 3	1 (4)

Conclusions

- **Pembrolizumab provided promising efficacy and manageable toxicity in heavily pre-treated patients with PD-L1^{+} advanced GEC**
- **Phase II and III trials (KEYNOTE-180 and -181) in patients with GEC are ongoing**

Doi et al. J Clin Oncol 2016; 34 (suppl): abstr 7

CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

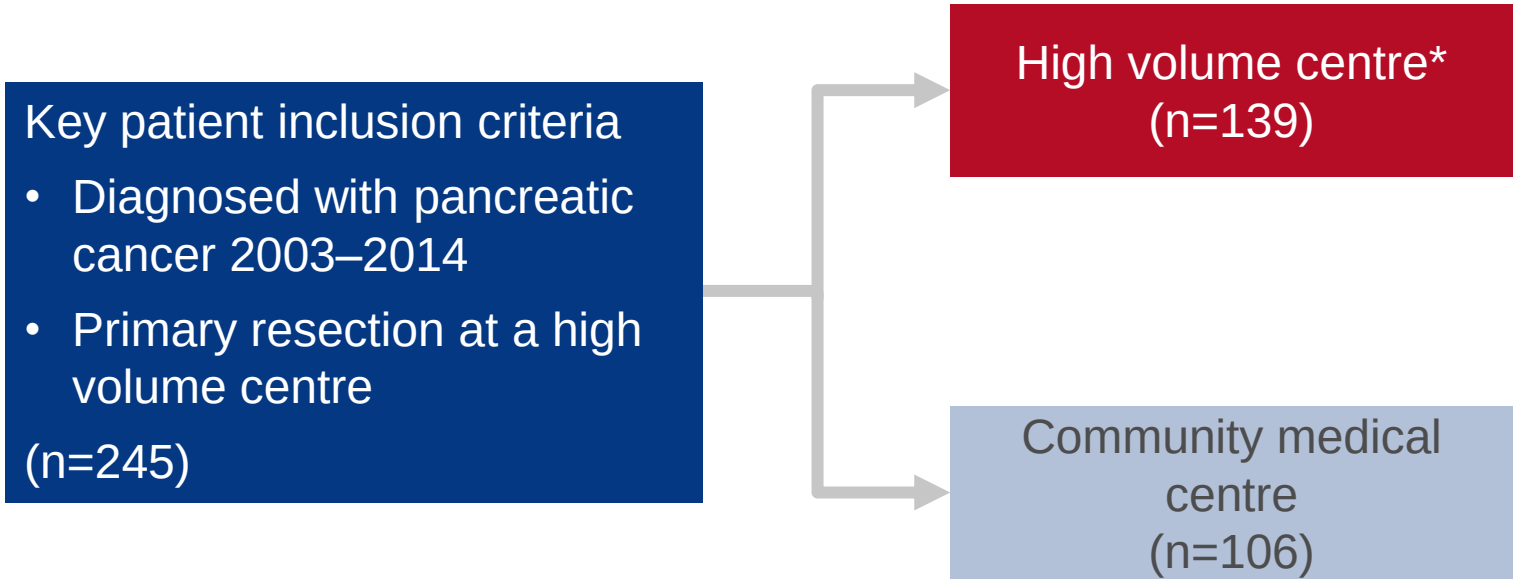
Cancers of the pancreas, small bowel and hepatobiliary tract

PANCREATIC CANCER

191: Resected pancreatic cancer (PC): Impact of adjuvant therapy (Rx) at a high-volume center (HVC) on overall survival (OS) – Mandelson MT, et al

Study objective

- To assess surgical outcomes with adjuvant therapy at high volume centres vs. community medical centres in patients with resected pancreatic cancer



PRIMARY ENDPOINT(S)

- 5-year OS

*Approximately 300 patients with pancreatic cancer per year

Mandelson et al. J Clin Oncol 2016; 34 (suppl): abstr 191

191: Resected pancreatic cancer (PC): Impact of adjuvant therapy (Rx) at a high-volume center (HVC) on overall survival (OS) – Mandelson MT, et al

Key results

- Baseline characteristics were generally comparable apart from age:
  - 63.1 vs. 68.2 years for high volume centre vs. community, respectively (p<0.01)

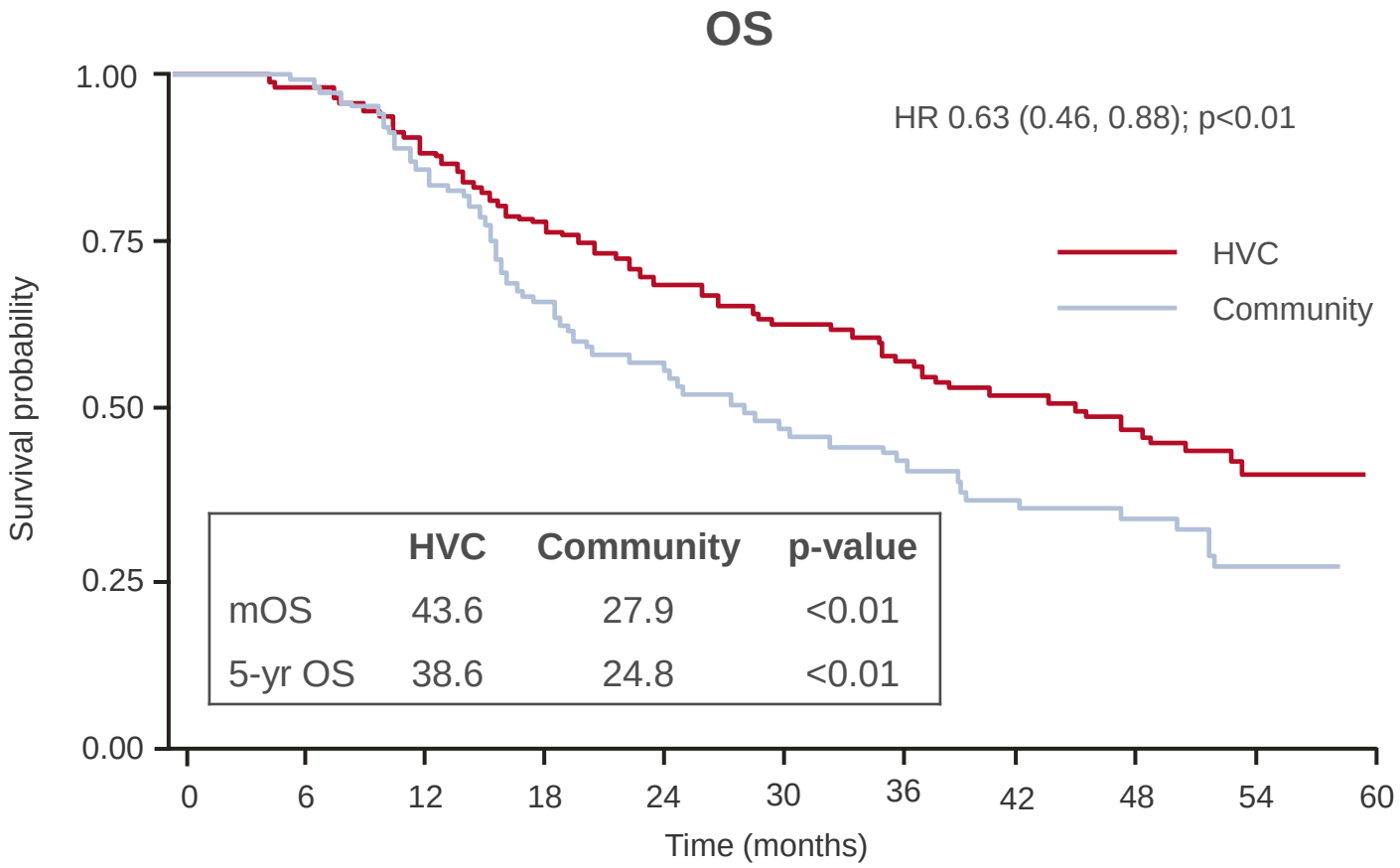
	High volume centre (n=139)	Community (n=106)	p-value
T stage 1 or 2, %	15	13	NS
Node positive, %	69	72	NS
Margin positive, %	22	20	NS

Treatment characteristics at high volume centre	%
Started CT	96
Multi-agent CT	81
CRT	53

Mandelson et al. J Clin Oncol 2016; 34 (suppl): abstr 191

191: Resected pancreatic cancer (PC): Impact of adjuvant therapy (Rx) at a high-volume center (HVC) on overall survival (OS) – Mandelson MT, et al

Key results (continued)



	HVC	Community	p-value
mOS	43.6	27.9	<0.01
5-yr OS	38.6	24.8	<0.01

HVC, high volume centre

Mandelson et al. J Clin Oncol 2016; 34 (suppl): abstr 191

191: Resected pancreatic cancer (PC): Impact of adjuvant therapy (Rx) at a high-volume center (HVC) on overall survival (OS) – Mandelson MT, et al

Conclusions

- **OS was superior in patients with resected pancreatic cancer receiving adjuvant therapy at a high volume centre compared with a community medical centre**
- **This study supports the use of high volume centres for patients receiving treatment for pancreatic cancer with curative intent**
- **Further investigations on the impact of patterns of care on OS are warranted in patients with pancreatic cancer**

Mandelson et al. J Clin Oncol 2016; 34 (suppl): abstr 191

193: Evofosfamide (TH-302) in combination with gemcitabine in previously untreated patients with metastatic or locally advanced unresectable pancreatic ductal adenocarcinoma: Primary analysis of the randomized, double-blind phase III MAESTRO study – Van Cutsem E, et al

Study objective

- To evaluate the efficacy and safety of evofosfamide* + gemcitabine vs. placebo + gemcitabine in patients with metastatic or locally advanced, unresectable PDAC

Key patient inclusion criteria

- Metastatic/locally advanced unresectable PDAC
- ECOG PS 0–1
- No prior CT/systemic therapy‡
- No neoadjuvant or adjuvant CT within 6 months

(n=693)

R 1:1

Evofosfamide† 340 mg/m² + gemcitabine† 1000 mg/m² (n=346) → PD

Stratification

- Disease extent
- ECOG PS
- Geographic region

Placebo† + gemcitabine† 1000 mg/m² (n=347) → PD

PRIMARY ENDPOINT(S)

- OS

SECONDARY ENDPOINTS

- PFS, ORR
- Safety, QoL, PK, biomarkers

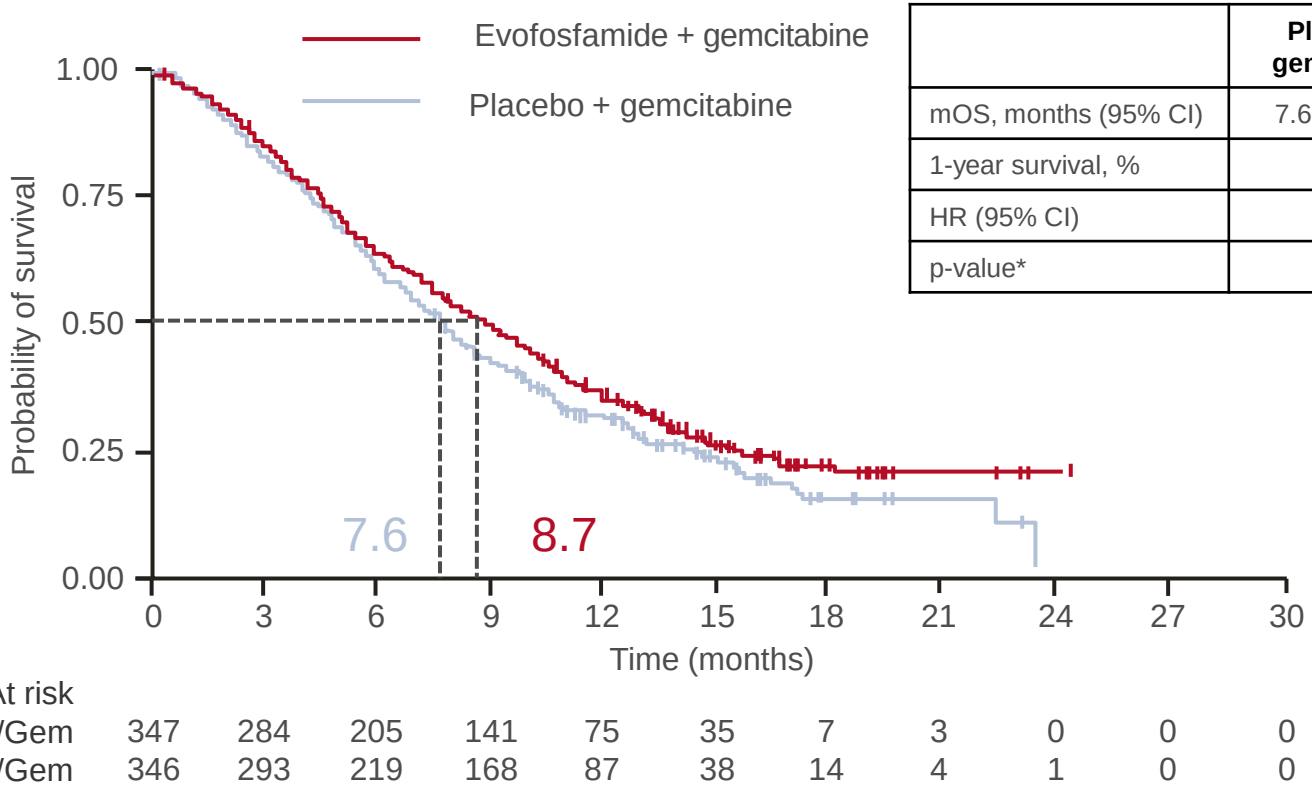
*Hypoxia-activated prodrug of bromo-isophosphoramide mustard; †d1, 8, 15 of a 28-day cycle; ‡Apart from radio-sensitising doses of 5-FU or gemcitabine

Van Cutsem et al. J Clin Oncol 2016; 34 (suppl): abstr 193

193: Evofosfamide (TH-302) in combination with gemcitabine in previously untreated patients with metastatic or locally advanced unresectable pancreatic ductal adenocarcinoma: Primary analysis of the randomized, double-blind phase III MAESTRO study – Van Cutsem E, et al

Key results

OS



	Placebo + gemcitabine	Evofosfamide + gemcitabine
mOS, months (95% CI)	7.6 (6.7, 8.3)	8.7 (7.6, 9.9)
1-year survival, %	29.8	34.2
HR (95% CI)	0.84 (0.71, 1.01)	
p-value*	0.059	

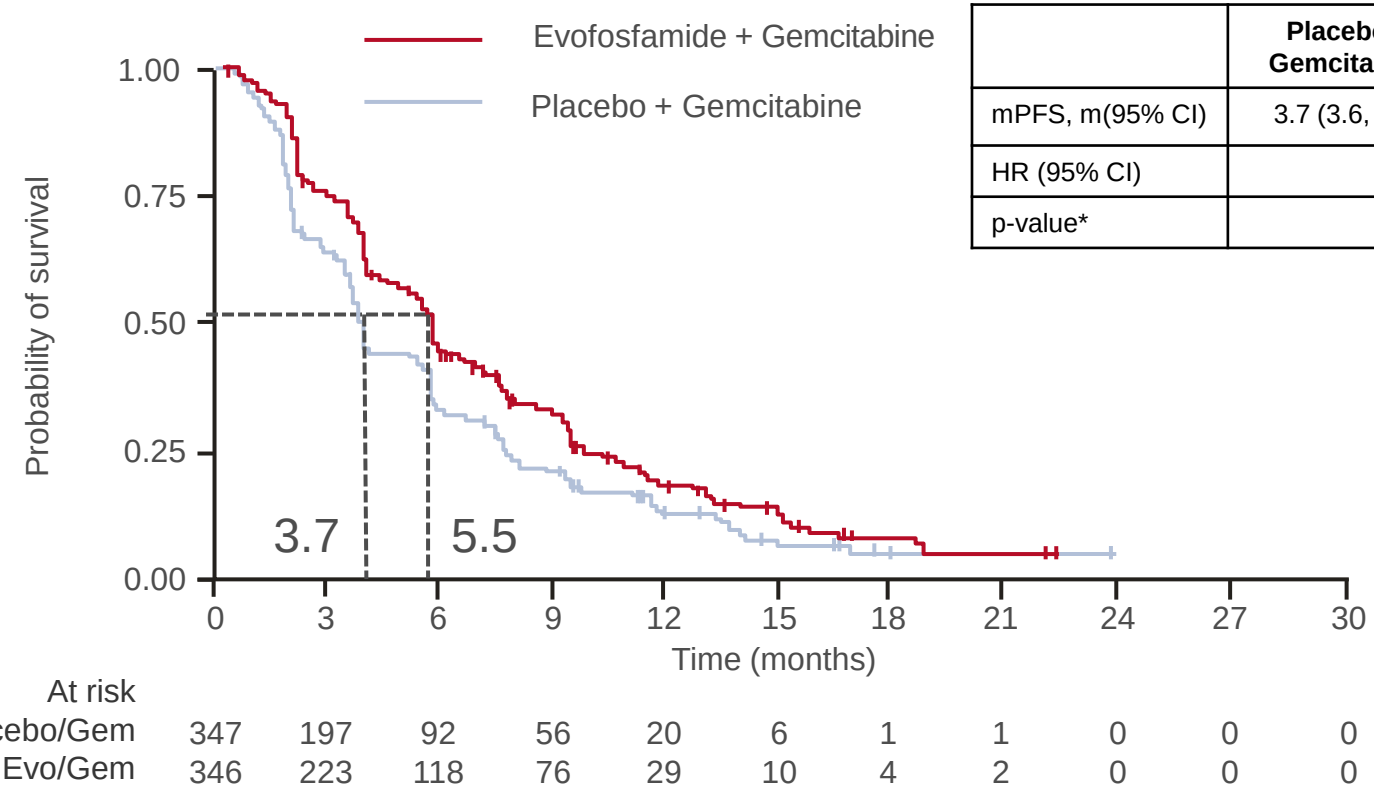
*Log rank (stratified). Evo, evofosfamide; Gem, gemcitabine

Van Cutsem et al. J Clin Oncol 2016; 34 (suppl): abstr 193

193: Evofosfamide (TH-302) in combination with gemcitabine in previously untreated patients with metastatic or locally advanced unresectable pancreatic ductal adenocarcinoma: Primary analysis of the randomized, double-blind phase III MAESTRO study – Van Cutsem E, et al

Key results (continued)

PFS



	Placebo + Gemcitabine	Evofosfamide + Gemcitabine
mPFS, m(95% CI)	3.7 (3.6, 3.8)	5.5 (4.8, 5.6)
HR (95% CI)	0.77 (0.65, 0.92)	
p-value*	0.004	

*Log rank (stratified)

Van Cutsem et al. J Clin Oncol 2016; 34 (suppl): abstr 193

193: Evofosfamide (TH-302) in combination with gemcitabine in previously untreated patients with metastatic or locally advanced unresectable pancreatic ductal adenocarcinoma: Primary analysis of the randomized, double-blind phase III MAESTRO study – Van Cutsem E, et al

Key results (continued)

	Evofosfamide (n=323)	Placebo (n=325)	OR (95% CI); p-value
ORR unconfirmed, %	20.4	16.3	1.32 (0.88, 1.97); 0.17
ORR confirmed, %	15.2	8.6	1.90 (1.16, 3.12); 0.0086

Reasons for treatment discontinuation, n (%)	Evofosfamide (n=346)	Placebo (n=347)
No treatment received	6 (1.7)	8 (2.3)
Treatment ongoing at data cut-off	12 (3.5)	16 (4.6)
Treatment completed/discontinued	328 (94.8)	323 (93.1)
AE	62 (17.9)	52 (15.6)
Protocol non-compliance	7 (2.0)	9 (2.6)
Disease progression	187 (54.0)	214 (61.7)
Death	12 (3.5)	17 (4.9)
Withdrawn consent	41 (11.8)	21 (6.1)
Other	19 (5.5)	8 (2.3)

Van Cutsem et al. J Clin Oncol 2016; 34 (suppl): abstr 193

193: Evofosfamide (TH-302) in combination with gemcitabine in previously untreated patients with metastatic or locally advanced unresectable pancreatic ductal adenocarcinoma: Primary analysis of the randomized, double-blind phase III MAESTRO study – Van Cutsem E, et al

Key results (continued)

AEs, %	Evofosfamide (n=338)	Placebo (n=341)
Any AE	99.1	98.8
AE leading to dose interruption	74.3	54.8
AE leading to dose reduction	62.4	37.5
Grade 3/4 AEs		
Nausea	2.7/0.0	3.8/0.0
Decreased appetite	1.8/0.3	2.9/0.0
Diarrhoea	4.4/0.3	1.8/0.0
Vomiting	3.0/0.3	4.1/0.0
Constipation	0.3/0.0	0.3/0.0
Fatigue	4.4/0.3	3.8/0.0

Conclusions

- **Evofosfamide did not significantly improve OS vs. placebo when added to gemcitabine in patients with unresectable PDAC**
- **However, evofosfamide demonstrated antitumor activity vs. placebo (OS, PFS, ORR)**
- **The safety profile for evofosfamide was consistent with previous studies**
- **Discontinuations and dose interruptions/reductions were more frequent with evofosfamide than placebo**

Van Cutsem et al. J Clin Oncol 2016; 34 (suppl): abstr 193

Cancers of the pancreas, small bowel and hepatobiliary tract

HEPATOCELLULAR CARCINOMA

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

Study objective

- To evaluate the efficacy and safety of doxorubicin + sorafenib vs. sorafenib alone in patients with advanced HCC

Key patient inclusion criteria
- Advanced HCC
- No prior systemic therapy
- Child-Pugh A
- ECOG PS 0–2

(n=346)

R

Doxorubicin 60 mg/m^2 q3w + sorafenib 400 mg po bid (n=173) → PD

Stratification
- Extent of disease (locally advanced; metastatic)

Sorafenib 400 mg po bid (n=173) → PD

PRIMARY ENDPOINT(S)
- OS

SECONDARY ENDPOINTS
- PFS, safety

Note: Based on data from abstract only. Presented by Alan Venook.

Abou-Alfa et al. J Clin Oncol 2016; 34 (suppl): abstr 192

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

Results

	Doxorubicin + sorafenib (n=173)	Sorafenib alone (n=173)
mOS, months (95% CI)	9.3 (7.1, 12.9)	10.5 (7.4, 14.3)
HR* (95% CI)	1.06 (0.8, 1.4)	
mPFS, months (95% CI)	3.6 (2.8, 4.6)	3.2 (2.3, 4.1)
HR* (95% CI)	0.90 (0.7, 1.2)	

	Doxorubicin + sorafenib (n=173)	Sorafenib alone (n=173)
Deaths on treatment, n	18	20
Possibly related to treatment, n	8†	3‡
Grade 3/4 haematological AEs, %	37.8	8.1
Non-haematological AEs, %	63.6	61.5

Conclusions

- **The addition of doxorubicin to sorafenib resulted in higher toxicity than sorafenib alone with no improvements in OS or PFS**
- **The mOS for sorafenib of about 10 months is consistent with previous studies**

*Doxorubicin + sorafenib vs. sorafenib alone; †1x each: sepsis, dysphagia, pneumonia, not specified, 2x each: cardiac, hepatic failure; ‡1x each: fatigue, hepatic failure, secondary malignancy

Based on data from abstract only. Presented by Alan Venook.

Abou-Alfa et al. J Clin Oncol 2016; 34 (suppl): abstr 192

197: Tumor and plasma biomarker analysis from the randomized controlled phase II trial (RCT) of tivantinib in second-line hepatocellular carcinoma (HCC) – Rimassa L, et al

Study objective

- To assess the prognostic and predictive value of tumour and circulating biomarkers in patients with HCC receiving 2L therapy with tivantinib (oral, ATP-independent MET inhibitor)

Study design

- Data were analysed from the Phase II ARQ 197-215 trial (2L tivantinib vs. placebo; n=107)
  - Circulating MET (n=102), HGF (n=102) and AFP (n=104) were centrally tested in serum using ELISA to determine high or low status*
    - The 75th percentile was used instead for AFP
  - Tumour MET was centrally analysed by IHC to determine high or low status*

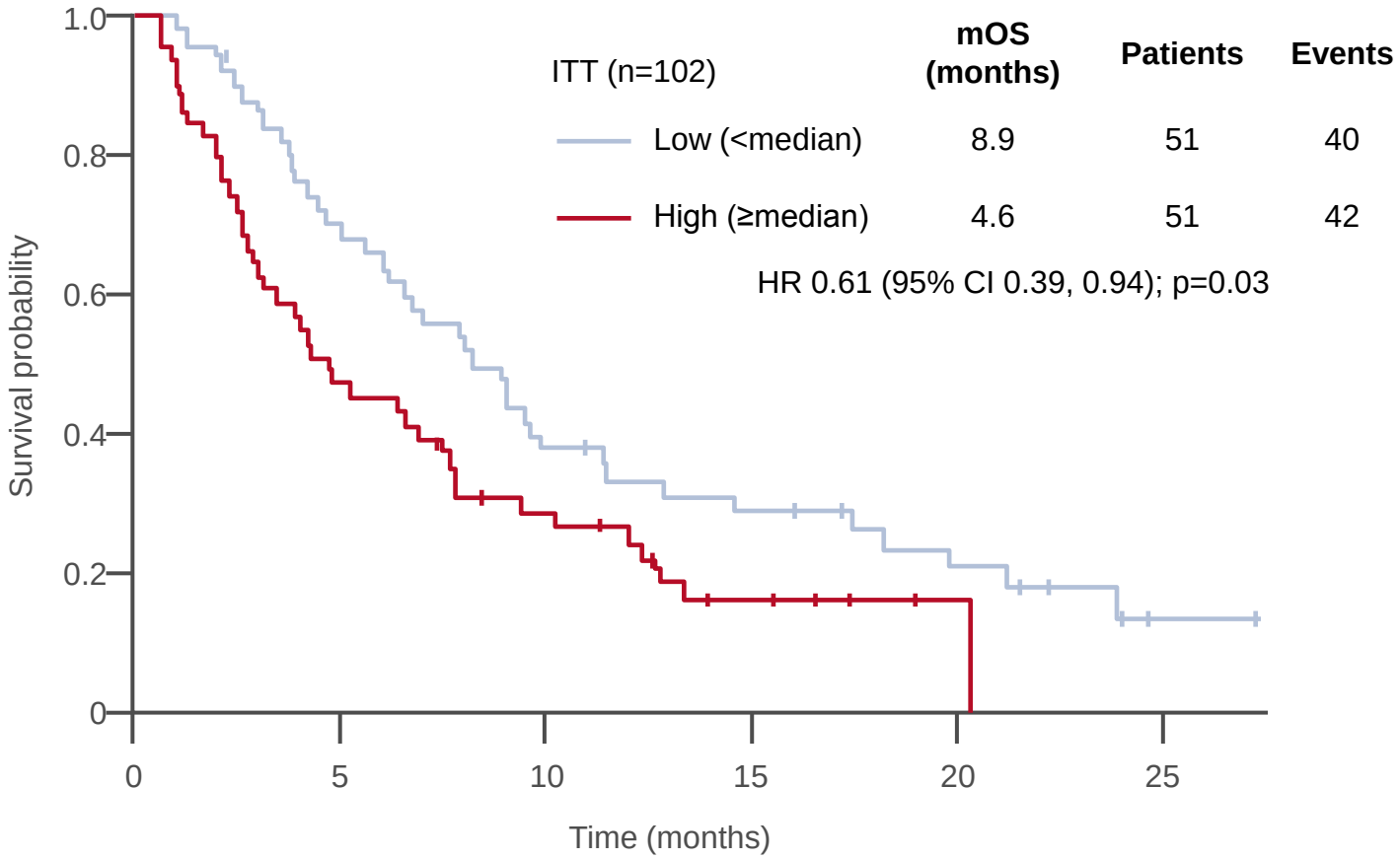
- Data were also analysed from the Phase III METIV HCC trial
  - Patients with MET-high HCC received tivantinib 120 mg bid (n=202) vs. placebo (n=101)
    - Child-Pugh A, ECOG PS 0–1, inoperable, PD after sorafenib

*High MET status: ≥2^{+} staining in ≥50% tumour cells

Rimassa et al. J Clin Oncol 2016; 34 (suppl): abstr 197

197: Tumor and plasma biomarker analysis from the randomized controlled phase II trial (RCT) of tivantinib in second-line hepatocellular carcinoma (HCC) – Rimassa L, et al

Key results



OS in MET-high patients with tivantinib vs. placebo: HR 0.55; p=0.07

Rimassa et al. J Clin Oncol 2016; 34 (suppl): abstr 197

197: Tumor and plasma biomarker analysis from the randomized controlled phase II trial (RCT) of tivantinib in second-line hepatocellular carcinoma (HCC) – Rimassa L, et al

Key results (continued)

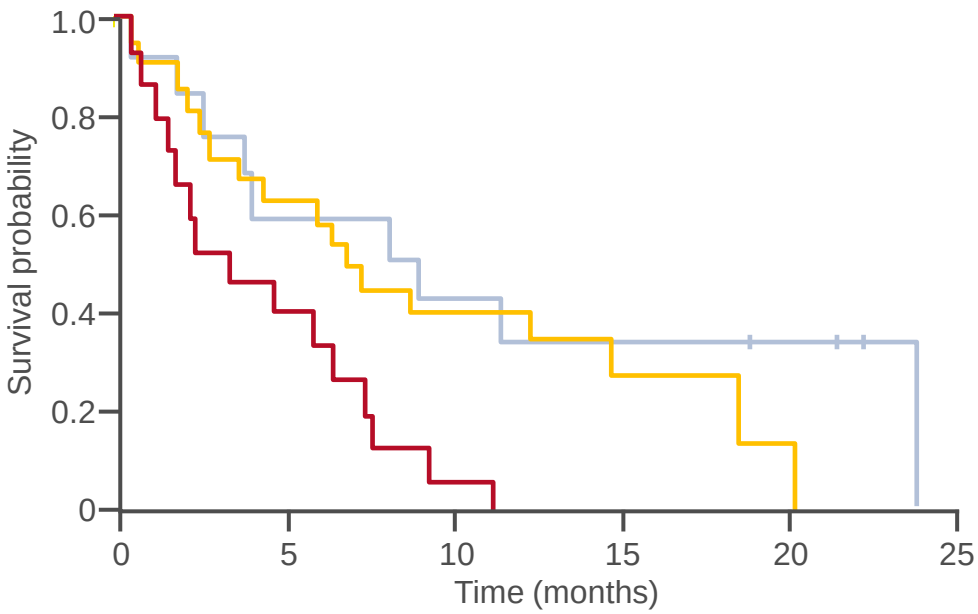
OS by circulating tumour MET status (ARQ 197-215 trial)

	mOS (months)	Patients	Events
Placebo MET-Low	9.0	13	9
Placebo MET-High	3.8	15	15

HR 0.34 (95% CI 0.13, 0.86); p=0.02

	mOS (months)	Patients	Events
Placebo MET-Low	9.0	13	9
Tivantinib MET-High	7.2	22	17

HR 0.72 (95% CI 0.30, 1.70); p=0.45



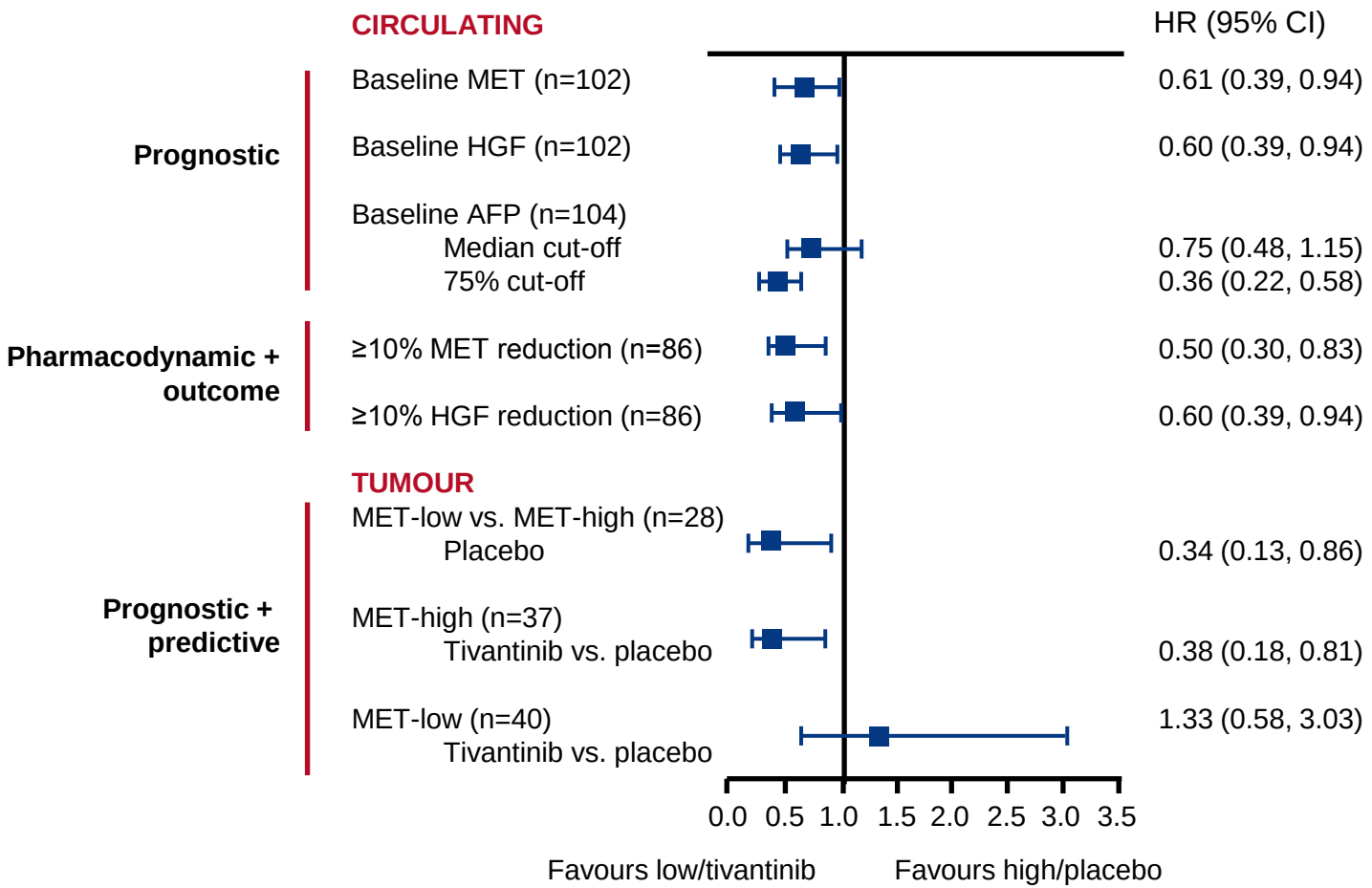
OS in MET-low patients: HR 1.33 (95% CI 0.58, 3.04); p=0.50
OS by MET status with tivantinib vs. placebo: p=0.04

Rimassa et al. J Clin Oncol 2016; 34 (suppl): abstr 197

197: Tumor and plasma biomarker analysis from the randomized controlled phase II trial (RCT) of tivantinib in second-line hepatocellular carcinoma (HCC) – Rimassa L, et al

Key results (continued)

Summary: ARQ 197-215 trial



Rimassa et al. J Clin Oncol 2016; 34 (suppl): abstr 197

197: Tumor and plasma biomarker analysis from the randomized controlled phase II trial (RCT) of tivantinib in second-line hepatocellular carcinoma (HCC) – Rimassa L, et al

Key results (continued)

- Initial results of the METIV-HCC study (currently ongoing)
  - A correlation was found between high MET status and sorafenib treatment ($p<0.0001$)
  - No correlation was found between MET status and:
    - Time on sorafenib
    - Reason for sorafenib discontinuation
    - Time between last sorafenib dose and biopsy
    - Time between diagnosis and biopsy
    - Prior local therapies

Conclusions

- **Tumour MET results are comparable between the ARQ 197-215 and METIV-HCC trials**
- **Circulating MET, HGF and AFP are prognostic markers in patients with HCC**
- **Circulating MET is a pharmacodynamic biomarker for tivantinib**
- **Tumour MET is the only prognostic and predictive marker**
- **This analysis supports the use of tivantinib in patients with MET-high tumours only**
- **The MET-HCC trial will validate the role of analysed biomarkers in HCC**

Rimassa et al. J Clin Oncol 2016; 34 (suppl): abstr 197

Cancers of the pancreas, small bowel and hepatobiliary tract

NEUROENDOCRINE TUMOUR

194: NETTER-1 phase III: Progression-free survival, radiographic response, and preliminary overall survival results in patients with midgut neuroendocrine tumors treated with 177-Lu-Dotatate – Strosberg JR, et al

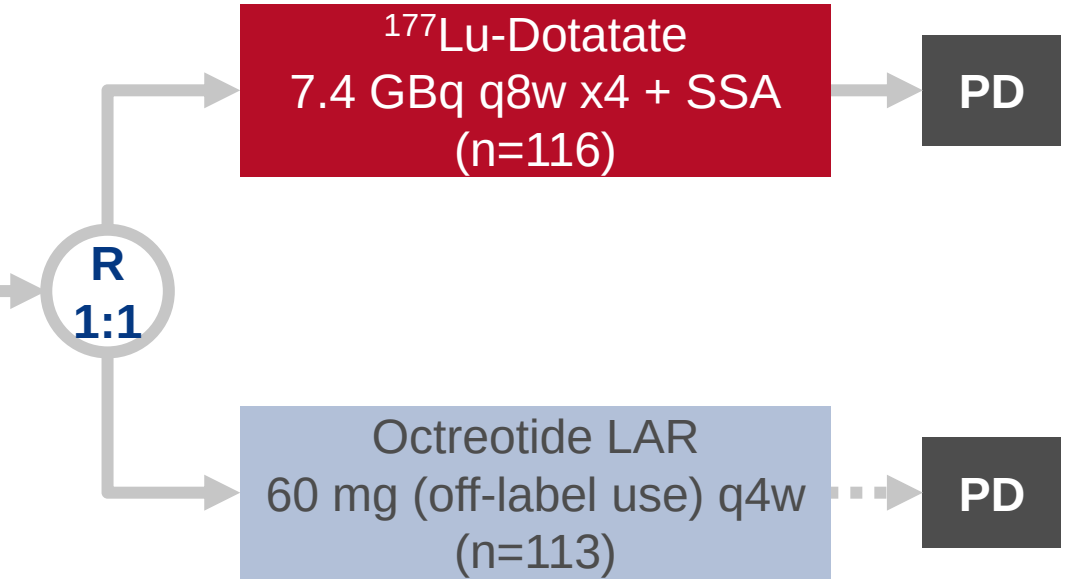
Study objective

- To assess the efficacy and safety of the somatostatin analogue ^{177}Lu-Dotatate vs. octreotide LAR in patients with inoperable, progressive, somatostatin receptor positive midgut NET

Key patient inclusion criteria

- Inoperable, somatostatin receptor positive midgut NET
- PD after octreotide LAR 20–30 mg (on-label use) q3/4w
- Ki67 index ≤20 (grade 1–2)
- Karnofsky PS ≥60

(n=229)



PRIMARY ENDPOINT(S)

- PFS (RECIST v1.1)

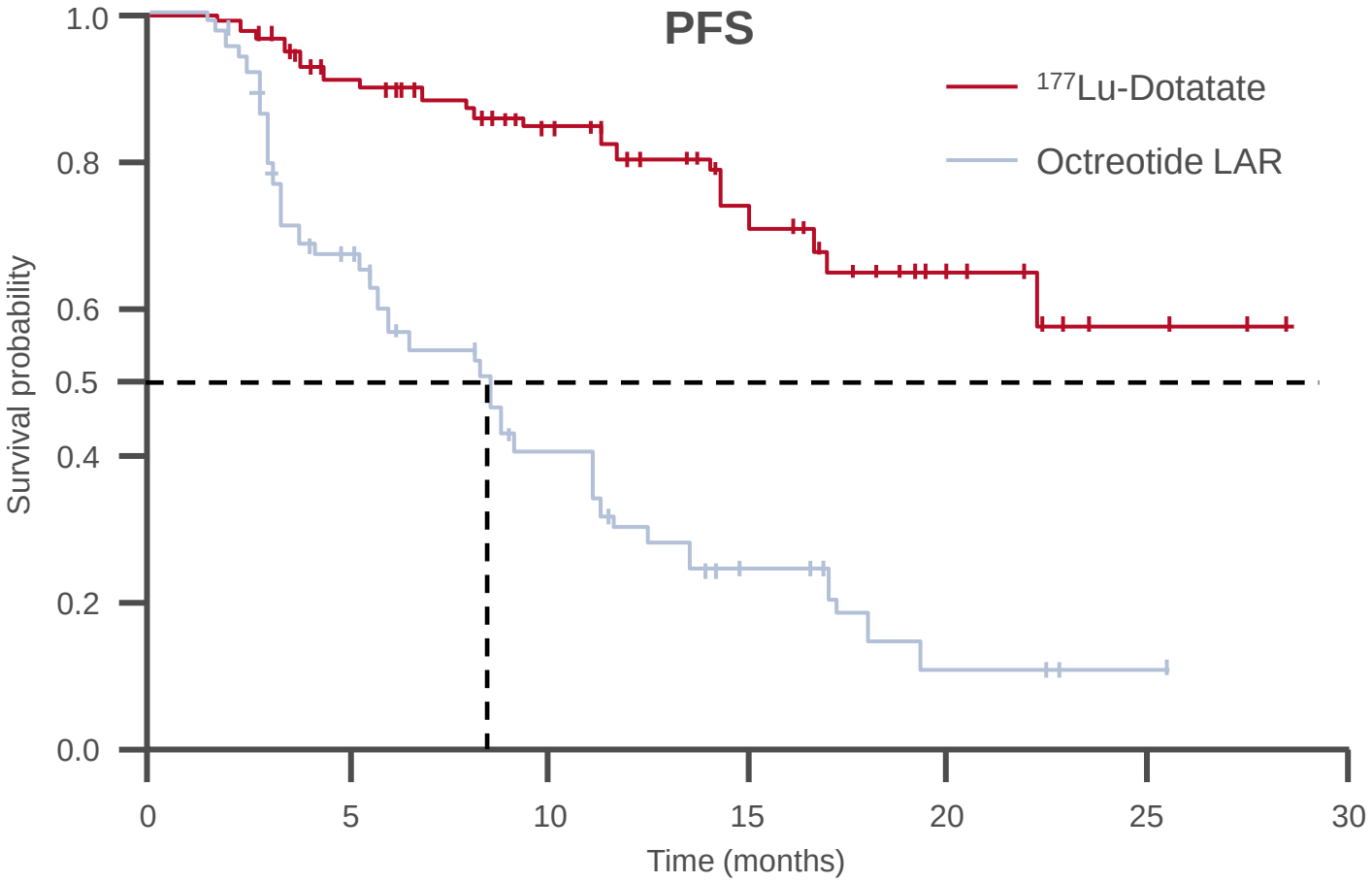
SECONDARY ENDPOINTS

- ORR, OS, TTP
- Toxicity, HR-QoL (EORTC QLQ-GI NET21)

Strosberg et al. J Clin Oncol 2016; 34 (suppl): abstr 194

194: NETTER-1 phase III: Progression-free survival, radiographic response, and preliminary overall survival results in patients with midgut neuroendocrine tumors treated with 177-Lu-Dotatate – Strosberg JR, et al

Key results



HR 0.21 (95% CI 0.129, 0.338); p<0.0001

↓

79% reduction in the risk of PD/death

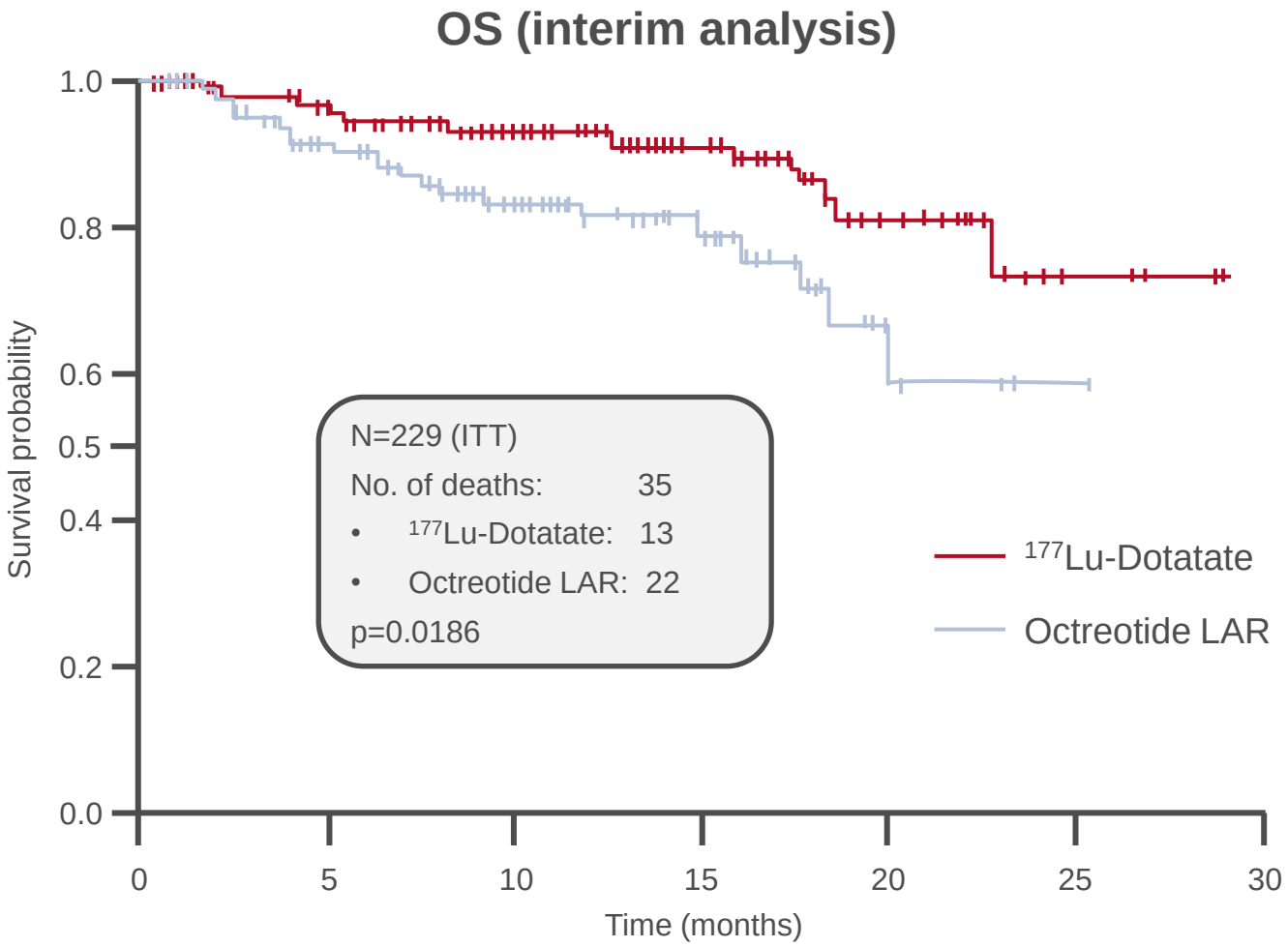
↓

Estimated mPFS with ^{177}Lu-Dotatate: ~40 months

Strosberg et al. J Clin Oncol 2016; 34 (suppl): abstr 194

194: NETTER-1 phase III: Progression-free survival, radiographic response, and preliminary overall survival results in patients with midgut neuroendocrine tumors treated with 177-Lu-Dotatate – Strosberg JR, et al

Key results (continued)



Strosberg et al. J Clin Oncol 2016; 34 (suppl): abstr 194

194: NETTER-1 phase III: Progression-free survival, radiographic response, and preliminary overall survival results in patients with midgut neuroendocrine tumors treated with 177-Lu-Dotatate – Strosberg JR, et al

Key results (continued)

	^{177}Lu-Dotatate (n=101)*	Octreotide LAR 60 mg (n=100)*
CR, n	1	0
PR, n	17	3
ORR, % (95% CI)	18 (10, 25)	3 (0, 6)
p-value	0.0008	

All patients	(n=116)	(n=113)
PD, n (%)	6 (5)	27 (24)
SD, n (%)	77 (66)	70 (62)

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

Strosberg et al. J Clin Oncol 2016; 34 (suppl): abstr 194

194: NETTER-1 phase III: Progression-free survival, radiographic response, and preliminary overall survival results in patients with midgut neuroendocrine tumors treated with 177-Lu-Dotatate – Strosberg JR, et al

Key results (continued)

Grade 3/4 AEs occurring in ≥3% of patients, %	^{177}Lu-Dotatate (n=111)	Octreotide LAR (n=110)
Nausea	4	2
Vomiting	7	0
Diarrhoea	3	2
Abdominal pain	3	5
Lymphopenia	9	0
Decreased appetite	0	3

Conclusions

- **^{177}Lu-Dotatate significantly improved PFS and ORR vs. octreotide LAR in patients with inoperable, progressive, somatostatin receptor positive midgut NET**
  - **Interim analysis also suggests improvements in OS with ^{177}Lu-Dotatate**
- **^{177}Lu-Dotatate had a favourable safety profile, with no clinically relevant findings**
- **^{177}Lu-Dotatate has a major therapeutic benefit in patients with midgut NET, for whom there are currently few available treatment options**

Strosberg et al. J Clin Oncol 2016; 34 (suppl): abstr 194

Cancers of the pancreas, small bowel and hepatobiliary tract

GENERAL

195: PD-1 blockade in mismatch repair deficient non-colorectal gastrointestinal cancers – Le DT, et al

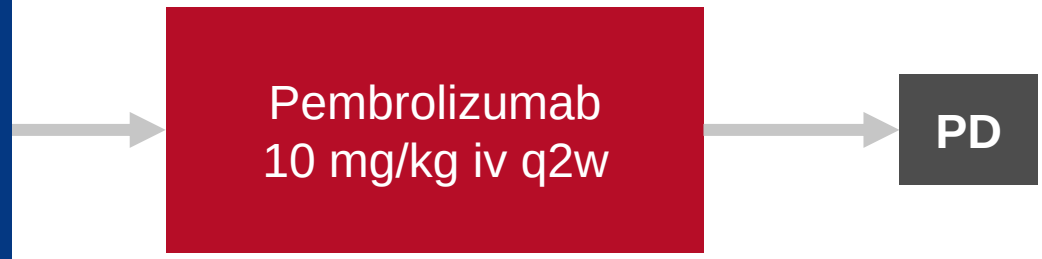
Study objective

- To investigate the efficacy and safety of pembrolizumab in patients with MMR deficient non-CRC advanced GI tumours

Key patient inclusion criteria

- Previously-treated, PD, advanced non-CRC GI cancer
- MMR deficient tumours
- ECOG PS 0–1
- No prior PD-1/PD-L1 therapy

(n=17)



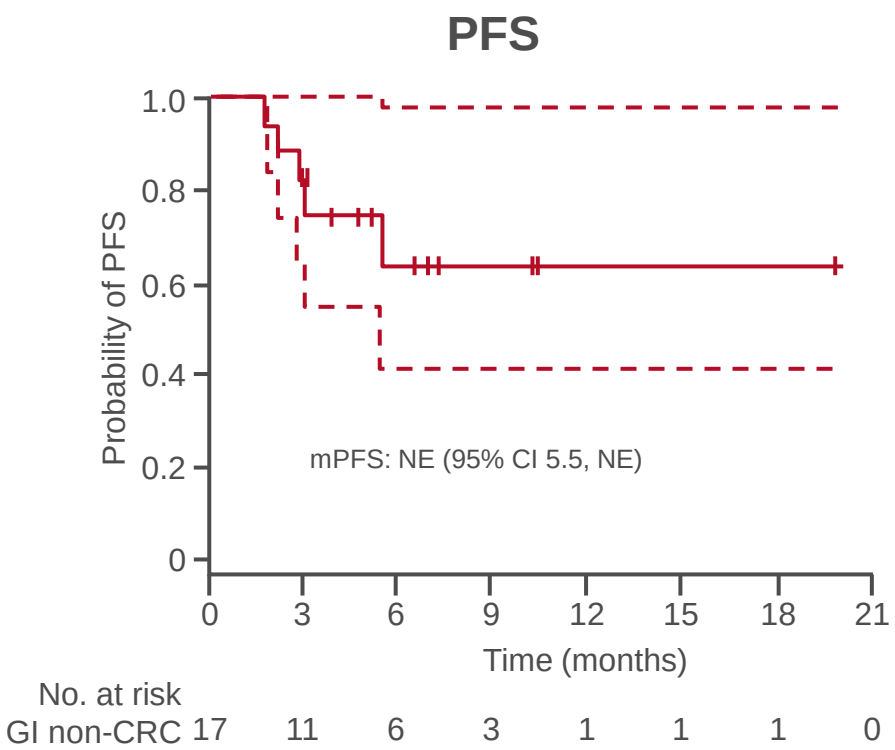
ENDPOINTS

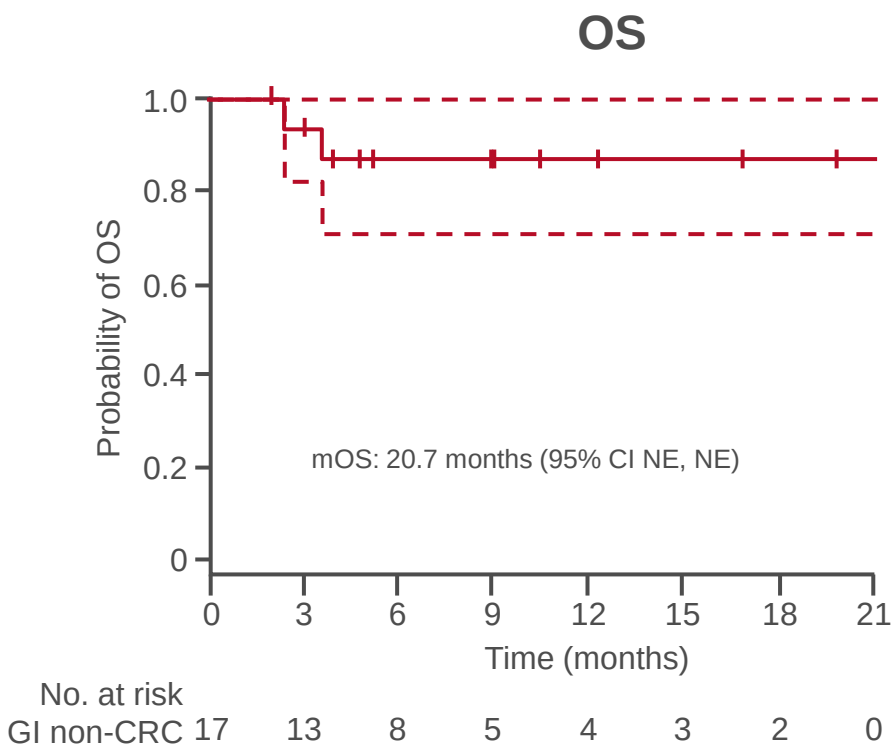
- ORR, PFS, OS
- Safety

Le et al. J Clin Oncol 2016; 34 (suppl): abstr 195

195: PD-1 blockade in mismatch repair deficient non-colorectal gastrointestinal cancers – Le DT, et al

Key results



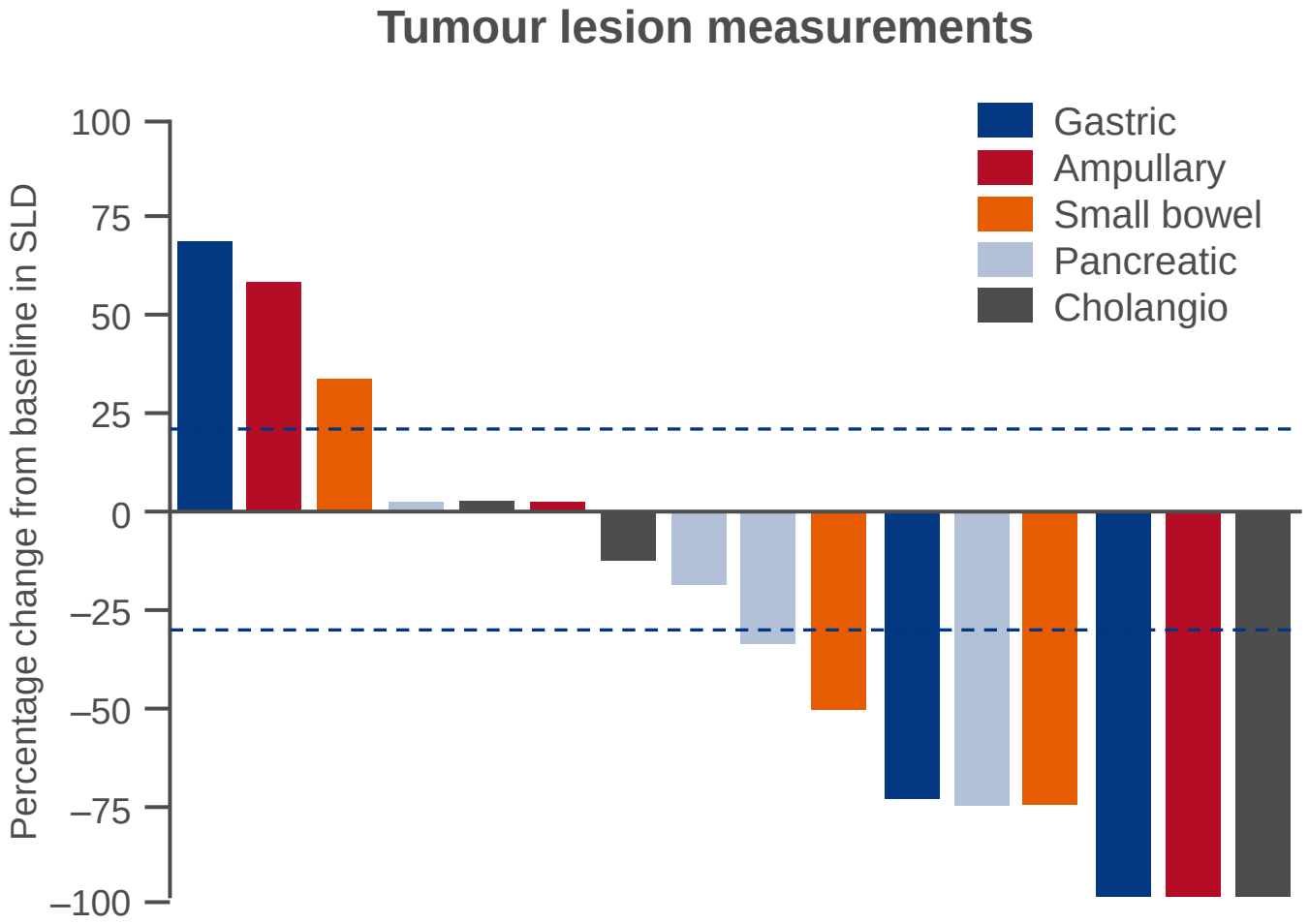


NE, not estimable

Le et al. J Clin Oncol 2016; 34 (suppl): abstr 195

195: PD-1 blockade in mismatch repair deficient non-colorectal gastrointestinal cancers – Le DT, et al

Key results (continued)



Le et al. J Clin Oncol 2016; 34 (suppl): abstr 195

195: PD-1 blockade in mismatch repair deficient non-colorectal gastrointestinal cancers – Le DT, et al

Key results (continued)

Objective responses	n=17
ORR, % (95% CI)	47 (23, 72)
DCR, % (95% CI)	76 (50, 93)
CR, n (%)	4 (24)
PR, n (%)	4 (24)
SD, n (%)	5 (29)
PD, n (%)	3 (18)
Not evaluable	1 (6)

Le et al. J Clin Oncol 2016; 34 (suppl): abstr 195

195: PD-1 blockade in mismatch repair deficient non-colorectal gastrointestinal cancers – Le DT, et al

Key results (continued)

TEAEs, n (%)	Any grade (n=17)	Grade 3 or 4 (n=17)
Any	13 (76)	2 (12)
Fatigue	4 (24)	0
Myalgia	2 (12)	0
Arthralgia	2 (12)	0
Nausea	3 (18)	0
Diarrhoea/colitis	3 (18)	2 (12)
Thyroiditis/hypothyroidism	4 (24)	0
Rash/pruritus	7 (41)	0

Conclusions

- **Pembrolizumab had promising activity in mismatch repair deficient GI cancers**
  - **Clinical benefit was observed in a range of tumours, including colon, stomach, duodenum, pancreas, ampulla and bile ducts**
- **Biochemical response correlated with radiological response**

Le et al. J Clin Oncol 2016; 34 (suppl): abstr 195

CANCERS OF THE COLON, RECTUM AND ANUS

Cancers of the colon, rectum and anus

COLORECTAL CANCER

488: Early detection of colorectal neoplasia: Combination of eight cancer-associated blood-based protein biomarker – Christensen IJ, et al

Study objective

- To assess the diagnostic value of eight blood-based protein markers in identifying CRC

Key patient inclusion criteria

- First-time colonoscopy patients, with symptoms potentially attributable to CRC

(n=4698)

→ Plasma levels of: AFP, CA19-9, CEA, hs-CRP, CyFra21-1, Ferritin, Galectin-3, TIMP-1 → **Assess**

PRIMARY & SECONDARY ENDPOINTS

- CRC + high risk adenomas vs. all others excluding non-CRC
- CRC vs. all other cancers excluding non-CRC
- All cancers vs. all others
- Non-CRC vs. all others

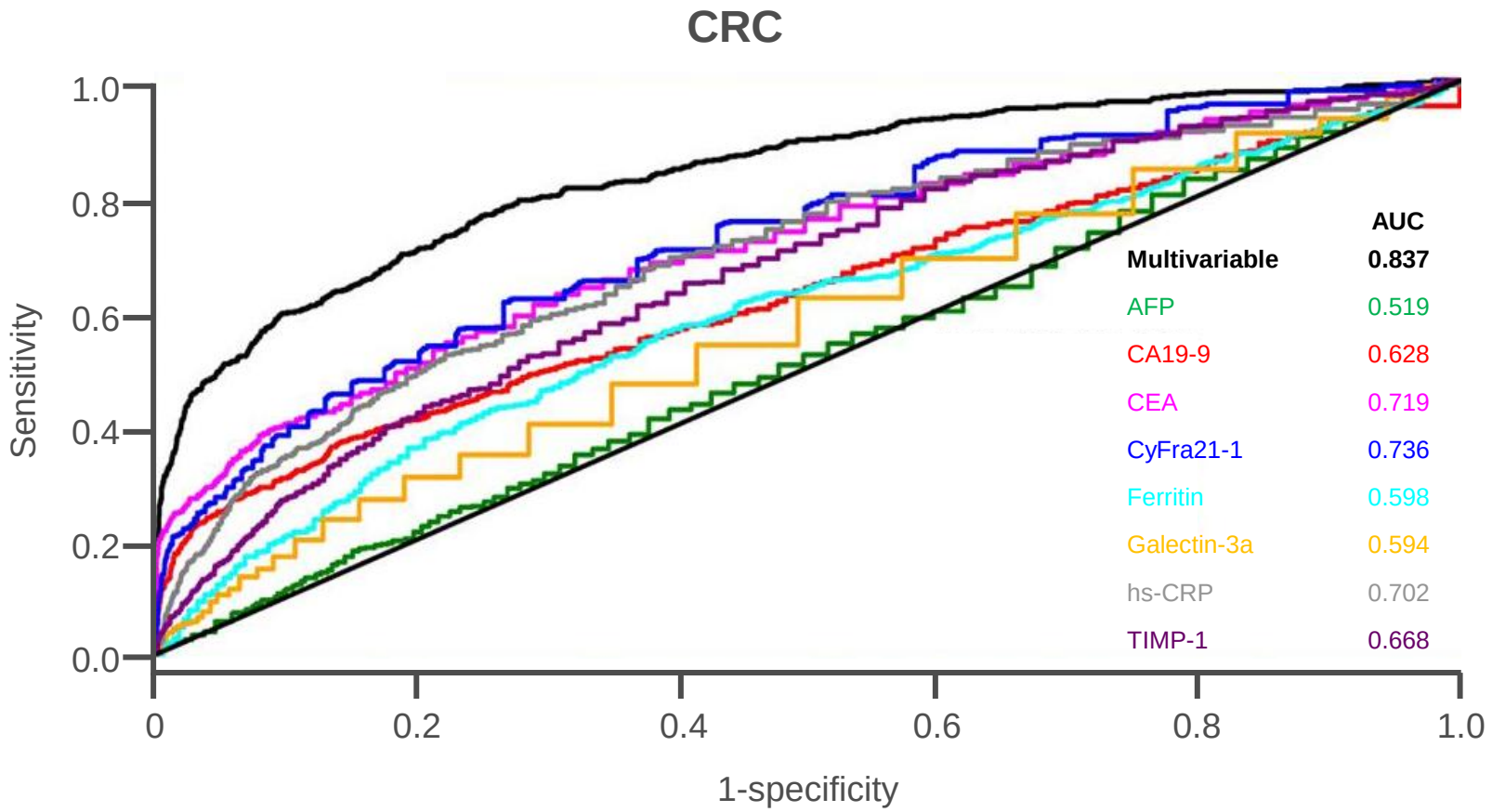
ANALYSIS

- Univariate and multivariate analyses were performed

Christensen et al. J Clin Oncol 2016; 34 (suppl): abstr 488

488: Early detection of colorectal neoplasia: Combination of eight cancer-associated blood-based protein biomarker – Christensen IJ, et al

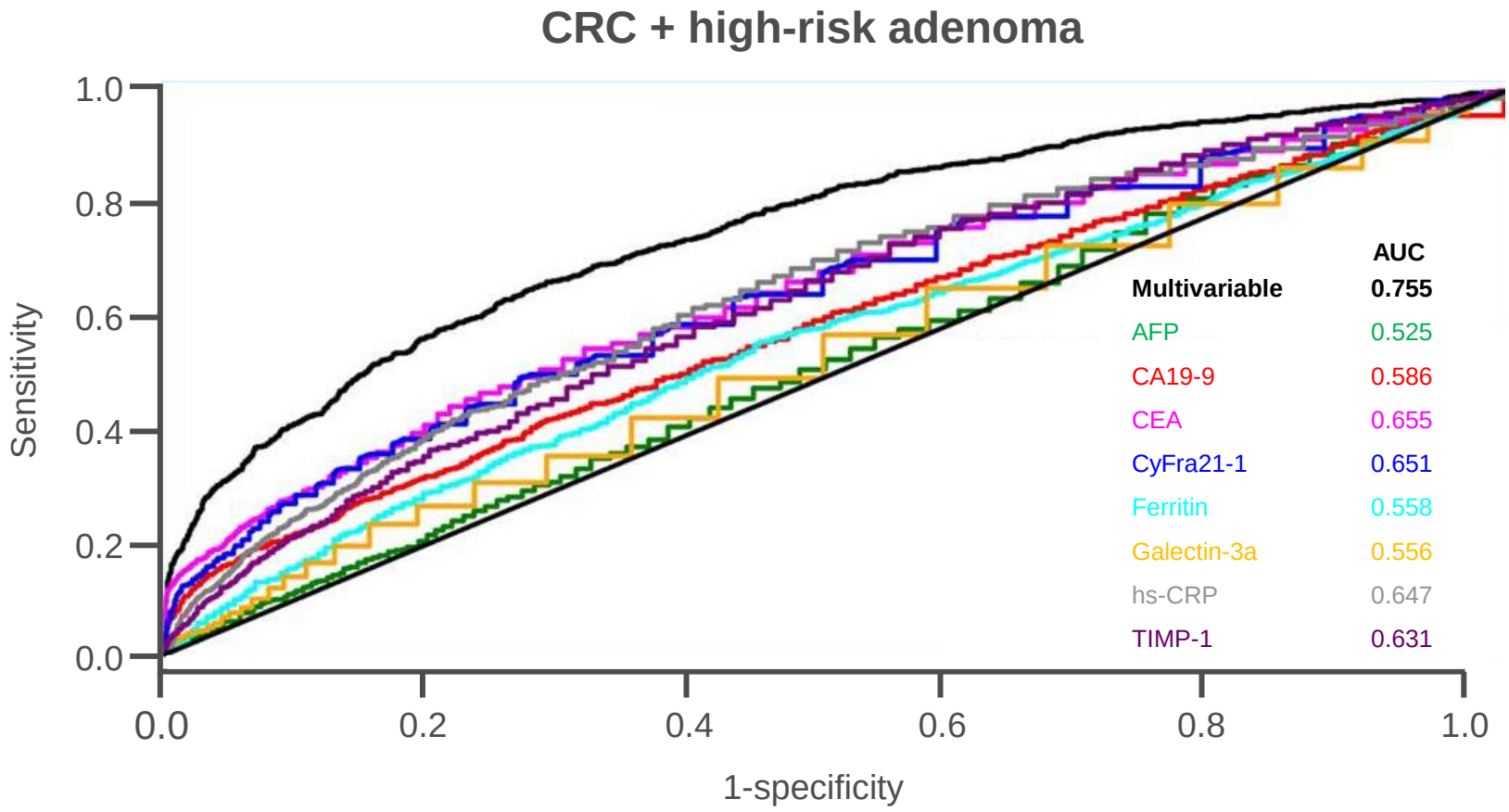
Results



Christensen et al. J Clin Oncol 2016; 34 (suppl): abstr 488

488: Early detection of colorectal neoplasia: Combination of eight cancer-associated blood-based protein biomarker – Christensen IJ, et al

Results (continued)



Christensen et al. J Clin Oncol 2016; 34 (suppl): abstr 488

488: Early detection of colorectal neoplasia: Combination of eight cancer-associated blood-based protein biomarker – Christensen IJ, et al

Results (continued)

Full model	Reduced model
CEA	CEA
hs-CRP	hs-CRP
Ferritin	Ferritin
CyFra21-1	CyFra21-1
Age	
Gender	

Endpoint	Full model AUC	Reduced model AUC
CRC + HRA	0.76	0.71
CRC	0.84	0.81

Conclusions

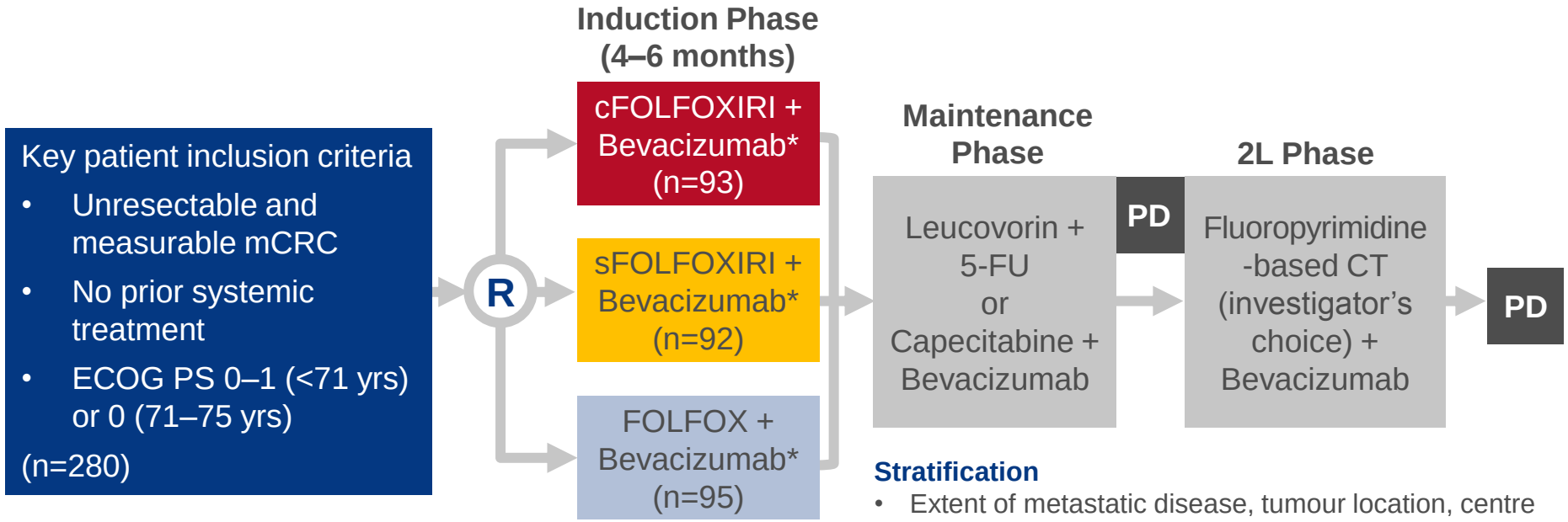
- A panel of blood-based biomarkers identified patients with a high risk of CRC
- A reduced model was almost as accurate as the complete model

Christensen et al. J Clin Oncol 2016; 34 (suppl): abstr 488

492: Overall response rate (ORR) in STEAM, a randomized, open-label, phase 2 trial of sequential and concurrent FOLFOXIRI-bevacizumab (BEV) vs FOLFOX-BEV for the first-line (1L) treatment (tx) of patients (pts) with metastatic colorectal cancer (mCRC) – Bendell JC, et al

Study objective

- To assess the efficacy of 1L bevacizumab with either concurrent or sequential FOLFOXIRI (cFOLFOXIRI vs. sFOLFOXIRI) or bevacizumab + FOLFOX in patients with mCRC



PRIMARY ENDPOINT(S)

- 1L ORR, 1L PFS

SECONDARY ENDPOINT(S)

- Resection and conversion to resectable disease rates
- Time to 2L PFS, OS, ORR

*5 mg/kg q2w

Bendell et al. J Clin Oncol 2016; 34 (suppl): abstr 492

492: Overall response rate (ORR) in STEAM, a randomized, open-label, phase 2 trial of sequential and concurrent FOLFOXIRI-bevacizumab (BEV) vs FOLFOX-BEV for the first-line (1L) treatment (tx) of patients (pts) with metastatic colorectal cancer (mCRC) – Bendell JC, et al

Key results

	cFOLFOXIRI-bevacizumab (n=93)	sFOLFOXIRI-bevacizumab (n=92)	FOLFOX-bevacizumab (n=95)
Median age, years (range)	58.0 (23–75)	56.0 (25–74)	58.0 (34–73)
Sex, male n (%)	51 (55)	52 (57)	59 (62)
ECOG PS, n (%)			
0	62 (67)	52 (57)	51 (54)
1	31 (33)	40 (43)	44 (46)
Cancer type at diagnosis			
Colon	68 (73)	64 (70)	76 (80)
Rectal	25 (27)	28 (30)	19 (20)
Prior cancer surgery, n (%)	48 (52)	55 (60)	61 (64)
Disease extent, liver limited disease, n (%)	28 (30)	28 (30)	27 (28)
Tumour location, right, n (%)*	43 (46)	38 (41)	40 (42)
Median follow-up, months (range)	13.7 (0.4–28.9)	13.1 (0.1–27.0)	12.4 (0.1–25.7)

*Right included the right colon and transverse up to splenic flexure

Bendell et al. J Clin Oncol 2016; 34 (suppl): abstr 492

492: Overall response rate (ORR) in STEAM, a randomized, open-label, phase 2 trial of sequential and concurrent FOLFOXIRI-bevacizumab (BEV) vs FOLFOX-BEV for the first-line (1L) treatment (tx) of patients (pts) with metastatic colorectal cancer (mCRC) – Bendell JC, et al

Key results (continued)

	cFOLFOXIRI-bevacizumab (n=93)	sFOLFOXIRI-bevacizumab (n=92)	Pooled FOLFOXIRI-bevacizumab (n=185)	FOLFOX-bevacizumab (n=95)
ORR, %	60.2	62.0	61.1	47.4
OR vs. FOLFOX-bevacizumab (90% CI); p-value	1.7 (1.05, 2.77); 0.075	1.8 (1.12, 2.97); 0.040	1.8 (1.16, 2.68); 0.025	
CR, %	4.3	0	2.2	1.1
PR, %	55.9	62.0	58.9	46.3
SD, %	31.2	32.6	31.9	40.0
PD, %	2.2	1.1	1.6	6.3
Unable to evaluate, %	6.5	4.3	5.4	6.3
Liver resection rates, %	15.1	9.8	12.4	7.4
R0 resection	15.1	8.7	11.9	6.3
% difference in resection rate vs. FOLFOX-bevacizumab (90% CI); p-value	7.7 (0.2, 15.2); 0.094	2.4 (-4.3, 9.2); 0.555	5.1 (-0.9, 11.0); 0.195	

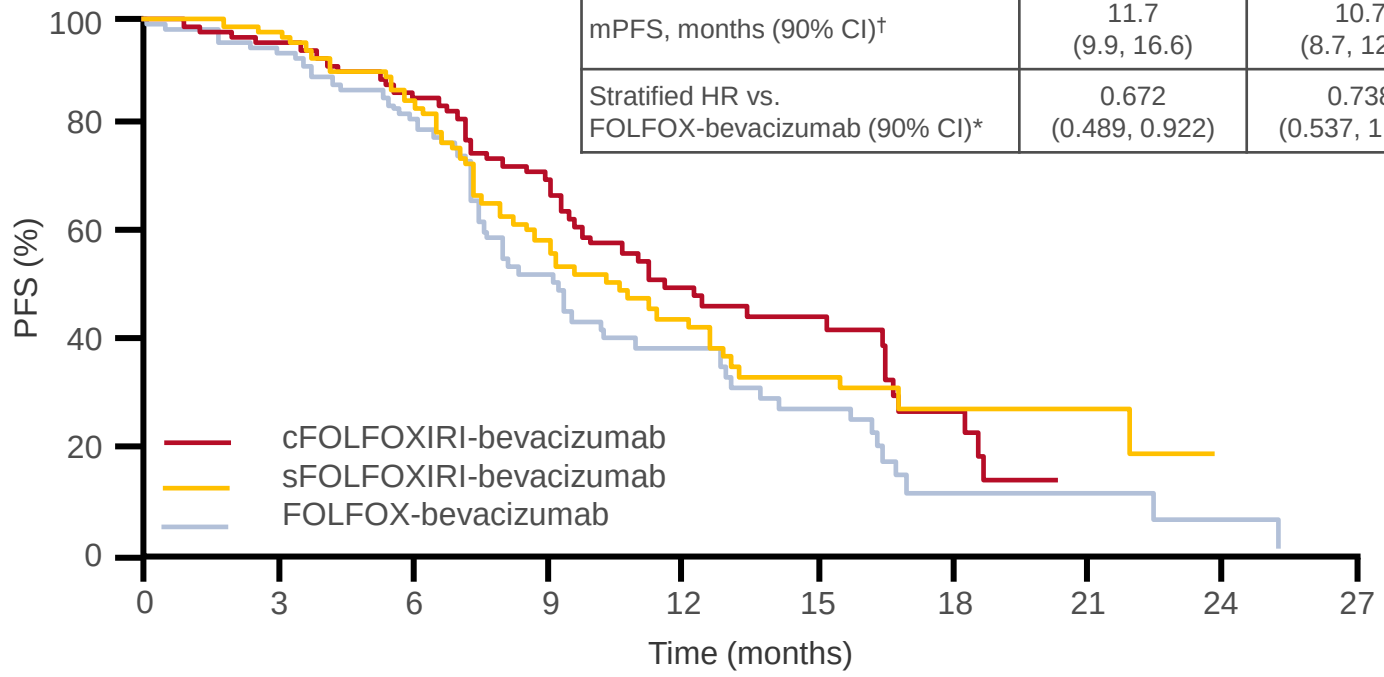
Bendell et al. J Clin Oncol 2016; 34 (suppl): abstr 492

492: Overall response rate (ORR) in STEAM, a randomized, open-label, phase 2 trial of sequential and concurrent FOLFOXIRI-bevacizumab (BEV) vs FOLFOX-BEV for the first-line (1L) treatment (tx) of patients (pts) with metastatic colorectal cancer (mCRC) – Bendell JC, et al

Key results (continued)

Interim PFS1 (ITT)

	cFOLFOXIRI-bevacizumab (n=93)	sFOLFOXIRI-bevacizumab (n=92)	FOLFOX-bevacizumab (n=95)
mPFS, months (90% CI)†	11.7 (9.9, 16.6)	10.7 (8.7, 12.7)	9.3 (7.7, 10.4)
Stratified HR vs. FOLFOX-bevacizumab (90% CI)*	0.672 (0.489, 0.922)	0.738 (0.537, 1.012)	



†PFS1 is defined as the time from randomisation to first occurrence of PD or death from any cause during 1L treatment, whichever occurs first. Patients without an event are censored at their last tumour assessment; *Stratified by extent of metastatic disease and tumour location after correction post-randomisation

Bendell et al. J Clin Oncol 2016; 34 (suppl): abstr 492

492: Overall response rate (ORR) in STEAM, a randomized, open-label, phase 2 trial of sequential and concurrent FOLFOXIRI-bevacizumab (BEV) vs FOLFOX-BEV for the first-line (1L) treatment (tx) of patients (pts) with metastatic colorectal cancer (mCRC) – Bendell JC, et al

Key results (continued)

	cFOLFOXIRI-bevacizumab (n=91)	sFOLFOXIRI-bevacizumab (n=90)	FOLFOX-bevacizumab (n=90)
Any TEAE, %	100	99	100
Grade ≥3 TEAE, %	90	87	82
Hypertension (AE of special interest)	20	16	12
TEAEs of special interest for bevacizumab, %	32	29	24
TEAE leading to withdrawal of study treatment, %	41	33	38
TEAE leading to study discontinuation, %	15	3	6
Fatal TEAE, %	3	4	3

Conclusions

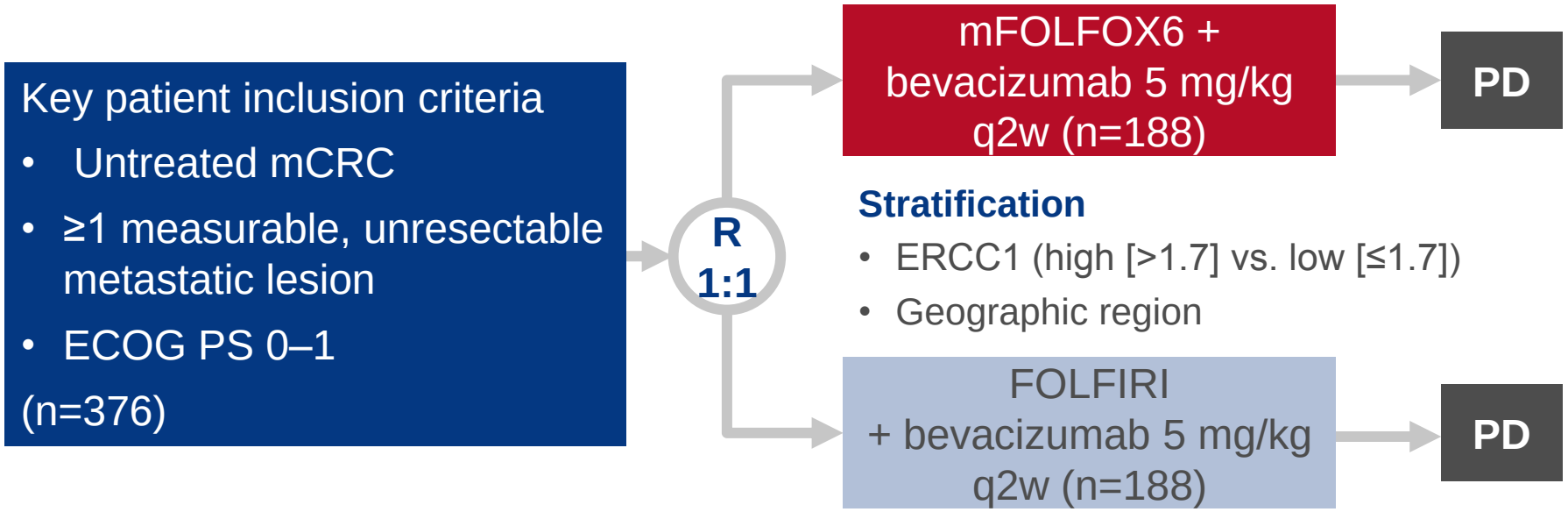
- **Triple therapy with cFOLFOXIRI + bevacizumab showed trends towards improved ORR, PFS and metastatic resection rates vs. FOLFOX + bevacizumab**
  - **Similar trends were observed for sFOLFOXIRI + bevacizumab and pooled FOLFOXIRI groups**
- **All treatments were well tolerated and consistent with the known safety profile for bevacizumab, although cFOLFOXIRI + bevacizumab was associated with a higher incidence of grade ≥3 hypertension**

Bendell et al. J Clin Oncol 2016; 34 (suppl): abstr 492

493: MAVERICC: A phase 2 study of the mFOLFOX6-bevacizumab (BV) vs. FOLFIRI-BV with biomarker stratification in patients (pts) with metastatic colorectal cancer (mCRC) – Lenz H-J, et al

Study objective

- To assess the efficacy and safety of 1L mFOLFOX6 + bevacizumab vs. FOLFIRI + bevacizumab in patients with mCRC



PRIMARY ENDPOINT(S)

- PFS

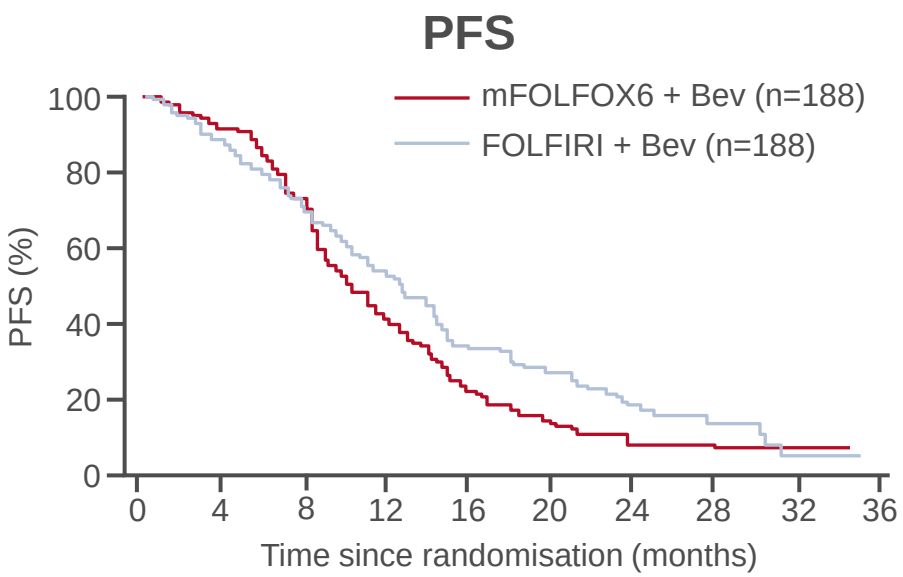
SECONDARY ENDPOINTS

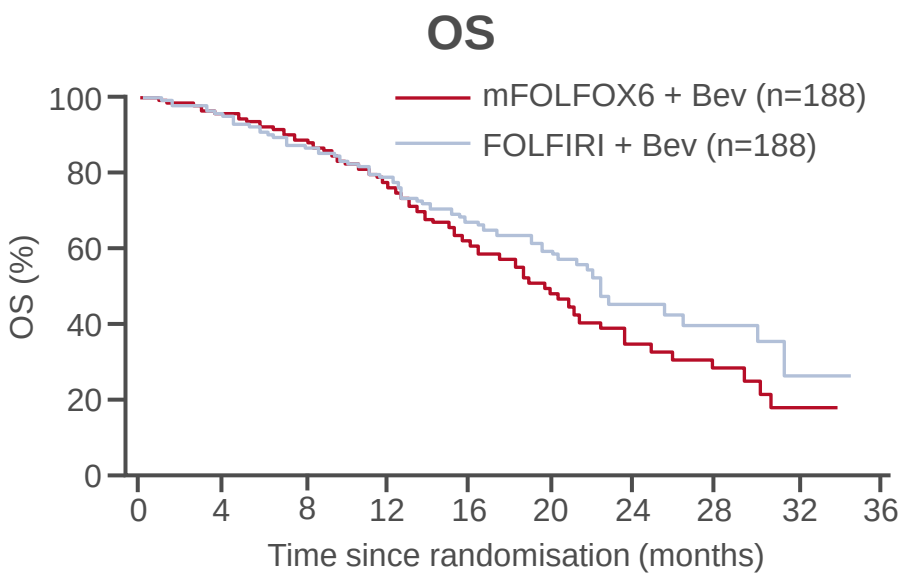
- OS, ORR
- Safety, biomarkers

Lenz et al. J Clin Oncol 2016; 34 (suppl): abstr 493

493: MAVERICC: A phase 2 study of the mFOLFOX6-bevacizumab (BV) vs. FOLFIRI-BV with biomarker stratification in patients (pts) with metastatic colorectal cancer (mCRC) – Lenz H-J, et al

Results





	mFOLFOX6 + Bev	FOLFIRI + Bev
mPFS, months	10.1	12.6
HR (95% CI); p-value	0.79 (0.61, 1.01); 0.056	

	mFOLFOX6 + Bev	FOLFIRI +Bev
mOS, months	23.9	27.5
HR (95% CI); p-value	0.76 (0.56, 1.04); 0.086	

BEV, bevacizumab

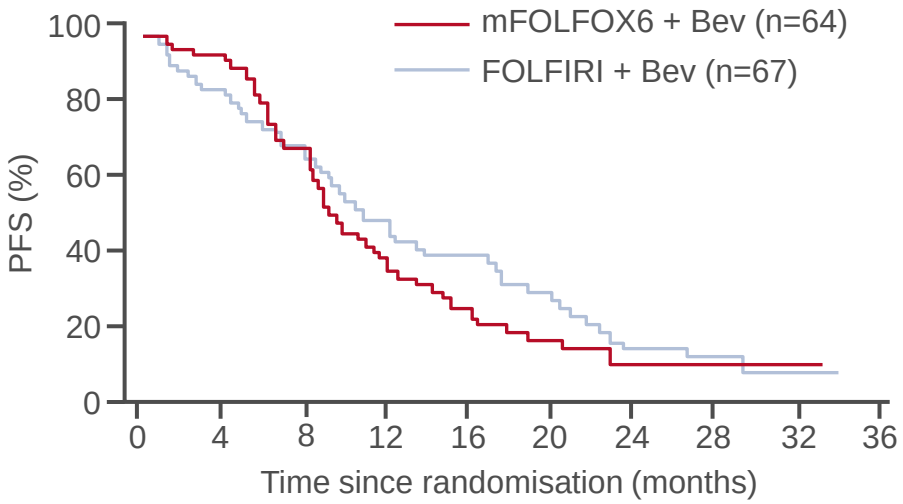
Lenz et al. J Clin Oncol 2016; 34 (suppl): abstr 493

493: MAVERICC: A phase 2 study of the mFOLFOX6-bevacizumab (BV) vs. FOLFIRI-BV with biomarker stratification in patients (pts) with metastatic colorectal cancer (mCRC) – Lenz H-J, et al

Results (continued)

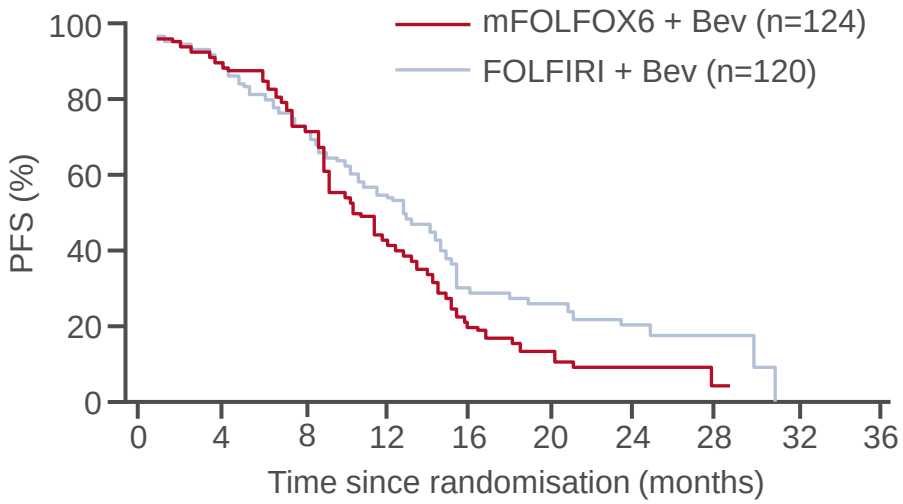
PFS by ERCC1 level

High (>1.7) baseline tumour ERCC1 (n=131)



	mFOLFOX6 + Bev	FOLFIRI + Bev
mPFS, months	9.9	11.2
HR (95% CI); p-value	0.84 (0.56, 1.26); 0.394	

Low (≤1.7) baseline tumour ERCC1 (n=244)



	mFOLFOX6 + Bev	FOLFIRI + Bev
mPFS, months	11.0	12.7
HR (95% CI); p-value	0.76 (0.55, 1.03); 0.079	

Bev, bevacizumab

Lenz et al. J Clin Oncol 2016; 34 (suppl): abstr 493

493: MAVERICC: A phase 2 study of the mFOLFOX6-bevacizumab (BV) vs. FOLFIRI-BV with biomarker stratification in patients (pts) with metastatic colorectal cancer (mCRC) – Lenz H-J, et al

Results (continued)

OS by ERCC1	mFOLFOX6 + Bev (n=188)		FOLFIRI + Bev (n=187)	
	High ERCC1 (n=64)	Low ERCC1 (n=124)	High ERCC1 (n=67)	Low ERCC1 (n=120)
mOS	22.5	25.5	26.5	27.9
HR* (95% CI)	1.14 (0.75, 1.73)		1.30 (0.81, 2.08)	
p-value	0.532		0.282	

PFS by tumour location	Right tumour (n=188)		Left tumour (n=187)	
	mFOLFOX6 + Bev (n=75)	FOLFIRI + Bev (n=79)	mFOLFOX6 + Bev (n=113)	FOLFIRI + Bev (n=109)
mPFS	10.0	11.2	10.2	13.8
HR† (95% CI)	0.88 (0.60, 1.28)		0.71 (0.51, 0.98)	
p-value	0.494		0.040	

*High vs. low ERCC1; †FOLFIRI vs. mFOLFOX6

Bev, bevacizumab

Lenz et al. J Clin Oncol 2016; 34 (suppl): abstr 493

493: MAVERICC: A phase 2 study of the mFOLFOX6-bevacizumab (BV) vs. FOLFIRI-BV with biomarker stratification in patients (pts) with metastatic colorectal cancer (mCRC) – Lenz H-J, et al

Results (continued)

AEs of special interest occurring in ≥2% of patients, n (%)	mFOLFOX6 + Bev (n=185)	FOLFIRI + Bev (n=183)
Hypertension (≥grade 3)	27 (14.6)	23 (12.6)
Venous thromboembolic event (≥grade 3)	14 (7.6)	18 (9.8)
GI perforation	8 (4.3)	4 (2.2)
Bleeding* (≥grade 3)	6 (3.2)	4 (2.2)
Bowel obstruction (≥grade 2)	5 (2.7)	3 (1.6)
Arterial thromboembolic event	4 (2.2)	9 (4.9)
Proteinuria (≥grade 3)	4 (2.2)	2 (1.1)

Conclusions

- **Among patients with mCRC and high ERRC1 tumour levels, PFS and OS were comparable with 1L mFOLFOX6 vs. FOLFIRI in combination with bevacizumab**
  - **Results should be interpreted cautiously due to lower prevalence of tumour ERCC1**
- **In the overall population, PFS and OS were comparable with mFOLFOX6 vs. FOLFIRI**
  - **A non-significant trend toward benefit was seen with FOLFIRI vs. mFOLFOX6, which may be related to the higher number of treatment cycles administered in the FOLFIRI arm**
- **Analyses for pVEGF-A and other biomarkers are ongoing**

*Other than pulmonary or CNS bleeding. Bev, bevacizumab

Lenz et al. J Clin Oncol 2016; 34 (suppl): abstr 493

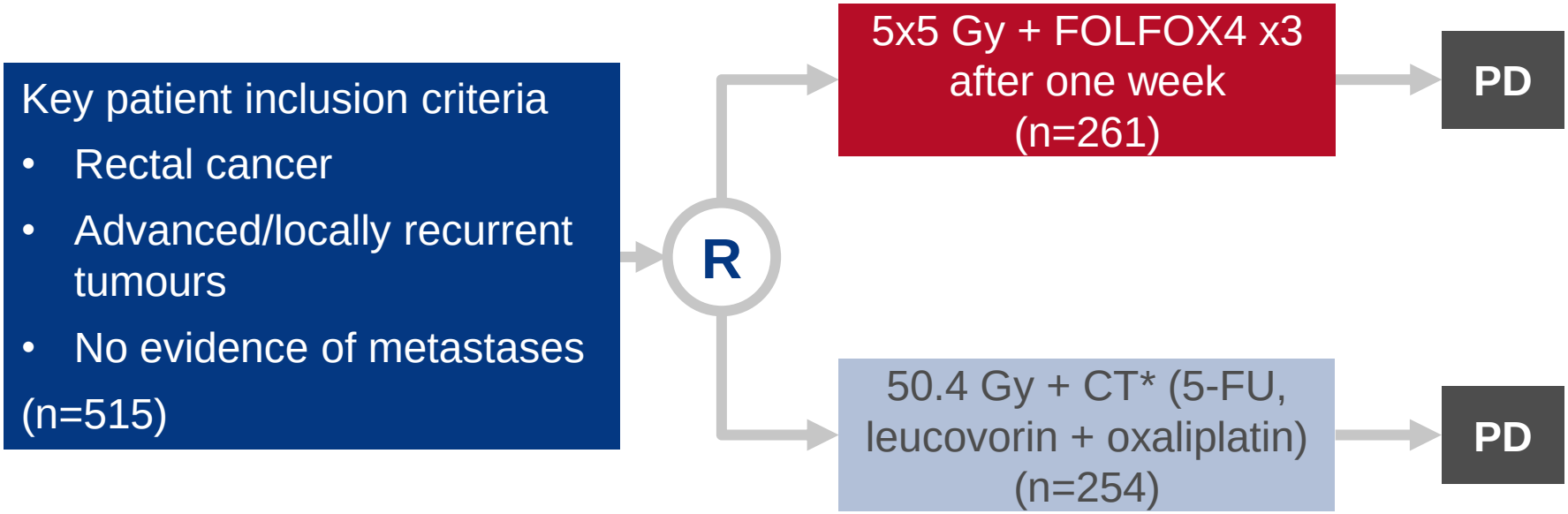
Cancers of the colon, rectum and anus

RECTAL CANCER

489: Neoadjuvant chemoradiation for fixed cT3 or cT4 rectal cancer: Results of a Polish II multicentre phase III study – Bujko K, et al

Study objective

- To test whether preoperative 5x5 Gy + consolidation CT was more efficacious locally than standard preoperative CRT in patients with unresectable rectal cancer



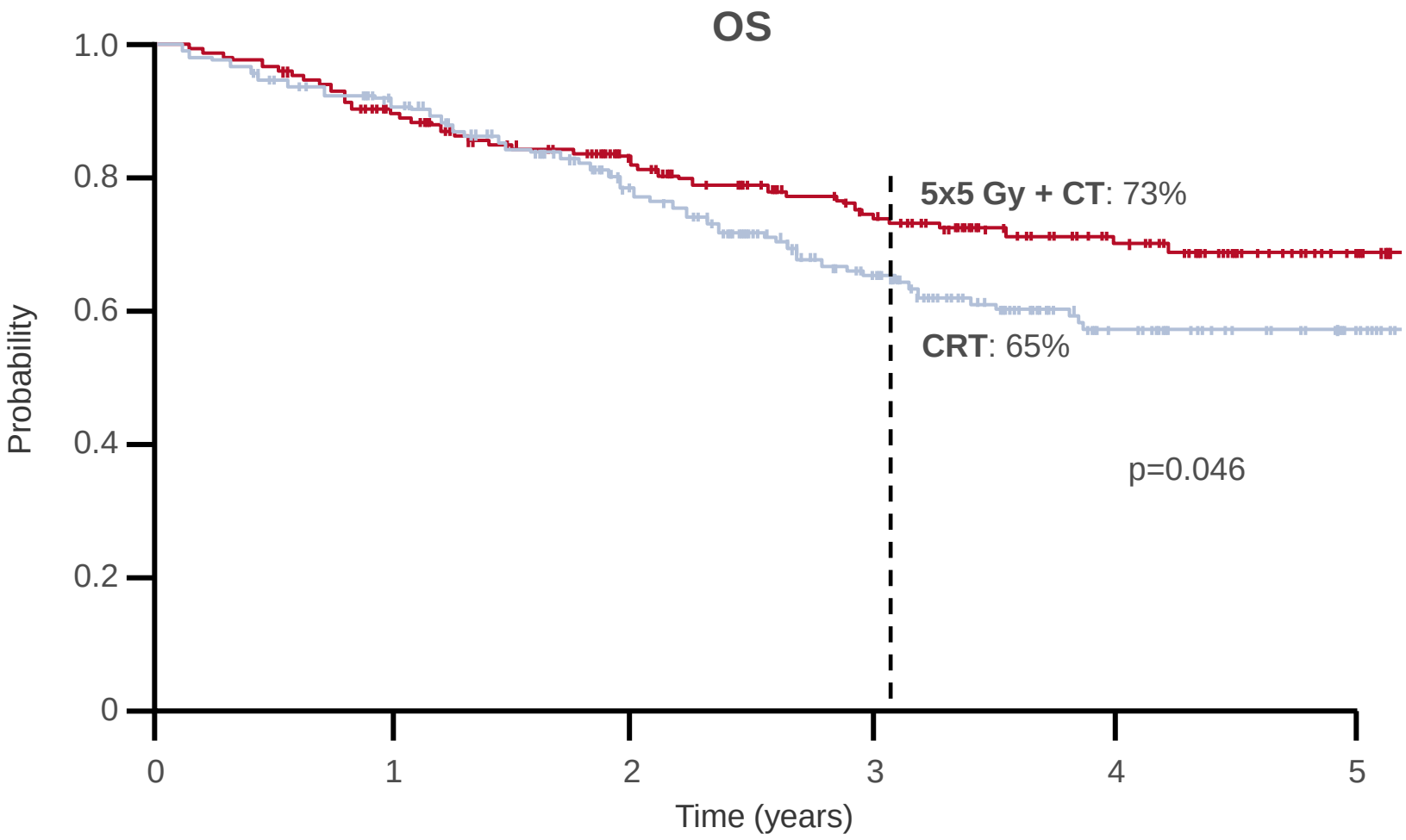
- Part 2: Oxaliplatin was given to both arms at the discretion of the participating centre
- Both arms underwent surgery at ~12 weeks after starting RT and ~6 weeks after neoadjuvant treatment

*2x 5-d cycles of bolus 5-FU 325 mg/m^2/d + leucovorin 20 mg/m^2/d, oxaliplatin 50 mg/m^2 qw

Bujko et al. J Clin Oncol 2016; 34 (suppl): abstr 489

489: Neoadjuvant chemoradiation for fixed cT3 or cT4 rectal cancer: Results of a Polish II multicentre phase III study – Bujko K, et al

Results



Bujko et al. J Clin Oncol 2016; 34 (suppl): abstr 489

489: Neoadjuvant chemoradiation for fixed cT3 or cT4 rectal cancer: Results of a Polish II multicentre phase III study – Bujko K, et al

Results (continued)

%	5x5 Gy + CT	CRT	p-value
DFS	52	53	0.85
Cumulative incidence of local failure	22	21	0.82
Cumulative incidence of distant metastases	30	27	0.26

%	5x5 Gy + CT	CRT	p-value
Postoperative complications	29	25	0.18
Reoperations	14	11	-
Surgery-related deaths (30 d)	0	2	-
R0 resection	77	71	0.07
R1 resection	7	8	-
R2 resection	0.5	2	-
pCR (ypT0N0)	16	12	0.21

Bujko et al. J Clin Oncol 2016; 34 (suppl): abstr 489

489: Neoadjuvant chemoradiation for fixed cT3 or cT4 rectal cancer: Results of a Polish II multicentre phase III study – Bujko K, et al

Results (continued)

Adherence, %	5x5 Gy + CT	CRT	p-value
Adherence to RT			
Dose reduction	0	8	<0.001
RT time prolongation (>7 d)	0	5	<0.001
Adherence to CT			
Dose reduction due to toxicity	20	26	0.15
Cycle delay without dose reduction	13	N/A*	-

Acute toxicity, %	5x5 Gy + CT	CRT	p-value
Grade 1–2	50	60	
Grade 3–4	23	21	0.006
Toxic deaths	1	3	

*Not allowed: all CT had to be given during irradiation

Bujko et al. J Clin Oncol 2016; 34 (suppl): abstr 489

489: Neoadjuvant chemoradiation for fixed cT3 or cT4 rectal cancer: Results of a Polish II multicentre phase III study – Bujko K, et al

Conclusions

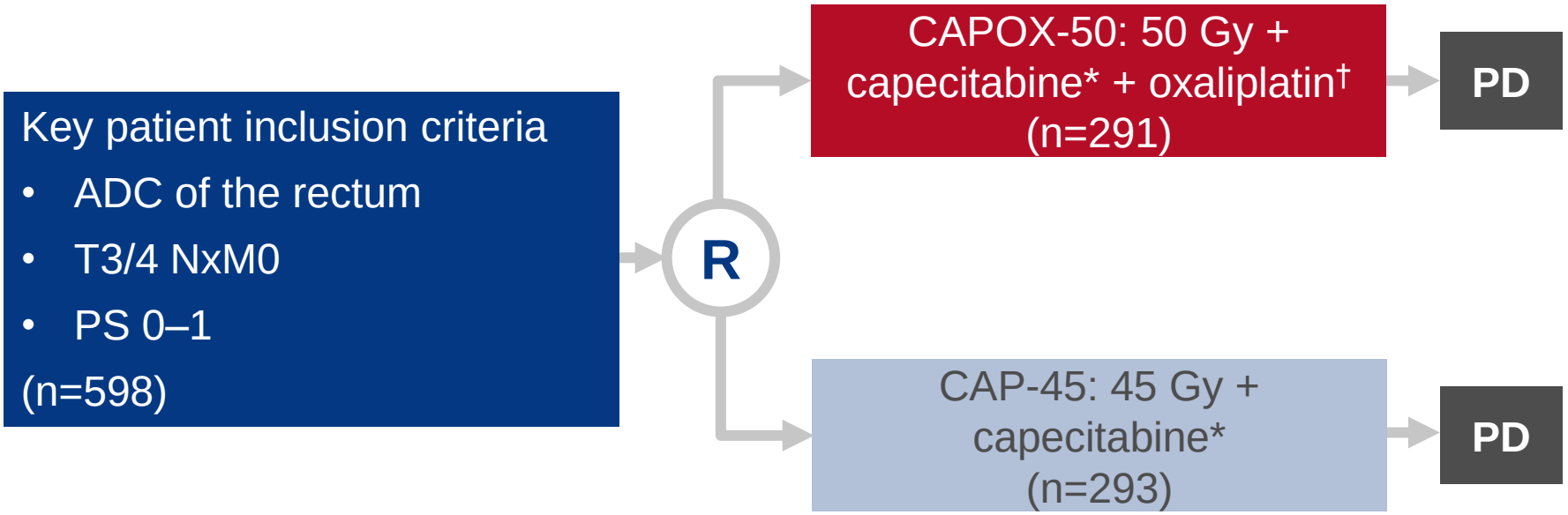
- **Local efficacy was comparable between preoperative 5x5 Gy + consolidation CT vs. conventional CRT in patients with unresectable rectal cancer**
- **Improved short-term OS and lower acute toxicity was observed with 5x5 Gy + consolidation chemotherapy**

Bujko et al. J Clin Oncol 2016; 34 (suppl): abstr 489

490: ACCORD12/0405-Prodige 2 phase III trial neoadjuvant treatment in rectal cancer: Results after 5 years of follow-up – Francois E, et al

Study objective

- To evaluate the efficacy and safety of adding oxaliplatin to standard neoadjuvant CRT vs. CRT alone in patients with rectal cancer



PRIMARY ENDPOINT(S)

- ypCR

SECONDARY ENDPOINTS

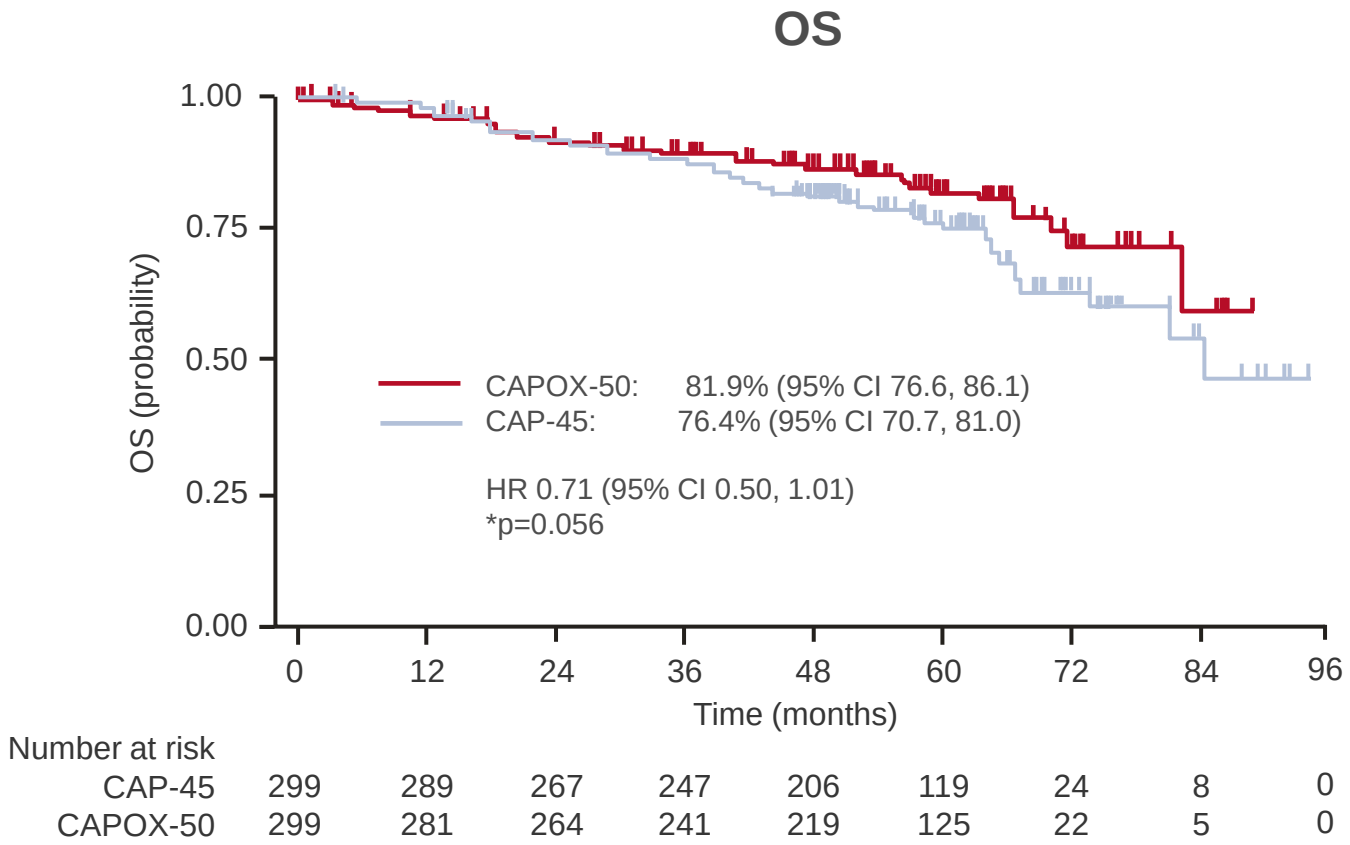
- OS, DFS, recurrence
- Safety

*1600 mg/m^2/d 5 d/w; †50 mg/m^2 qw

Francois et al. J Clin Oncol 2016; 34 (suppl): abstr 490

490: ACCORD12/0405-Prodige 2 phase III trial neoadjuvant treatment in rectal cancer: Results after 5 years of follow-up – Francois E, et al

Results

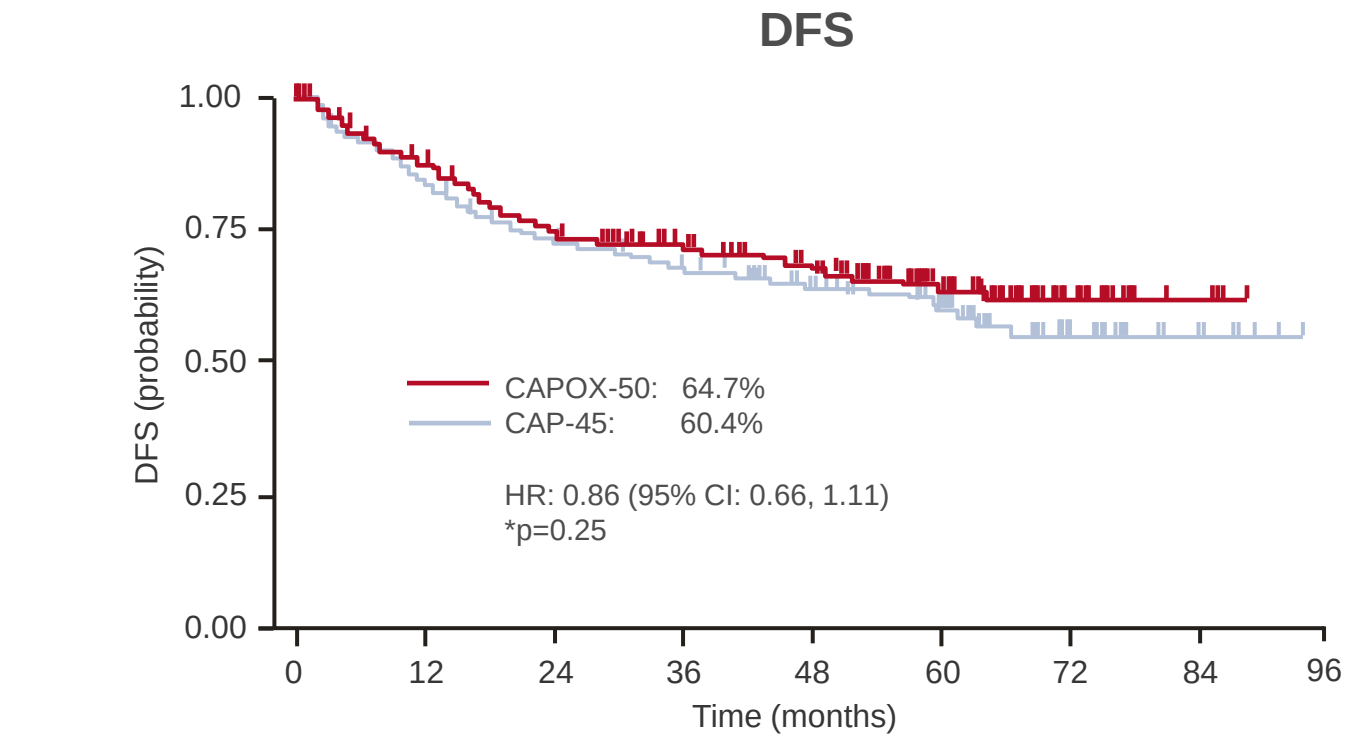


*Log-rank test

Francois et al. J Clin Oncol 2016; 34 (suppl): abstr 490

490: ACCORD12/0405-Prodige 2 phase III trial neoadjuvant treatment in rectal cancer: Results after 5 years of follow-up – Francois E, et al

Results (continued)



Number at risk									
RT45-Cap	299	246	212	189	159	91	17	6	0
RT50-Capox	299	256	216	196	173	95	18	4	0

*Log-rank test

Francois et al. J Clin Oncol 2016; 34 (suppl): abstr 490

490: ACCORD12/0405-Prodige 2 phase III trial neoadjuvant treatment in rectal cancer: Results after 5 years of follow-up – Francois E, et al

Results (continued)

- Local recurrence: CAPOX-50 7.8% vs. CAP-45 8.8%; HR 0.92 (95% CI 0.51, 1.66); p=0.78

Prognostic factors	OS		DFS	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Dworak score				
Other responses	1	-	1	-
TRG3 + TRG4	0.71 (0.59, 0.85)	<0.001	0.37 (0.25, 0.54)	<0.001
ypN				
ypN0	1	-	1	-
ypN1	1.39 (0.89, 2.17)	0.152	1.42 (1.01, 1.99)	0.043
ypN2	3.51 (2.41, 5.77)	<0.001	2.73 (1.82, 4.09)	<0.001
Age, years				
<75	1	-	1	-
≥75	2.70 (1.62, 4.52)	<0.001	2.44 (1.61, 3.68)	<0.001

Francois et al. J Clin Oncol 2016; 34 (suppl): abstr 490

490: ACCORD12/0405-Prodige 2 phase III trial neoadjuvant treatment in rectal cancer: Results after 5 years of follow-up – Francois E, et al

Results (continued)

Grade 3/4 AEs, %	CAPOX-50	CAP-45	p-value
Overall (at 5 years)	1.9	1.8	0.13
Overall (during 5 years)	6.7	7.4	0.82
Diarrhoea	0.0	0.4	0.46
Anal incontinence	1.1	2.1	0.19

Conclusions

- **There were no significant differences in OS, DFS, pCR or recurrence with CAPOX + RT vs. capecitabine + RT in patients with rectal cancer**
- **Oxaliplatin was associated with a higher frequency of toxicity**
- **This study suggests that the standard neoadjuvant therapy for patients with rectal cancer should be 50 Gy + capecitabine**

Francois et al. J Clin Oncol 2016; 34 (suppl): abstr 490

491: The incidence of secondary pelvic tumors after previous (chemo)radiation for rectal cancer – Rombouts AJM, et al

Study objective

- To analyse the association between RT for rectal cancer and the development of second primary tumours

Key patient inclusion criteria

- Retrospective review of data from the population-based Netherlands Cancer Registry (NCR)
- Included all surgically treated, non-metastasised primary rectal cancer patients (no metastases) diagnosed between 1989 and 2007

(n=29,214)

- Standardised IR were calculated for comparison with the incidence of primary tumours in the general population, taking in account sex, age and calendar year
- Multivariate analyses were performed with Cox regression

Rombouts et al. J Clin Oncol 2016; 34 (suppl): abstr 491

491: The incidence of secondary pelvic tumors after previous (chemo)radiation for rectal cancer – Rombouts AJM, et al

Key results

- A total of 29,214 patients were included; median follow-up was 6.2 years (range 0–24)

n (%)	RT (n=15,454)	No RT (n=13,760)
Mean age at diagnosis, years (range)	64 (14–95)	68 (19–98)
Gender		
Male	9384 (60.7)	7479 (54.4)
Female	6070 (39.3)	6281 (45.6)
Tumour differentiation grade		
Well	749 (4.8)	1394 (10.1)
Intermediate	8918 (57.7)	9393 (68.3)
Poor	2294 (14.8)	1264 (9.2)
Undifferentiated	23 (0.1)	15 (0.1)
Unknown	3470 (22.5)	1694 (12.3)

Rombouts et al. J Clin Oncol 2016; 34 (suppl): abstr 491

491: The incidence of secondary pelvic tumors after previous (chemo)radiation for rectal cancer – Rombouts AJM, et al

Key results (continued)

n (%)	RT (n=15,454)	No RT (n=13,760)
Treatment of rectal cancer		
Neoadjuvant		
CRT	1589 (10.3)	–
RT	10,287 (66.6)	–
CT	17 (0.1)	3 (0.0)
Adjuvant		
RT	3742 (24.2)	–
CT	1231 (8.0)	744 (5.4)
Number of second tumours		
1	1569 (10.2)	1739 (12.6)
2	129 (0.8)	185 (1.3)
>2	15 (0.1)	16 (0.1)

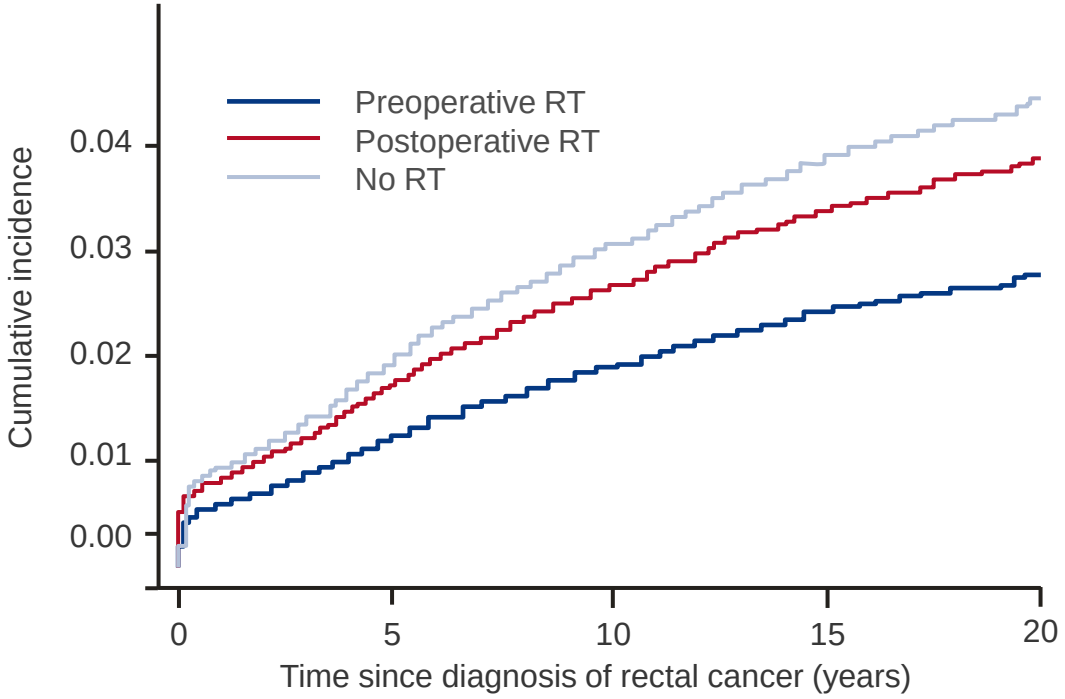
Rombouts et al. J Clin Oncol 2016; 34 (suppl): abstr 491

491: The incidence of secondary pelvic tumors after previous (chemo)radiation for rectal cancer – Rombouts AJM, et al

Key results (continued)

- Compared with the cancer incidence in the Dutch population, the standardised IR was 1.14 (95% CI 1.10, 1.17) with an absolute excess risk of 23.31 per 10,000 persons per year

Cumulative incidence risk of secondary pelvic tumours



- The risk of second cancer was lower among patients who received RT than those who did not (standardised HR 0.70; 95% CI 0.61, 0.81)
- Second cancers were more common after postoperative RT than after preoperative RT (standardised HR 1.37; 95% CI 1.10,1.70)

Rombouts et al. J Clin Oncol 2016; 34 (suppl): abstr 491

491: The incidence of secondary pelvic tumors after previous (chemo)radiation for rectal cancer – Rombouts AJM, et al

Key results (continued)

- The cumulative incidence risk of rectosigmoid tumours was lower following preoperative RT than after postoperative RT (standardised HR 0.59; 95% CI 0.37, 0.94)
- RT reduced the risk of secondary pelvic tumours (HR 0.78; 95% CI 0.66, 0.92), particularly for prostate cancer (standardised HR 0.51; 95% CI 0.43, 0.62)
  - Sex-specific analyses illustrated that this effect remained for men (standardised HR 0.59; 95% CI 0.50, 0.69), but there was no protective or detrimental effect for women (standardised HR 1.00; 95% CI 0.76, 1.33)

Conclusions

- **RT appears to protect against the development of secondary tumours, particularly for prostate cancer**
- **Among patients with rectal cancer there was:**
  - **A marginal increased risk of second cancer compared with the general population**
  - **No increase in second tumours after previous RT for rectal cancer**

Rombouts et al. J Clin Oncol 2016; 34 (suppl): abstr 491