GI SLIDE DECK 2019

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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 2019. This slide set specifically focuses on the **2019 American Society of Clinical Oncology Annual Meeting** and is available in English, French, Chinese 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. We 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
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(ESDO Governing Board)

esdo

european society of digestive oncology

ESDO Medical Oncology Slide Deck
Editors 2019

COLORECTAL CANCERS




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PANCREATIC CANCER AND HEPATOBILIARY TUMOURS



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GASTRO-OESOPHAGEAL AND NEUROENDOCRINE TUMOURS


Prof Côme Lepage	University Hospital & INSERM, Dijon, France
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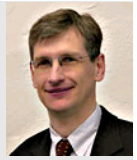
BIOMARKERS

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

1/2L	first-/second-line
5FU	5-fluorouracil
ACC	adenocarcinoma
ACS	active symptom control
AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
bCTCs	baseline circulating tumour cells
Bev	bevacizumab
BICR	blinded-independent central review
bid	twice daily
BCLC	Barcelona clinic liver cancer
BOR	best overall response
BSC	best supportive care
CA19-9	carbohydrate antigen 19-9
CAPOX	oxaliplatin + capecitabine
CATEM	capecitabine + temozolomide
CI	confidence interval
CMS	consensus molecular subtypes
CPS	combined positive score
CR	complete response
(m)CRC	(metastatic) colorectal cancer
CRCA	Colorectal Cancer Assigner
CT	chemotherapy
ctDNA	circulating tumour DNA
D	day
DCR	disease control rate
DFS	disease-free survival
DoR	duration of response
ECF	epirubicin + cisplatin + 5-fluorouracil
ECOG	Eastern Cooperative Oncology Group
ECX	epirubicin + oxaliplatin + capecitabine
FL(OX)	5-fluorouracil + leucovorin (+ oxaliplatin)
FOLFIRI	irinotecan + leucovorin + 5-fluorouracil
(m)FOLFOX	(modified) leucovorin + 5-fluorouracil + oxaliplatin
(m)FOLFOXIRI	(modified) irinotecan + oxaliplatin + leucovorin + 5-fluorouracil
GEJ	gastro-oesophageal junction
GEM	gemcitabine
GI	gastrointestinal
Gy	Gray
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HER2	human epidermal growth factor receptor 2
HR	hazard ratio
IS	Immunoscore
ITT	intent-to-treat
KM	Kaplan-Meier
LN	lymph node
max	maximum
mCRC	metastatic colorectal cancer
min	minimum
mo	months
MSI-H	microsatellite instability-high
Nab-p	nab-paclitaxel
neg	negative
NI	non-inferiority
OR	odds ratio
ORR	overall/objective response rate
(m)OS	(median) overall survival
PBO	placebo
PD	progressive disease
PD-L1	programmed death-ligand 1
Pembro	pembrolizumab
(m)PFS	(median) progression-free survival
PFS1	time to first progression
(m)PFS2	(median) time to second progression
pos	positive
PR	partial response
PS	performance status
q(2/3/4)w	every (2/3/4) week(s)
R	randomised
R0/1/2	resection 0/1/2
(m)RECIST	(modified) Response Evaluation Criteria In Solid tumours
RFA	radiofrequency ablation
RFS	recurrence-free survival
RPS	Recombination Proficiency Score
RT	radiotherapy
S-1	tegafur + gimeracil + oteracil
SCC	squamous cell carcinoma
SD	stable disease
SOX	S-1 + oxaliplatin
SSP	single sample predictor
TEAE	treatment-emergent adverse event
TRAE	treatment-related adverse event
TRG	tumour regression grade
TTF	time to treatment failure
TTP	time to progression
TTR	time to response
UCB	upper confidence bound
WT	wild type

Contents

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

CANCERS OF THE OESOPHAGUS AND STOMACH

LBA4007: Pembrolizumab with or without chemotherapy versus chemotherapy for advanced gastric or gastroesophageal junction (G/GEJ) adenocarcinoma: The phase III KEYNOTE-062 study – Tabernero J, et al

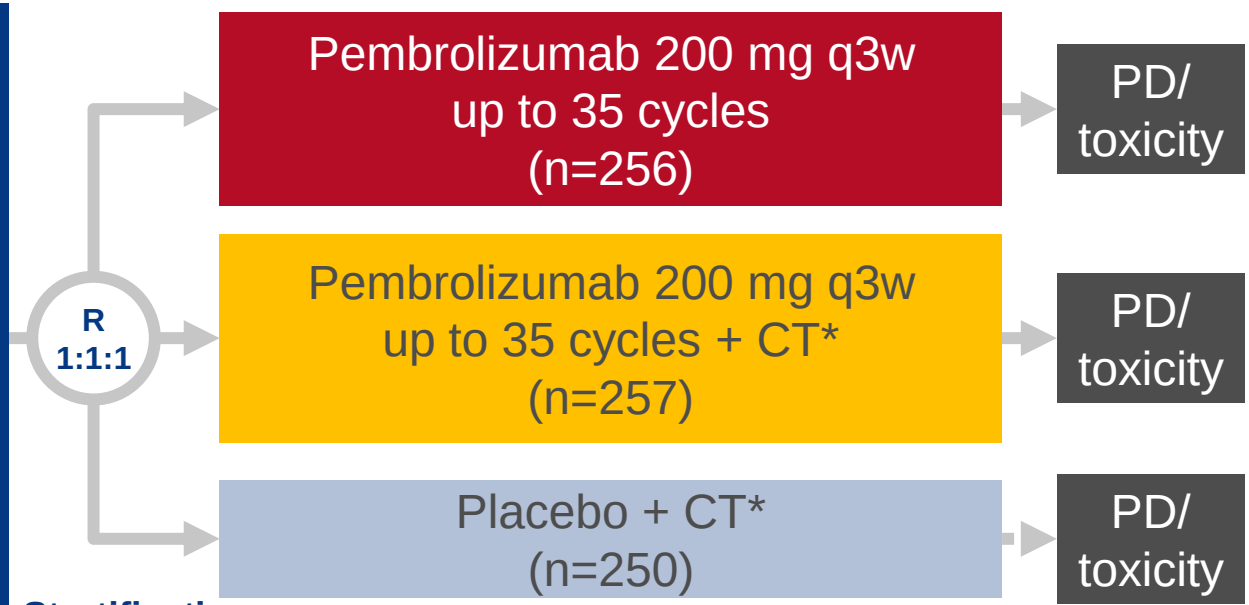
Study objective

- To assess the efficacy and safety of pembrolizumab with or without CT vs. CT alone in patients with advanced gastric and GEJ adenocarcinoma

Key patient inclusion criteria

- Locally advanced, unresectable or metastatic gastric and GEJ adenocarcinoma
- HER2/neu negative, PD-L1-positive disease (CPS ≥1)
- ECOG PS 0–1

(n=763)



Stratification

- Region; locally advanced or metastatic disease; 5FU or capecitabine

PRIMARY ENDPOINTS

- OS, PFS

SECONDARY ENDPOINTS

- ORR, safety

*Cisplatin 80 mg/m^2 q3w + 5FU 800 mg/m^2/day for 5 days q3w (cisplatin may be capped at 6 cycles per country guidelines) or capecitabine bid D1–14 q3w

Tabernero J, et al. J Clin Oncol 2019;37(suppl):abstr LBA4007

LBA4007: Pembrolizumab with or without chemotherapy versus chemotherapy for advanced gastric or gastroesophageal junction (G/GEJ) adenocarcinoma: The phase III KEYNOTE-062 study – Tabernero J, et al

Key results

Characteristic, n (%) [unless otherwise specified]	Pembrolizumab (n=254)	Pembrolizumab + CT (n=257)	CT (n=250)
Median age, years (range)	61.0 (20–83)	62.0 (22–83)	62.5 (23–87)
Male	180 (70)	195 (76)	179 (72)
ECOG PS 1	125 (49)	138 (54)	135 (54)
Metastatic disease	245 (96)	243 (95)	235 (94)
CPS ≥10	92 (36)	99 (39)	90 (36)
MSI-H	14 (5)	17 (7)	19 (8)
Region			
Europe/North America/Australia	148 (58)	148 (58)	147 (59)
Asia	62 (24)	64 (25)	61 (24)
Rest of World	46 (18)	45 (18)	42 (17)
Primary tumour location			
Stomach	176 (69)	170 (66)	181 (72)
GEJ	79 (31)	85 (33)	67 (27)
Backbone therapy[a]			
5FU	-	98 (38)	95 (38)
Capecitabine	-	159 (62)	155 (62)

[a]Per stratification; data cut-off: March 26, 2019

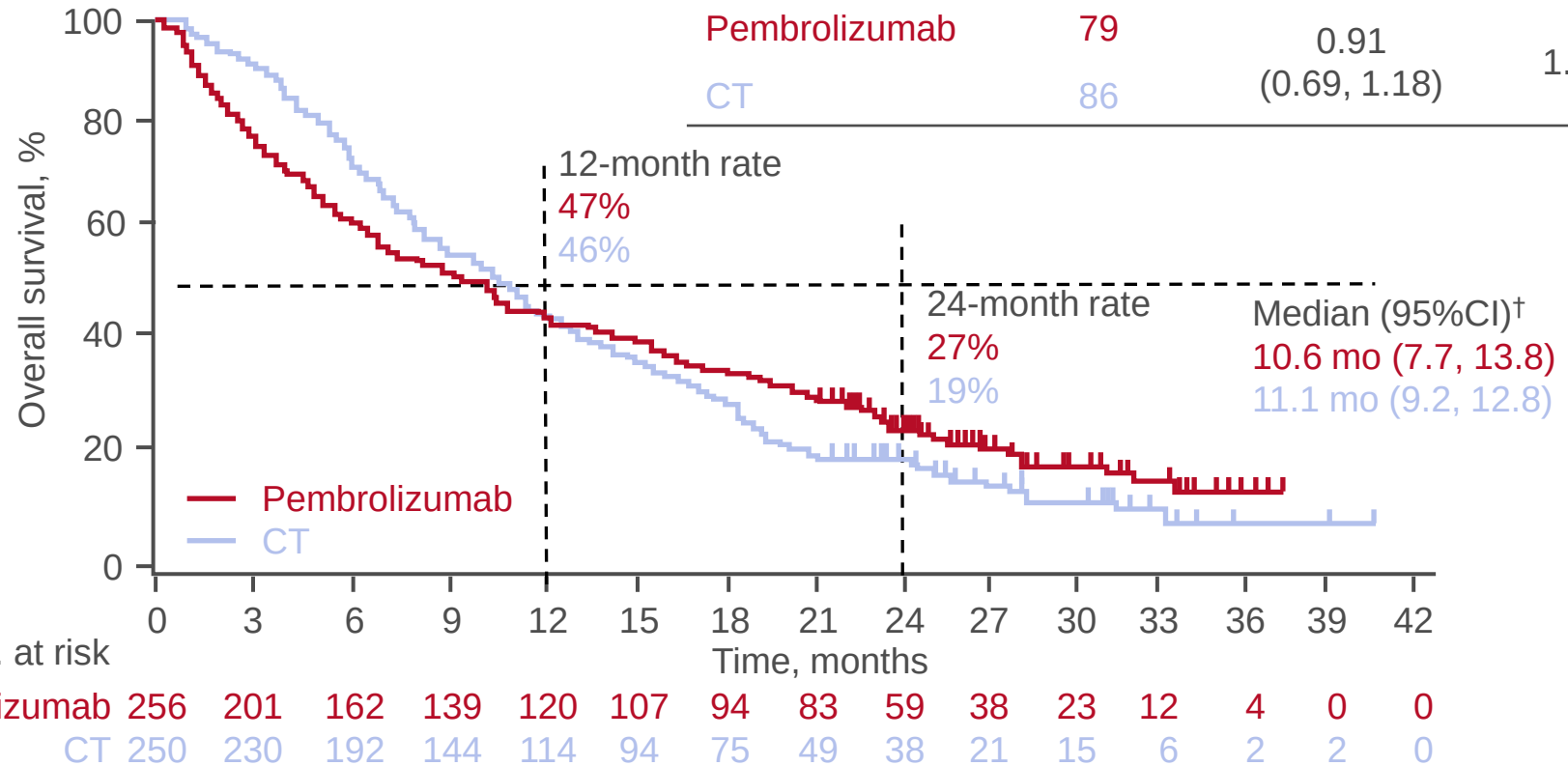
Tabernero J, et al. J Clin Oncol 2019;37(suppl):abstr LBA4007

LBA4007: Pembrolizumab with or without chemotherapy versus chemotherapy for advanced gastric or gastroesophageal junction (G/GEJ) adenocarcinoma: The phase III KEYNOTE-062 study – Tabernero J, et al

Key results (cont.)

OS (CPS ≥1) for pembrolizumab vs. CT

	Events, %	HR (99.2%CI)	NI*
Pembrolizumab	79	0.91 (0.69, 1.18)	1.2
CT	86		



No. at risk

Pembrolizumab	256	201	162	139	120	107	94	83	59	38	23	12	4	0	0
CT	250	230	192	144	114	94	75	49	38	21	15	6	2	2	0

*Non-inferiority margin;†HR 0.91 (95%CI 0.74, 1.10)

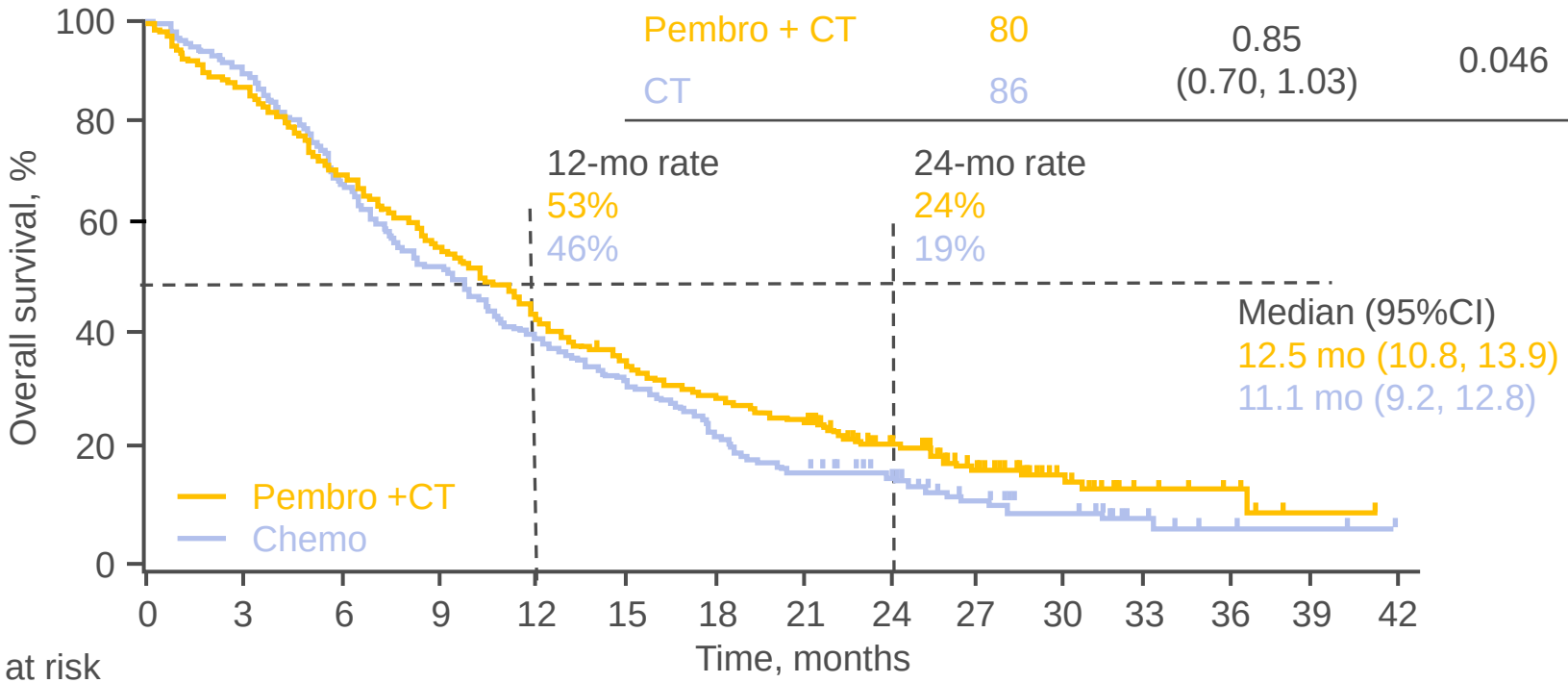
Tabernero J, et al. J Clin Oncol 2019;37(suppl):abstr LBA4007

LBA4007: Pembrolizumab with or without chemotherapy versus chemotherapy for advanced gastric or gastroesophageal junction (G/GEJ) adenocarcinoma: The phase III KEYNOTE-062 study – Tabernero J, et al

Key results (cont.)

OS (CPS ≥1) for pembrolizumab + CT vs. CT

	Events, %	HR (99.2%CI)	p-value
Pembro + CT	80	0.85 (0.70, 1.03)	0.046
CT	86		



No. at risk

Pembro + CT	257	229	194	165	136	105	88	74	52	33	17	8	5	1	0
CT	250	230	192	144	114	94	75	49	38	21	15	6	2	2	0

Tabernero J, et al. J Clin Oncol 2019;37(suppl):abstr LBA4007

LBA4007: Pembrolizumab with or without chemotherapy versus chemotherapy for advanced gastric or gastroesophageal junction (G/GEJ) adenocarcinoma: The phase III KEYNOTE-062 study – Tabernero J, et al

Key results (cont.)

Outcomes	CPS ≥1			CPS ≥10		
	Pembro	Pembro + CT	CT	Pembro	Pembro + CT	CT
OS						
Events	79	80	86	66	76	83
HR (95%CI) vs. CT	0.91 (0.69, 1.18)	0.85 (0.70, 1.03)	- -	0.69 (0.49, 0.97)	0.85 (0.62, 1.17)	- -
mOS, mo (95%CI)	10.6 (7.7, 13.8)	12.5 (10.8, 13.9)	11.1 (9.2, 12.8)	17.4 (9.1, 23.1)	12.3 (9.5, 14.8)	10.8 (8.5, 13.8)
PFS						
Events	88	83	89	80	79	89
HR (95%CI) vs. CT	1.66 (1.37, 2.01)	0.84 (0.70, 1.02)*	- -	1.10 (0.79, 1.51)	0.73 (0.53, 1.00)	- -
mPFS, mo (95%CI)	2.0 (1.5, 2.8)	6.9 (5.7, 7.3)	6.4 (5.7, 7.0)	2.9 (1.6, 5.4)	5.7 (5.5, 8.2)	6.1 (5.3, 6.9)
ORR, %	14.8	48.6	37.2	25.0	52.5	37.8
DoR, mo (range)	13.7 (1.4+–33.6+)	6.8 (1.4+–34.7+)	6.8 (1.4+–30.4+)	19.3 (1.4+–33.6+)	8.3 (1.6+–34.7+)	37.8 (1.5+–30.4+)

*p=0.039

Tabernero J, et al. J Clin Oncol 2019;37(suppl):abstr LBA4007

LBA4007: Pembrolizumab with or without chemotherapy versus chemotherapy for advanced gastric or gastroesophageal junction (G/GEJ) adenocarcinoma: The phase III KEYNOTE-062 study – Tabernero J, et al

Key results (cont.)

TRAEs (CPS ≥1), %	Pembrolizumab (n=254)	Pembrolizumab + CT (n=250)	CT (n=244)
Any	54	94	92
Grade 3–4	16	71	68
Led to discontinuation	4	27	18
Led to death	1*	2†	1‡
Immune-mediated events and infusion reactions	21	24	8

Conclusions

- **In patients with advanced gastric or GEJ cancer with CPS ≥1, there was a comparable improvement in OS for those receiving 1L pembrolizumab vs. CT although there was a modest OS improvement in those with CPS ≥10**
- **Pembrolizumab + CT also demonstrated some additional benefit to CT alone**
- **Pembrolizumab had a more favourable tolerability profile compared with CT and the safety profile for pembrolizumab + CT was manageable**

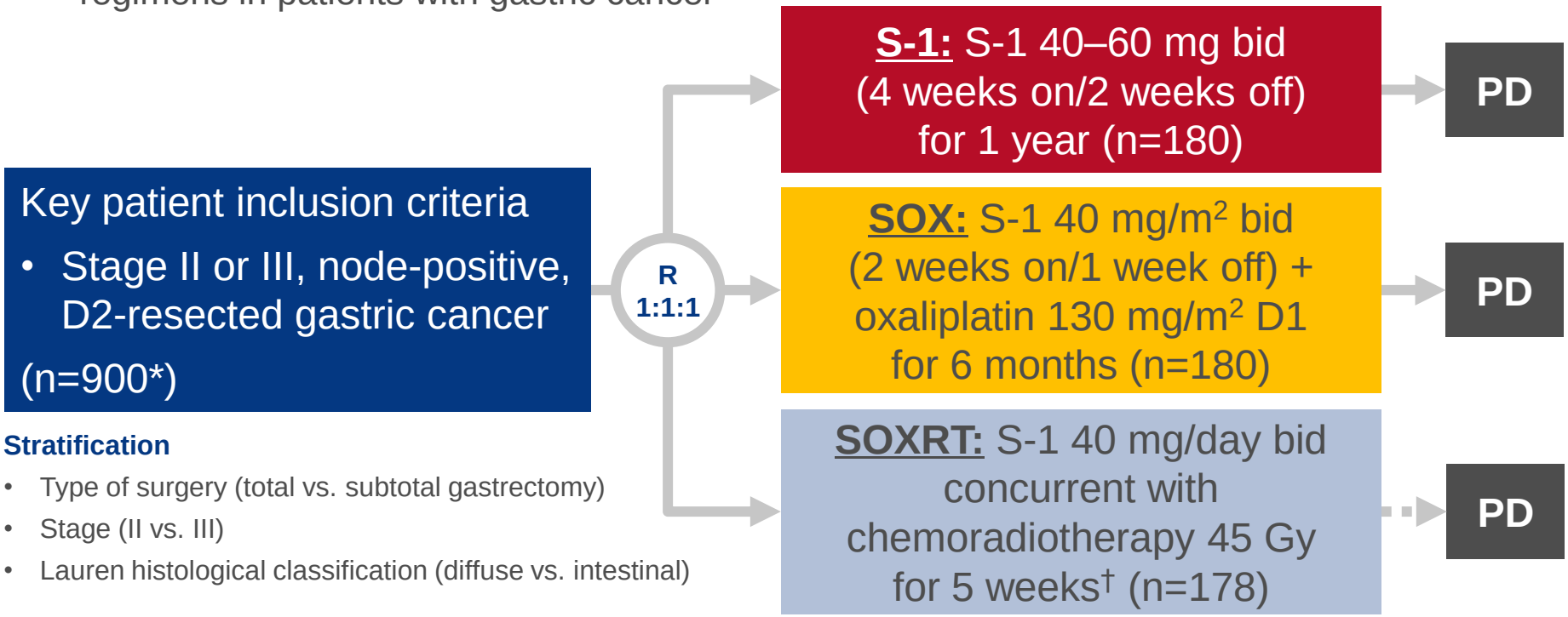
*Pneumonitis, malignant neoplasm progression, pericardial effusion (n=1 each); †febrile neutropenia, myocardial ischaemia, colitis, sepsis, malignant progression; ‡multiple organ failure, pneumonitis, pulmonary embolism (n=1 each)

Tabernero J, et al. J Clin Oncol 2019;37(suppl):abstr LBA4007

4001: ARTIST 2: Interim results of a phase III trial involving adjuvant chemotherapy and/or chemoradiotherapy after D2-gastrectomy in stage II/III gastric cancer (GC) – Park SH, et al

Study objective

- To investigate the efficacy and safety of different chemotherapy and chemoradiotherapy regimens in patients with gastric cancer



Stratification

- Type of surgery (total vs. subtotal gastrectomy)
- Stage (II vs. III)
- Lauren histological classification (diffuse vs. intestinal)

PRIMARY ENDPOINT

- DFS

SECONDARY ENDPOINTS

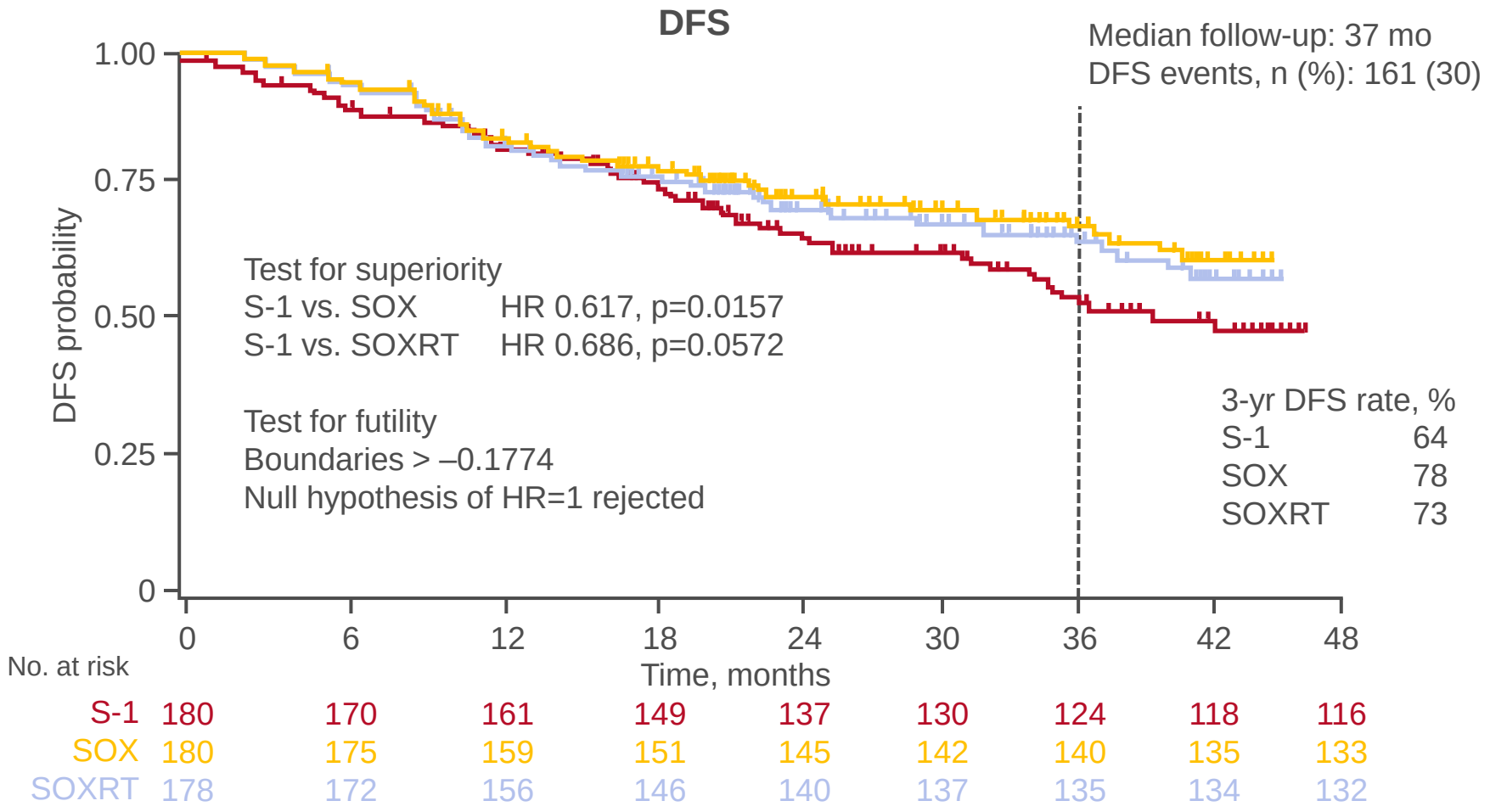
- OS, recurrence, safety

*Interim analysis of 538 patients; †2 cycles prior to adjuvant chemoradiotherapy and 4 cycles after of S-1 40 mg/m^2 bid (2 weeks on/1 week off) + oxaliplatin 130 mg/m^2 D1

Park SH, et al. J Clin Oncol 2019;37(suppl):abstr 4001

4001: ARTIST 2: Interim results of a phase III trial involving adjuvant chemotherapy and/or chemoradiotherapy after D2-gastrectomy in stage II/III gastric cancer (GC) – Park SH, et al

Key results



Park SH, et al. J Clin Oncol 2019;37(suppl):abstr 4001

4001: ARTIST 2: Interim results of a phase III trial involving adjuvant chemotherapy and/or chemoradiotherapy after D2-gastrectomy in stage II/III gastric cancer (GC) – Park SH, et al

Key results (cont.)

Grade 3–4 AEs, n (%)	S-1 (n=180)	SOX (n=179)	SOXRT (n=177)
Anaemia	7 (4)	14 (8)	12 (7)
Neutropenia	2 (1)	5 (3)	5 (3)
Nausea	2 (1)	2 (1)	0
Vomiting	1 (1)	4 (2)	0
Constipation	0	0	0
Diarrhoea	7 (4)	3 (2)	4 (2)
Anorexia	5 (3)	7 (4)	2 (1)
Fatigue	2 (2)	4 (2)	0
Skin	0	0	0
Neuropathy	0	21 (12)	11 (6)

Conclusions

- **In patients with stage II/III node-positive, D2-resected gastric cancer, adjuvant SOX and SOXRT demonstrated longer DFS than S-1 alone**
- **All three regimens were generally well tolerated**

Park SH, et al. J Clin Oncol 2019;37(suppl):abstr 4001

4010: Pembrolizumab versus chemotherapy as second-line therapy for advanced esophageal cancer: Phase 3 KEYNOTE-181 study – Shah MA, et al

Study objective

- To investigate the efficacy and safety of 2L pembrolizumab in patients with advanced or metastatic squamous cell carcinoma (SCC) or adenocarcinoma (ACC) of the oesophagus

Key patient inclusion criteria

- Advanced or metastatic SCC or ACC of oesophagus or Siewert type I GEJ adenocarcinoma
- Progression on/after 1L therapy
- ECOG PS 0–1

(n=628)

R 1:1

Pembrolizumab
200 mg q3w for up to 2 years
(n=314)

→ PD

Stratification

- Histology (SCC vs. ACC)
- Region (Asia vs. rest of world)

Chemotherapy
Paclitaxel 80–100 mg/m^2 D1, 8, 15 q4w,
docetaxel 75 mg/m^2 q3w or
irinotecan 180 mg/m^2 q2w
(n=314)

→ PD

PRIMARY ENDPOINT

- OS in SCC, PD-L1 CPS ≥10 and ITT populations

SECONDARY ENDPOINTS

- PFS, ORR, safety

Shah MA, et al. J Clin Oncol 2019;37(suppl):abstr 4010

4010: Pembrolizumab versus chemotherapy as second-line therapy for advanced esophageal cancer: Phase 3 KEYNOTE-181 study – Shah MA, et al

Key results

Characteristic, n (%) [unless otherwise specified]	Pembrolizumab (n=314)	Chemotherapy (n=314)
Median age, years (range)	63 (23–84)	62 (24–84)
>65 years, n (%)	139 (44)	133 (42)
Male	273 (87)	271 (86)
Region		
Asia	121 (39)	122 (39)
Rest of World	193 (61)	192 (61)
ECOG PS 1	187 (60)	197 (63)
Tumour type		
SCC	198 (63)	203 (65)
ACC	116 (37)	111 (35)
PD-L1 status		
CPS ≥10	107 (34)	115 (37)
CPS <10	201 (64)	196 (62)
CPS not evaluable	6 (2)	3 (1)

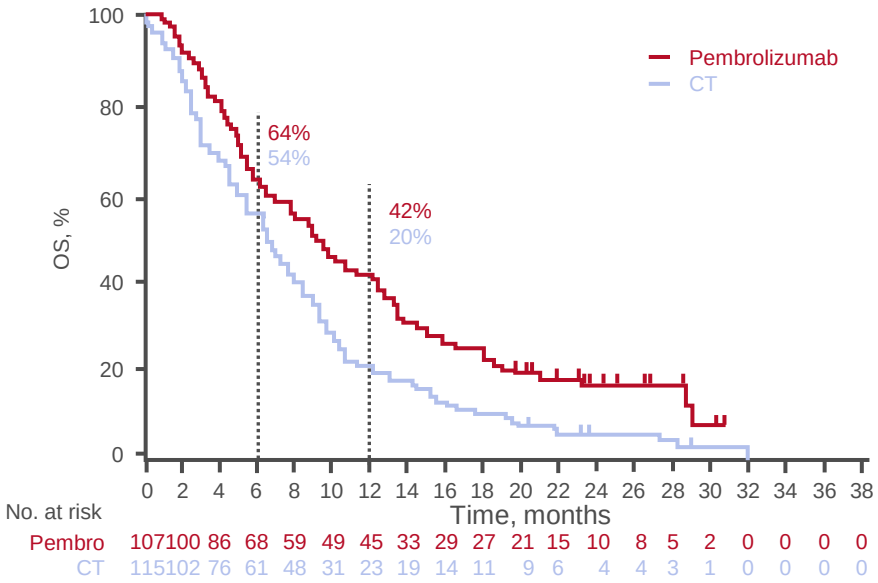
Shah MA, et al. J Clin Oncol 2019;37(suppl):abstr 4010

4010: Pembrolizumab versus chemotherapy as second-line therapy for advanced esophageal cancer: Phase 3 KEYNOTE-181 study – Shah MA, et al

Key results (cont.)

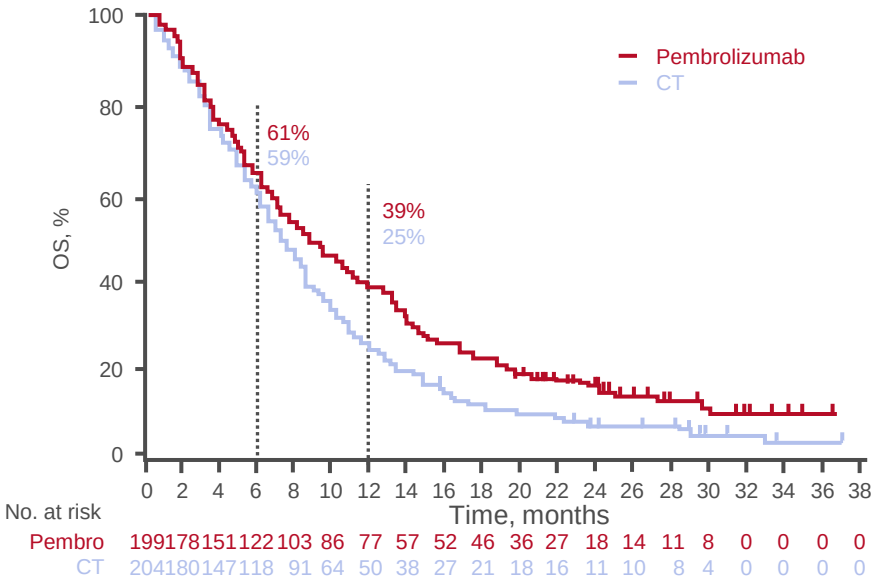
PD-L1 CPS ≥10

	Events	Median, mo (95%CI)	HR* (95%CI)	p-value†
Pembrolizumab	84	9.3 (6.6, 12.5)	0.67 (0.50, 0.89)	0.0029
CT	95	6.7 (5.1, 8.2)		



SCC population

	Events	Median, mo (95%CI)	HR* (95%CI)	p-value†
Pembrolizumab	86	8.2 (6.7, 10.0)	0.75 (0.61, 0.93)	0.0035
CT	93	7.1 (6.1, 8.2)		



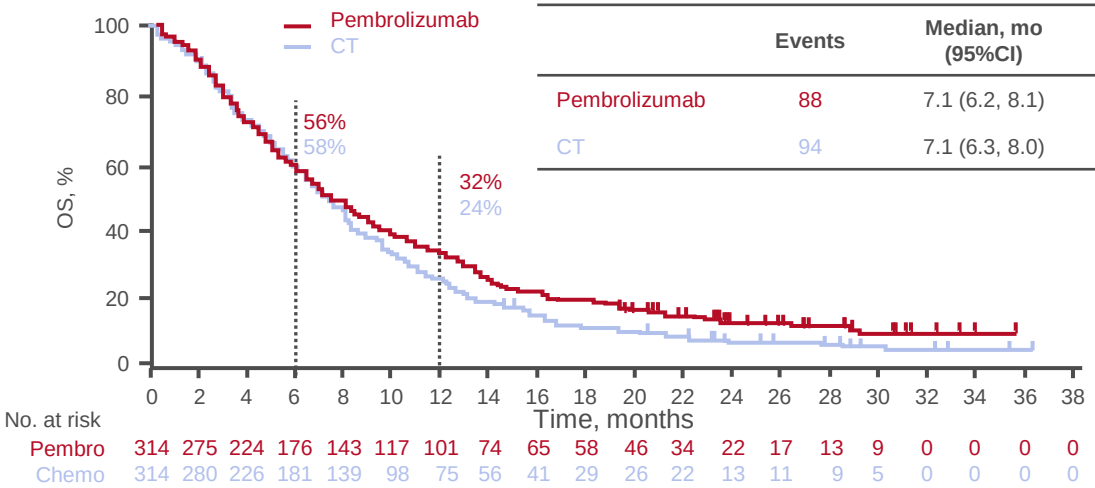
*Based on Cox regression model with treatment as a covariate stratified by region and histology; †p-values are nominal

Shah MA, et al. J Clin Oncol 2019;37(suppl):abstr 4010

4010: Pembrolizumab versus chemotherapy as second-line therapy for advanced esophageal cancer: Phase 3 KEYNOTE-181 study – Shah MA, et al

Key results (cont.)

ITT population



	Events	Median, mo (95%CI)	HR* (95%CI)	p-value†
Pembrolizumab	88	7.1 (6.2, 8.1)	0.85 (0.72, 1.01)	0.0031
CT	94	7.1 (6.3, 8.0)		

Conclusions

- **In previously treated patients with advanced ACC of the oesophagus and PD-L1 CPS ≥10, pembrolizumab demonstrated improvement in OS after an additional four months of follow-up**
- **There were also clinically meaningful OS benefits in previously treated patients with advanced SCC of the oesophagus**

*Based on Cox regression model with treatment as a covariate stratified by region and histology; †p-values are nominal

Shah MA, et al. J Clin Oncol 2019;37(suppl):abstr 4010

CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

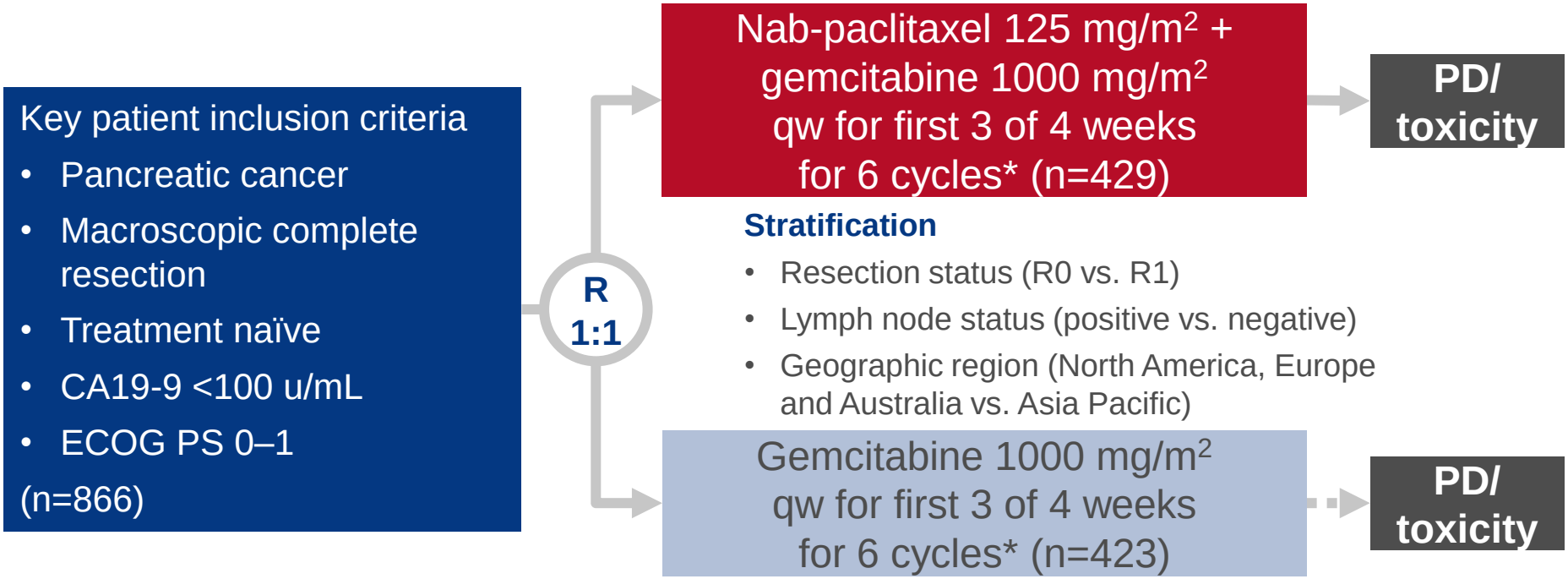
Cancers of the pancreas, small bowel and hepatobiliary tract

PANCREATIC CANCER

4000: APACT: phase III, multicenter, international, open-label, randomized trial of adjuvant nab-paclitaxel + gemcitabine (nab-P/G) vs gemcitabine (G) for surgically resected pancreatic adenocarcinoma – Tempero MA, et al

Study objective

- To investigate the efficacy and safety of nab-paclitaxel + gemcitabine compared with gemcitabine in patients with surgically resected pancreatic cancer



PRIMARY ENDPOINT

- Independently assessed DFS

SECONDARY ENDPOINTS

- OS, safety

*Treatment initiated ≤12 weeks post-surgery

Tempero MA, et al. J Clin Oncol 2019;37(suppl):abstr 4000

4000: APACT: phase III, multicenter, international, open-label, randomized trial of adjuvant nab-paclitaxel + gemcitabine (nab-P/G) vs gemcitabine (G) for surgically resected pancreatic adenocarcinoma – Tempero MA, et al

Key results

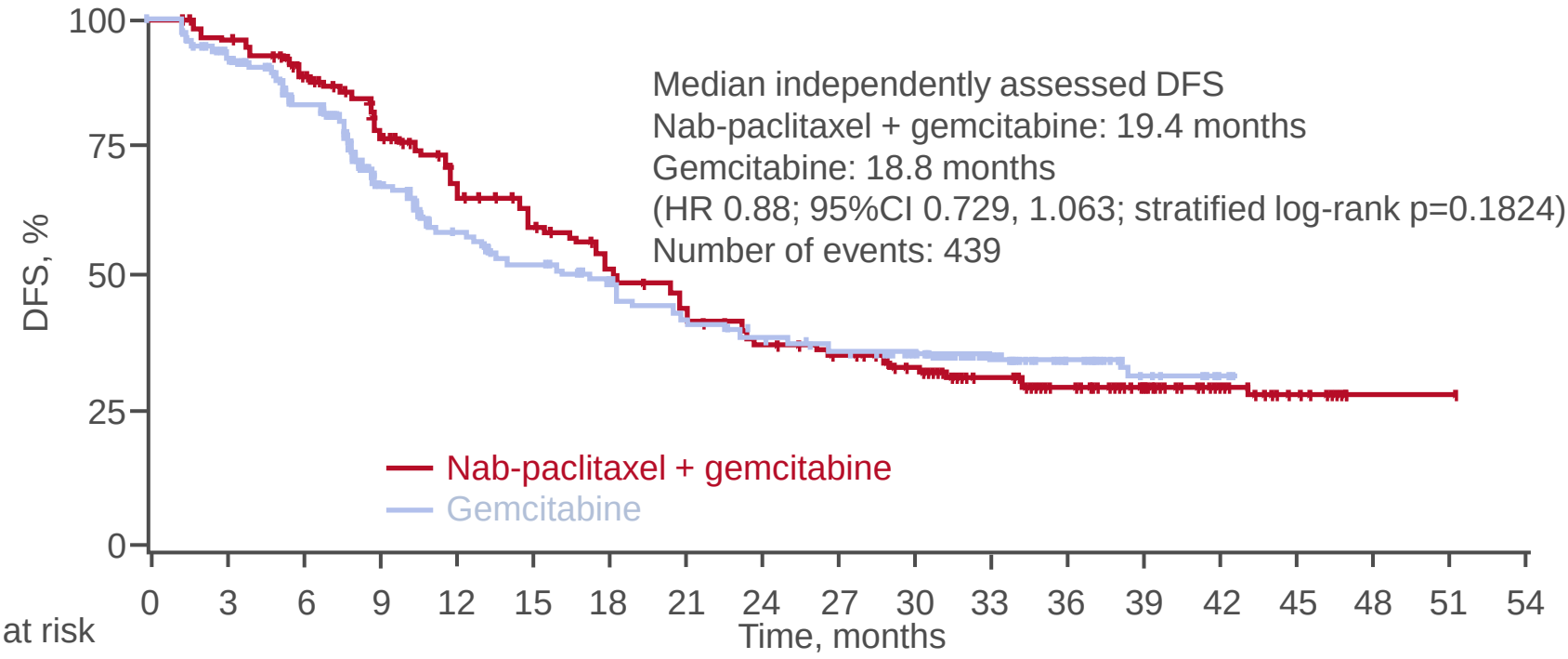
Characteristic, n (%) [unless otherwise specified]	Nab-paclitaxel + Gem (n=432)	Gem (n=434)	Total (n=866)
Median age, years (range)	64.0 (34–83)	64.0 (38–86)	64.0 (34–86)
Male	228 (53)	253 (58)	481 (56)
ECOG PS			
0	252 (58)	268 (62)	520 (60)
1	180 (42)	166 (38)	346 (40)
Resection status			
R0 (tumour-free margin)	327 (76)	334 (77)	661 (76)
R1 (microscopically positive margin)	105 (24)	100 (23)	205 (24)
Nodal status			
LN negative	121 (28)	122 (28)	243 (28)
LN positive	311 (72)	312 (72)	623 (72)
Baseline CA19-9			
n	423	429	852
Median, U/mL	14.31	12.90	13.65
Tumour grade			
Well differentiated	49 (11)	55 (13)	104 (12)
Moderately differentiated	264 (61)	241 (56)	505 (58)
Poorly differentiated	101 (23)	155 (26)	216 (25)
Undifferentiated	1 (<1)	2 (<1)	3 (<1)
Other/unknown	17 (4)	21 (5)	38 (4)

Tempero MA, et al. J Clin Oncol 2019;37(suppl):abstr 4000

4000: APACT: phase III, multicenter, international, open-label, randomized trial of adjuvant nab-paclitaxel + gemcitabine (nab-P/G) vs gemcitabine (G) for surgically resected pancreatic adenocarcinoma – Tempero MA, et al

Key results (cont.)

DFS (independently assessed)



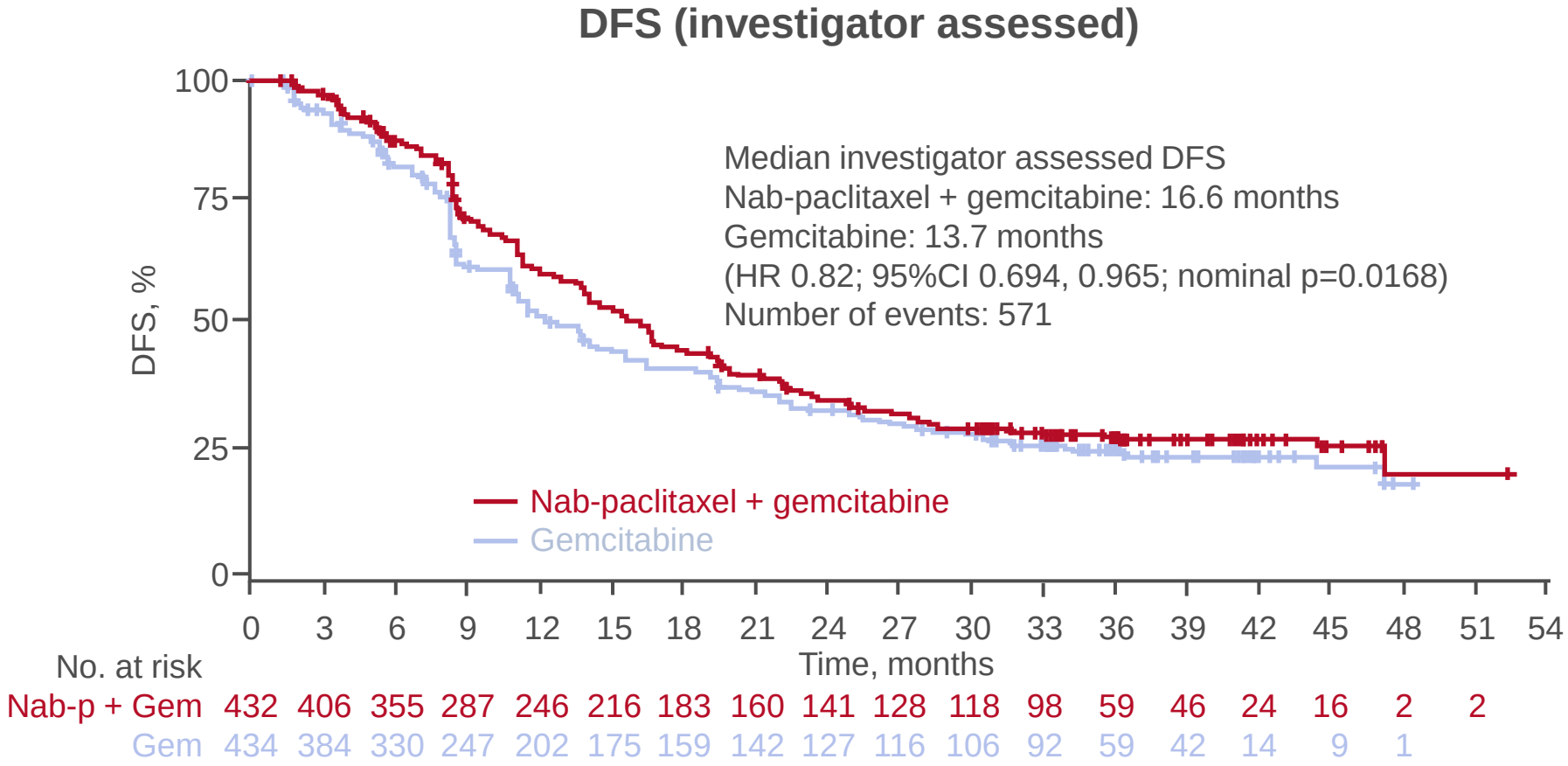
No. at risk

Nab-p + Gem	432	391	338	279	236	204	167	138	121	112	99	88	54	43	20	14	2	2
Gem	434	368	309	235	183	157	147	127	116	105	98	88	59	42	15	10	1	

Tempero MA, et al. J Clin Oncol 2019;37(suppl):abstr 4000

4000: APACT: phase III, multicenter, international, open-label, randomized trial of adjuvant nab-paclitaxel + gemcitabine (nab-P/G) vs gemcitabine (G) for surgically resected pancreatic adenocarcinoma – Tempero MA, et al

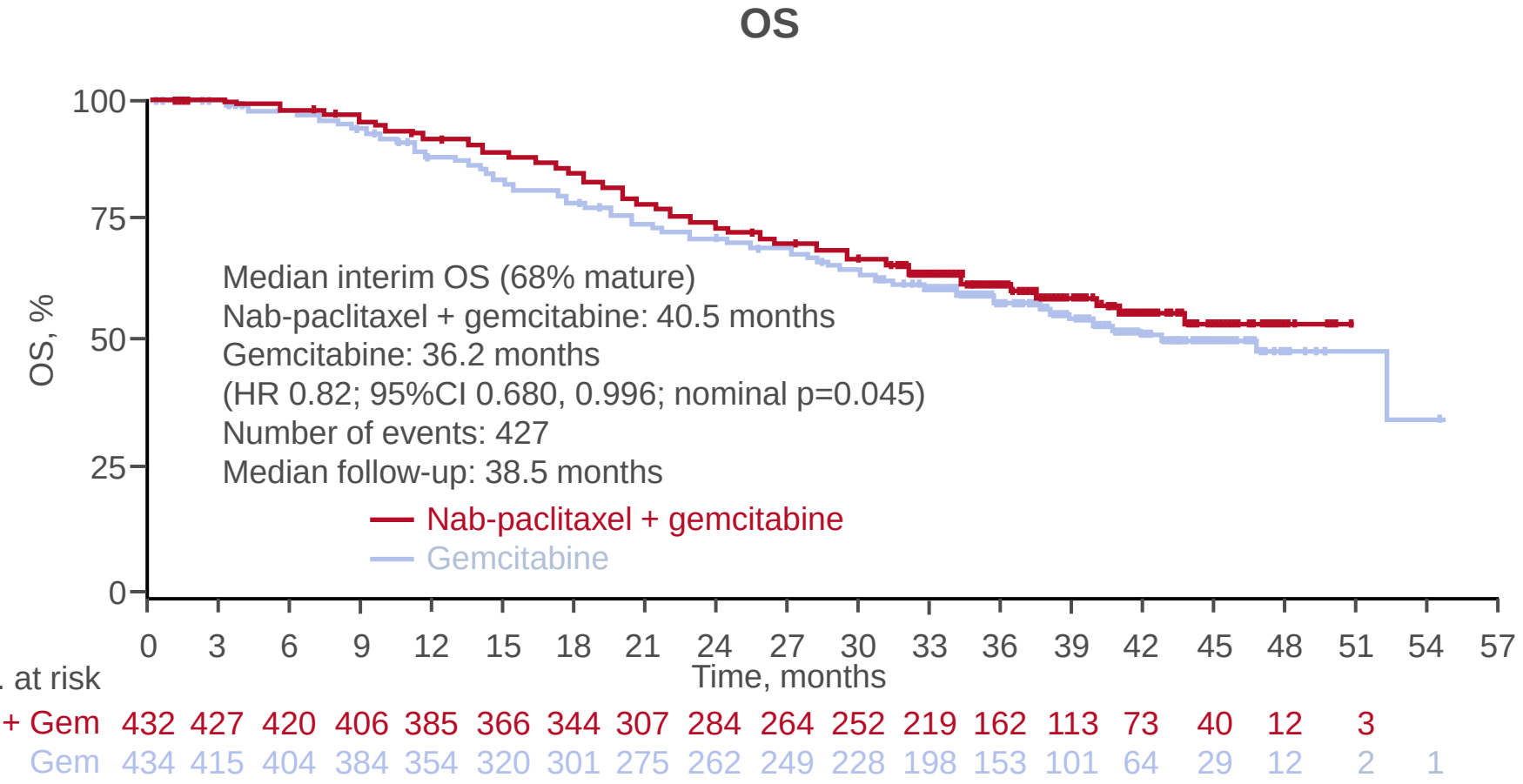
Key results (cont.)



Tempero MA, et al. J Clin Oncol 2019;37(suppl):abstr 4000

4000: APACT: phase III, multicenter, international, open-label, randomized trial of adjuvant nab-paclitaxel + gemcitabine (nab-P/G) vs gemcitabine (G) for surgically resected pancreatic adenocarcinoma – Tempero MA, et al

Key results (cont.)



No. at risk																		
Nab-p + Gem	432	427	420	406	385	366	344	307	284	264	252	219	162	113	73	40	12	3
Gem	434	415	404	384	354	320	301	275	262	249	228	198	153	101	64	29	12	2	1

Tempero MA, et al. J Clin Oncol 2019;37(suppl):abstr 4000

4000: APACT: phase III, multicenter, international, open-label, randomized trial of adjuvant nab-paclitaxel + gemcitabine (nab-P/G) vs gemcitabine (G) for surgically resected pancreatic adenocarcinoma – Tempero MA, et al

Key results (cont.)

Event, n (%)	Nab-paclitaxel + gemcitabine (n=429)	Gemcitabine (n=423)
Patients with ≥1 grade ≥3 TEAE	371 (86)	286 (68)
Patients with ≥1 serious TEAE	176 (41)	96 (23)
Grade ≥3 haematological TEAE (in ≥5% of patients in either arm)		
Any haematological TEAEs	250 (58)	204 (48)
Neutropenia	212 (49)	184 (43)
Anaemia	63 (15)	33 (8)
Leukopenia	36 (8)	20 (5)
Febrile neutropenia	21 (5)	4 (1)
Grade ≥3 non-haematological TEAEs (in ≥5% of patients in either arm)		
Peripheral neuropathy (SMQ)[a]	64 (15)	0
Fatigue	43 (10)	13 (3)
Diarrhoea	22 (5)	4 (1)
Asthenia	21 (5)	8 (2)
Hypertension	17 (4)	27 (6)

[a]Reported as a group term

Tempero MA, et al. J Clin Oncol 2019;37(suppl):abstr 4000

4000: APACT: phase III, multicenter, international, open-label, randomized trial of adjuvant nab-paclitaxel + gemcitabine (nab-P/G) vs gemcitabine (G) for surgically resected pancreatic adenocarcinoma – Tempero MA, et al

Conclusions

- **In patients with surgically resected pancreatic cancer, nab-paclitaxel + gemcitabine did not significantly improve DFS vs. gemcitabine although there was a significant improvement in OS**
- **The safety profile of nab-paclitaxel + gemcitabine was consistent with previous findings**

Tempero MA, et al. J Clin Oncol 2019;37(suppl):abstr 4000

LBA4: Olaparib as maintenance treatment following first-line platinum-based chemotherapy (PBC) in patients with a germline BRCA mutation and metastatic pancreatic cancer (mPC): Phase III POLO trial – Kindler HL, et al

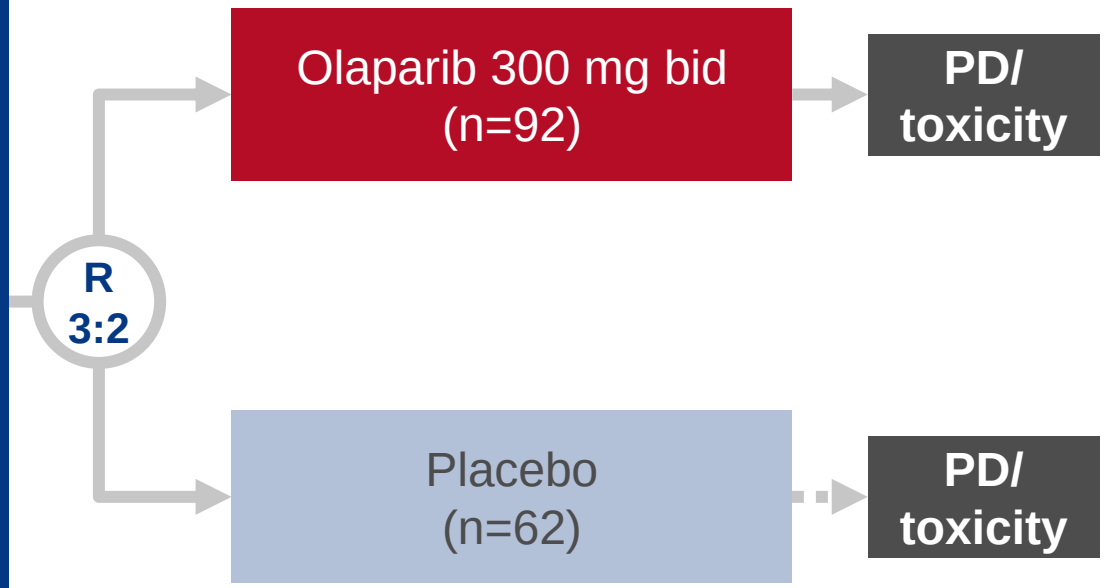
Study objective

- To assess the efficacy and safety of olaparib as 2L therapy in patients with a germline BRCA mutation and metastatic pancreatic cancer

Key patient inclusion criteria

- Metastatic pancreatic cancer
- Deleterious or suspected deleterious germline BRCA1 or BRCA2 mutation
- ≥16 weeks of 1L platinum-based CT with no limit to duration, without progression (CR, PR or SD)

(n=154)



PRIMARY ENDPOINT

- PFS (RECIST v1.1)

SECONDARY ENDPOINTS

- PFS2, ORR (modified RECIST v1.1), OS, safety

Kindler HL, et al. J Clin Oncol 2019;37(suppl):abstr LBA4

LBA4: Olaparib as maintenance treatment following first-line platinum-based chemotherapy (PBC) in patients with a germline BRCA mutation and metastatic pancreatic cancer (mPC): Phase III POLO trial – Kindler HL, et al

Key results

Characteristic, n (%) [unless otherwise specified]	Olaparib (n=92)	Placebo (n=62)
Median age, years (range)	57.0 (37–84)	57.0 (36–75)
≥65 years, n (%)	28 (30.4)	13 (21.0)
Male	53 (57.6)	31 (50.0)
Caucasian	82 (89.1)	59 (95.2)
ECOG PS		
0	65 (70.7)	38 (61.3)
1	25 (27.2)	23 (37.1)
BRCA mutation status		
BRCA1	29 (31.5)	16 (25.8)
BRCA2	62 (67.4)	46 (74.2)
Both	1 (1.1)	0 (0)
Primary tumour location in pancreas		
Head	46 (50.0)	34 (54.8)
Body	41 (44.6)	17 (27.4)
Tail	29 (31.5)	22 (35.5)
Biliary stent present	1 (1.1)	4 (6.5)
Median albumin concentration, g/dL (range)	4.1 (3.2–4.8)	4.0 (3.4–5.0)

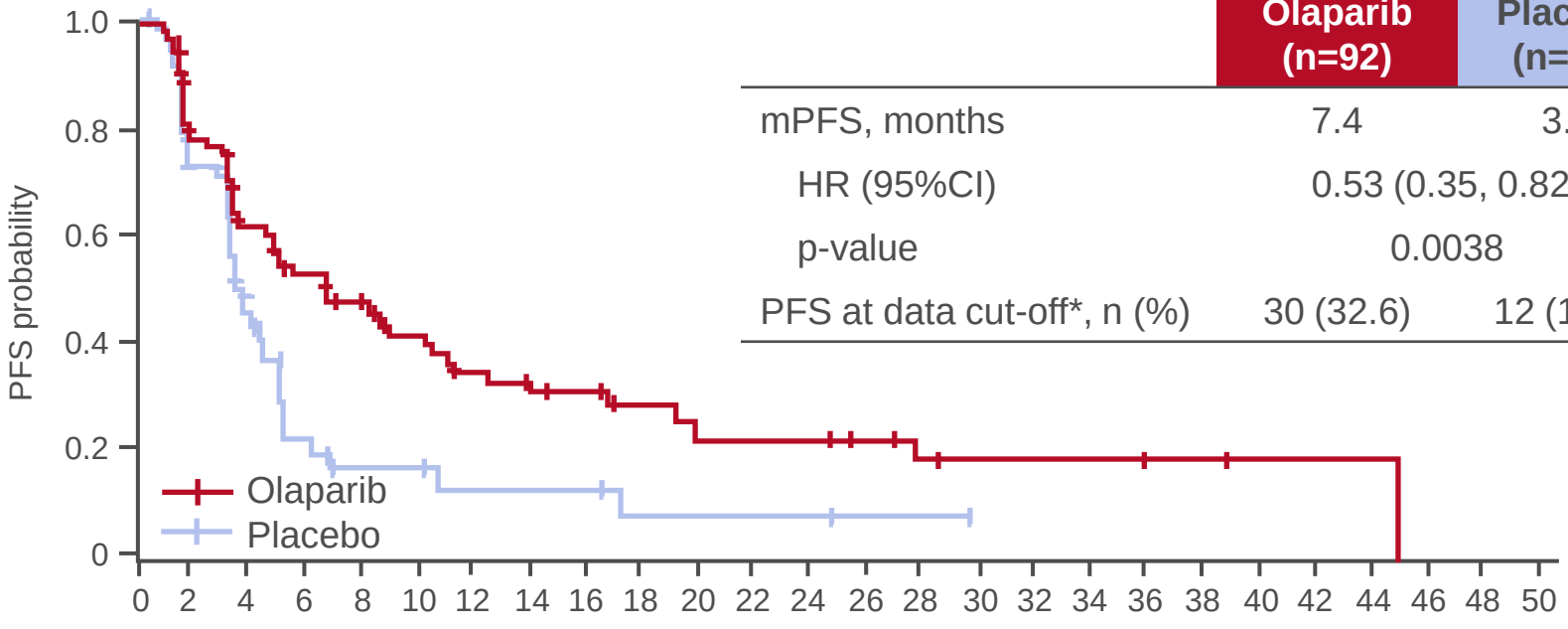
*Patients may be counted in >1 category

Kindler HL, et al. J Clin Oncol 2019;37(suppl):abstr LBA4

LBA4: Olaparib as maintenance treatment following first-line platinum-based chemotherapy (PBC) in patients with a germline BRCA mutation and metastatic pancreatic cancer (mPC): Phase III POLO trial – Kindler HL, et al

Key results (cont.)

Primary endpoint: PFS by blinded independent central review



	Olaparib (n=92)	Placebo (n=62)
mPFS, months	7.4	3.8
HR (95%CI)	0.53 (0.35, 0.82)	
p-value	0.0038	
PFS at data cut-off*, n (%)	30 (32.6)	12 (19.4)

No. at risk

Olaparib	92	69	50	41	34	24	18	17	14	10	10	8	8	7	5	3	3	3	3	2	1	1	1	0
Placebo	62	39	23	10	6	6	4	4	4	2	2	2	2	1	1	0								

*January 15, 2019

Kindler HL, et al. J Clin Oncol 2019;37(suppl):abstr LBA4

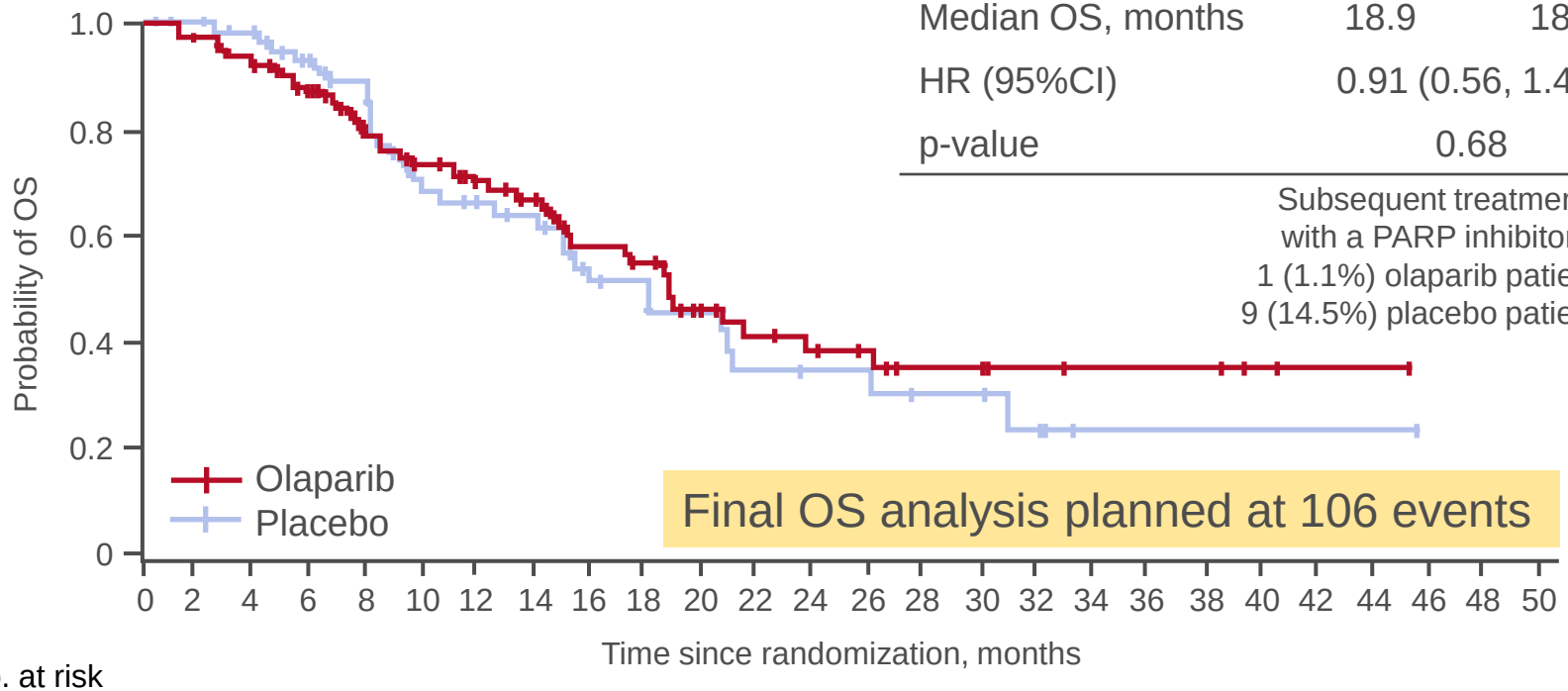
LBA4: Olaparib as maintenance treatment following first-line platinum-based chemotherapy (PBC) in patients with a germline BRCA mutation and metastatic pancreatic cancer (mPC): Phase III POLO trial – Kindler HL, et al

Key results (cont.)

Overall survival (46% maturity)

	Olaparib (n=92)	Placebo (n=62)
Median OS, months	18.9	18.1
HR (95%CI)	0.91 (0.56, 1.46)	
p-value	0.68	

Subsequent treatment with a PARP inhibitor:
1 (1.1%) olaparib patient
9 (14.5%) placebo patients



Final OS analysis planned at 106 events

No. at risk

Olaparib	92	87	80	71	61	51	46	39	31	28	20	16	14	12	9	6	5	4	4	4	2	1	1	0
Placebo	62	60	56	50	44	32	29	27	20	18	14	10	8	8	6	6	4	1	1	1	1	1	1	0

Kindler HL, et al. J Clin Oncol 2019;37(suppl):abstr LBA4

LBA4: Olaparib as maintenance treatment following first-line platinum-based chemotherapy (PBC) in patients with a germline BRCA mutation and metastatic pancreatic cancer (mPC): Phase III POLO trial – Kindler HL, et al

Key results (cont.)

ORR in patients with measurable disease by BICR

	Olaparib (n=78)	Placebo (n=52)
ORR, n (%)	18 (23.1)	6 (11.5)
Median time to onset of response, months	5.4	3.6
Median DoR, months	24.9	3.7

- Two patients who received olaparib had a CR
  - Both CRs were ongoing at the data cut-off*

*January 15, 2019

LBA4: Olaparib as maintenance treatment following first-line platinum-based chemotherapy (PBC) in patients with a germline BRCA mutation and metastatic pancreatic cancer (mPC): Phase III POLO trial – Kindler HL, et al

Key results (cont.)

AEs and exposure	Olaparib (n=91)	Placebo (n=60)
Any grade, n (%)	87 (95.6)	56 (93.3)
Grade ≥3, n (%)	36 (39.6)	14 (23.3)
AEs leading to dose interruption, n (%)	32 (35.2)	3 (5.0)
AEs leading to dose reduction, n (%)	15 (16.5)	2 (3.3)
AEs leading to discontinuation, n (%)	5 (5.5)	1 (1.7)
Median duration of treatment, months (range)	6.0 (0.8–45.3)	3.7 (0.1–30.1)

Conclusions

- **In patients with metastatic pancreatic cancer and a germline BRCA mutation who had not progressed on platinum-based CT, maintenance olaparib was associated with a significant and clinically meaningful improvement in PFS**
- **The tolerability profile of olaparib was manageable and consistent with that observed in other tumour types**
- **These are the first data to demonstrate the benefit of a targeted treatment in biomarker-selected patients with metastatic pancreatic cancer and suggest that germline BRCA mutation testing should be performed**

Kindler HL, et al. J Clin Oncol 2019;37(suppl):abstr LBA4

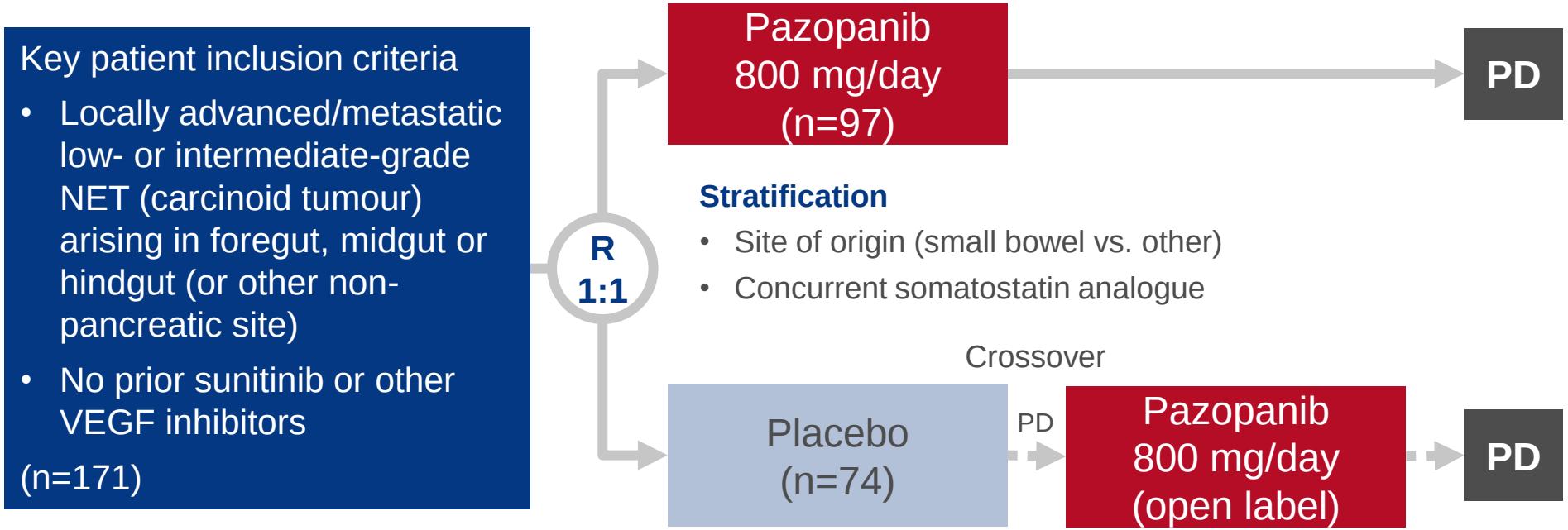
Cancers of the pancreas, small bowel and hepatobiliary tract

NEUROENDOCRINE TUMOUR

4005: Prospective randomized phase II trial of pazopanib versus placebo in patients with progressive carcinoid tumors (CARC)(Alliance A021202) – Bergsland EK, et al

Study objective

- To investigate the efficacy and safety of pazopanib (a multi-kinase inhibitor) in patients with progressive carcinoid tumours



PRIMARY ENDPOINT

- PFS (RECIST v1.1)

SECONDARY ENDPOINTS

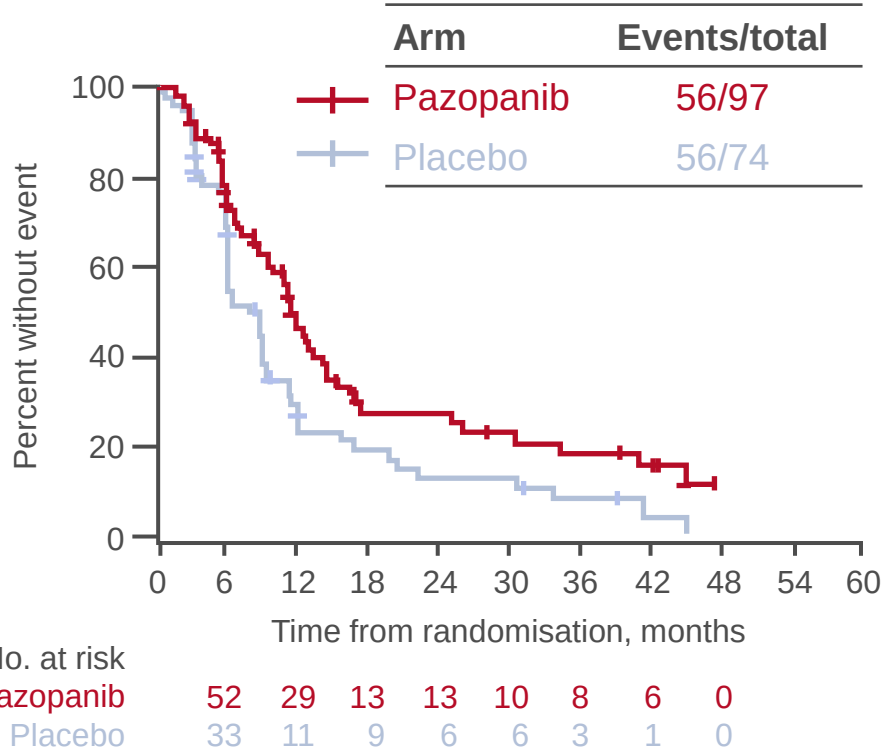
- OS, ORR, DoR, TTF, safety

Bergsland EK, et al. J Clin Oncol 2019;37(suppl):abstr 4005

4005: Prospective randomized phase II trial of pazopanib versus placebo in patients with progressive carcinoid tumors (CARC)(Alliance A021202) – Bergsland EK, et al

Key results

Progression-free survival (central review, ITT)



	Pazopanib (n=97)	Placebo (n=74)
No. of events, %	56	56
12-mo PFS, % (90% UCB)	46.4 (54.7)	22.9 (31.4)
mPFS, months (90% UCB)	11.6 (13.0)	8.5 (8.9)
HR (90% UCB)	0.53 (0.69)	REF
Stratified log-rank p-value = 0.0005		
Adj. HR* (90% UCB)	0.57 (0.74)	REF
Adjusted log-rank p-value = 0.0020		

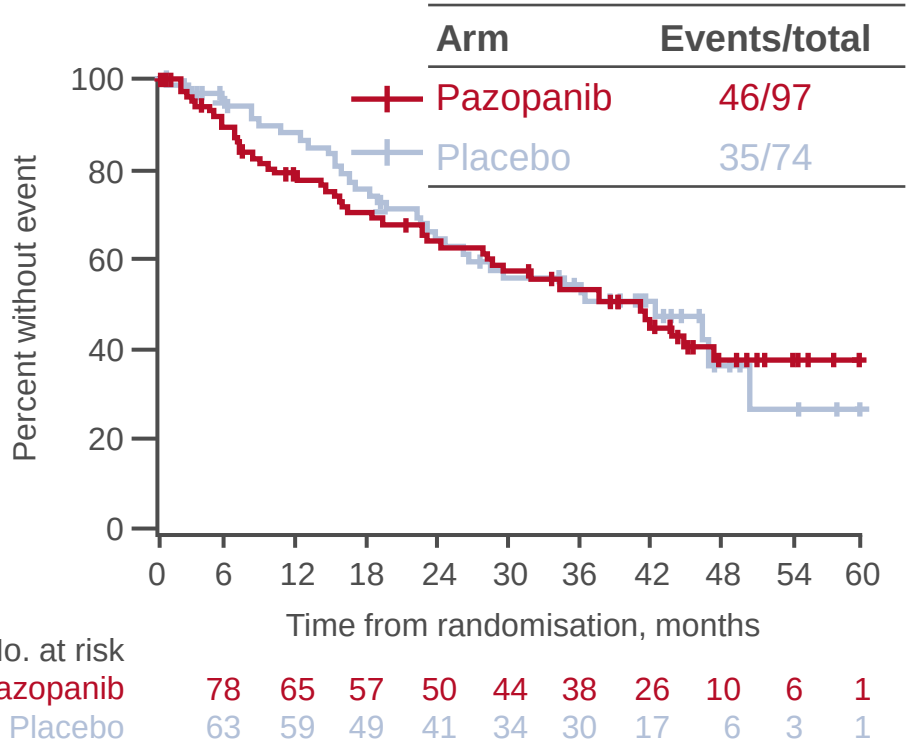
*Gender, functional tumour, age and stratification factors (concurrent somatostatin analogue, site of primary)

Bergsland EK, et al. J Clin Oncol 2019;37(suppl):abstr 4005

4005: Prospective randomized phase II trial of pazopanib versus placebo in patients with progressive carcinoid tumors (CARC)(Alliance A021202) – Bergsland EK, et al

Key results (cont.)

Overall survival (preliminary, ITT)



	Pazopanib (n=97)	Placebo (n=74)
No. of deaths, %	46	35
12-mo OS, % (90% UCB)	79.3 (85.1)	88.3 (93.4)
mOS, months (90% UCB)	41.3 (44.8)	42.4 (50.8)
HR (90% UCB)	1.13 (1.51)	REF
Stratified log-rank p-value = 0.7000		
Adj. HR* (90% UCB)	1.21 (1.64)	REF
Adjusted log-rank p-value = 0.7246		

*Gender, functional tumour, age and stratification factors (concurrent somatostatin analogue, site of primary)

Bergsland EK, et al. J Clin Oncol 2019;37(suppl):abstr 4005

4005: Prospective randomized phase II trial of pazopanib versus placebo in patients with progressive carcinoid tumors (CARC)(Alliance A021202) – Bergsland EK, et al

Key results (cont.)

Grade ≥3 TRAEs, n (%)	Pazopanib (n=89)	Placebo (n=72)	p-value
Fatigue	7 (7.9)	2 (2.8)	0.1896
Nausea	4 (4.5)	1 (1.4)	0.3813
Hypertension	24 (26.9)	3 (4.2)	<0.0001
AST increased	8 (9)	0 (0)	0.0088
ALT increased	8 (9)	0 (0)	0.0088
Diarrhoea	4 (4.5)	3 (4.2)	1.0000
Blood bilirubin increased	2 (2.2)	1 (1.4)	1.0000
Vomiting	3 (3.4)	2 (2.8)	1.0000

Conclusions

- **In patients with progressive carcinoid tumours, pazopanib demonstrated improvement in PFS, but not OS (which may have been confounded by crossover)**
- **Pazopanib was associated with more grade ≥3 AEs, in particular, hypertension**
- **Further studies are warranted in this patient population to determine those most likely to benefit and to determine strategies to lessen the toxicities**

Bergsland EK, et al. J Clin Oncol 2019;37(suppl):abstr 4005

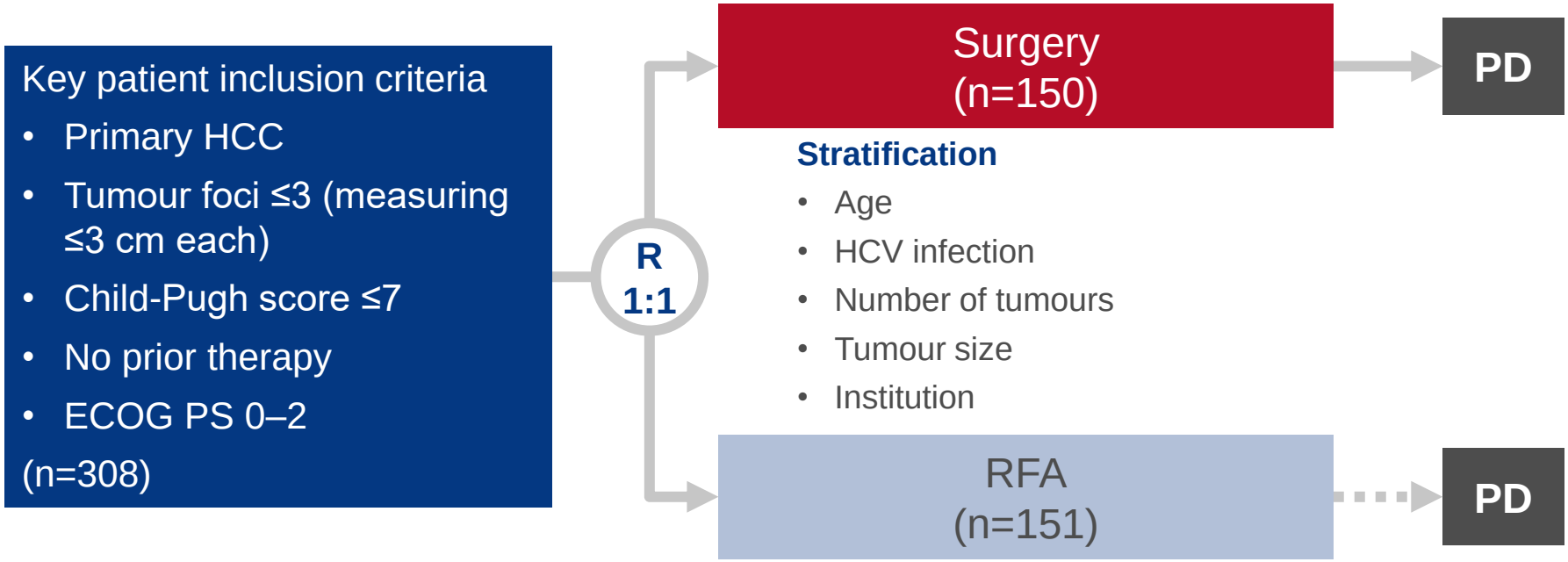
Cancers of the pancreas, small bowel and hepatobiliary tract

HEPATOCELLULAR CARCINOMA

4002: A multicenter randomized controlled trial to evaluate the efficacy of surgery vs. radiofrequency ablation for small hepatocellular carcinoma (SURF trial) – Izumi N, et al

Study objective

- To investigate the efficacy and safety of surgery compared with RFA in patients with HCC



PRIMARY ENDPOINTS

- RFS, OS

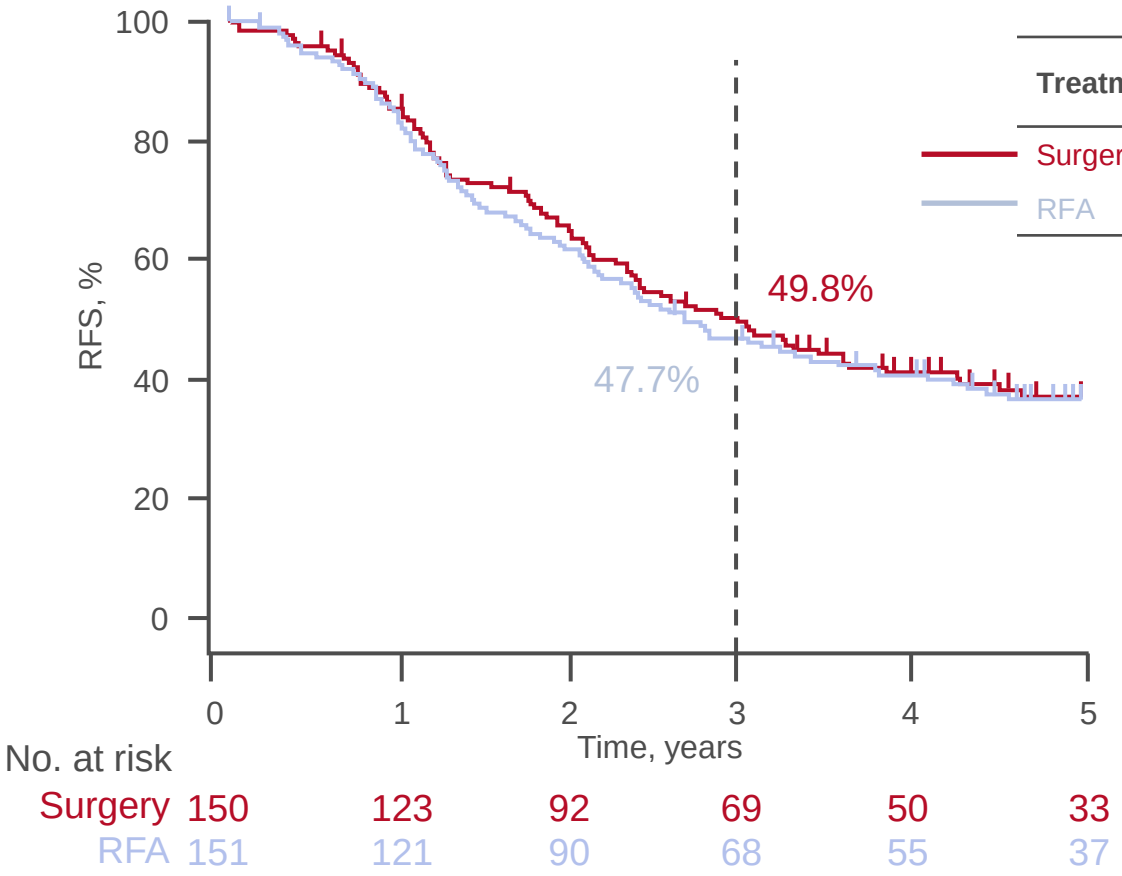
SECONDARY ENDPOINT

- Safety

Izumi N, et al. J Clin Oncol 2019;37(suppl):abstr 4002

4002: A multicenter randomized controlled trial to evaluate the efficacy of surgery vs. radiofrequency ablation for small hepatocellular carcinoma (SURF trial) – Izumi N, et al

Key results



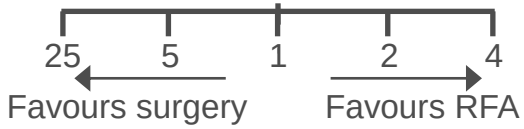
Treatment	Median RFS, years (95%CI)	p-value
Surgery	2.98 (2.33, 3.86)	0.793
RFA	2.76 (2.17, 3.80)	

Izumi N, et al. J Clin Oncol 2019;37(suppl):abstr 4002

4002: A multicenter randomized controlled trial to evaluate the efficacy of surgery vs. radiofrequency ablation for small hepatocellular carcinoma (SURF trial) – Izumi N, et al

Key results (cont.)

	Surgery		RFA			
	Recurrence	Registered	Recurrence	Registered	HR	95%CI
All	99	150	96	151	0.96	(0.72, 1.28)
Age						
<60 years	12	29	9	28	1.05	(0.43, 2.59)
≥60 years	87	121	87	123	0.95	(0.70, 1.29)
HCV infection						
Negative	33	53	33	57	1.01	(0.61, 1.65)
Positive	66	97	63	94	0.94	(0.66, 1.34)
No. of tumours						
Solitary	87	135	84	136	0.98	(0.73, 1.34)
Multiple	12	15	12	15	0.79	(0.32, 1.93)
Tumour size, cm						
≤2.0	61	98	59	101	1.07	(0.74, 1.55)
>2.0	38	52	37	50	0.80	(0.50, 1.28)
Child-Pugh score						
5	75	117	78	129	1.00	(0.72, 1.39)
6–7	23	32	18	22	0.72	(0.34, 1.49)



Izumi N, et al. J Clin Oncol 2019;37(suppl):abstr 4002

4002: A multicenter randomized controlled trial to evaluate the efficacy of surgery vs. radiofrequency ablation for small hepatocellular carcinoma (SURF trial) – Izumi N, et al

Key results (cont.)

	Surgery	RFA	p-value*
Median length of hospital stay, days (range)	17.0 (12.0–23.0)	10.0 (7.0–15.5)	<0.01
Median operation/procedure time, min (range)	274.0 (203.0–341.0)	40.0 (24.0–70.0)	<0.01

Conclusions

- **In patients with early stage HCC and tumours <3 cm in diameter, RFS was comparable for those undergoing surgical resection and RFA**
- **Both approaches were safe with no mortality in either group**

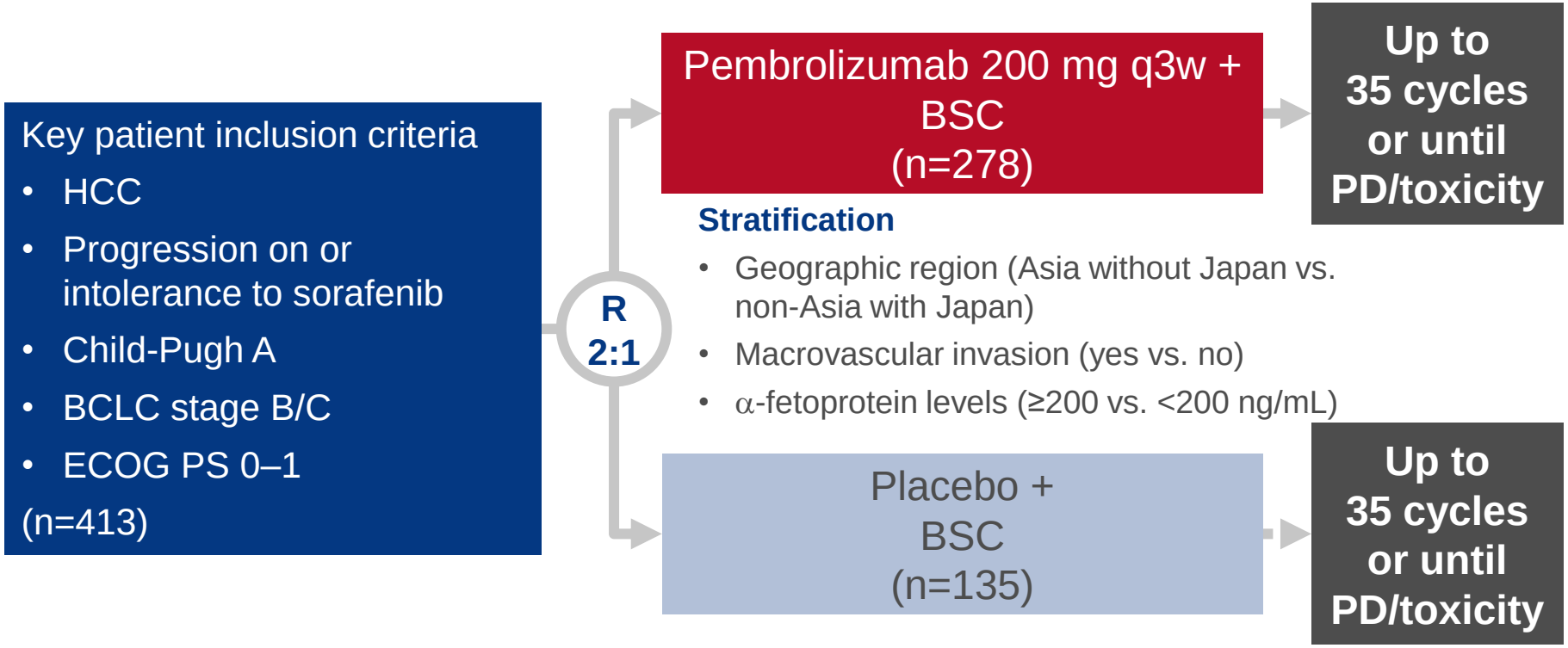
*Wilcoxon rank sum test

Izumi N, et al. J Clin Oncol 2019;37(suppl):abstr 4002

4004: Results of KEYNOTE-240: phase 3 study of pembrolizumab (Pembro) vs best supportive care (BSC) for second line therapy in advanced hepatocellular carcinoma (HCC) – Finn RS, et al

Study objective

- To investigate the efficacy and safety of pembrolizumab in patients with previously treated advanced HCC



CO-PRIMARY ENDPOINTS

- OS, PFS

SECONDARY ENDPOINTS

- ORR, DoR, DCR, TTP, safety

Finn RS, et al. J Clin Oncol 2019;37(suppl):abstr 4004

4004: Results of KEYNOTE-240: phase 3 study of pembrolizumab (Pembro) vs best supportive care (BSC) for second line therapy in advanced hepatocellular carcinoma (HCC) – Finn RS, et al

Key results

Characteristic, n (%) [unless otherwise specified]	Pembrolizumab (n=278)	Placebo (n=135)
Median age, years (range)	67 (18–91)	65 (23–89)
Male	226 (81.3)	112 (83)
ECOG PS 1	116 (41.7)	64 (47.4)
Child-Pugh score		
A	277 (99.6)	133 (98.5)
B	1 (0.4)	2 (1.5)
Overall BCLC stage		
B	56 (20.1)	29 (21.5)
C	222 (79.9)	106 (78.5)
HBV positive	72 (25.9)	29 (21.5)
HCV positive	43 (15.5)	21 (15.6)
Discontinuation of prior sorafenib		
Intolerance	36 (12.9)	18 (13.3)
PD	242 (87.1)	117 (86.7)
Extrahepatic disease	195 (70.1)	93 (68.9)
Macrovascular invasion	36 (12.9)	16 (11.9)
Baseline α-fetoprotein ≥200 ng/mL	129 (46.4)	58 (43.0)

Finn RS, et al. J Clin Oncol 2019;37(suppl):abstr 4004

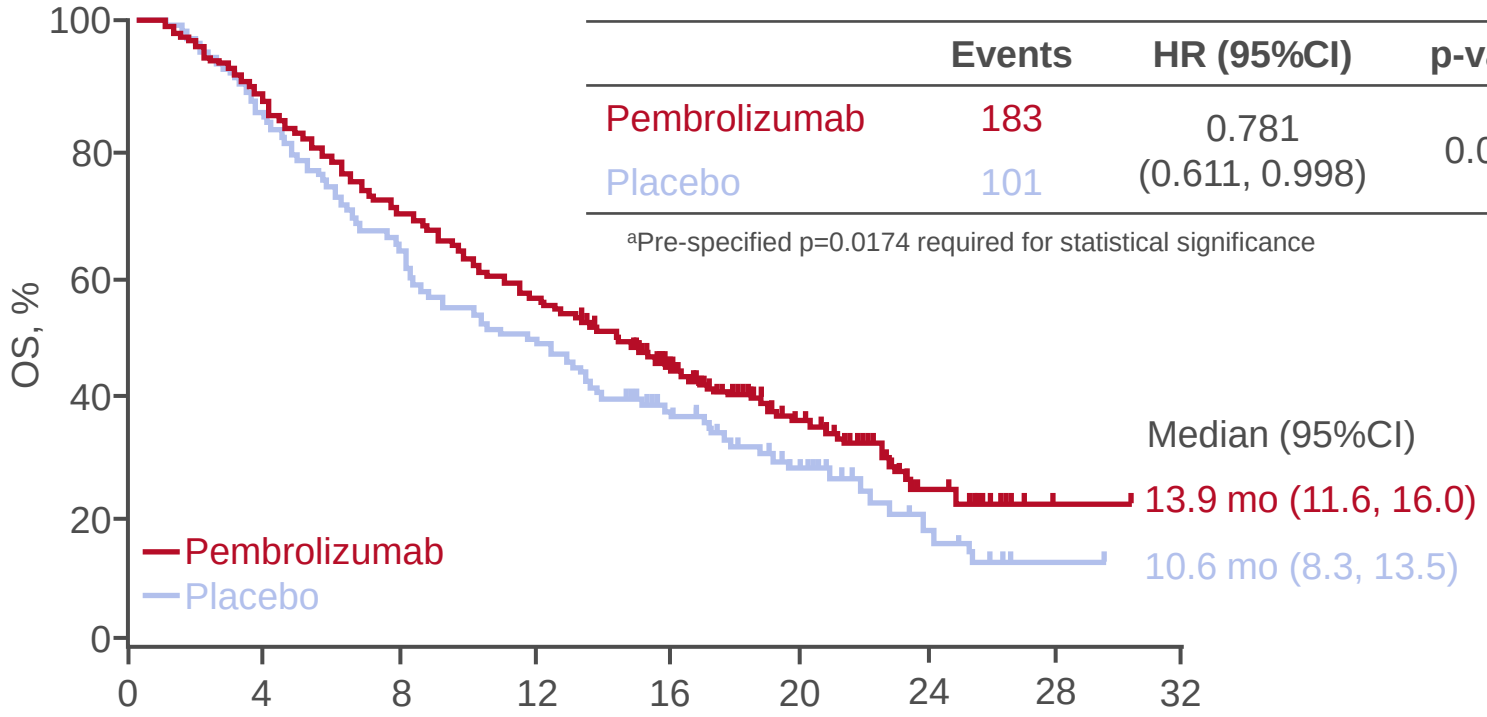
4004: Results of KEYNOTE-240: phase 3 study of pembrolizumab (Pembro) vs best supportive care (BSC) for second line therapy in advanced hepatocellular carcinoma (HCC) – Finn RS, et al

Key results (cont.)

OS

	Events	HR (95%CI)	p-value[a]
Pembrolizumab	183	0.781 (0.611, 0.998)	0.0238
Placebo	101		

[a]Pre-specified p=0.0174 required for statistical significance



No.at risk

Pembrolizumab	278	237	190	152	110	57	16	1	0
Placebo	135	113	84	65	42	23	8	1	0

Finn RS, et al. J Clin Oncol 2019;37(suppl):abstr 4004

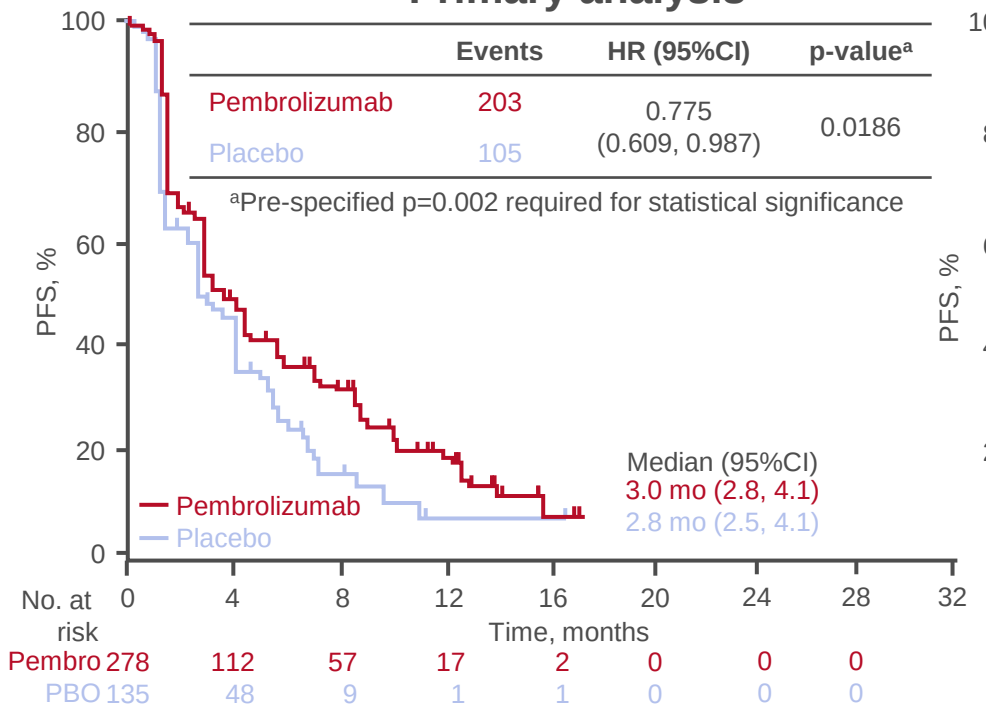
4004: Results of KEYNOTE-240: phase 3 study of pembrolizumab (Pembro) vs best supportive care (BSC) for second line therapy in advanced hepatocellular carcinoma (HCC) – Finn RS, et al

Key results (cont.)

Primary analysis

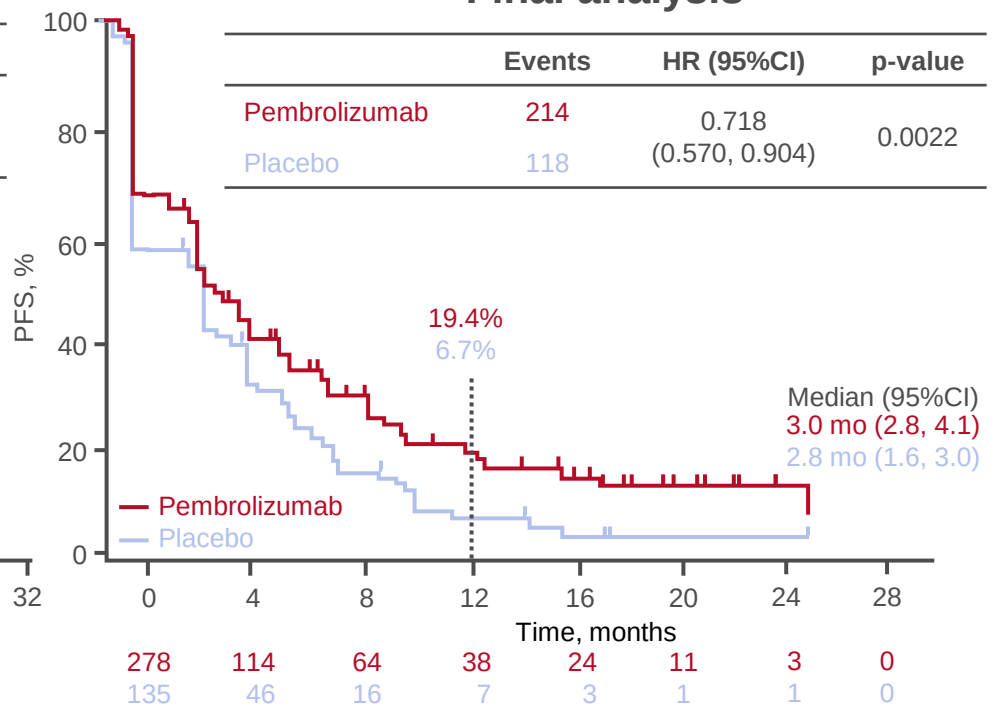
	Events	HR (95%CI)	p-value[a]
Pembrolizumab	203	0.775 (0.609, 0.987)	0.0186
Placebo	105		

[a]Pre-specified p=0.002 required for statistical significance



Final analysis

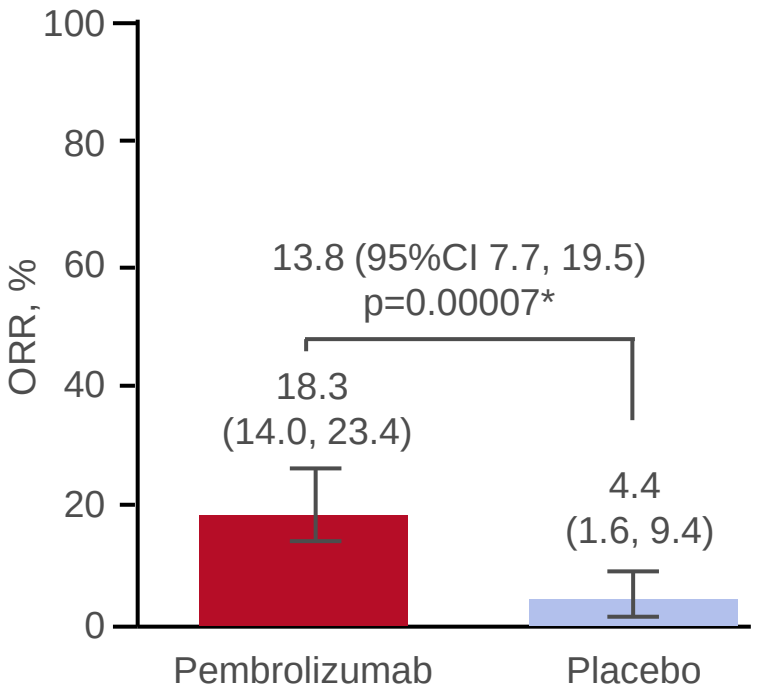
	Events	HR (95%CI)	p-value
Pembrolizumab	214	0.718 (0.570, 0.904)	0.0022
Placebo	118		



Finn RS, et al. J Clin Oncol 2019;37(suppl):abstr 4004

4004: Results of KEYNOTE-240: phase 3 study of pembrolizumab (Pembro) vs best supportive care (BSC) for second line therapy in advanced hepatocellular carcinoma (HCC) – Finn RS, et al

Key results (cont.)



BOR, n (%)	Pembrolizumab (n=278)	Placebo (n=135)
CR	6 (2.2)	0 (0)
PR	45 (16.2)	6 (4.4)
SD	122 (43.9)	66 (48.9)
SD ≥23 weeks	37 (18.3)	20 (14.8)
PD	90 (32.4)	57 (42.2)
DCR (CR + PR + SD)	173 (62.2)	72 (53.3)

Duration of response, median (range), months†

- Pembrolizumab: 13.8 mo (1.5+–23.6+)
- Placebo: Not reached (2.8–20.4+)

*Nominal one-sided p-value based on the Miettinen and Nurminen method stratified by randomisation factors; †from product-limit (Kaplan-Meier) method for censored data; "+" symbol indicates no PD by the time of last disease assessment

Finn RS, et al. J Clin Oncol 2019;37(suppl):abstr 4004

4004: Results of KEYNOTE-240: phase 3 study of pembrolizumab (Pembro) vs best supportive care (BSC) for second line therapy in advanced hepatocellular carcinoma (HCC) – Finn RS, et al

Key results (cont.)

AEs, n (%)	Pembrolizumab (n=279)	Placebo (n=134)
TRAEs	170 (60.9)	65 (48.5)
Grade 3–4*	52 (18.6)	10 (7.5)
Led to discontinuation	18 (6.5)	1 (0.7)
Led to death	1 (0.4)†	0 (0)
Immune-mediated	51 (18.3)	11 (8.2)
Grade 3–4	20 (7.2)	1 (0.7)
Led to discontinuation	10 (3.6)	0 (0)
Immune-mediated hepatic-related	10 (3.6)	0 (0)

Conclusions

- **In patients with advanced HCC, 2L pembrolizumab improved PFS and reduced the risk of death, but did not reach the pre-specified statistical boundaries for survival compared with BSC**
- **The safety profile of pembrolizumab was consistent with that found in other tumour types**

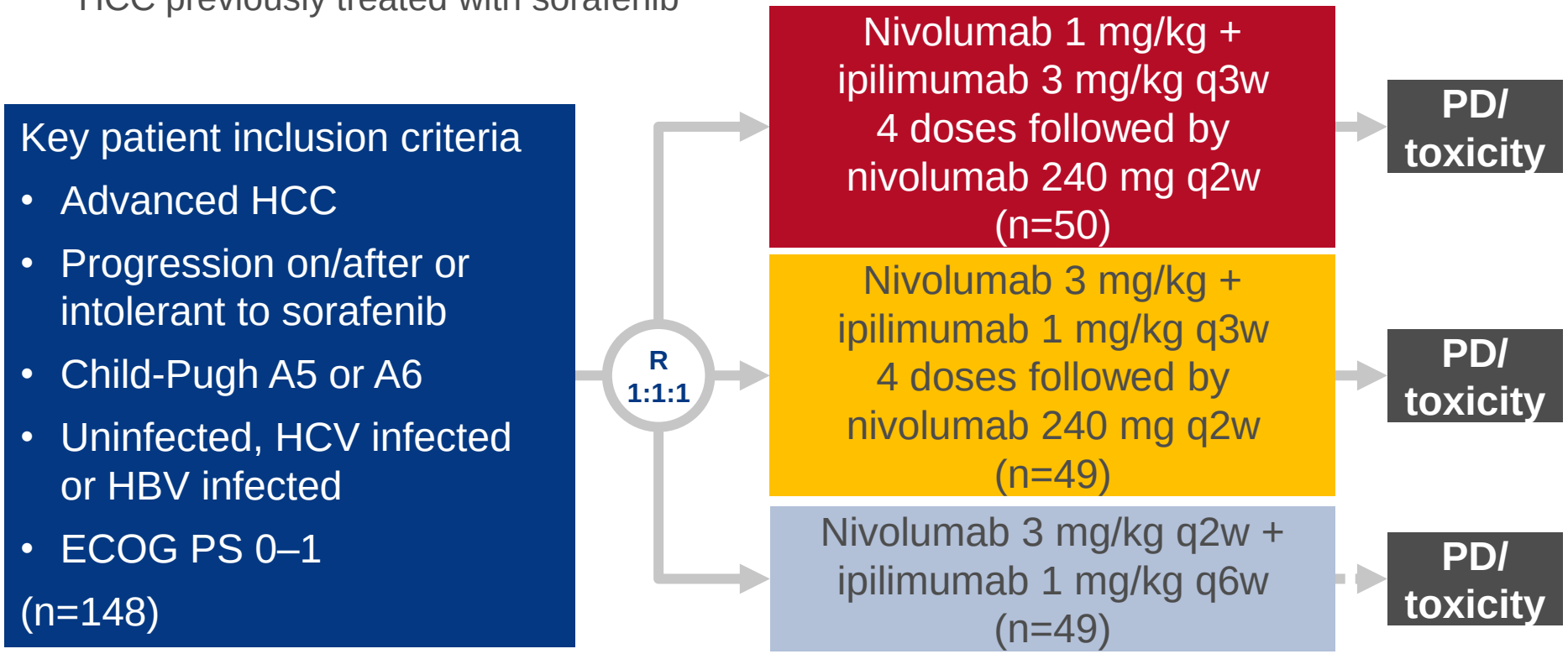
*One grade 5 event in pembrolizumab arm that led to death;
†malignant neoplasm progression possibly treatment related

Finn RS, et al. J Clin Oncol 2019;37(suppl):abstr 4004

4012: Nivolumab (NIVO) + ipilimumab (IPI) combination therapy in patients (pts) with advanced hepatocellular carcinoma (aHCC): Results from CheckMate 040 – Yau T, et al

Study objective

- To investigate the efficacy and safety of nivolumab + ipilimumab in patients with advanced HCC previously treated with sorafenib



PRIMARY ENDPOINTS

- Safety, ORR (RECIST v1.1)

SECONDARY ENDPOINTS

- DCR, DoR, TTR, TTP, PFS, OS

Yau T, et al. J Clin Oncol 2019;37(suppl):abstr 4012

4012: Nivolumab (NIVO) + ipilimumab (IPI) combination therapy in patients (pts) with advanced hepatocellular carcinoma (aHCC): Results from CheckMate 040 – Yau T, et al

Key results

TRAEs, n (%)	Nivolumab 1 mg/kg + ipilimumab 3 mg/kg q3w (n=49)		Nivolumab 3 mg/kg + ipilimumab 1 mg/kg q3w (n=49)		Nivolumab 3 mg/kg q2w + ipilimumab 1 mg/kg q6w (n=48)	
	Any grade	Grade 3–4	Any grade	Grade 3–4	Any grade	Grade 3–4
Any	46 (94)	26 (53)	35 (71)	14 (29)	38 (79)	15 (31)
Pruritus	22 (45)	2 (4)	16 (33)	0	14 (29)	0 (0)
Rash	14 (29)	2 (4)	11 (22)	2 (4)	8 (17)	0 (0)
Diarrhoea	12 (24)	2 (4)	6 (12)	1 (2)	8 (17)	1 (2)
AST increased	10 (20)	8 (16)	10 (20)	4 (8)	6 (13)	2 (4)
Lipase increased	7 (14)	6 (12)	6 (12)	3 (6)	8 (17)	4 (8)
Fatigue	9 (18)	1 (2)	6 (12)	0 (0)	5 (10)	0 (0)
ALT increased	8 (16)	4 (8)	7 (14)	3 (6)	4 (8)	0 (0)
Hypothyroidism	10 (20)	0 (0)	4 (8)	0 (0)	4 (8)	0 (0)
Rash maculopapular	7 (14)	2 (4)	4 (8)	0 (0)	3 (6)	0 (0)
Decreased appetite	6 (12)	0 (0)	4 (8)	0 (0)	3 (6)	0 (0)
Malaise	6 (12)	1 (2)	3 (6)	0 (0)	3 (6)	0 (0)
Adrenal insufficiency	7 (14)	1 (2)	3 (6)	0 (0)	2 (4)	0 (0)
Nausea	5 (10)	0 (0)	4 (8)	0 (0)	1 (2)	0 (0)
Pyrexia	2 (4)	0 (0)	4 (8)	0 (0)	5 (10)	0 (0)

Yau T, et al. J Clin Oncol 2019;37(suppl):abstr 4012

4012: Nivolumab (NIVO) + ipilimumab (IPI) combination therapy in patients (pts) with advanced hepatocellular carcinoma (aHCC): Results from CheckMate 040 – Yau T, et al

Key results (cont.)

	Nivolumab 1 mg/kg + ipilimumab 3 mg/kg q3w (n=49)	Nivolumab 3 mg/kg + ipilimumab 1 mg/kg q3w (n=49)	Nivolumab 3 mg/kg q2w + ipilimumab 1 mg/kg q6w (n=49)
ORR by BICR, n (%)	16 (32)	15 (31)	15 (31)
CR	4 (8)	3 (6)	0
PR	12 (24)	12 (24)	15 (31)
SD, n (%)	9 (18)	5 (10)	9 (18)
PD, n (%)	20 (40)	24 (49)	21 (43)
Unable to determine, n (%)	3 (6)	4 (8)	4 (8)
DCR, n (%)	27 (54)	21 (43)	24 (49)
Median TTR, months (range)	2.0 (1.1–12.8)	2.6 (1.2–5.5)	2.7 (1.2–8.7)
Median DoR, months (range)	17.5 (4.6–30.5+)	22.2 (4.2–29.9+)	16.6 (4.1+–32.0+)
ORR by investigator assessment, n (%)	16 (32)	13 (27)	14 (29)

Conclusions

- **In patients with advanced HCC previously treated with sorafenib, nivolumab + ipilimumab was associated with a higher ORR than nivolumab alone**
- **The tolerability profile of nivolumab + ipilimumab was similar to nivolumab alone**

Yau T, et al. J Clin Oncol 2019;37(suppl):abstr 4012

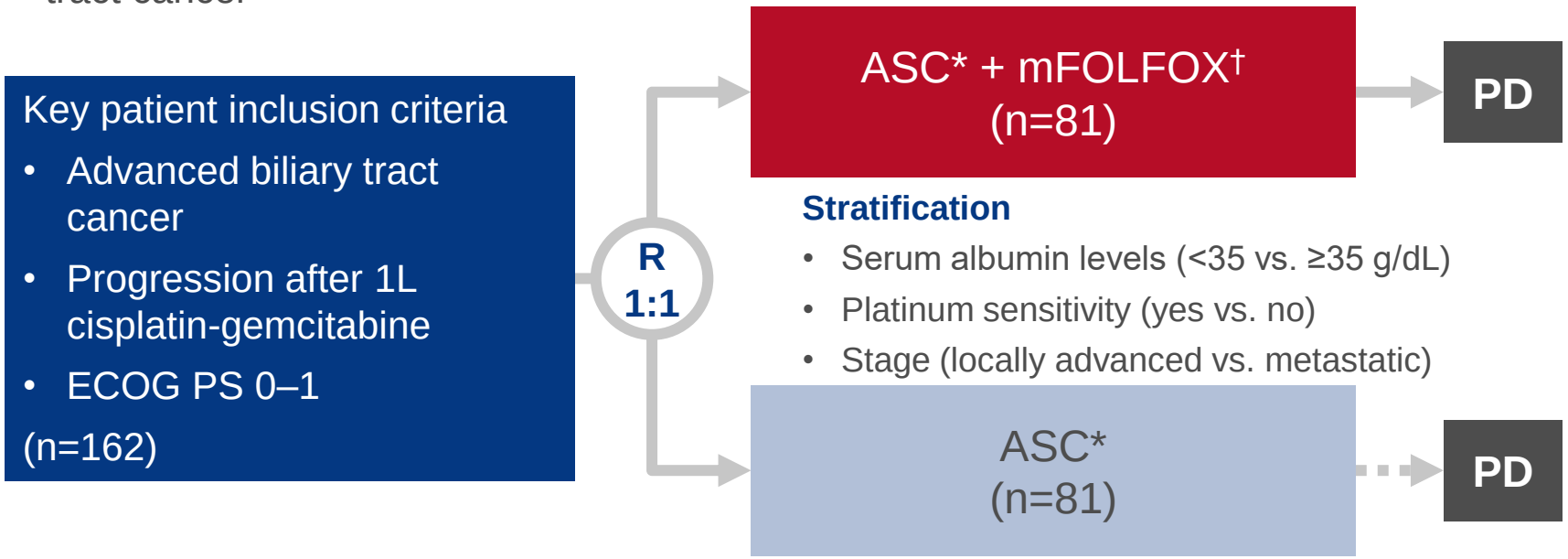
Cancers of the pancreas, small bowel and hepatobiliary tract

BILIARY TRACT CANCER

4003: ABC-06 | A randomised phase III, multi-centre, open-label study of active symptom control (ASC) alone or ASC with oxaliplatin / 5-FU chemotherapy (ASC+mFOLFOX) for patients (pts) with locally advanced / metastatic biliary tract cancers (ABC) previously-treated with cisplatin/gemcitabine (CisGem) chemotherapy – Lamarca A, et al

Study objective

- To investigate the efficacy and safety of active symptom control (ASC) with or without mFOLFOX in previously treated patients with locally advanced or metastatic biliary tract cancer



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, response rates, safety

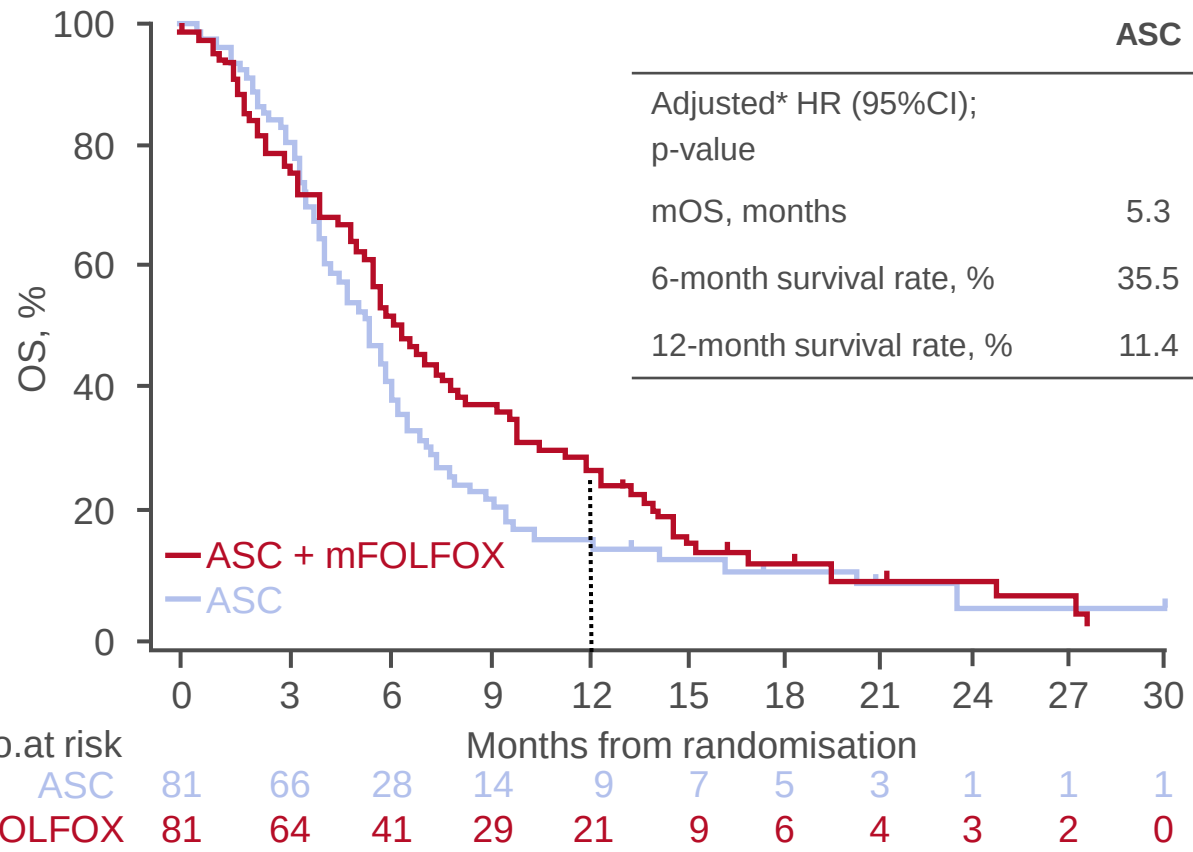
*Includes: biliary drainage, antibiotics, analgesia, steroids, anti-emetics, etc.; †oxaliplatin 85 mg/m^2, L-folinic acid 175 mg (or folinic acid 350 mg), 5FU 400 mg/mg^2 (bolus), 5FU 2400 mg/m^2 continuous infusion q2w up to 12 cycles

Lamarca A, et al. J Clin Oncol 2019;37(suppl):abstr 4003

4003: ABC-06 | A randomised phase III, multi-centre, open-label study of active symptom control (ASC) alone or ASC with oxaliplatin / 5-FU chemotherapy (ASC+mFOLFOX) for patients (pts) with locally advanced / metastatic biliary tract cancers (ABC) previously-treated with cisplatin/gemcitabine (CisGem) chemotherapy – Lamarca A, et al

Key results

OS



	ASC	ASC + mFOLFOX
Adjusted* HR (95%CI); p-value	0.69 (0.50, 0.97); 0.031	
mOS, months	5.3	6.2
6-month survival rate, %	35.5	50.6
12-month survival rate, %	11.4	25.9

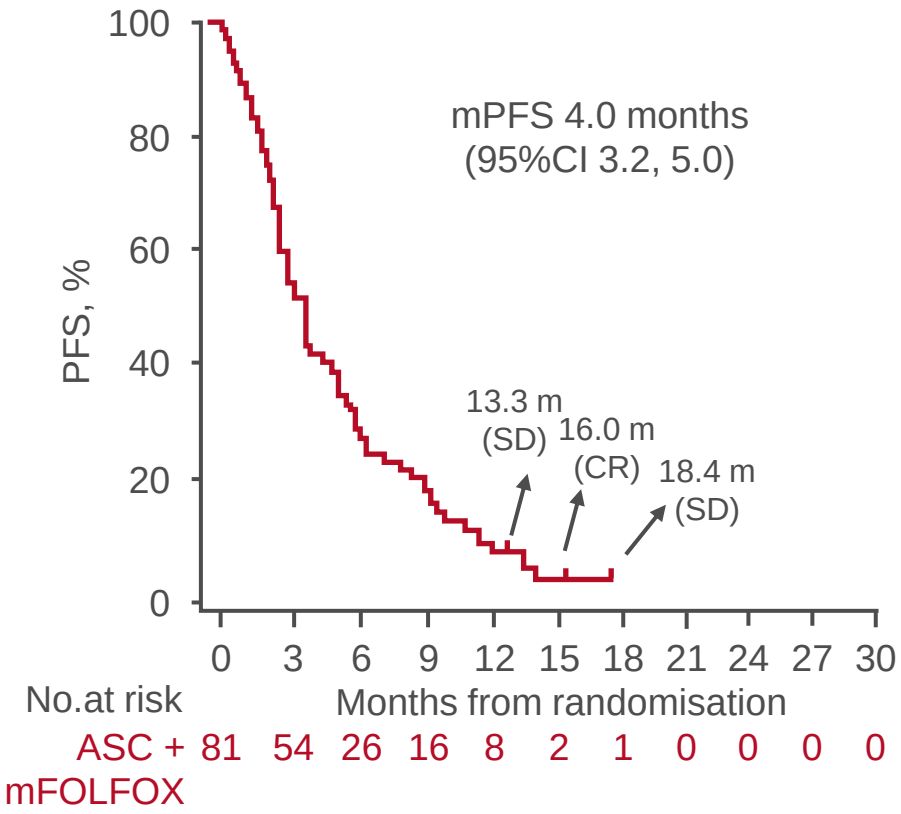
*No marked evidence was identified against the key proportional hazards assumption, which confirmed the validity of using Cox regression

Lamarca A, et al. J Clin Oncol 2019;37(suppl):abstr 4003

4003: ABC-06 | A randomised phase III, multi-centre, open-label study of active symptom control (ASC) alone or ASC with oxaliplatin / 5-FU chemotherapy (ASC+mFOLFOX) for patients (pts) with locally advanced / metastatic biliary tract cancers (ABC) previously-treated with cisplatin/gemcitabine (CisGem) chemotherapy – Lamarca A, et al

Key results (cont.)

Radiological PFS



BOR (RECIST v1.1), n (%)	ASC + mFOLFOX (n=81)
CR	1 (1)
PR	3 (4)
SD	23 (28)
Response rate (CR + PR)	4 (5)
DCR (CR + PR + SD)	27 (33)
PD	30 (37)
Death	23 (28)
Not evaluable (non-measurable disease)	1 (1)

Lamarca A, et al. J Clin Oncol 2019;37(suppl):abstr 4003

4003: ABC-06 | A randomised phase III, multi-centre, open-label study of active symptom control (ASC) alone or ASC with oxaliplatin / 5-FU chemotherapy (ASC+mFOLFOX) for patients (pts) with locally advanced / metastatic biliary tract cancers (ABC) previously-treated with cisplatin/gemcitabine (CisGem) chemotherapy – Lamarca A, et al

Key results (cont.)

Grade 3–4 AEs occurring in ≥2%, n (%)	ASC (n=81)	ASC + mFOLFOX (n=81)†
Fatigue/lethargy	6 (7)	15 (19)
Neutrophil count decreased	0 (0)	10 (12)
Infection (lung/urinary/fever/unspecified)	1 (1)	11 (14)
Biliary event (obstruction/infection/others*)	12 (15)	15 (19)
Anorexia	6 (7)	1 (1)
Nausea and vomiting	1 and 3 (1 and 4, respectively)	1 and 3 (1 and 3, respectively)
Thromboembolic events	4 (5)	0 (0)
Constipation	1 (1)	2 (2)
Diarrhoea	2 (2)	2 (2)
Anaemia	1 (1)	2 (2)
Catheter-related infection	0 (0)	3 (4)

*Including liver infection, increased bilirubin/alkaline phosphatase and hepatitis; †other AEs (%) in the ASC + mFOLFOX group included hyperglycaemia (2), allergic reaction (1), neuropathy (1), febrile neutropenia (1), myocardial infarction (1), oral mucositis/dry mouth (1 and 1, respectively) and acute kidney injury (1)

Lamarca A, et al. J Clin Oncol 2019;37(suppl):abstr 4003

4003: ABC-06 | A randomised phase III, multi-centre, open-label study of active symptom control (ASC) alone or ASC with oxaliplatin / 5-FU chemotherapy (ASC+mFOLFOX) for patients (pts) with locally advanced / metastatic biliary tract cancers (ABC) previously-treated with cisplatin/gemcitabine (CisGem) chemotherapy – Lamarca A, et al

Conclusions

- In previously treated patients with locally advanced or metastatic biliary tract cancer, ASC + mFOLFOX provided improvements in OS compared with ASC
- In patients with locally advanced or metastatic biliary tract cancer, 2L mFOLFOX + ASC should be considered as a new standard of care

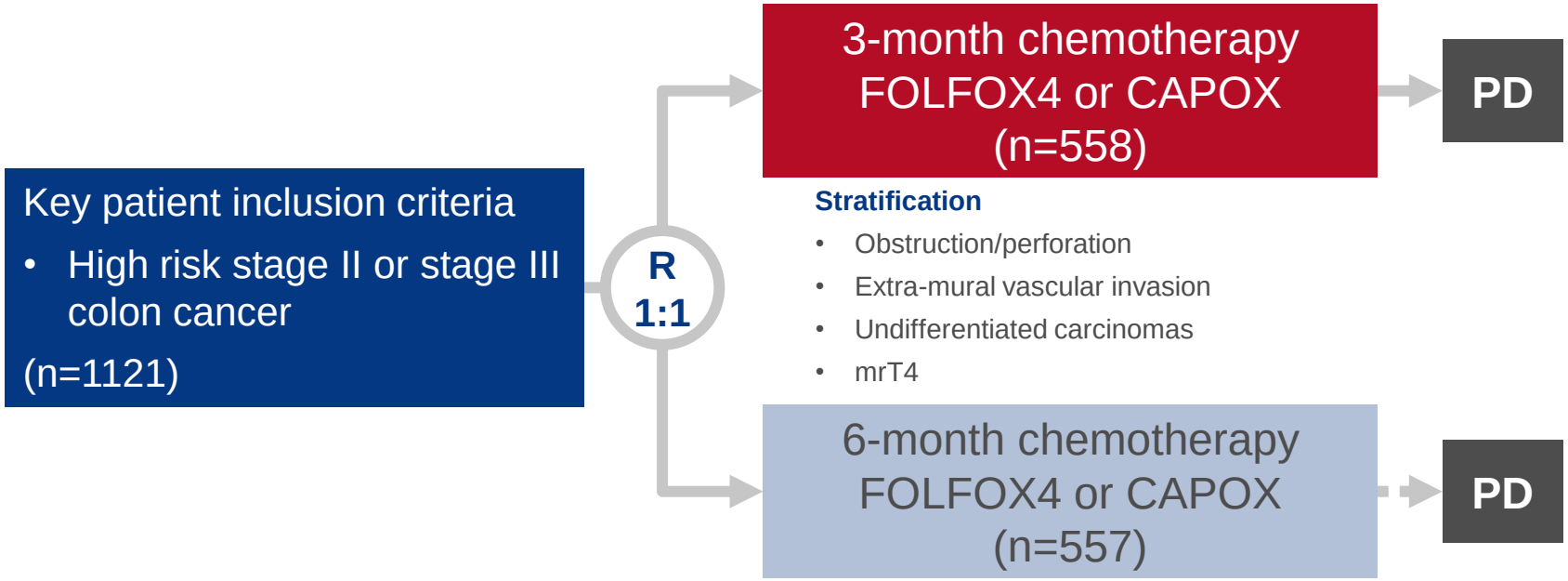
Lamarca A, et al. J Clin Oncol 2019;37(suppl):abstr 4003

CANCERS OF THE COLON, RECTUM AND ANUS

3500: Three versus six months adjuvant FOLFOX or CAPOX for high risk stage II and stage III colon cancer patients: The efficacy results of Hellenic Oncology Research Group (HORG) participation to the International Duration Evaluation of Adjuvant chemotherapy (IDEA) project – Souglakos I, et al

Study objective

- To investigate the efficacy and safety of 3 vs. 6 months of oxaliplatin + fluoropyrimidine-based adjuvant chemotherapy in patients with high risk stage II or stage III colon cancer



PRIMARY ENDPOINT

- 3-year DFS

SECONDARY ENDPOINT

- Safety

Souglakos I, et al. J Clin Oncol 2019;37(suppl):abstr 3500

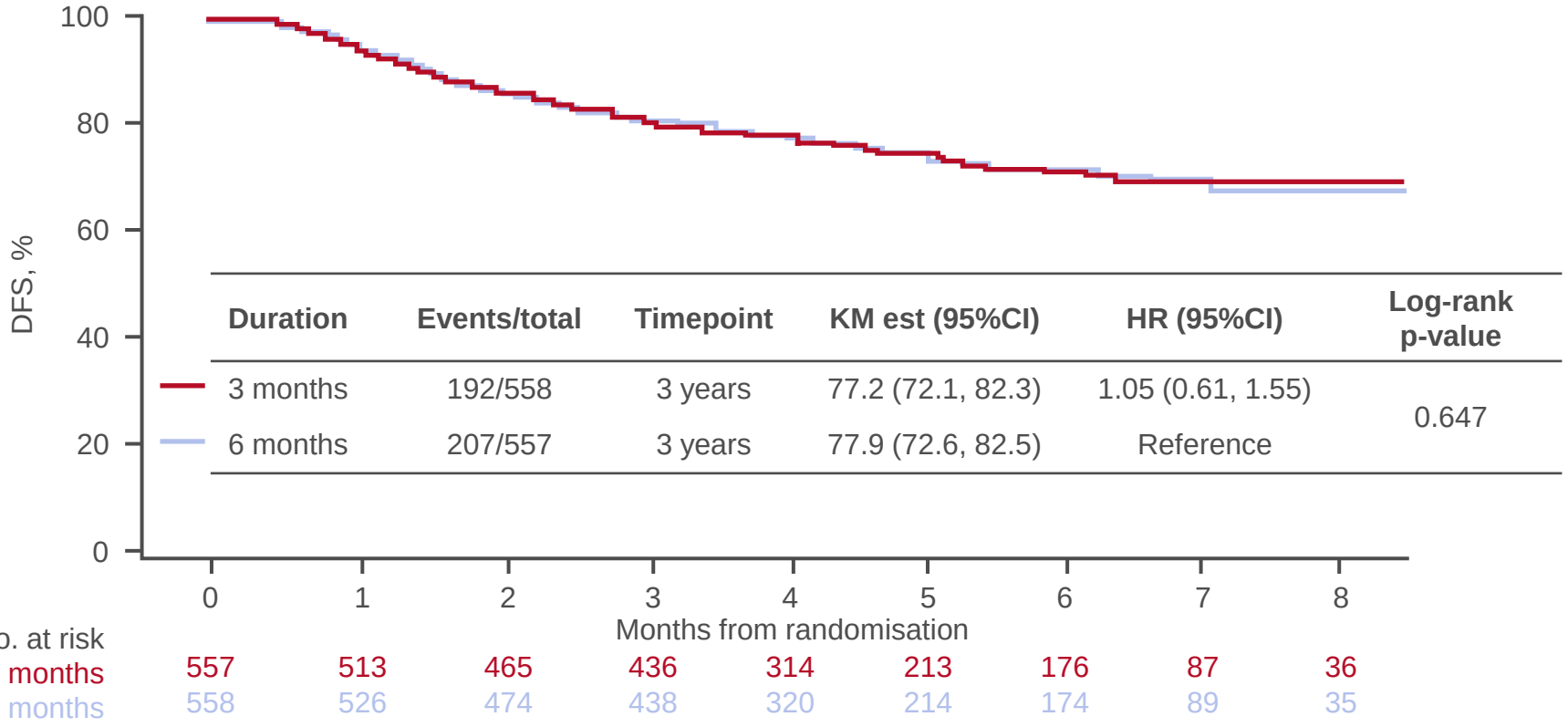
3500: Three versus six months adjuvant FOLFOX or CAPOX for high risk stage II and stage III colon cancer patients: The efficacy results of Hellenic Oncology Research Group (HORG) participation to the International Duration Evaluation of Adjuvant chemotherapy (IDEA) project – Souglakos I, et al

Key results

3-year DFS

ITT population (n=1115)

Median follow-up 67.0 (min-max: 38.3–126.0) months



Duration	Events/total	Timepoint	KM est (95%CI)	HR (95%CI)	Log-rank p-value
3 months	192/558	3 years	77.2 (72.1, 82.3)	1.05 (0.61, 1.55)	0.647
6 months	207/557	3 years	77.9 (72.6, 82.5)	Reference	

No. at risk									
3 months	557	513	465	436	314	213	176	87	36
6 months	558	526	474	438	320	214	174	89	35

Souglakos I, et al. J Clin Oncol 2019;37(suppl):abstr 3500

3500: Three versus six months adjuvant FOLFOX or CAPOX for high risk stage II and stage III colon cancer patients: The efficacy results of Hellenic Oncology Research Group (HORG) participation to the International Duration Evaluation of Adjuvant chemotherapy (IDEA) project – Souglakos I, et al

Key results (cont.)

AEs in all patients, %	3 months (n=558)	6 months (n=557)	p-value
Any	20	32	**0.037**
Neutropenia	11	14	0.482
Febrile neutropenia	1.4	1.2	0.517
Fatigue	2.8	6.0	**0.002**
Nausea	1.4	1.8	0.603
Diarrhoea	5	8	**0.019**

Conclusions

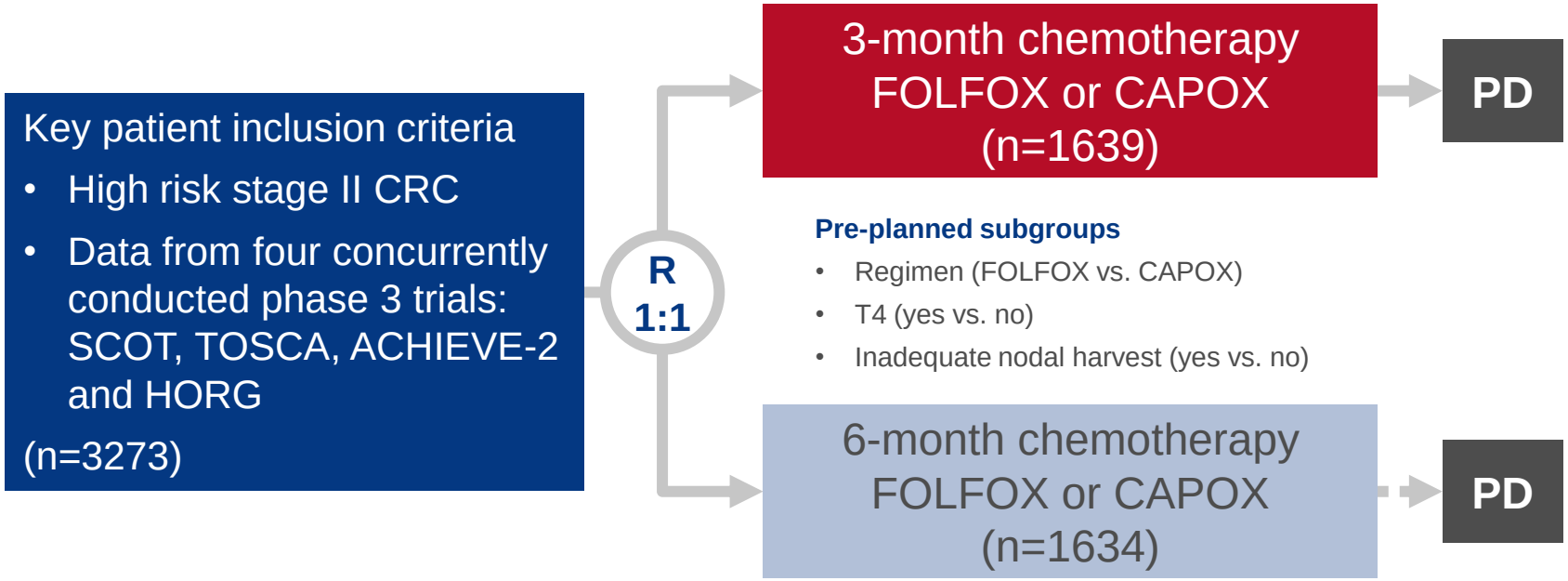
- **In patients with high risk, stage II and III colon cancer, there was little difference between those receiving adjuvant FOLFOX or CAPOX for 3 or 6 months**
- **The safety profile of adjuvant FOLFOX or CAPOX was manageable, but there was a higher proportion of AEs observed with 6 vs. 3 months of treatment**

Souglakos I, et al. J Clin Oncol 2019;37(suppl):abstr 3500

3501: Prospective pooled analysis of four randomized trials investigating duration of adjuvant (adj) oxaliplatin-based therapy (3 vs 6 months {m}) for patients (pts) with high-risk stage II colorectal cancer (CC) – Iveson T, et al

Study objective

- To investigate the efficacy and safety of 3 vs. 6 months of oxaliplatin-based adjuvant chemotherapy in patients with high risk stage II CRC



PRIMARY ENDPOINT

- DFS

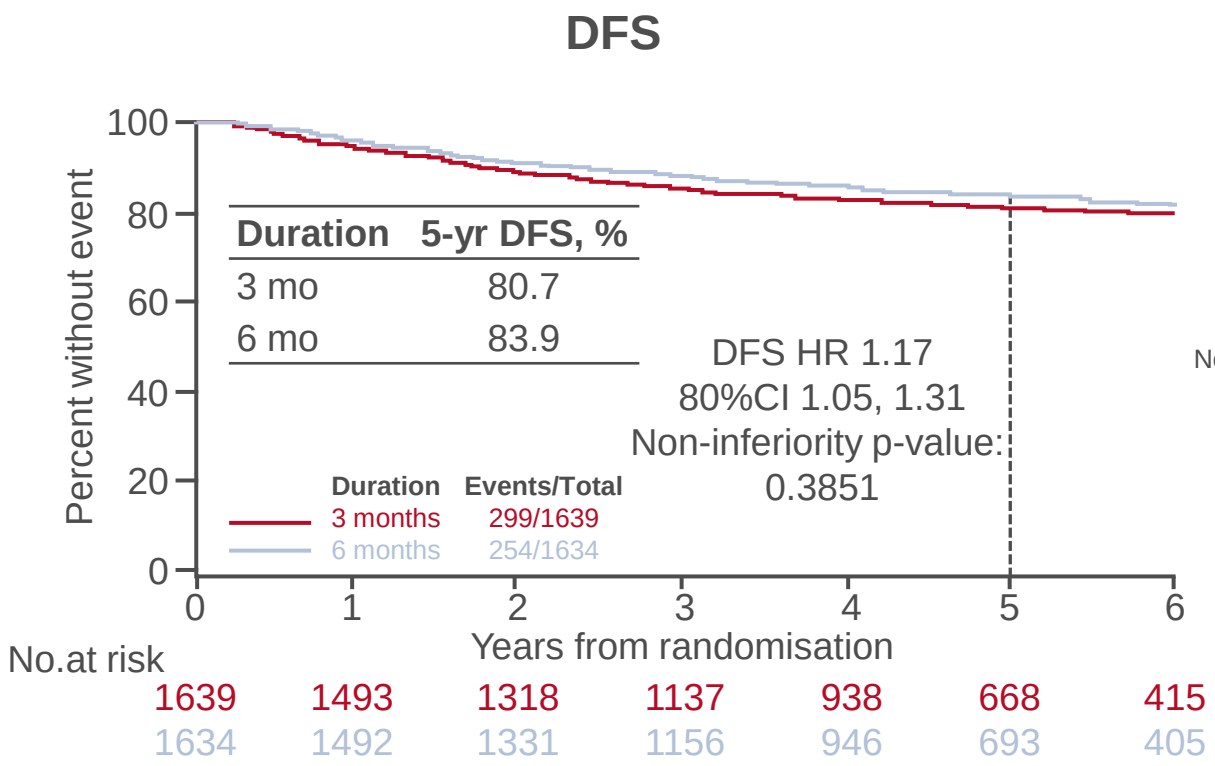
SECONDARY ENDPOINT

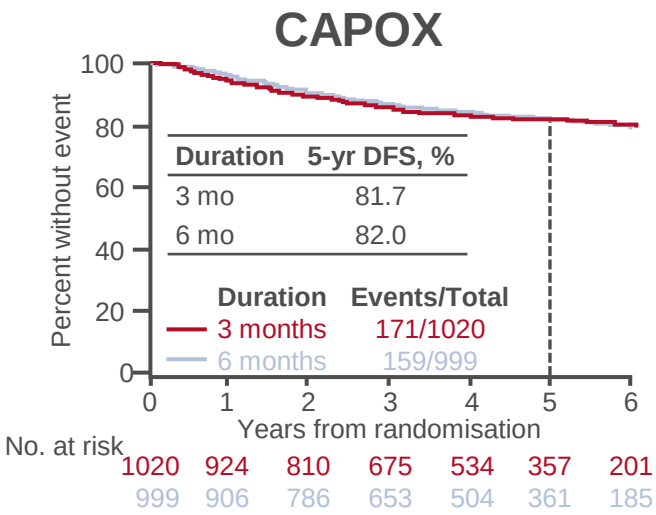
- Safety

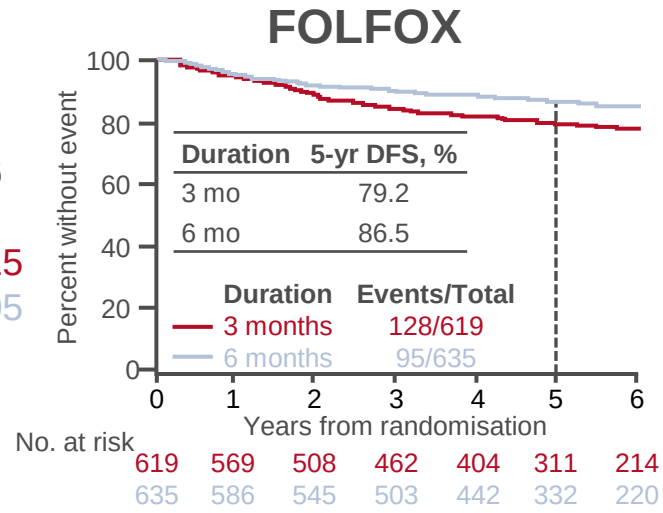
Iveson T, et al. J Clin Oncol 2019;37(suppl):abstr 3501

3501: Prospective pooled analysis of four randomized trials investigating duration of adjuvant (adj) oxaliplatin-based therapy (3 vs 6 months {m}) for patients (pts) with high-risk stage II colorectal cancer (CC) – Iveson T, et al

Key results







Iveson T, et al. J Clin Oncol 2019;37(suppl):abstr 3501

3501: Prospective pooled analysis of four randomized trials investigating duration of adjuvant (adj) oxaliplatin-based therapy (3 vs 6 months {m}) for patients (pts) with high-risk stage II colorectal cancer (CC) – Iveson T, et al

Key results (cont.)

	FOLFOX			CAPOX			Overall		
AEs, %	**3 mo**	**6 mo**	**p-value**	**3 mo**	**6 mo**	**p-value**	**3 mo**	**6 mo**	**p-value**
Overall									
Grade 2	33	36	<0.0001	35	47	<0.0001	34	42	<0.0001
Grade 3–5	31	51		22	32		26	40	
Neurotoxicity									
Grade 2	9	26	<0.0001	14	29	<0.0001	12	28	<0.0001
Grade 3–5	1	9		2	8		1	8	
Diarrhoea									
Grade 2	7	12	0.0031	7	12	0.0026	7	12	0.0002
Grade 3–5	4	6		5	7		5	7	

Conclusions

- **In patients with high risk stage II CRC, DFS was comparable between 3 and 6 months of treatment, however, it appeared that efficacy with 3 months of FOLFOX was inferior to 6 months**
- **There was significantly more toxicity with the 6-month regimens**

Iveson T, et al. J Clin Oncol 2019;37(suppl):abstr 3501

3503: Association of colon cancer (CC) molecular signatures with prognosis and oxaliplatin prediction-benefit in the MOSAIC trial (Multicenter International Study of Oxaliplatin/5FU-LV in the Adjuvant Treatment of Colon Cancer) – Pogue-Geile KL, et al

Study objective

- To investigate the use of molecular signatures as prognostic markers for predicting response to oxaliplatin in patients with colon cancer

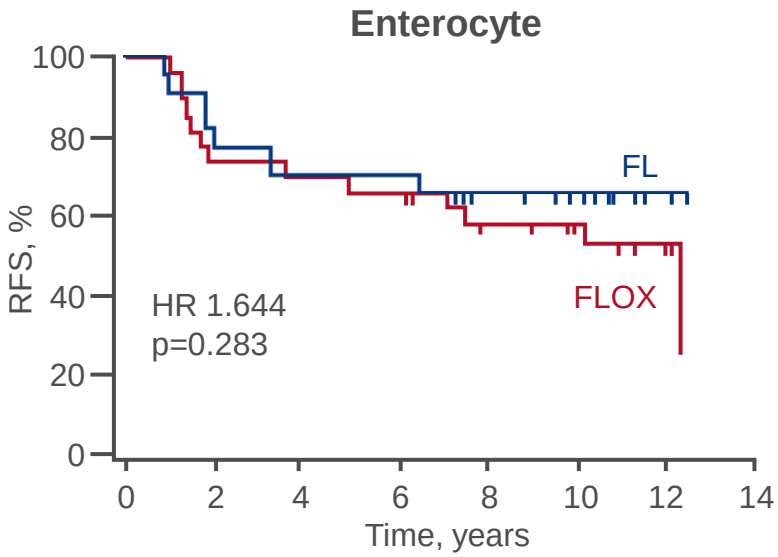
Methods

- A custom-designed nCounter code set (n=298 genes) was used to determine the gene expression profiles of patients with stage III colon cancer (n=926)
- Colorectal Cancer Assigner (CRCA) subtype and consensus molecular subtypes (CMS) were determined using a locked down algorithm based on a re-estimated centroid of 72 genes and a modified single sample predictor (SSP) of 84 genes, respectively
- Recombination Proficiency Score (RPS) was evaluated along with signature predictions (blinded to clinical outcome) and signature performance (blinded to gene expression) for associations with DFS
- Patients were treated with 5FU + leucovorin with (FLOX) or without (FL) oxaliplatin

Pogue-Geile KL, et al. J Clin Oncol 2019;37(suppl):abstr 3503

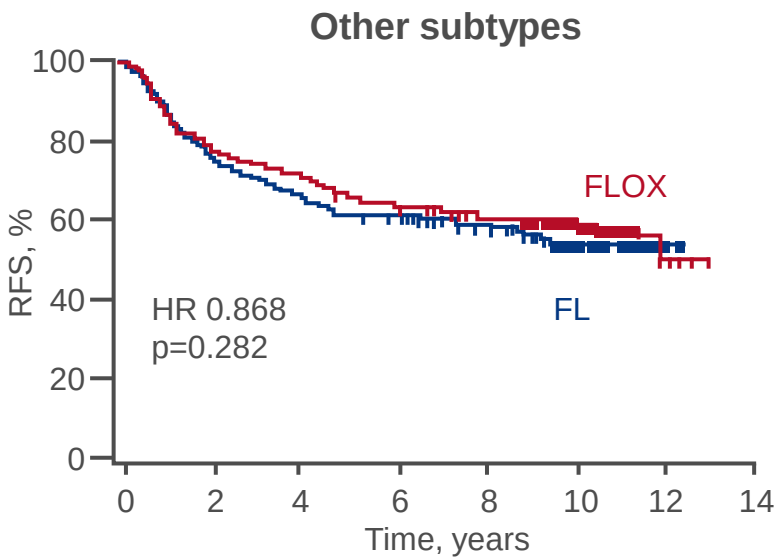
3503: Association of colon cancer (CC) molecular signatures with prognosis and oxaliplatin prediction-benefit in the MOSAIC trial (Multicenter International Study of Oxaliplatin/5FU-LV in the Adjuvant Treatment of Colon Cancer) – Pogue-Geile KL, et al

Key results



No. at risk

FLOX	29	21	20	19	14	10	0	0
FL	22	17	16	16	11	8	2	0



No. at risk

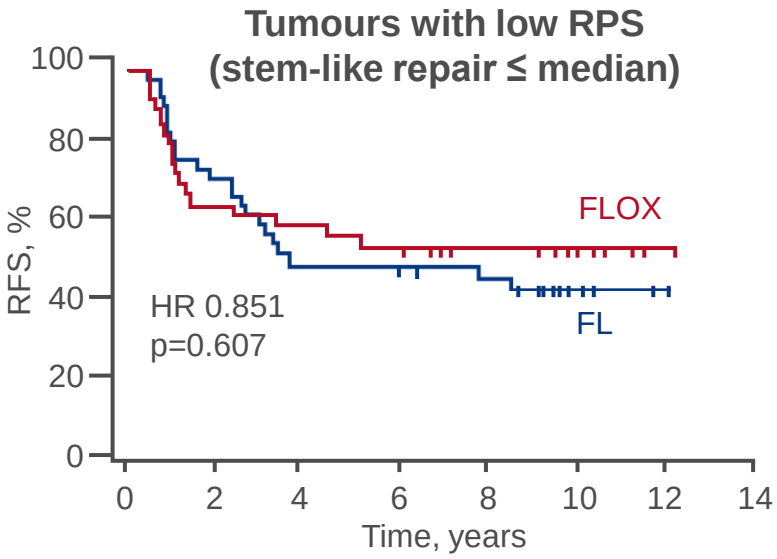
FLOX	274	213	194	172	156	120	22	0
FL	263	195	168	155	139	93	25	0

Pogue-Geile KL, et al. J Clin Oncol 2019;37(suppl):abstr 3503

3503: Association of colon cancer (CC) molecular signatures with prognosis and oxaliplatin prediction-benefit in the MOSAIC trial (Multicenter International Study of Oxaliplatin/5FU-LV in the Adjuvant Treatment of Colon Cancer) – Pogue-Geile KL, et al

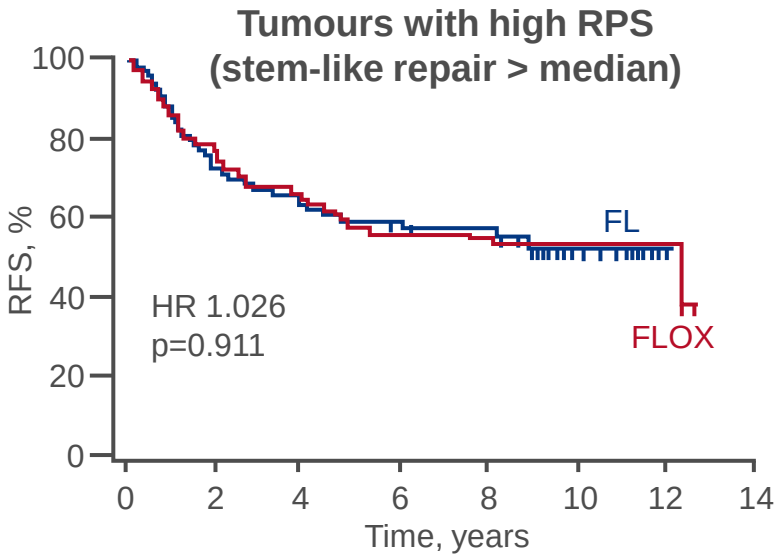
Key results (cont.)

Oxaliplatin did not provide benefit in stem-like tumours with low RPS



No. at risk

FLOX	39	25	23	21	17	11	1	0
FL	41	29	20	20	18	10	2	0



No. at risk

FLOX	77	56	48	40	39	33	4	0
FL	69	48	41	38	34	21	6	0

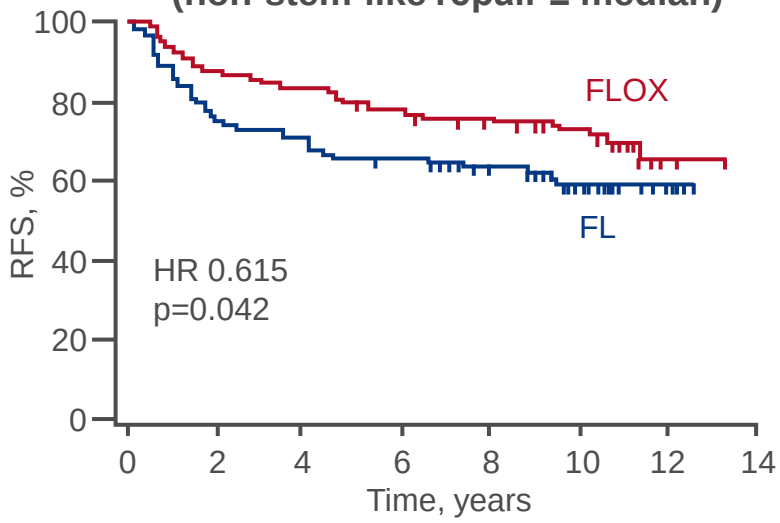
Pogue-Geile KL, et al. J Clin Oncol 2019;37(suppl):abstr 3503

3503: Association of colon cancer (CC) molecular signatures with prognosis and oxaliplatin prediction-benefit in the MOSAIC trial (Multicenter International Study of Oxaliplatin/5FU-LV in the Adjuvant Treatment of Colon Cancer) – Pogue-Geile KL, et al

Key results (cont.)

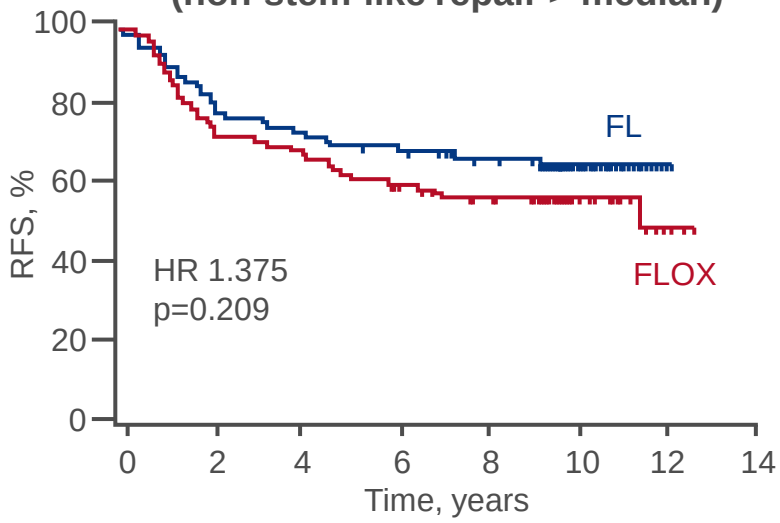
Oxaliplatin did not provide benefit in patients with non-stem-like tumours and low RPS scores

Tumours with low RPS scores (non-stem-like repair ≤ median)



No. at risk								
FLOX	109	95	91	84	76	59	10	0
FL	101	75	70	64	55	38	10	0

Tumours with high RPS scores (non-stem-like repair > median)



No. at risk								
FLOX	78	58	52	46	38	27	7	0
FL	74	60	53	49	43	32	9	0

Pogue-Geile KL, et al. J Clin Oncol 2019;37(suppl):abstr 3503

3503: Association of colon cancer (CC) molecular signatures with prognosis and oxaliplatin prediction-benefit in the MOSAIC trial (Multicenter International Study of Oxaliplatin/5FU-LV in the Adjuvant Treatment of Colon Cancer) – Pogue-Geile KL, et al

Conclusions

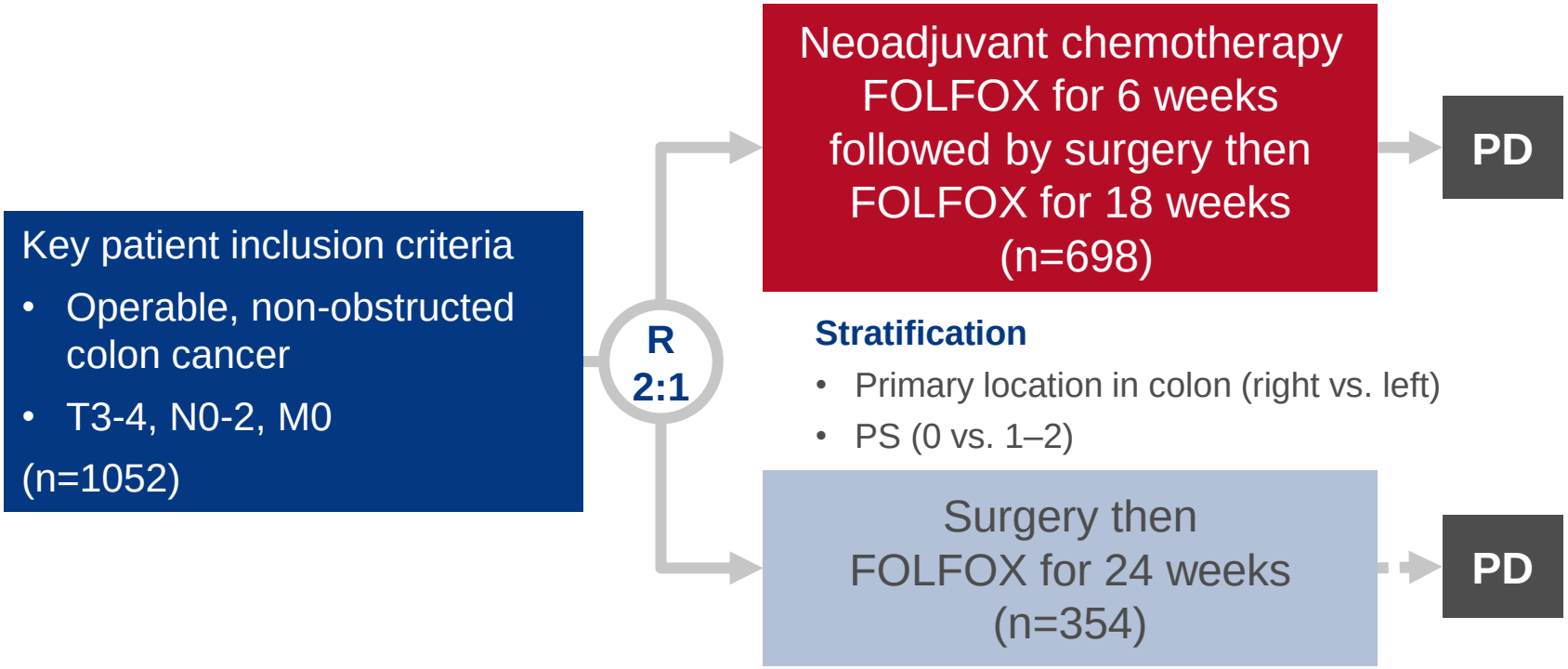
- In patients with stage III colon cancer classified as having CRCA and CMS subtypes, combining oxaliplatin with 5FU + leucovorin did not provide any additional benefit
- In patients with non-stem-like tumours and low RPS, oxaliplatin did provide benefit when combined with 5FU + leucovorin while there was no benefit in those with stem-like tumours and low RPS

Pogue-Geile KL, et al. J Clin Oncol 2019;37(suppl):abstr 3503

3504: FOxTROT: an international randomised controlled trial in 1052 patients (pts) evaluating neoadjuvant chemotherapy (NAC) for colon cancer – Seymour MT, et al

Study objective

- To investigate the efficacy and safety of neoadjuvant chemotherapy in patients with colon cancer compared with surgery then chemotherapy



PRIMARY ENDPOINT

- 2-year DFS

SECONDARY ENDPOINTS

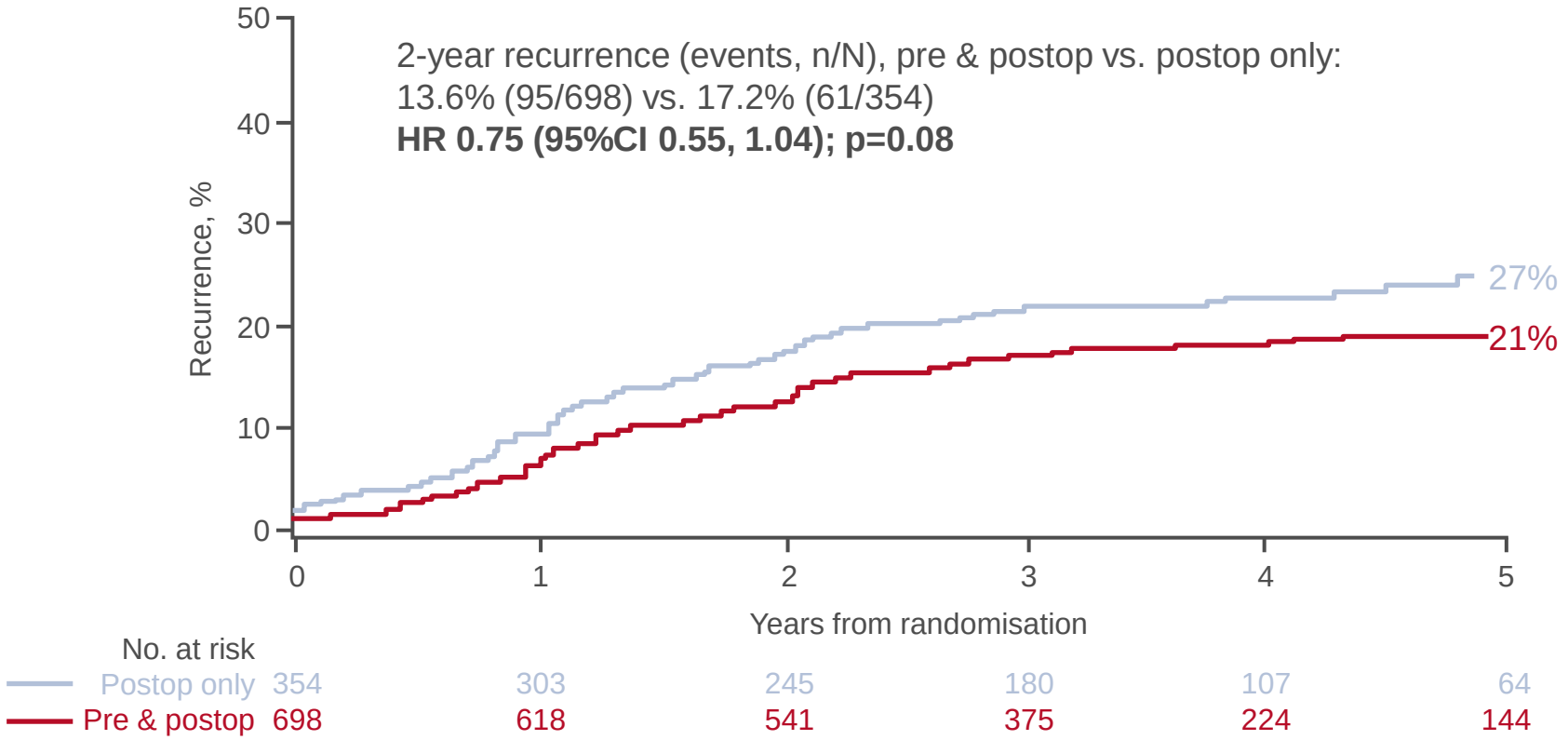
- Resection rate, safety

Seymour MT, et al. J Clin Oncol 2019;37(suppl):abstr 3504

3504: FOxTROT: an international randomised controlled trial in 1052 patients (pts) evaluating neoadjuvant chemotherapy (NAC) for colon cancer – Seymour MT, et al

Key results

Recurrence – by treatment allocation



Seymour MT, et al. J Clin Oncol 2019;37(suppl):abstr 3504

3504: FOxTROT: an international randomised controlled trial in 1052 patients (pts) evaluating neoadjuvant chemotherapy (NAC) for colon cancer – Seymour MT, et al

Key results (cont.)

Local pathologist score*, %	Pre & postop CT (n=689)	Postop CT only (n=353)	p-value
Did not proceed to surgery	0.6	0.6	
Surgery but no resection	0.3	1.1	0.001
R2 – macroscopically incomplete	0.3	1.1	
R1 – microscopically incomplete	4.2	8.8	
R0 – microscopically complete	93.1	88.4	

*Concordance of local vs. central assessment of resection margins = 99% (n=904)

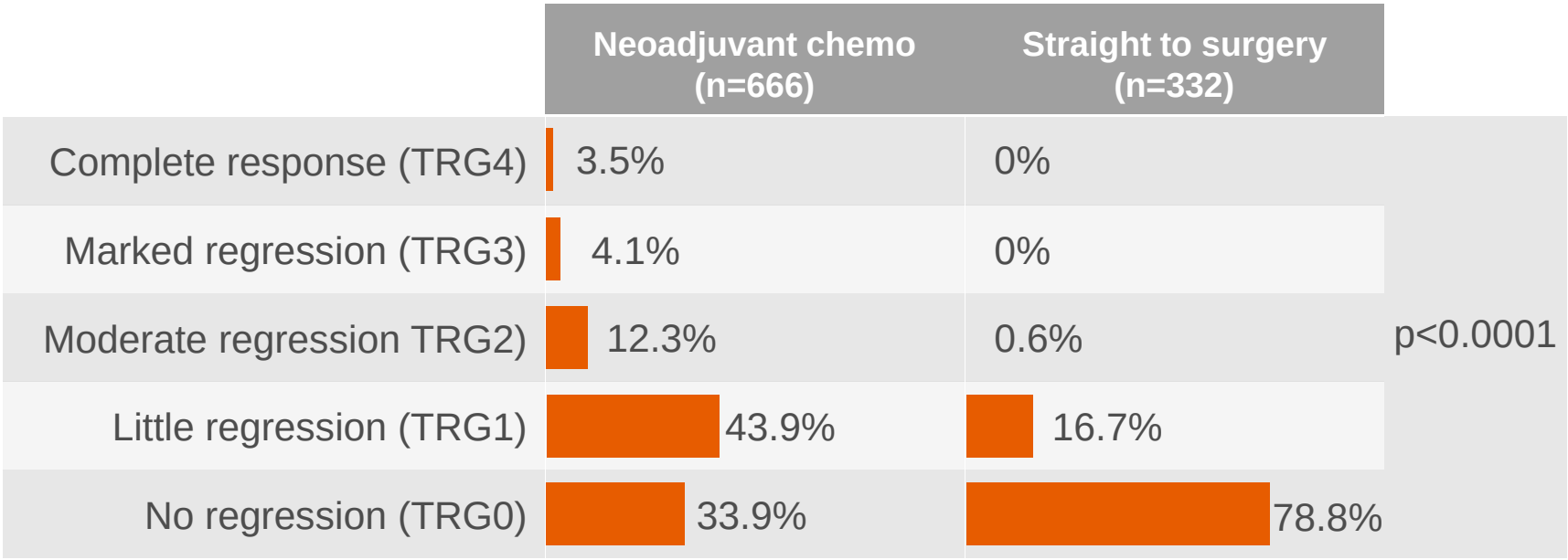
Seymour MT, et al. J Clin Oncol 2019;37(suppl):abstr 3504

3504: FOxTROT: an international randomised controlled trial in 1052 patients (pts) evaluating neoadjuvant chemotherapy (NAC) for colon cancer – Seymour MT, et al

Key results (cont.)

Tumour regression grade (TRG)* at surgery

91% scored blind by central pathologist
9% scored by local pathologists



*Dworak et al. Intl J Colorectal Dis 1997;12:19–23.

Seymour MT, et al. J Clin Oncol 2019;37(suppl):abstr 3504

3504: FOxTROT: an international randomised controlled trial in 1052 patients (pts) evaluating neoadjuvant chemotherapy (NAC) for colon cancer – Seymour MT, et al

Conclusions

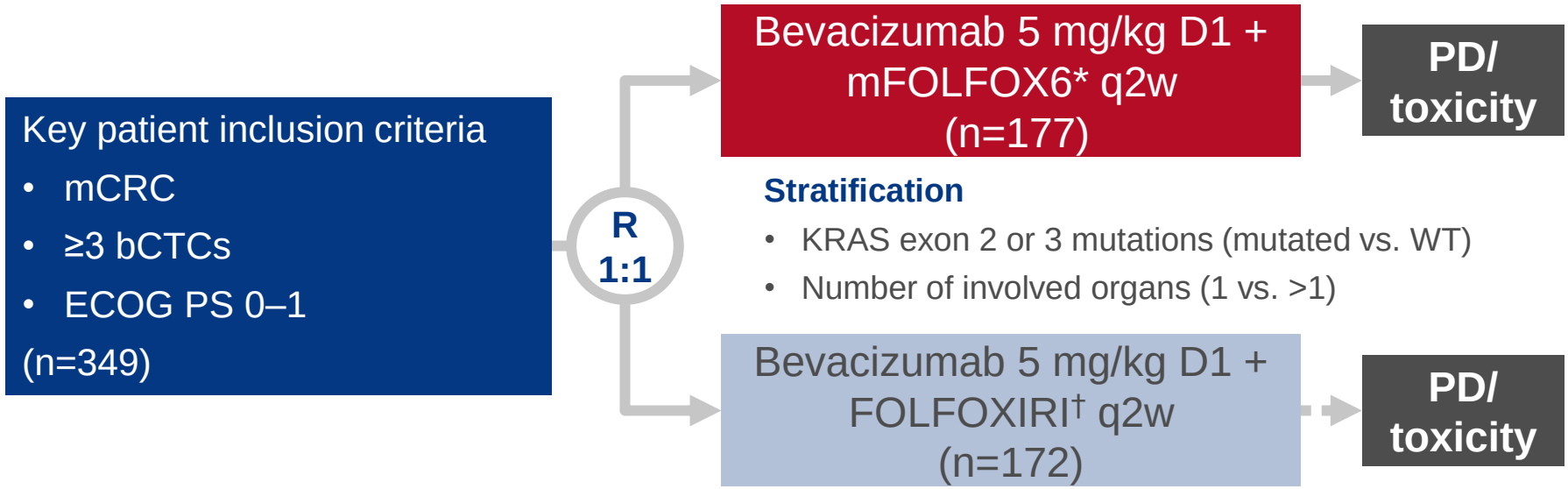
- In patients with colon cancer, neoadjuvant CT did not provide a significant improvement in DFS, but did significantly down-stage tumours and reduced the number of incomplete resections compared with surgery followed by CT
- This regimen may be considered as a potential new option for patients with locally advanced, operable colon cancer

Seymour MT, et al. J Clin Oncol 2019;37(suppl):abstr 3504

3507: Randomized phase III study comparing FOLFOX + bevacizumab versus FOLFOXIRI + bevacizumab (BEV) as 1st line treatment in patients with metastatic colorectal cancer (mCRC) with ≥3 baseline circulating tumour cells (bCTCs) – Sastre J, et al

Study objective

- To investigate the efficacy and safety of bevacizumab + FOLFOX vs. bevacizumab + FOLFOXIRI in patients with mCRC and ≥3 baseline circulating tumour cells (bCTCs)



PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

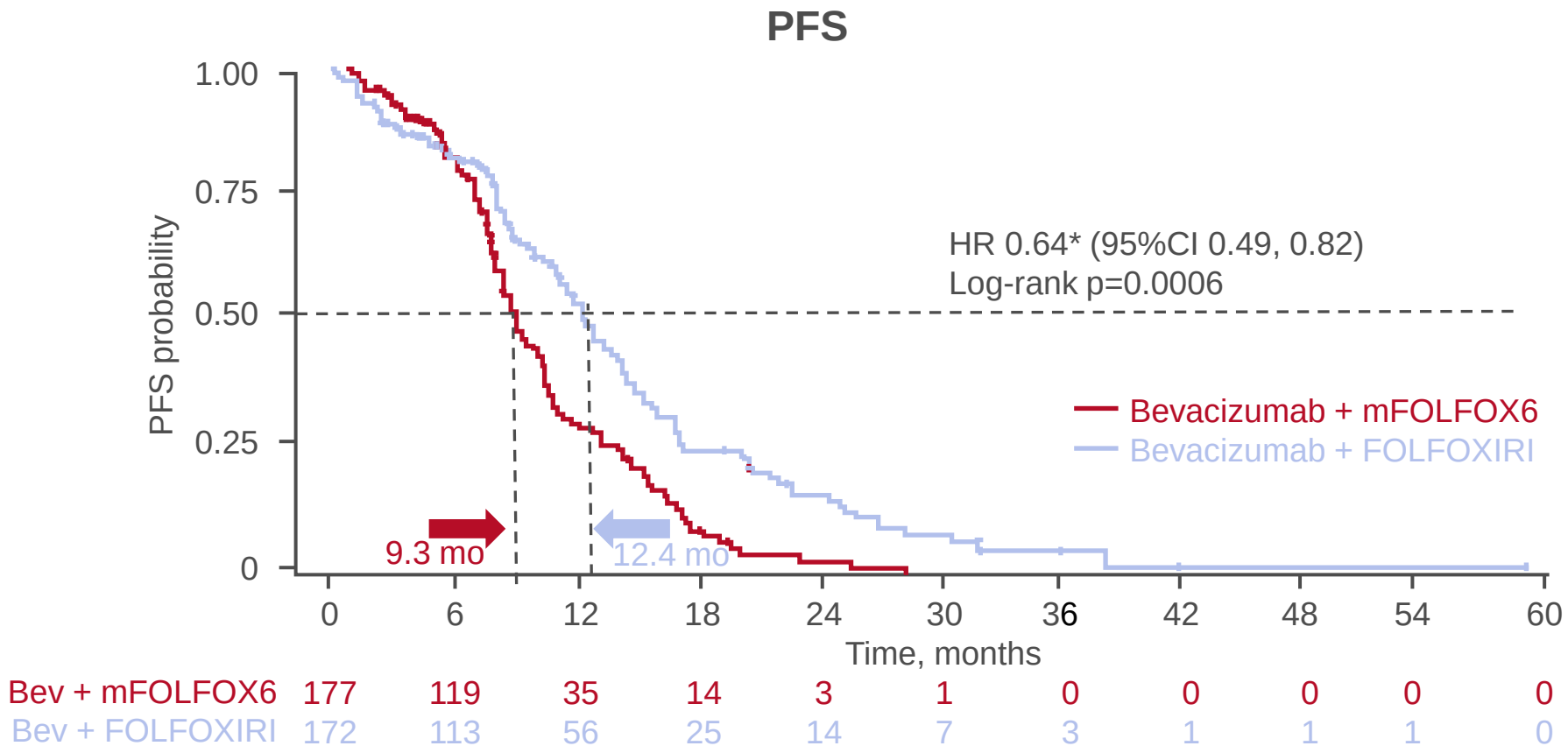
- OS, ORR, safety

*Oxaliplatin 85 mg/m^2 D1, leucovorin 400 mg/m^2 D1, 5FU 400 mg/m^2 bolus D1, 5FU 2400 mg/m^2 continuous infusion; †irinotecan 15 mg/m^2 D1, oxaliplatin 85 mg/m^2 D1, leucovorin 400 mg/m^2 D1, 5FU 3200 mg/m^2 continuous infusion

Sastre J, et al. J Clin Oncol 2019;37(suppl):abstr 3507

3507: Randomized phase III study comparing FOLFOX + bevacizumab versus FOLFOXIRI + bevacizumab (BEV) as 1st line treatment in patients with metastatic colorectal cancer (mCRC) with ≥3 baseline circulating tumour cells (bCTCs) – Sastre J, et al

Key results

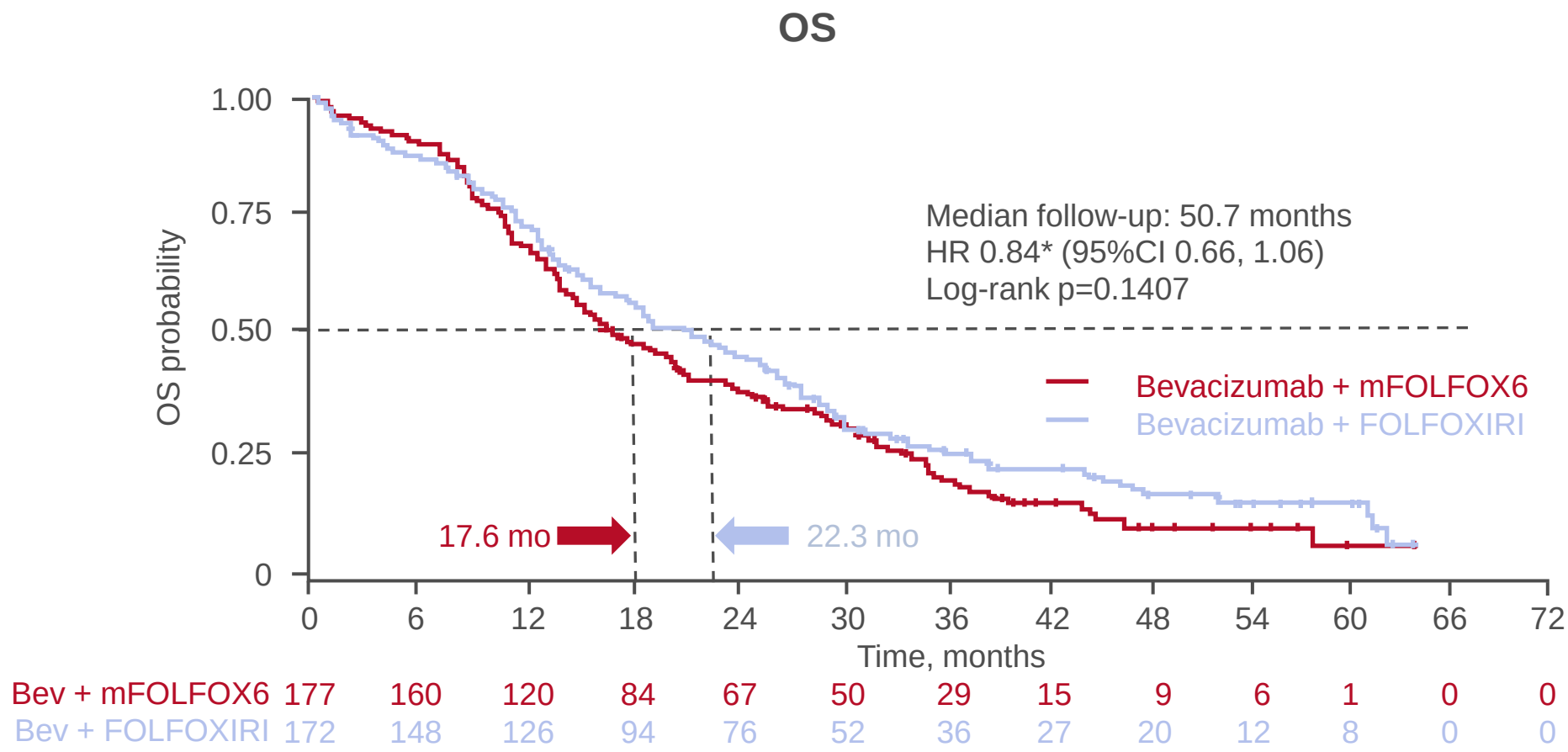


*Cox model proportional hazard assumption is not met

Sastre J, et al. J Clin Oncol 2019;37(suppl):abstr 3507

3507: Randomized phase III study comparing FOLFOX + bevacizumab versus FOLFOXIRI + bevacizumab (BEV) as 1st line treatment in patients with metastatic colorectal cancer (mCRC) with ≥3 baseline circulating tumour cells (bCTCs) – Sastre J, et al

Key results (cont.)

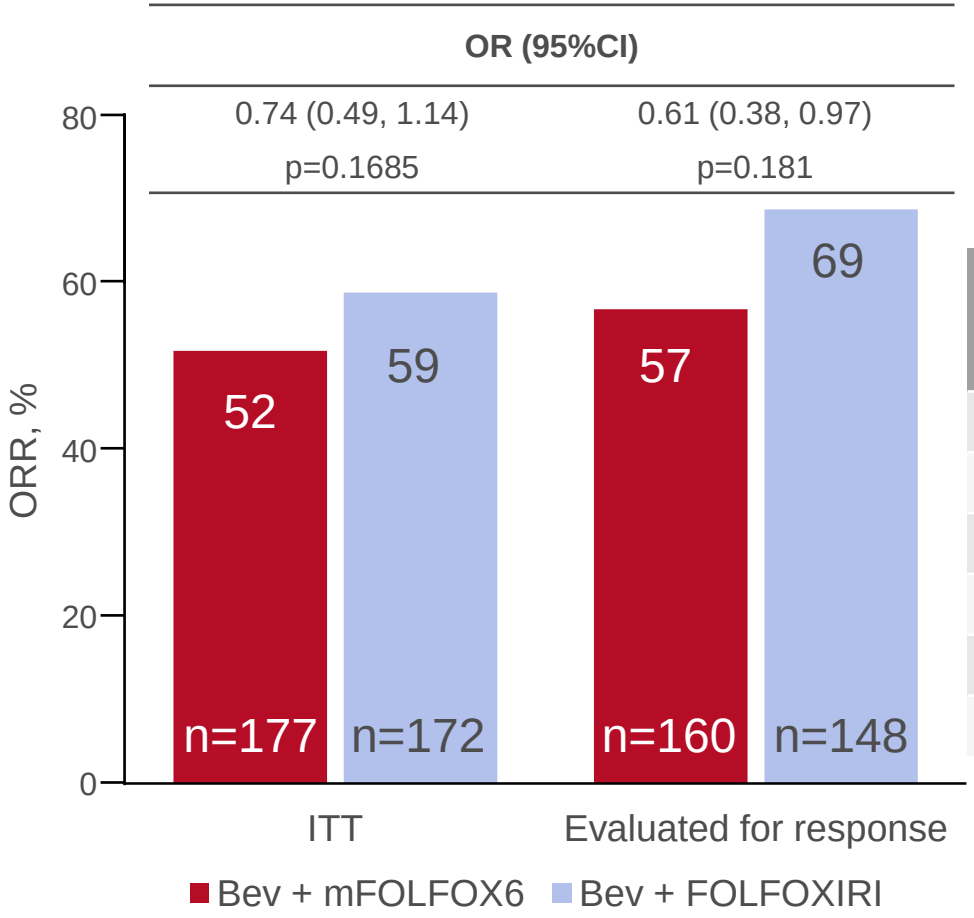


*Cox model proportional hazard assumption is not met

Sastre J, et al. J Clin Oncol 2019;37(suppl):abstr 3507

3507: Randomized phase III study comparing FOLFOX + bevacizumab versus FOLFOXIRI + bevacizumab (BEV) as 1st line treatment in patients with metastatic colorectal cancer (mCRC) with ≥3 baseline circulating tumour cells (bCTCs) – Sastre J, et al

Key results (cont.)



	Bevacizumab + mFOLFOX6 (n=177)	Bevacizumab + FOLFOXIRI (n=172)
Rescue surgery		
No	144 (81.4)	141 (82.0)
Yes	33 (18.6)	31 (18.0)
R0		
No	163 (92.1)	160 (93.0)
Yes	14 (7.9)	12 (7.0)

Sastre J, et al. J Clin Oncol 2019;37(suppl):abstr 3507

3507: Randomized phase III study comparing FOLFOX + bevacizumab versus FOLFOXIRI + bevacizumab (BEV) as 1st line treatment in patients with metastatic colorectal cancer (mCRC) with ≥3 baseline circulating tumour cells (bCTCs) – Sastre J, et al

Key results (cont.)

Grade ≥3 TRAEs occurring in ≥5%, n (%)	Bev + mFOLFOX6 (n=177)	Bev + FOLFOXIRI (n=170)	p-value
Any	119 (67)	133 (78)	**0.022**
Asthenia	12 (7)	27 (16)	**0.007**
Diarrhoea	10 (6)	35 (21)	**<0.001**
Febrile neutropenia	4 (2)	16 (9)	**0.004**
Neutropenia	46 (26)	59 (35)	0.077
Mucositis	7 (4)	15 (9)	0.063
Neurotoxicity	42 (24)	32 (19)	0.265
Death	6 (3)	8 (5)	0.553

Conclusions

- **In patients with mCRC with ≥3 bCTCs, bevacizumab + FOLFOXIRI as 1L treatment was associated with a significant improvement in PFS**
- **These data suggest that this treatment regimen could be a potential option for patients with mCRC and ≥3 bCTCs**
- **Further evaluation is required to fully elucidate the predictive value of CTCs**

Sastre J, et al. J Clin Oncol 2019;37(suppl):abstr 3507

3508: Updated results of TRIBE2, a phase III, randomized strategy study by GONO in the first- and second-line treatment of unresectable mCRC – Cremolini C, et al

Study objective

- To investigate the efficacy and safety of bevacizumab + FOLFOX vs. bevacizumab + FOLFIRI in patients with unresectable mCRC

Key patient inclusion criteria

- Unresectable mCRC
- No prior treatment for metastases or oxaliplatin-containing chemotherapy
- ECOG PS ≤2

(n=679)

R 1:1

Bevacizumab + FOLFOX* followed by bevacizumab + FOLFIRI* after PD (n=340)

Stratification

- ECOG PS (0 vs. 1)
- Prior adjuvant CT (yes vs. no)
- Number of metastatic sites (1 vs. >1)
- Liver only disease (yes vs. no)

Bevacizumab + FOLFOXIRI* followed by reintroduction of same regimen* after PD (n=339)

PRIMARY ENDPOINT

- PFS2

SECONDARY ENDPOINTS

- PFS1, response rates, OS, safety

*Up to 8 cycles and then 5FU + bevacizumab maintenance

Cremolini C, et al. J Clin Oncol 2019;37(suppl):abstr 3508

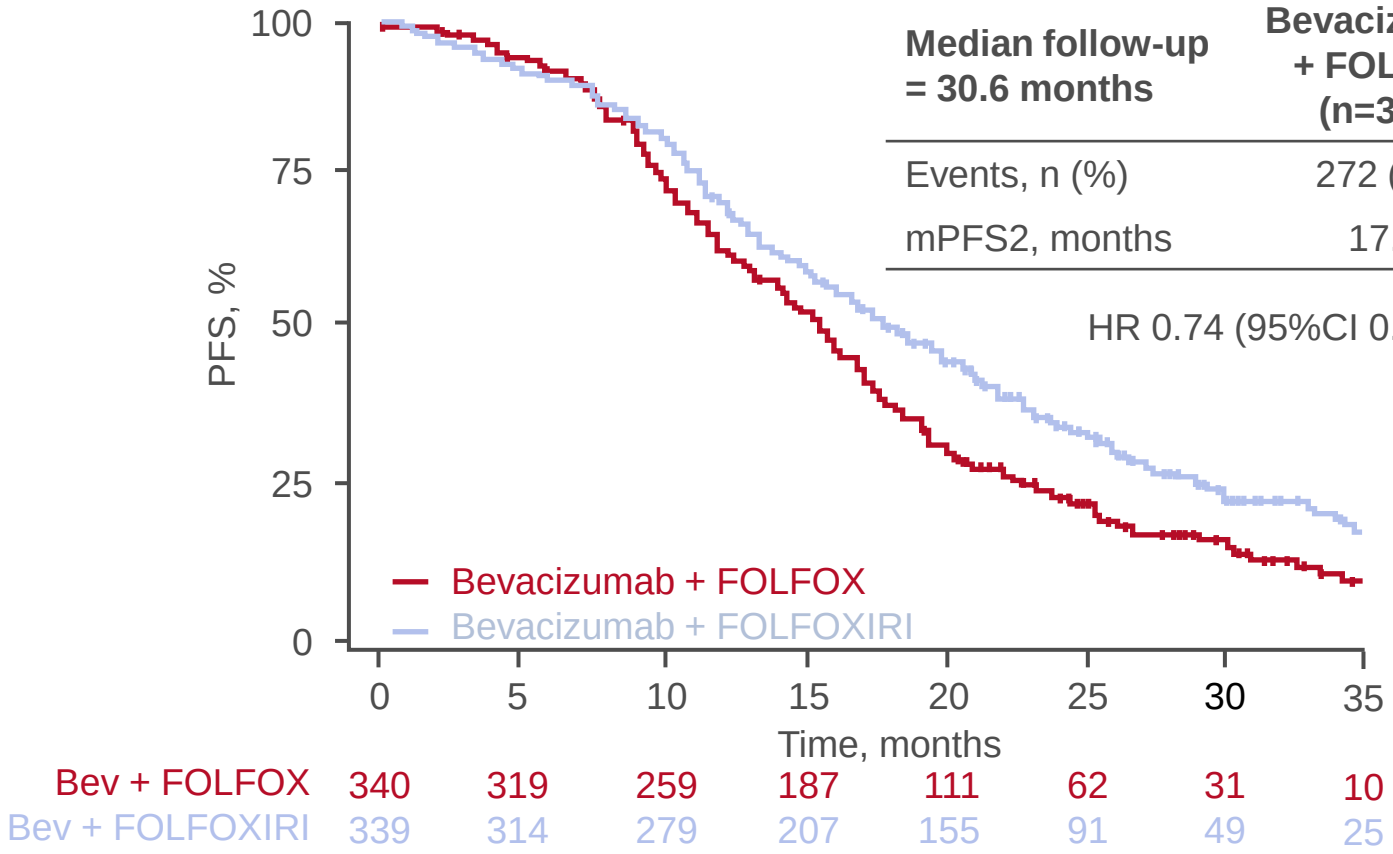
3508: Updated results of TRIBE2, a phase III, randomized strategy study by GONO in the first- and second-line treatment of unresectable mCRC – Cremolini C, et al

Key results

PFS2

Median follow-up = 30.6 months	Bevacizumab + FOLFOX (n=340)	Bevacizumab + FOLFOXIRI (n=339)
Events, n (%)	272 (80)	242 (71)
mPFS2, months	17.5	19.1

HR 0.74 (95%CI 0.62, 0.88); p<0.001



Cremolini C, et al. J Clin Oncol 2019;37(suppl):abstr 3508

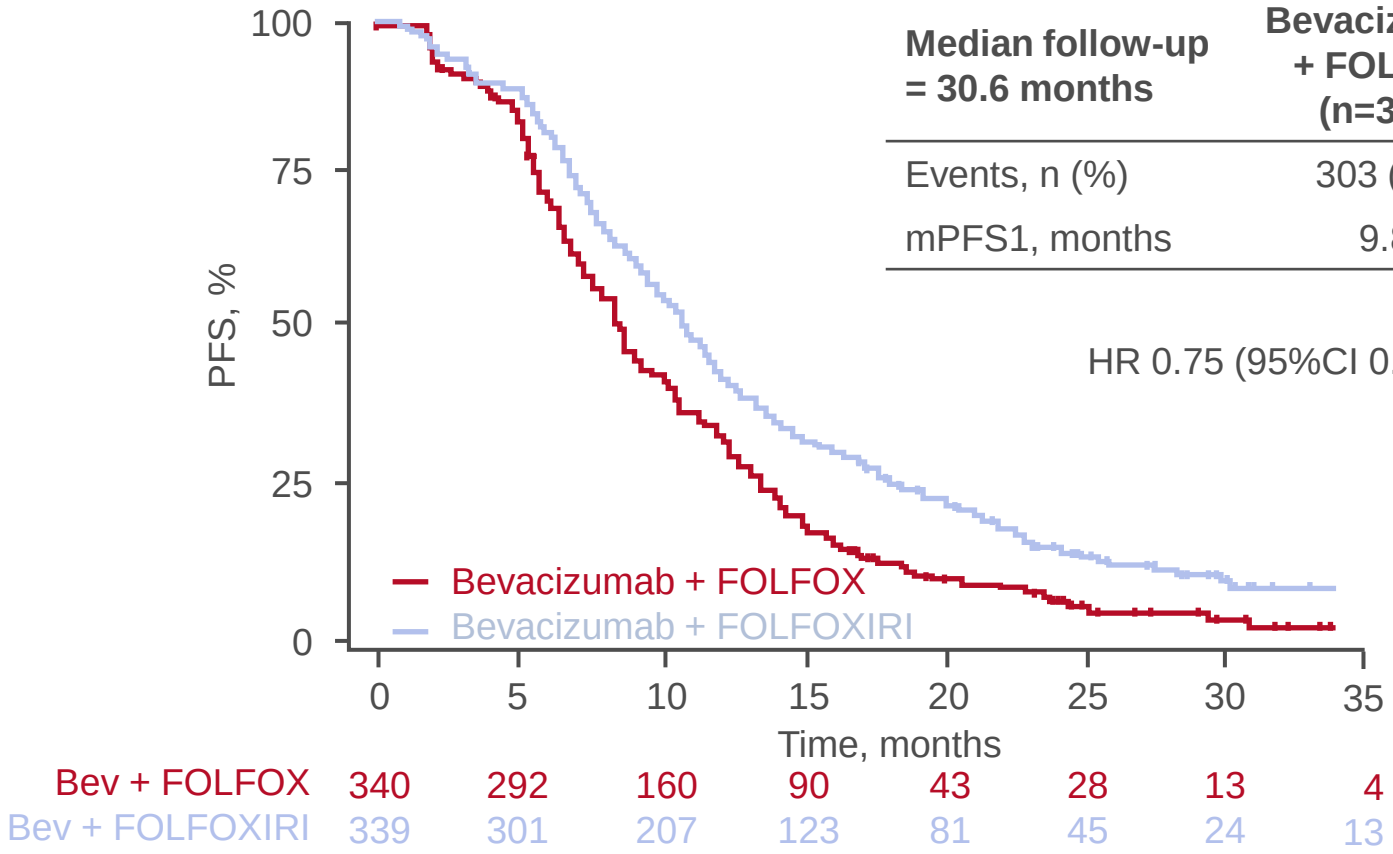
3508: Updated results of TRIBE2, a phase III, randomized strategy study by GONO in the first- and second-line treatment of unresectable mCRC – Cremolini C, et al

Key results (cont.)

PFS1

Median follow-up = 30.6 months	Bevacizumab + FOLFOX (n=340)	Bevacizumab + FOLFOXIRI (n=339)
Events, n (%)	303 (89)	291 (86)
mPFS1, months	9.8	12.0

HR 0.75 (95%CI 0.63, 0.88); p<0.001



Cremolini C, et al. J Clin Oncol 2019;37(suppl):abstr 3508

3508: Updated results of TRIBE2, a phase III, randomized strategy study by GONO in the first- and second-line treatment of unresectable mCRC – Cremolini C, et al

Key results (cont.)

	Bevacizumab + FOLFOX	Bevacizumab + FOLFOXIRI	OR (95%CI); p-value
1L response, %	n=340	n=339	
CR	4	3	
PR	46	59	
Response rate	50	62	1.61 (1.19, 2.18); 0.002
SD	40	29	
PD	7	4	
Not assessed	3	5	
2L response, %	n=195	n=129	
CR	1	2	
PR	11	17	
Response rate	12	19	1.83 (0.99, 3.39); 0.057
SD	52	58	
DCR	64	77	1.78 (1.05, 3.04); 0.037
PD	30	14	
Not assessed	6	9	

Cremolini C, et al. J Clin Oncol 2019;37(suppl):abstr 3508

3508: Updated results of TRIBE2, a phase III, randomized strategy study by GONO in the first- and second-line treatment of unresectable mCRC – Cremolini C, et al

Key results (cont.)

Grade 3/4 AEs, %*	1L		2L	
	Bev + FOLFOX (n=336)	Bev + FOLFOXIRI (n=336)	Bev + FOLFOX (n=195)	Bev + FOLFOXIRI (n=129)
Nausea	3	6	3	6
Vomiting	2	3	2	3
Diarrhoea	5	17†	6	9
Stomatitis	3	5	3	5
Neutropenia	21	50†	24	24
Febrile neutropenia	3	7†	2	2
Neurotoxicity	1	2	0	5†
Asthenia	6	7	6	8
Hypertension	10	7	2	3
Venous thromboembolism	6	4	1	1

Conclusions

- **In patients with unresectable mCRC, 1L bevacizumab + FOLFOXIRI did not impact the efficacy of other treatments after progression and may have long-term benefits**
- **Using bevacizumab + FOLFOXIRI after progression demonstrated some additional benefit with only a modest impact on tolerability**

*Per protocol population; †significant difference between the two treatment groups

Cremolini C, et al. J Clin Oncol 2019;37(suppl):abstr 3508

3509: A randomized phase II trial of second-line CAPTEM versus FOLFIRI in MGMT methylated, RAS mutated metastatic colorectal cancer (mCRC) patients – Pietrantonio F, et al

Study objective

- To investigate the efficacy and safety of CATEM vs. FOLFIRI in patients with MGMT methylated, RAS-mutant mCRC

Key patient inclusion criteria

- mCRC
- RAS mutated with MGMT methylation
- Failed 1L fluoropyrimidine-oxaliplatin ± bevacizumab
- ECOG PS 0–1

(n=82)

R 1:1

Capecitabine 1500 mg/m^2/day D1–14 + temozolomide 150 mg/m^2/day D10–14 q4w (n=41)

Stratification

- Time from start of oxaliplatin-based therapy to PD (<9 vs. ≥9 months)
- Prior bevacizumab (yes vs. no)

FOLFIRI* (n=41)

PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

- Response rate, DoR, OS, safety

*Irinotecan 180 mg/m^2 D1, leucovorin 200 mg/m^2 D1, 2, 5FU 400 mg/m^2 D1, 2 bolus then 5FU 600 mg/m^2 protracted venous infusion D1, 2 q2w

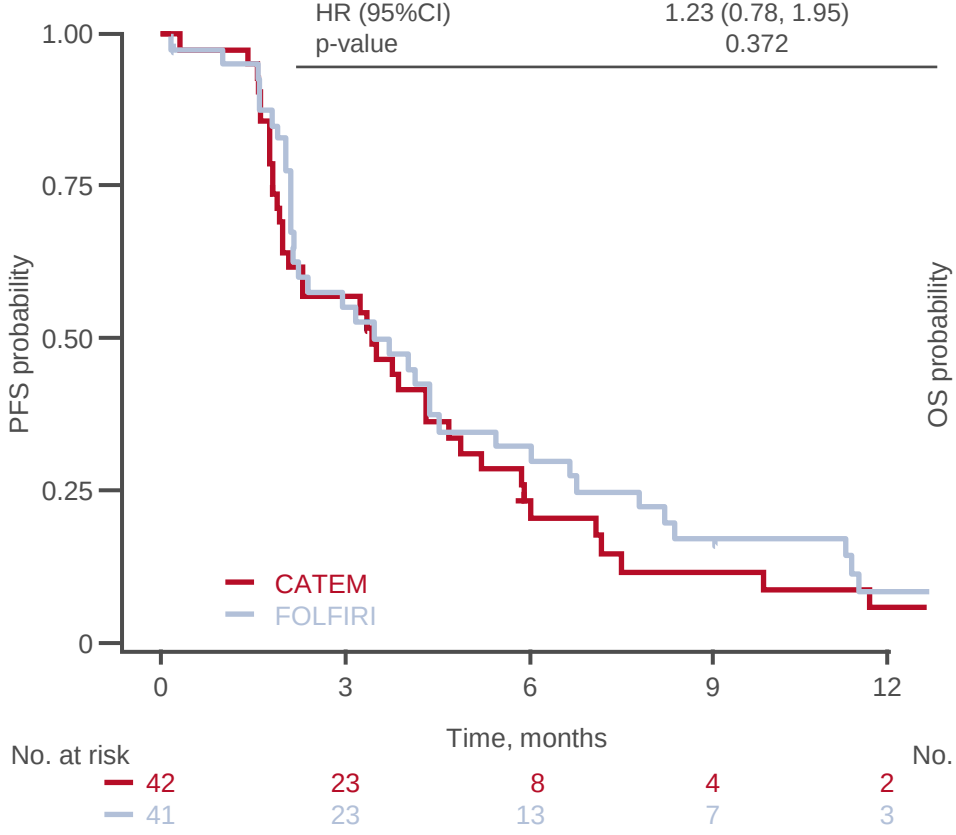
Pietrantonio F, et al. J Clin Oncol 2019;37(suppl):abstr 3509

3509: A randomized phase II trial of second-line CAPTEM versus FOLFIRI in MGMT methylated, RAS mutated metastatic colorectal cancer (mCRC) patients – Pietrantonio F, et al

Key results

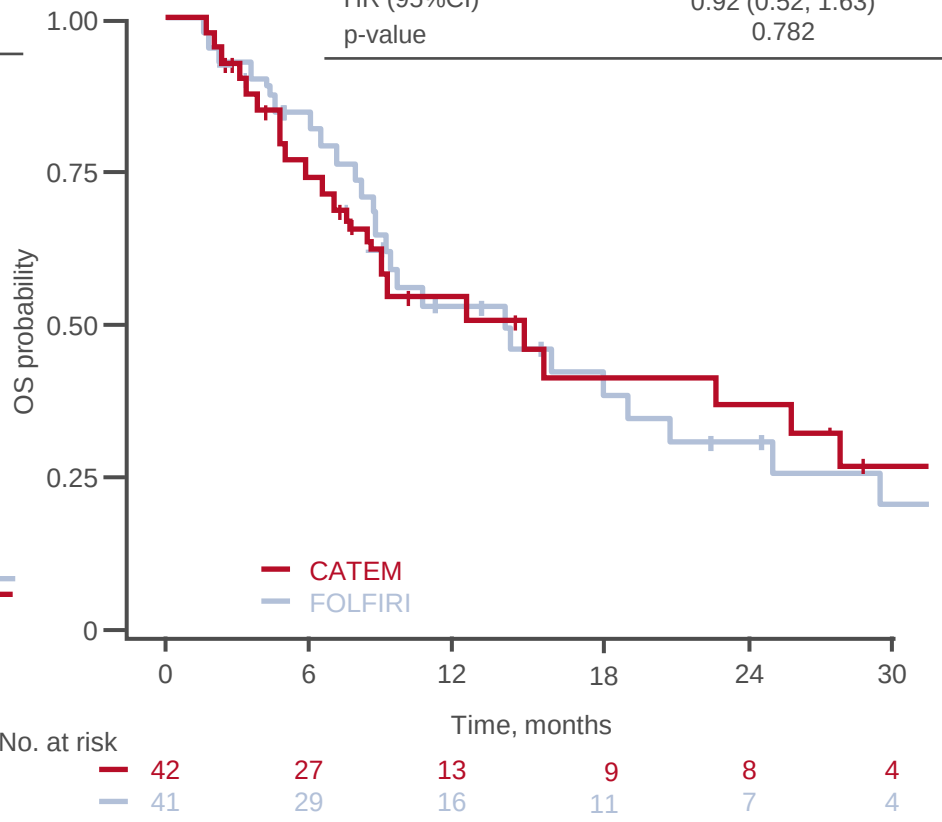
PFS

Median follow-up = 27.4 mo	CATEM (n=42)	FOLFIRI (n=41)
mPFS, mo	3.5	3.7
HR (95%CI)	1.23 (0.78, 1.95)	
p-value	0.372	



OS

Median follow-up = 27.4 mo	CATEM (n=42)	FOLFIRI (n=41)
mOS, mo	14.8	14.0
HR (95%CI)	0.92 (0.52, 1.63)	
p-value	0.782	



Pietrantonio F, et al. J Clin Oncol 2019;37(suppl):abstr 3509

3509: A randomized phase II trial of second-line CAPTEM versus FOLFIRI in MGMT methylated, RAS mutated metastatic colorectal cancer (mCRC) patients – Pietrantonio F, et al

Key results (cont.)

Grade 3–4 TRAEs, %	CATEM (n=42)	FOLFIRI (n=41)
All events	16.7	48.8
Diarrhoea	2.4	14.6
Nausea	2.4	2.4
Vomiting	4.8	2.4
Stomatitis	0	7.3
Fatigue	2.4	4.9
Neutropenia	2.4	26.8
Febrile neutropenia	0	0
Thrombocytopenia	7.1	0
Anaemia	2.4	9.8
Hand-foot syndrome	0	2.4

Conclusions

- **In patients with MGMT methylated, RAS-mutant mCRC, CATEM provided similar improvements in PFS and OS to FOLFIRI and was generally well-tolerated**
- **Further phase 3 studies are required to validate these findings**

Pietrantonio F, et al. J Clin Oncol 2019;37(suppl):abstr 3509

3511: Final results and OS of the randomized phase II VOLFI trial (AIO-KRK0109): mFOLFOXIRI + panitumumab versus FOLFOXIRI as first-line treatment in patients with RAS wild-type metastatic colorectal cancer (mCRC) – Geissler M, et al

Study objective

- To investigate the efficacy and safety of mFOLFOXIRI + panitumumab vs. FOLFOXIRI in patients with mCRC

Key patient inclusion criteria

- Non-resectable mCRC
- WT RAS
- No prior treatment
- ECOG PS 0–1

(n=96)

R 2:1

mFOLFOXIRI* + panitumumab 6 mg/kg q2w (n=63)

Stratification

- Unresectable metastatic disease; symptomatic/ large tumour load (Cohort 1)
- Chance of secondary resection with curative intent (Cohort 2)

FOLFOXIRI† q2w (n=33)

PRIMARY ENDPOINT

- ORR (RECIST v1.1)

SECONDARY ENDPOINTS

- PFS, OS, DCR, secondary resection rate, safety

*Irinotecan 150 mg/m^2, oxaliplatin 85 mg/m^2, leucovorin 200 mg/m^2, 5FU 3000 mg/m^2 continuous infusion; †irinotecan 165 mg/m^2, oxaliplatin 85 mg/m^2, leucovorin 200 mg/m^2, 5FU 3200 mg/m^2 continuous infusion

Geissler M, et al. J Clin Oncol 2019;37(suppl):abstr 3511

3511: Final results and OS of the randomized phase II VOLFI trial (AIO-KRK0109): mFOLFOXIRI + panitumumab versus FOLFOXIRI as first-line treatment in patients with RAS wild-type metastatic colorectal cancer (mCRC) – Geissler M, et al

Key results

Objective response rate

Full analysis set

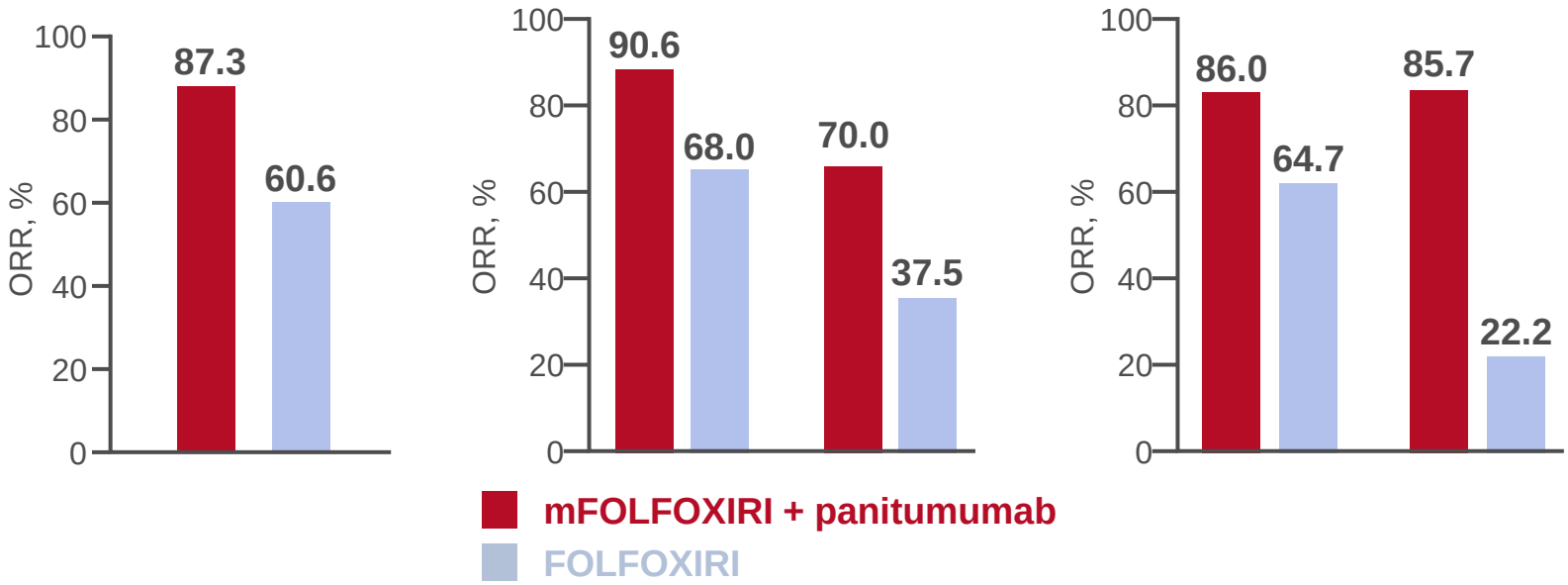
n=96
p=0.004
OR 4.47
95%CI 1.61, 12.38

By tumour sidedness

Left	Right
n=78	n=18
p=0.021	p=0.345
OR 4.52	OR 3.89
1.30, 15.72	0.54, 27.89

By genotype

RAS/BRAF WT	BRAS mut
n=60	n=16
p=0.081	p=0.041
OR 3.36	OR 21.0
0.90, 12.55	1.50, 293.25

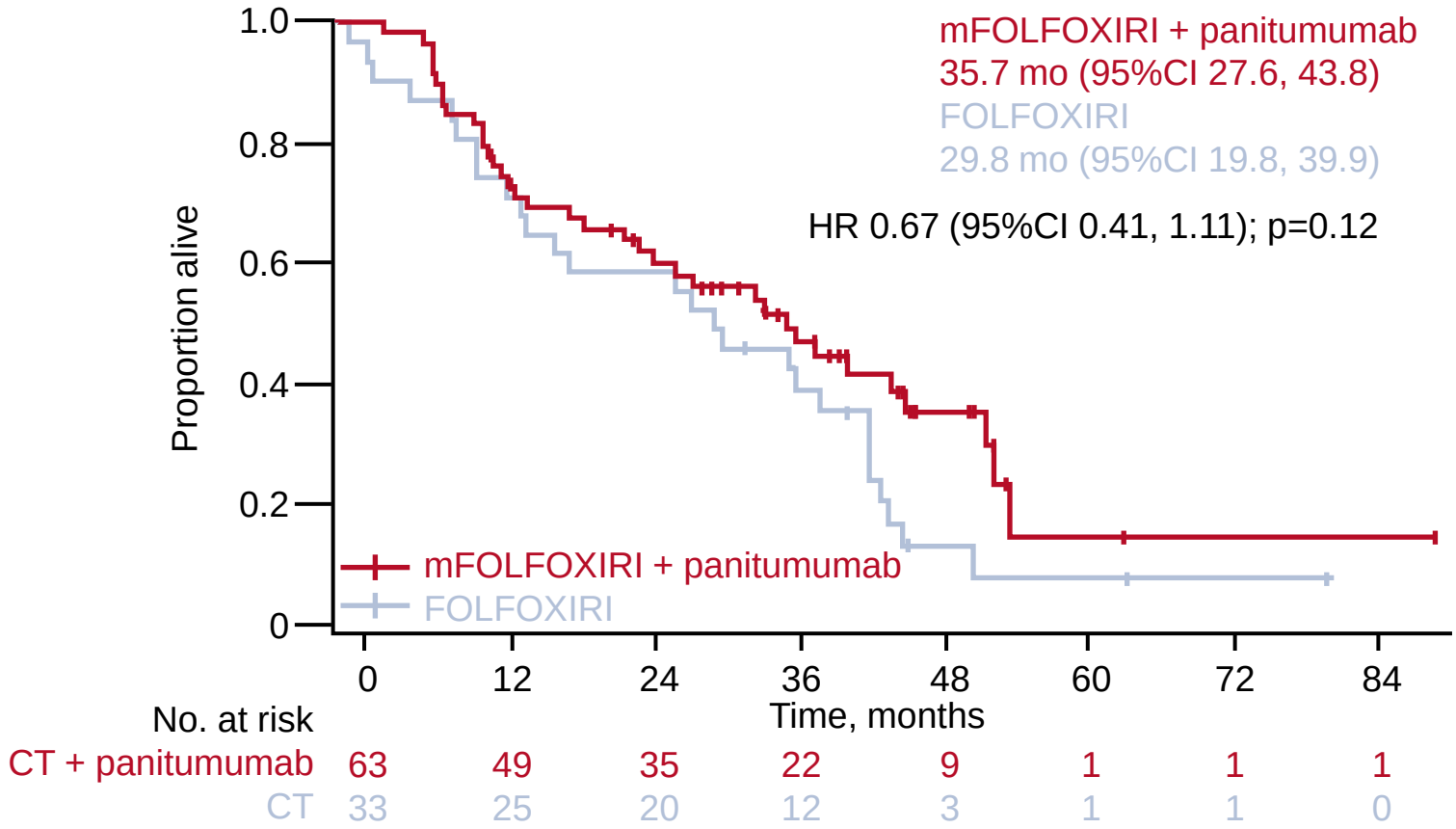


Geissler M, et al. J Clin Oncol 2019;37(suppl):abstr 3511

3511: Final results and OS of the randomized phase II VOLFI trial (AIO-KRK0109): mFOLFOXIRI + panitumumab versus FOLFOXIRI as first-line treatment in patients with RAS wild-type metastatic colorectal cancer (mCRC) – Geissler M, et al

Key results (cont.)

Overall survival



Geissler M, et al. J Clin Oncol 2019;37(suppl):abstr 3511

3511: Final results and OS of the randomized phase II VOLFI trial (AIO-KRK0109): mFOLFOXIRI + panitumumab versus FOLFOXIRI as first-line treatment in patients with RAS wild-type metastatic colorectal cancer (mCRC) – Geissler M, et al

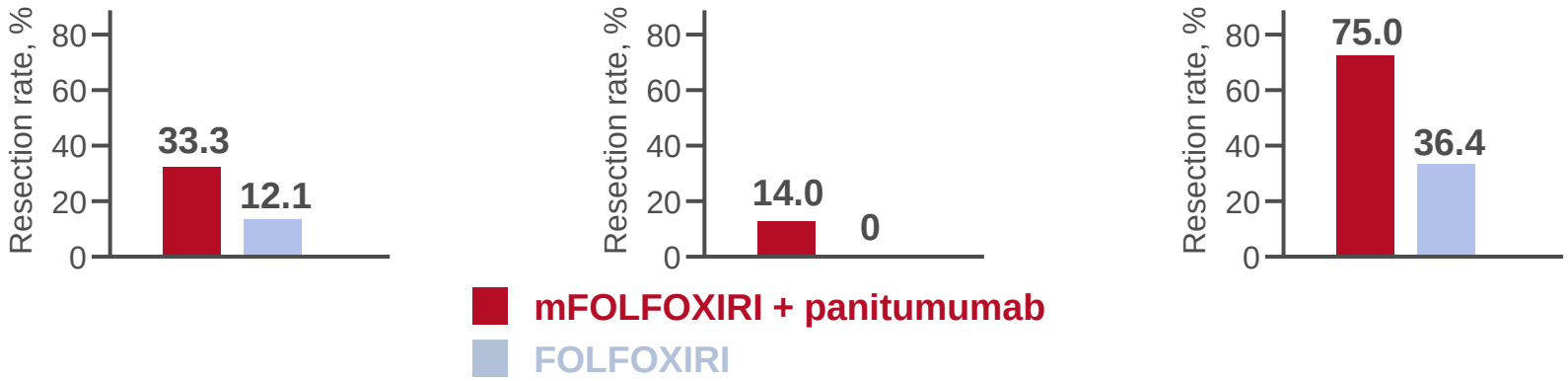
Key results (cont.)

Secondary resection rate

Full analysis set
n=96
p=0.02
OR 3.63
95%CI 1.13, 11.67

Cohort 1
n=65
p=0.08
OR 7.80
95%CI 0.42, 145.2

Cohort 2
n=31
p=0.05
OR 5.25
95%CI 1.07, 25.8



Conclusions

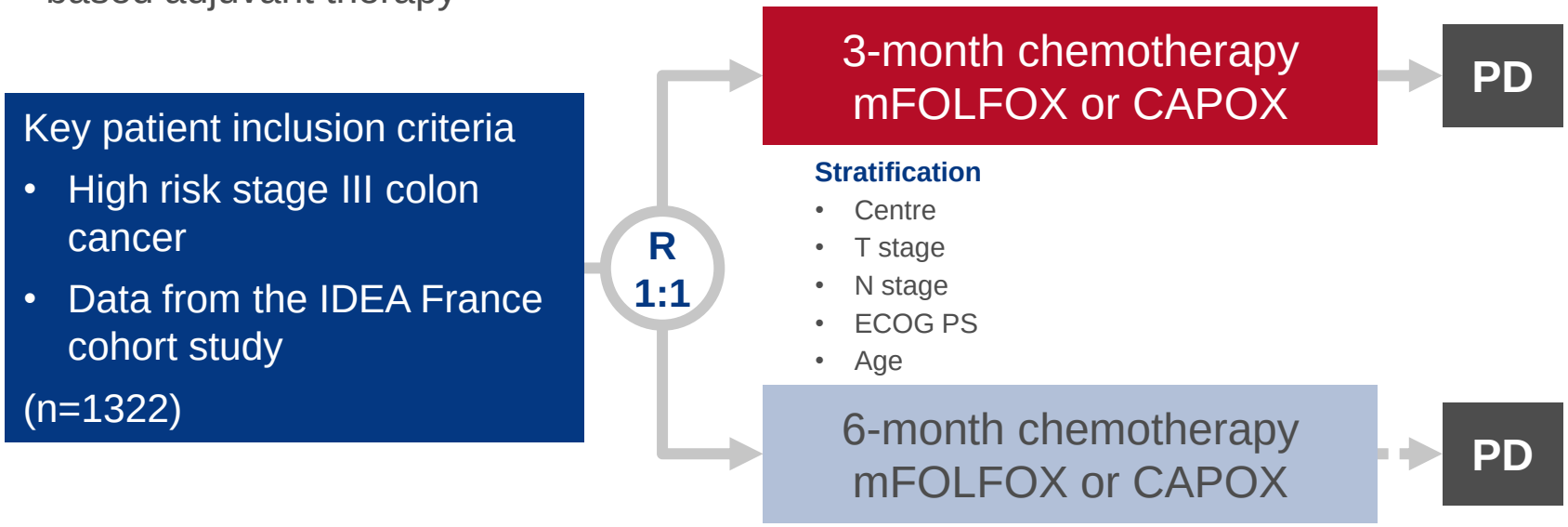
- **In patients with RAS WT mCRC, mFOLFOXIRI + panitumumab may be a potential option for those with high tumour load and/or possibility of secondary resection of metastases although further studies are required to confirm these findings**

Geissler M, et al. J Clin Oncol 2019;37(suppl):abstr 3511

3513: Validation of the Immunoscore prognostic value in stage III colon cancer patients treated with oxaliplatin in the prospective IDEA France cohort study (PRODIGE-GERCOR) – Pagès F, et al

Study objectives

- To investigate and validate whether the Immunoscore (IS)* test can identify patients at high risk of relapse or death in patients with stage III colon cancer receiving oxaliplatin-based adjuvant therapy



PRIMARY ENDPOINT

- DFS

SECONDARY ENDPOINT

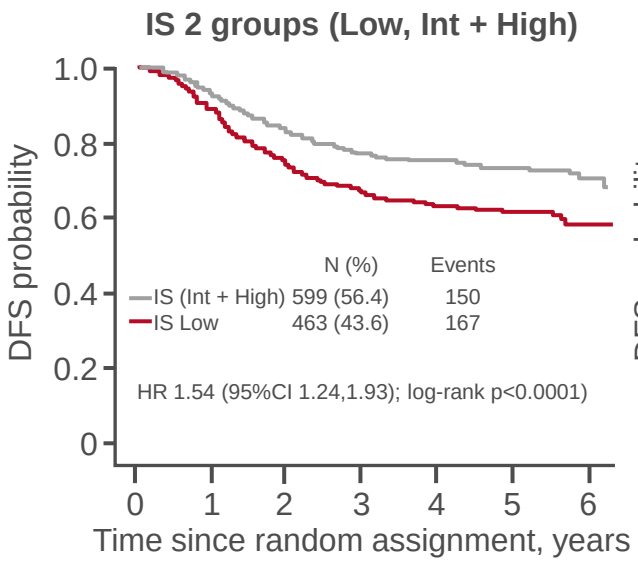
- Safety

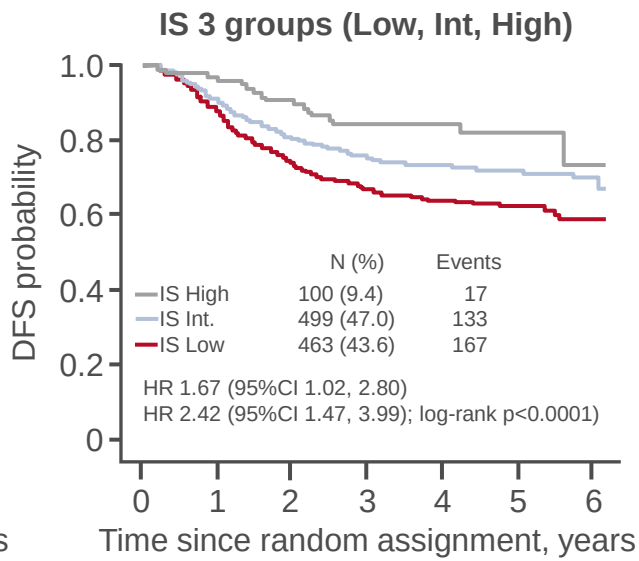
*Digital pathology is used to quantify the densities of CD3+ and cytotoxic CD8+ T cells in core tumour and invasive margin and converted to predefined cut-offs and grouped as either low, intermediate or high or as low or intermediate + high or as a continuous score

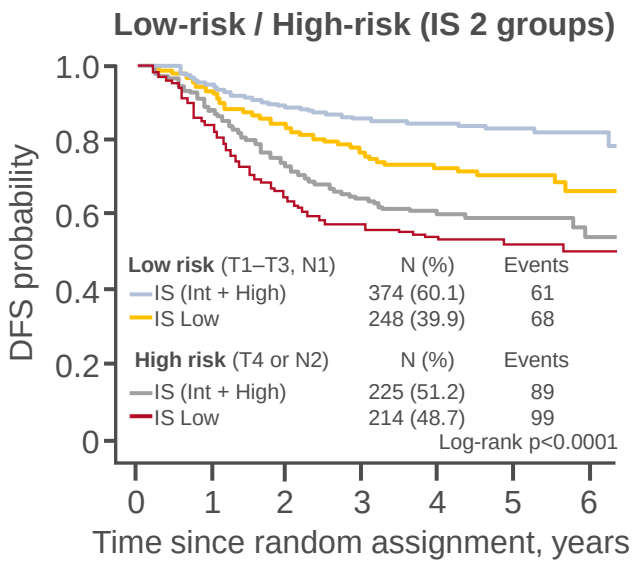
Pagès F, et al. J Clin Oncol 2019;37(suppl):abstr 3513

3513: Validation of the Immunoscore prognostic value in stage III colon cancer patients treated with oxaliplatin in the prospective IDEA France cohort study (PRODIGE-GERCOR) – Pagès F, et al

Key results







	N	Events	HR	95%CI	p-value
Immunoscore classification					
High	100	17	1		
Intermediate	499	133	1.745	1.053, 2.892	
Low	463	167	2.321	1.409, 3.824	0.0008
Histopathological classification					
Low risk (T1–3, N1)	622	129	1		
High risk (T4 or N2)	439	188	2.343	1.871, 2.935	<0.0001

Pagès F, et al. J Clin Oncol 2019;37(suppl):abstr 3513

3513: Validation of the Immunoscore prognostic value in stage III colon cancer patients treated with oxaliplatin in the prospective IDEA France cohort study (PRODIGE-GERCOR) – Pagès F, et al

Key results (cont.)

Efficacy of mFOLFOX6 3 vs. 6 months according to Immunoscore status

Immunoscore status	All patients		Low risk (T1-T3, N1)		High risk (T4 &/or N2)	
	3 months	6 months	3 months	6 months	3 months	6 months
Intermediate + High						
Events, n/N	86/275	49/275	35/172	17/168	51/103	32/107
HR (95%CI)	0.53 (0.37, 0.75)		0.47 (0.26, 0.83)		0.54 (0.35, 0.84)	
p-value	0.0003		0.01		0.006	
Low						
Events, n/N	81/217	72/206	89/118	80/106	79/98	89/100
HR (95%CI)	0.84 (0.61, 1.15)		0.86 (0.52, 1.42)		0.76 (0.51, 1.15)	
p-value	0.270		0.557		0.199	

Conclusions

- **In patients with stage III colon cancer, the Immunoscore can be considered as a prognostic factor for DFS**
- **The findings demonstrated that 6 months of mFOLFOX6 only benefitted those patients who had an intermediate or high Immunoscore regardless of whether they are low or high risk**

Pagès F, et al. J Clin Oncol 2019;37(suppl):abstr 3513

3518: A pooled analysis of multicenter cohort studies of post-surgery circulating tumour DNA (ctDNA) in early stage colorectal cancer (CRC) – Tie J, et al

Study objective

- To investigate ctDNA post-surgery in patients with early stage CRC

Methods

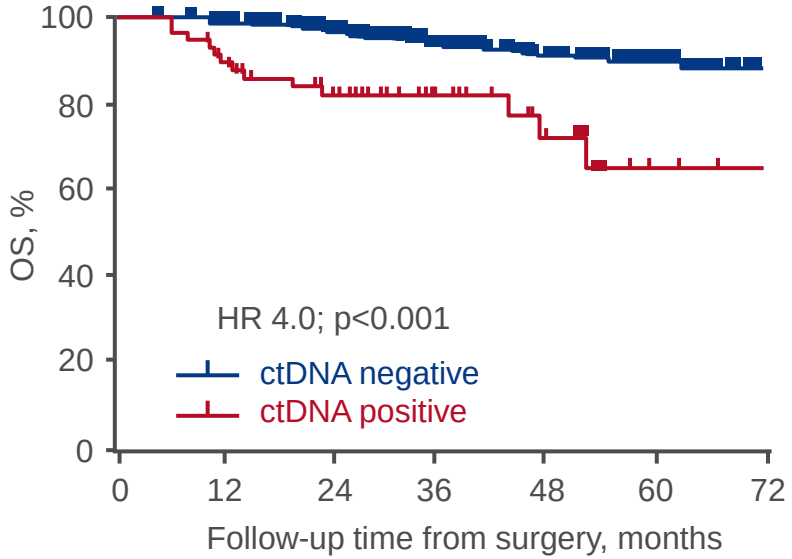
- Data were collected from three prospective cohort studies for patients with stage II or III CRC (n=485)
- Plasma samples were collected 4–10 weeks after surgery and mutations were detected in ctDNA using the Safe-SeqS assay
- Outcomes were assessed over a 5-year follow-up period

Tie J, et al. J Clin Oncol 2019;37(suppl):abstr 3518

3518: A pooled analysis of multicenter cohort studies of post-surgery circulating tumour DNA (ctDNA) in early stage colorectal cancer (CRC) – Tie J, et al

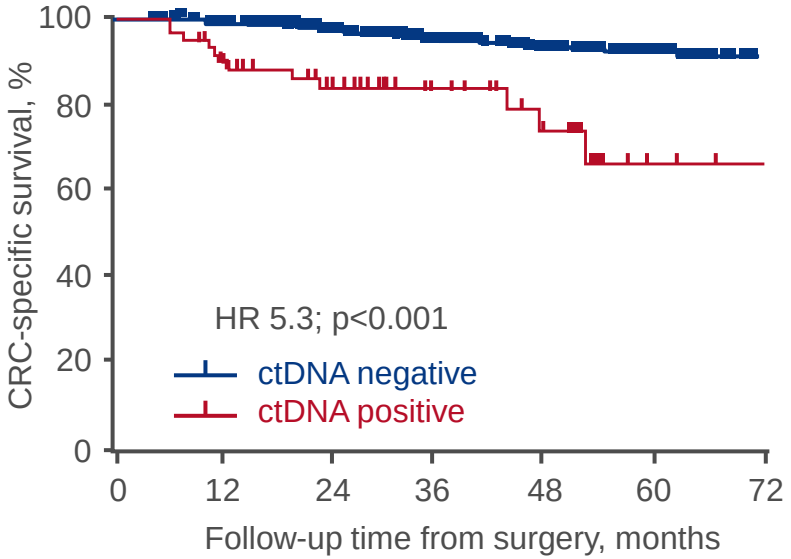
Key results

OS – all patients



	n	Events	5-year OS, %
ctDNA neg	426	34	89
ctDNA pos	59	13	65

CRC-specific survival – all patients

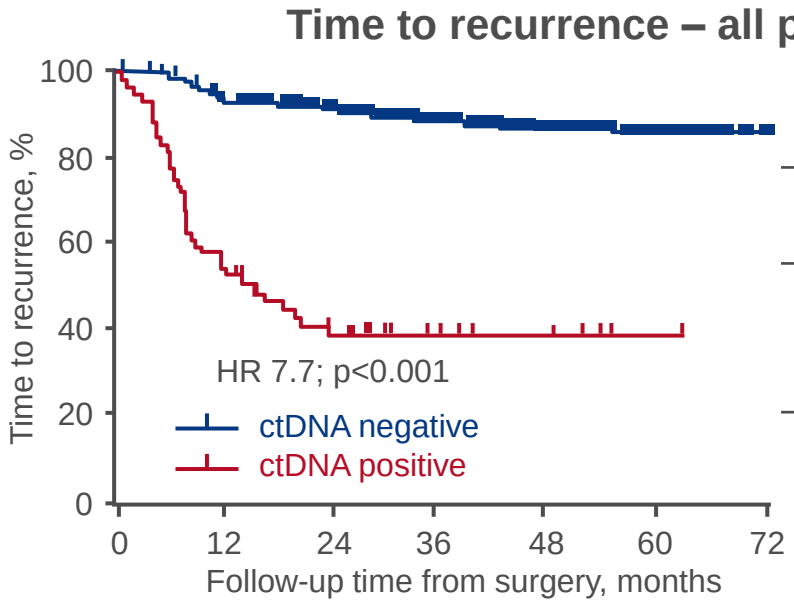


	n	Events	5-year CRC-specific survival, %
ctDNA neg	426	24	92
ctDNA pos	59	12	66

Tie J, et al. J Clin Oncol 2019;37(suppl):abstr 3518

3518: A pooled analysis of multicenter cohort studies of post-surgery circulating tumour DNA (ctDNA) in early stage colorectal cancer (CRC) – Tie J, et al

Key results (cont.)



	n	Events	5-year time to recurrence, %
ctDNA neg	426	55	85
ctDNA pos	59	35	39

Conclusions

- In patients with stage II or III CRC, ctDNA detected 4–10 weeks post-surgery was associated with a significantly worse OS, CRC-specific survival and a shorter time to recurrence
- The prognostic value of ctDNA detection could be enhanced by combining with an analysis of mutation allele frequency

Tie J, et al. J Clin Oncol 2019;37(suppl):abstr 3518