GI SLIDE DECK 2019

Selected abstracts from:

ESMO 21st World Congress on Gastrointestinal Cancer

3–6 July 2019 | Barcelona, Spain

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 **ESMO 21st World Congress on Gastrointestinal Cancer** 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,

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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


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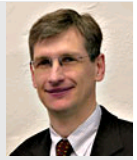

Prof Eric Van Cutsem	Digestive Oncology, University Hospitals, Leuven, Belgium
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esdo

Glossary

1L	first-line
5FU	5-fluorouracil
AST	aspartate aminotransferase
ATP	adenosine triphosphate
BICR	blinded-independent central review
bid	twice daily
BOR	best overall response
BSC	best supportive care
BTK	Bruton's tyrosine kinase
BTLC	best target lesion change
CA19-9	carbohydrate antigen 19-9
CAR	chimeric antigen receptor
CBR	clinical benefit rate
CI	confidence interval
CR	complete response
CRC	colorectal cancer
CRM	circumferential resection margin
CRP	C-reactive protein
CT	chemotherapy
ctDNA	circulating tumour DNA
D	day
DCR	disease control rate
DFS	disease-free survival
DLT	dose-limiting toxicity
DoR	duration of response
ECOG	Eastern Cooperative Oncology Group
EORTC	European Organisation for Research and Treatment of Cancer
FGFR	fibroblast growth factor receptor
FOLFIRI	leucovorin + 5-fluorouracol + irinotecan
FOLFOX	leucovorin + 5-fluorouracil + oxaliplatin
G	grade
GEJ	gastro-oesophageal junction
GGT	gamma-glutamyl transferase
GI	gastrointestinal
Gy	Gray
HER2	human epidermal growth factor receptor 2
HR	hazard ratio
HRc	hormone receptor
HRQoL	health-related quality of life
IHC	immunohistochemistry
(m)ITT	(modified) intent-to-treat
IV	intravenous
mCRC	metastatic colorectal cancer
mAb	monoclonal antibody
MASC	Mammary analogue secretory carcinoma
MSI(-H)	microsatellite instability (-high)
MSS	microsatellite stable
nal-IRI	liposomal irinotecan
NAR	neoadjuvant rectal
NCI	National Cancer Institute
NE	not evaluable
NOS	not otherwise specified
NR	not reached
ORR	overall/objective response rate
(m)OS	(median) overall survival
pCR	pathological complete response
PD	progressive disease
PDAC	pancreatic ductal adenocarcinoma
PD-L1	programmed death-ligand 1
(m)PFS	(median) progression-free survival
PR	partial response
PS	performance status
q(2/3/4/5)w	every (2/3/4/5) week(s)
QLQ-C30	quality of life questionnaire C30
QoL	quality of life
R	randomised
R0/1	resection 0/1
RECIST	Response Evaluation Criteria In Solid Tumors
SD	stable disease
TMB	tumour mutational burden
TGR	tumour growth rate
TRAE	treatment-related adverse event
TRG	tumour regression grade
TTF	time to treatment failure
Tx	treatment
WT	wild type

Contents

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

CANCERS OF THE OESOPHAGUS AND STOMACH

LBA-003: A phase III study of TAS-118 plus oxaliplatin versus S-1 plus cisplatin as first-line chemotherapy in patients with advanced gastric cancer (SOLAR study) – Kang Y-K, et al

Study objective

- To investigate the efficacy and safety of TAS-118 + oxaliplatin vs. S-1 + cisplatin in patients with advanced gastric or GEJ cancer

Key patient inclusion criteria
- Advanced gastric or GEJ cancer
- Treatment naïve
- Negative or unknown for HER2 testing
- ECOG PS 0–1

(n=711)

R 1:1

TAS-118 40–60 mg bid D1–7 + oxaliplatin 85 mg/m^2 D1, 15 q2w (n=347) → PD/ toxicity

S-1 40–60 mg bid D1–21 + cisplatin 60 mg/m^2 D1 or 8 q5w (n=334) → PD/ toxicity

Stratification
- ECOG PS (0 vs. 1)
- Measurable lesion (yes vs. no)
- Country (Japan vs. Korea)

PRIMARY ENDPOINT
- OS

SECONDARY ENDPOINTS
- PFS, TTF, ORR, DCR, safety

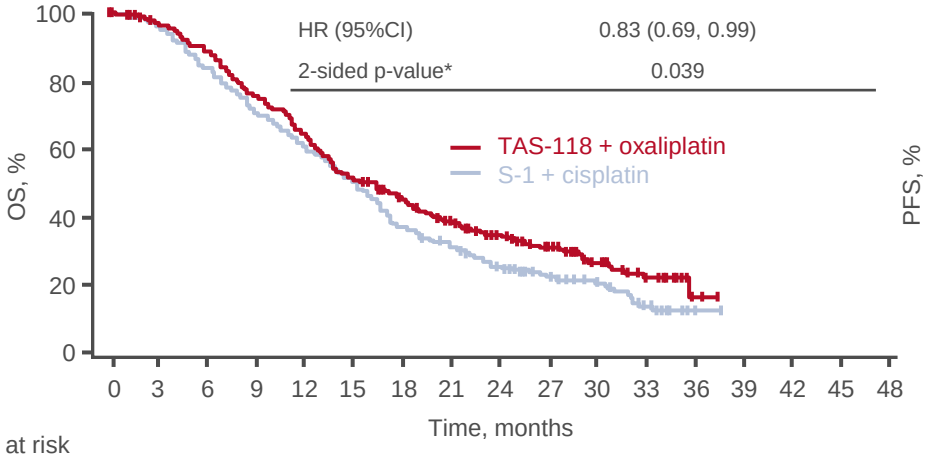
Kang Y-K, et al. Ann Oncol 2019;30(suppl):abstr LBA-003

LBA-003: A phase III study of TAS-118 plus oxaliplatin versus S-1 plus cisplatin as first-line chemotherapy in patients with advanced gastric cancer (SOLAR study) – Kang Y-K, et al

Key results

OS

	TAS-118 + oxaliplatin (n=347)	S-1 + cisplatin (n=334)
Events	233	258
Median, months	16.0	15.1
HR (95%CI)	0.83 (0.69, 0.99)	
2-sided p-value*	0.039	

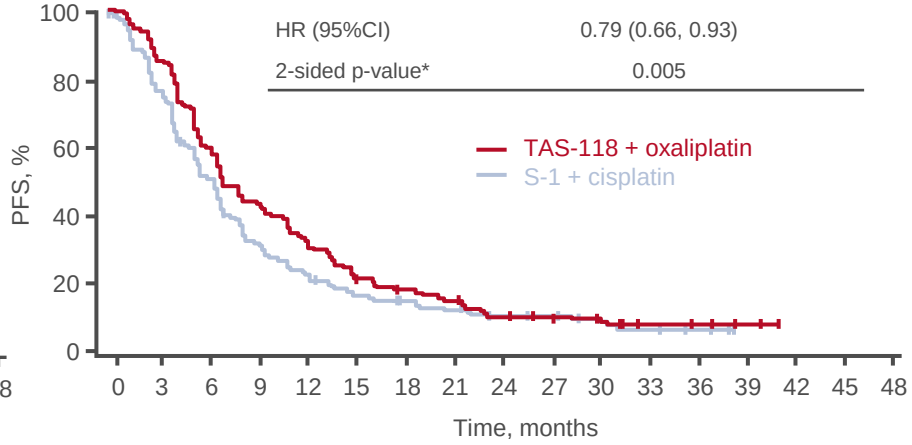


No. at risk

TAS-118	347	330	304	255	217	174	143	103	69	48	28	17	2	0	0	0	0
S-1	334	323	280	236	202	167	111	83	53	38	26	12	1	0	0	0	0

PFS

	TAS-118 + oxaliplatin (n=347)	S-1 + cisplatin (n=334)
Events	268	278
Median, months	7.1	6.4
HR (95%CI)	0.79 (0.66, 0.93)	
2-sided p-value*	0.005	



	347	280	180	123	87	60	40	31	20	17	12	5	5	2	0	0	0
	334	249	153	88	61	42	32	19	14	13	10	6	4	0	0	0	0

*Log-rank test

Kang Y-K, et al. Ann Oncol 2019;30(suppl):abstr LBA-003

LBA-003: A phase III study of TAS-118 plus oxaliplatin versus S-1 plus cisplatin as first-line chemotherapy in patients with advanced gastric cancer (SOLAR study) – Kang Y-K, et al

Key results (cont.)

Grade ≥3 AEs occurring in ≥5%, %	TAS-118 + oxaliplatin (n=352)	S-1 + cisplatin (n=348)
Anaemia	15.9	18.4
Neutropenia	15.3	25.3
Thrombocytopenia	2.0	5.7
Diarrhoea	9.4	4.3
Decreased appetite	15.1	13.2
Peripheral sensory neuropathy	8.5	0.3
Weight decreased	5.4	2.9

Conclusions

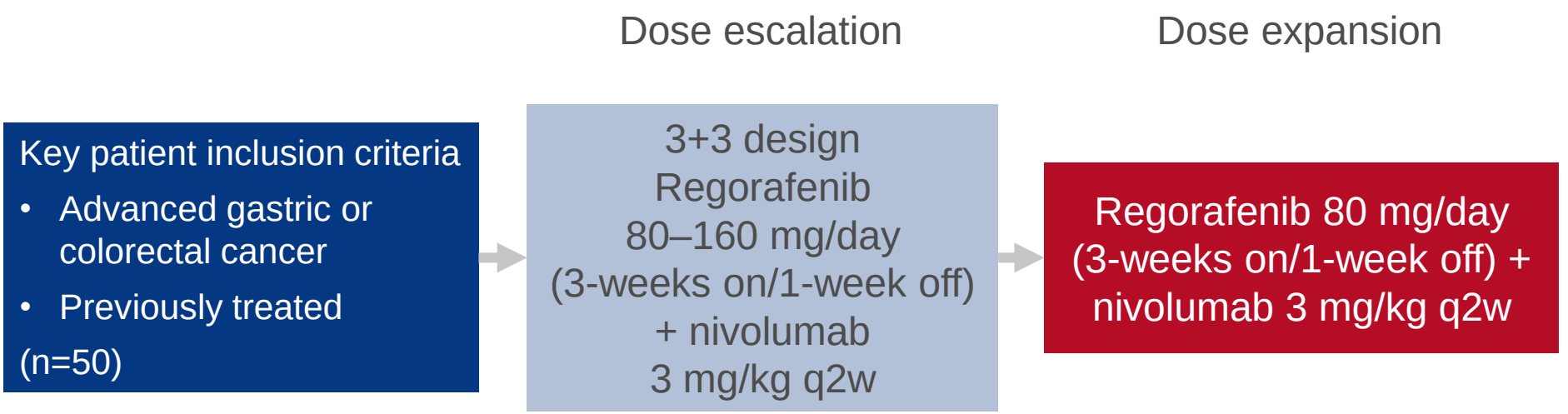
- **In patients with advanced gastric or GEJ cancer, 1L TAS-118 + oxaliplatin demonstrated significant improvements in survival compared with S-1 + cisplatin**
- **The proportion of patients experiencing non-haematological AEs was higher with TAS-118 + oxaliplatin than S-1 + cisplatin**

Kang Y-K, et al. Ann Oncol 2019;30(suppl):abstr LBA-003

SO-007: Regorafenib plus nivolumab in patients with advanced colorectal (CRC) or gastric cancer (GC): an open-label, dose-finding, and dose-expansion phase 1b trial (REGONIVO, EPOC1603) – Hara H, et al

Study objective

- To investigate the efficacy and safety of regorafenib + nivolumab in patients with advanced gastric or colorectal cancer



PRIMARY ENDPOINT

- DLT

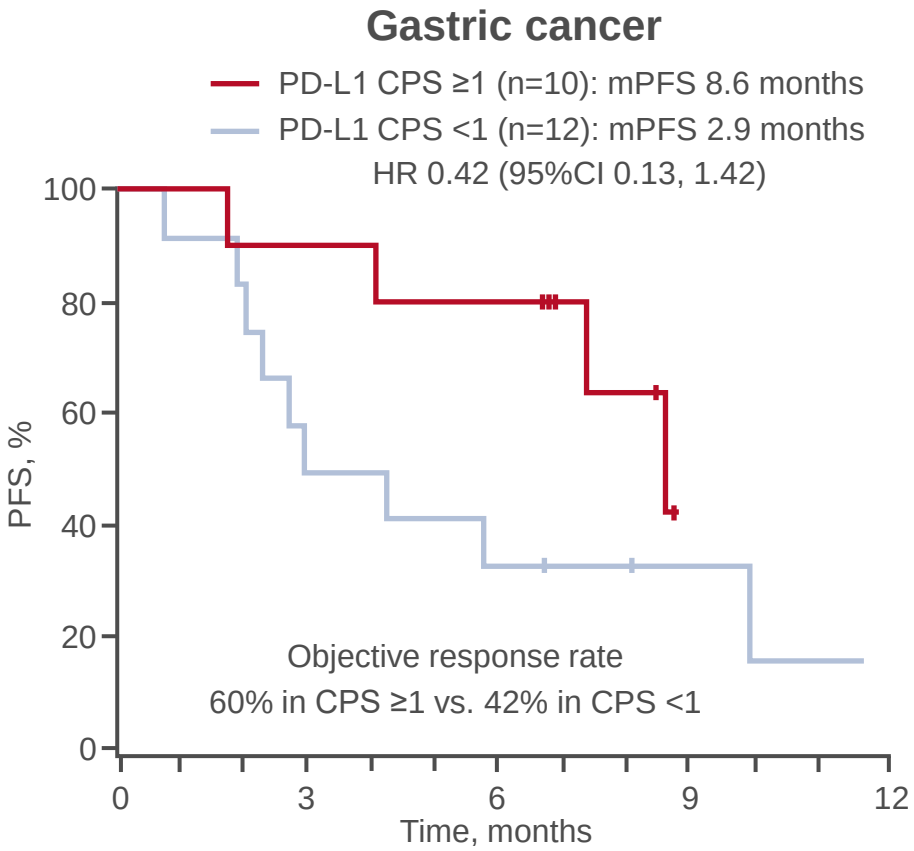
SECONDARY ENDPOINTS

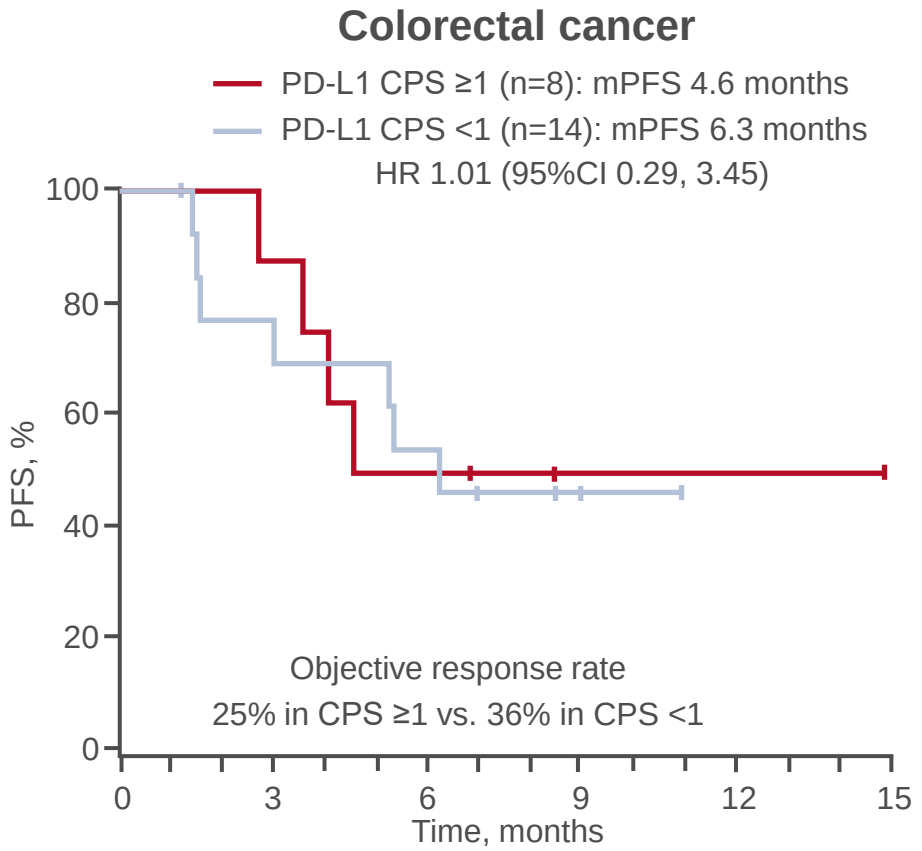
- PFS according to PD-L1 and TMB

Hara H, et al. Ann Oncol 2019;30(suppl):abstr SO-007

SO-007: Regorafenib plus nivolumab in patients with advanced colorectal (CRC) or gastric cancer (GC): an open-label, dose-finding, and dose-expansion phase 1b trial (REGONIVO, EPOC1603) – Hara H, et al

Key results

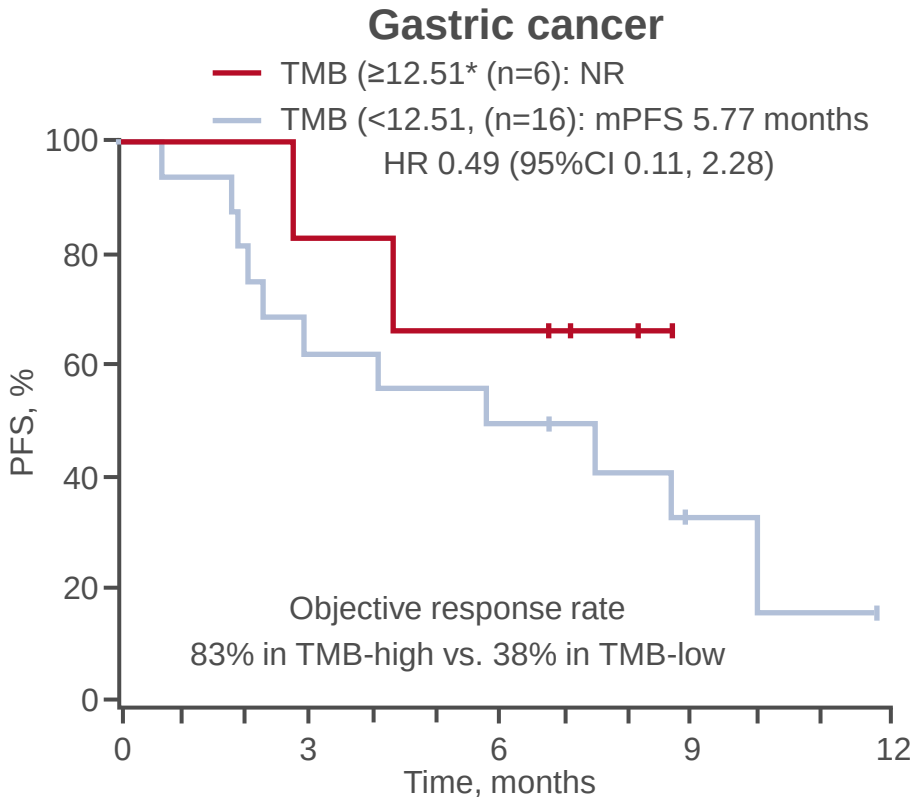


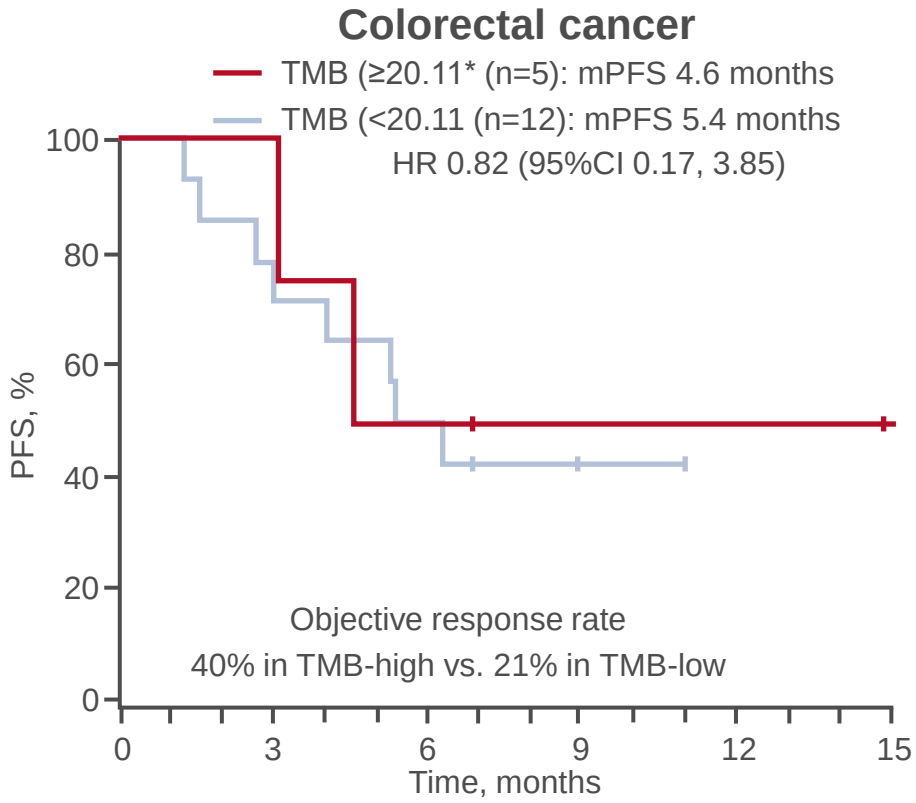


Hara H, et al. Ann Oncol 2019;30(suppl):abstr SO-007

SO-007: Regorafenib plus nivolumab in patients with advanced colorectal (CRC) or gastric cancer (GC): an open-label, dose-finding, and dose-expansion phase 1b trial (REGONIVO, EPOC1603) – Hara H, et al

Key results (cont.)





Conclusion

- **In patients with advanced CRC or gastric cancer, combining regorafenib with nivolumab provided promising antitumor activity regardless of PD-L1 expression or TMB**

*Top quarter (measured by oncomine tumour mutation load assay)

Hara H, et al. Ann Oncol 2019;30(suppl):abstr SO-007

CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

Cancers of the pancreas, small bowel and hepatobiliary tract

PANCREATIC CANCER

O-001: An international, randomized, open-label, phase III trial of adjuvant nab paclitaxel plus gemcitabine (nab-P/Gem) vs gemcitabine (Gem) alone for surgically resected pancreatic adenocarcinoma (APACT): Primary analysis and quality of life outcomes – Reni M, et al

Study objective

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

Key patient inclusion criteria

- Pancreatic cancer
- Macroscopic complete resection
- No prior neoadjuvant, radiation or systemic therapy
- CA19-9 <100 u/mL
- ECOG PS 0–1

(n=866)

R 1:1

Nab-paclitaxel 125 mg/m^2 + gemcitabine 1000 mg/m^2 qw for first 3 of 4 weeks for 6 cycles* (n=429) → PD/ toxicity

Stratification

- Resection status (R0 vs. R1)
- Lymph node status (positive vs. negative)
- Geographic region (North America, Europe and Australia vs. Asia Pacific)

Gemcitabine 1000 mg/m^2 qw for first 3 of 4 weeks for 6 cycles* (n=423) → PD/ toxicity

PRIMARY ENDPOINT

- Independently assessed DFS

SECONDARY ENDPOINTS

- OS, safety, QoL

*Treatment initiated ≤12 weeks post-surgery

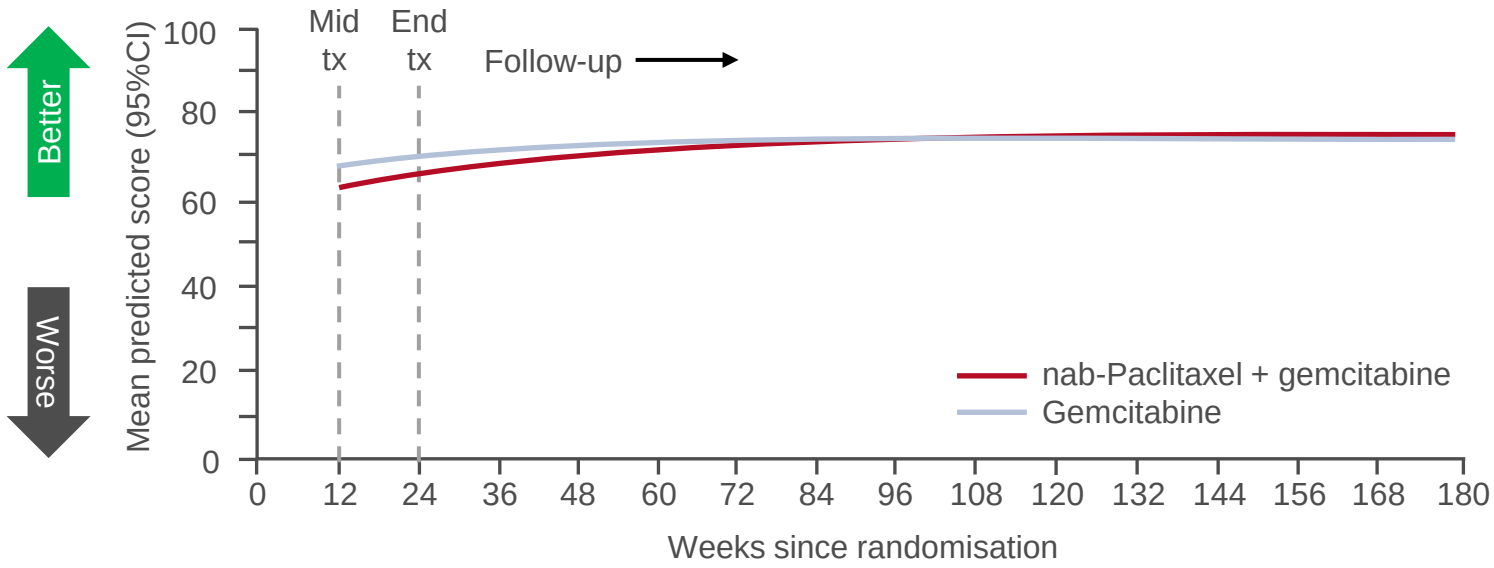
Reni M, et al. Ann Oncol 2019;30(suppl):abstr O-001

O-001: An international, randomized, open-label, phase III trial of adjuvant nab paclitaxel plus gemcitabine (nab-P/Gem) vs gemcitabine (Gem) alone for surgically resected pancreatic adenocarcinoma (APACT): Primary analysis and quality of life outcomes – Reni M, et al

Key results

- Although HRQoL was initially worse with nab-paclitaxel + gemcitabine, over time there were no meaningful differences observed and HRQoL was similar between the two groups

Global health status/QoL (EORTC QLQ-C30)



Conclusion

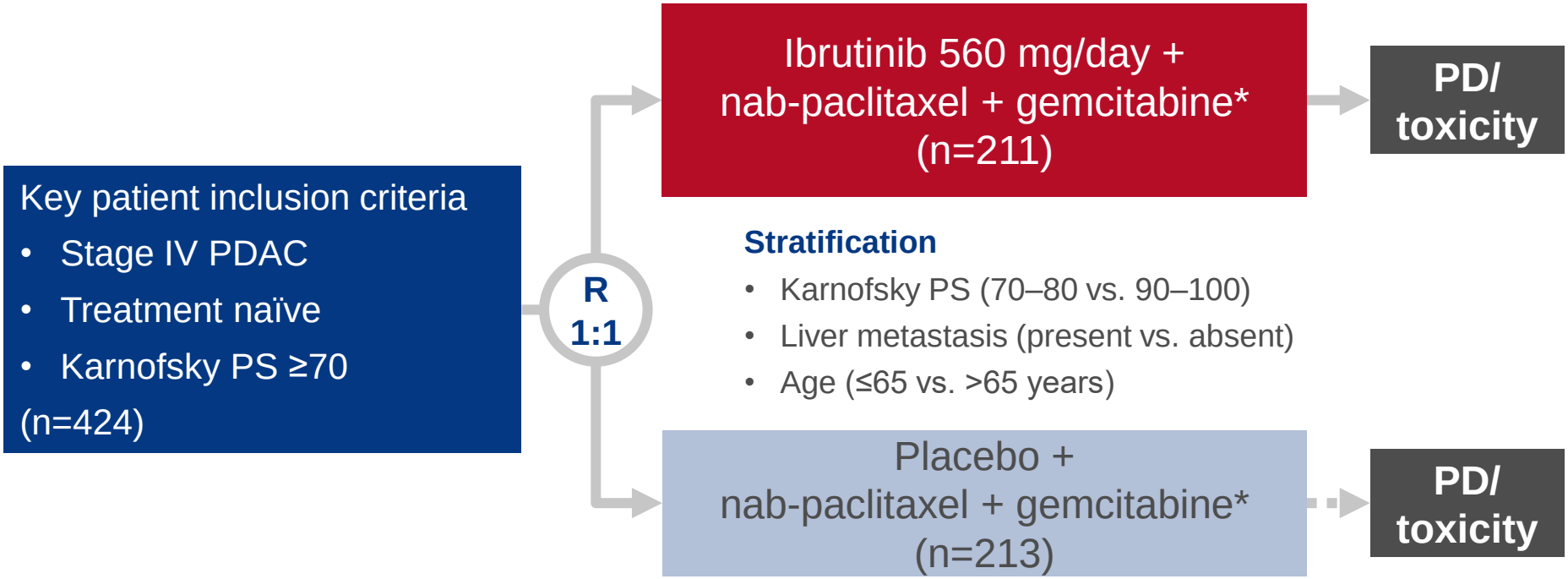
- **In patients with pancreatic cancer, the combination of nab-paclitaxel + gemcitabine did not impact HRQoL and was comparable with gemcitabine alone**

Reni M, et al. Ann Oncol 2019;30(suppl):abstr O-001

O-002: Ibrutinib in combination with nab-paclitaxel and gemcitabine as first-line treatment for patients with metastatic pancreatic adenocarcinoma: Results from the phase 3 RESOLVE study – Tempero M, et al

Study objective

- To investigate the efficacy and safety of ibrutinib, a BTK inhibitor, combined with nab-paclitaxel + gemcitabine in patients with metastatic PDAC



PRIMARY ENDPOINTS

- OS, PFS

SECONDARY ENDPOINTS

- ORR, safety

*Nab-paclitaxel 125 mg/m^2 + gemcitabine 1000 mg/m^2 D1, 8, 15 q4w

Tempero M, et al. Ann Oncol 2019;30(suppl):abstr O-002

O-002: Ibrutinib in combination with nab-paclitaxel and gemcitabine as first-line treatment for patients with metastatic pancreatic adenocarcinoma: Results from the phase 3 RESOLVE study – Tempero M, et al

Key results

Characteristic, n (%) [unless otherwise stated]	Ibrutinib + nab-paclitaxel + gemcitabine (n=211)	Placebo + nab-paclitaxel + gemcitabine (n=213)
Median age, years (range)	64 (32–82)	64 (32–85)
Male	114 (54)	121 (57)
Race white	146 (69)	142 (67)
Karnofsky PS (electronic data capture)		
100	39 (18)	46 (22)
90	108 (51)	101 (47)
80	54 (26)	53 (25)
≤70	10 (5)	13 (6)
ECOG PS		
0	99 (47)	88 (41)
≥1	112 (53)	125 (59)
Number of metastatic sites		
1	79 (37)	73 (34)
2	85 (40)	62 (29)
>2	47 (22)	78 (37)
Liver metastases		
Present	169 (80)	172 (81)
Absent	42 (20)	41 (19)

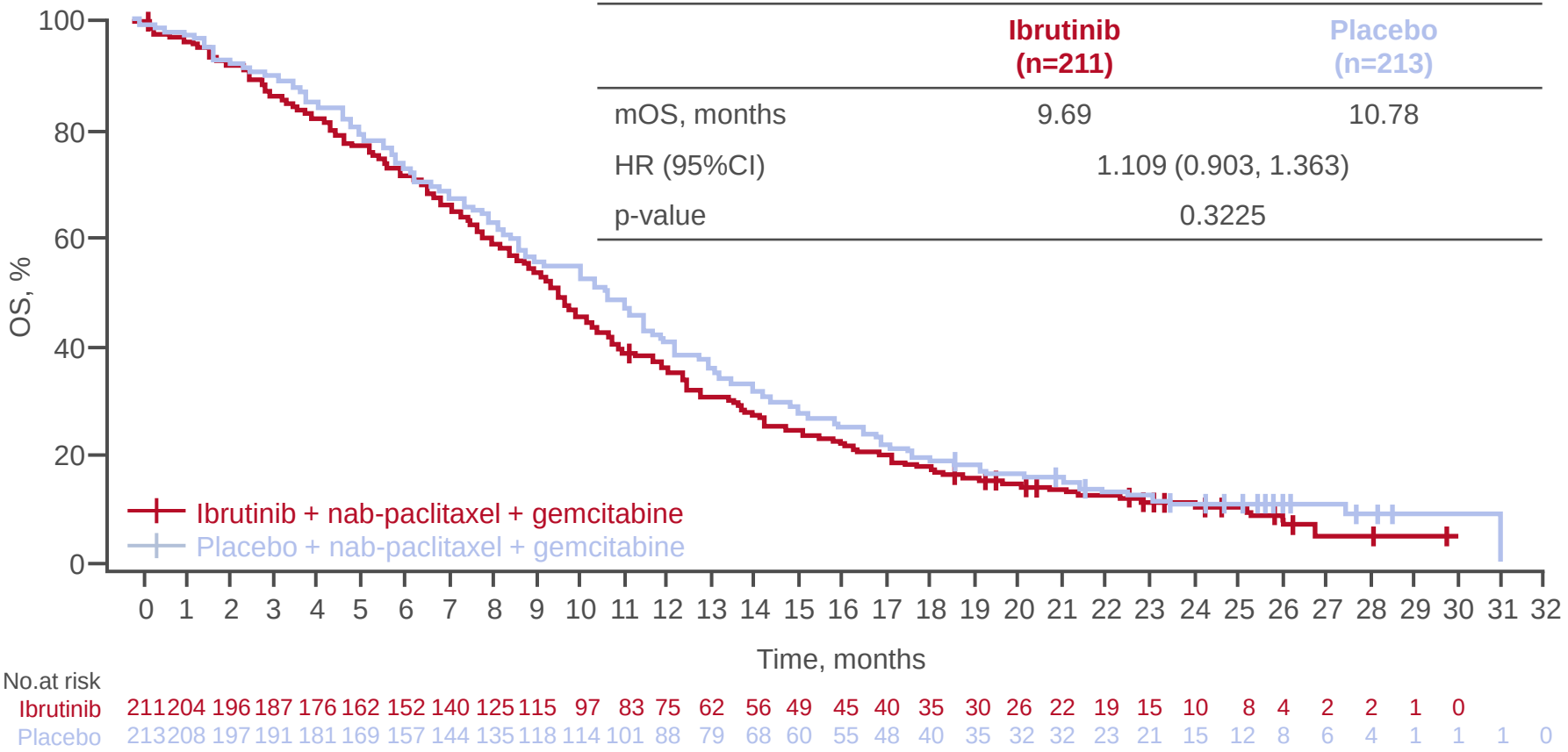
Tempero M, et al. Ann Oncol 2019;30(suppl):abstr O-002

O-002: Ibrutinib in combination with nab-paclitaxel and gemcitabine as first-line treatment for patients with metastatic pancreatic adenocarcinoma: Results from the phase 3 RESOLVE study – Tempero M, et al

Key results (cont.)

OS

	Ibrutinib (n=211)	Placebo (n=213)
mOS, months	9.69	10.78
HR (95%CI)	1.109 (0.903, 1.363)	
p-value	0.3225	



No.at risk

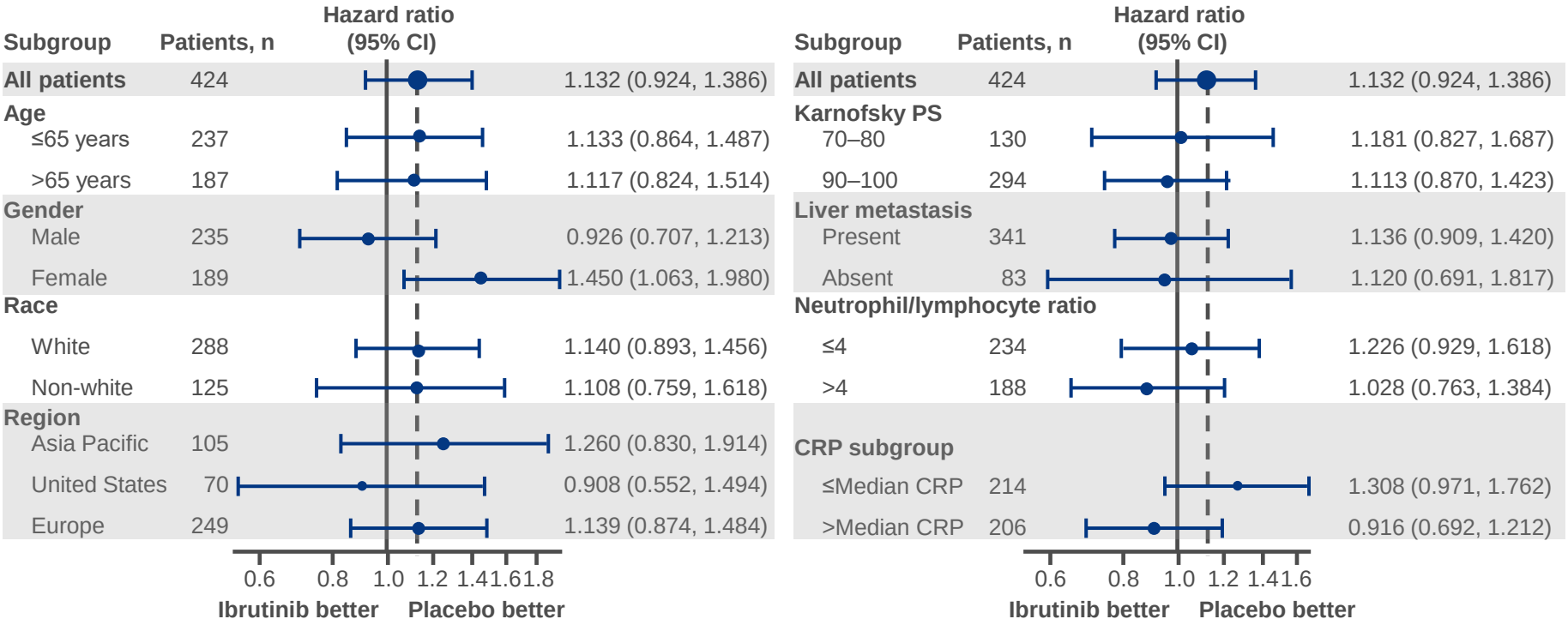
Ibrutinib	211	204	196	187	176	162	152	140	125	115	97	83	75	62	56	49	45	40	35	30	26	22	19	15	10	8	4	2	2	1	0
Placebo	213	208	197	191	181	169	157	144	135	118	114	101	88	79	68	60	55	48	40	35	32	32	23	21	15	12	8	6	4	1	1	1	0

Tempero M, et al. Ann Oncol 2019;30(suppl):abstr O-002

O-002: Ibrutinib in combination with nab-paclitaxel and gemcitabine as first-line treatment for patients with metastatic pancreatic adenocarcinoma: Results from the phase 3 RESOLVE study – Tempero M, et al

Key results (cont.)

OS by subgroups



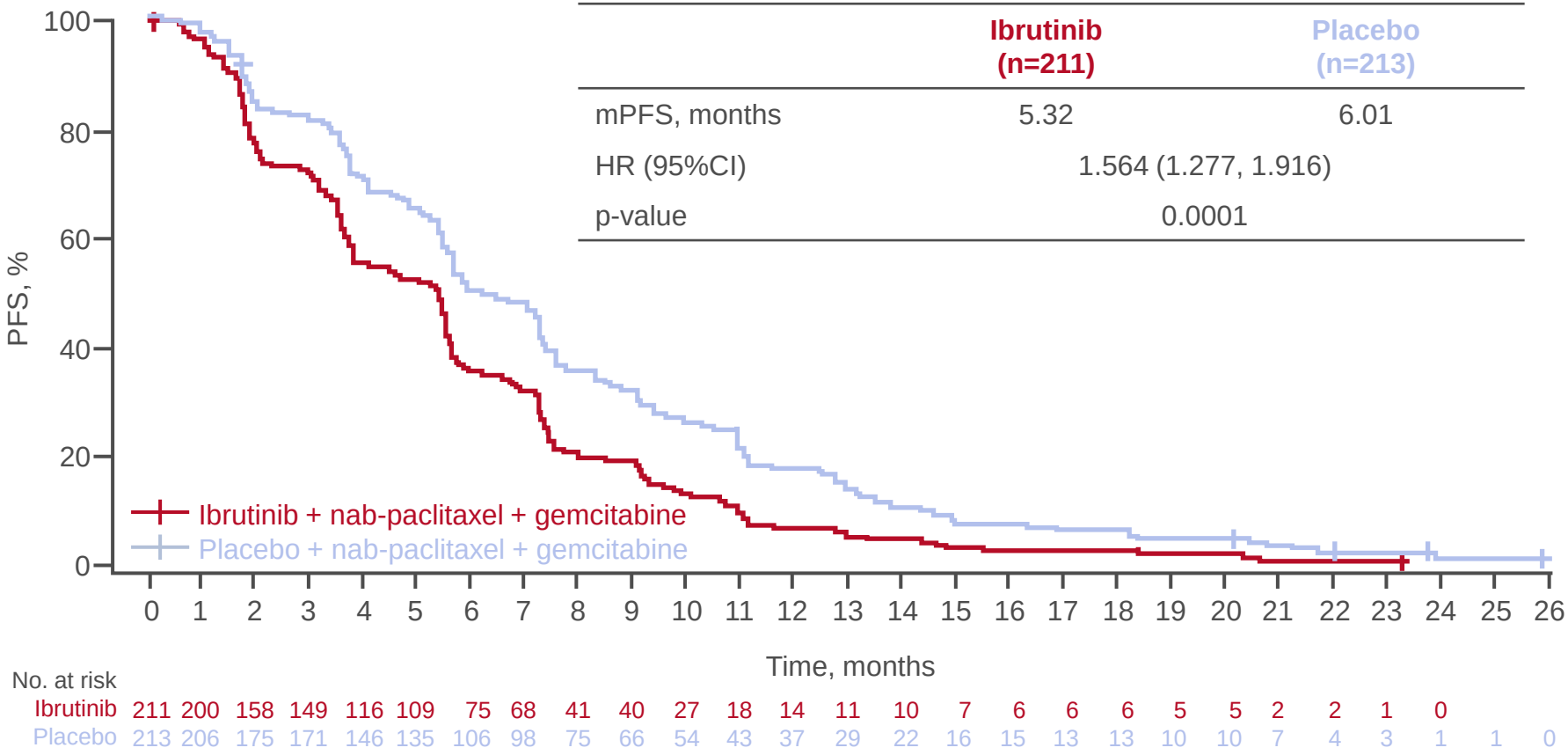
Tempero M, et al. Ann Oncol 2019;30(suppl):abstr O-002

O-002: Ibrutinib in combination with nab-paclitaxel and gemcitabine as first-line treatment for patients with metastatic pancreatic adenocarcinoma: Results from the phase 3 RESOLVE study – Tempero M, et al

Key results (cont.)

PFS

	Ibrutinib (n=211)	Placebo (n=213)
mPFS, months	5.32	6.01
HR (95%CI)	1.564 (1.277, 1.916)	
p-value	0.0001	



Tempero M, et al. Ann Oncol 2019;30(suppl):abstr O-002

O-002: Ibrutinib in combination with nab-paclitaxel and gemcitabine as first-line treatment for patients with metastatic pancreatic adenocarcinoma: Results from the phase 3 RESOLVE study – Tempero M, et al

Key results (cont.)

Grade ≥3 AEs occurring in ≥10%, n (%)	Ibrutinib + nab-paclitaxel + gemcitabine (n=208)	Placebo + nab-paclitaxel + gemcitabine (n=212)
Any	178 (86)	184 (87)
Neutropenia	50 (24)	74 (35)
Peripheral sensory neuropathy	35 (17)	16 (8)
Anaemia	34 (16)	36 (17)
Asthenia	33 (16)	25 (12)
Diarrhoea	30 (14)	19 (9)
Thrombocytopenia	20 (10)	21 (10)

Conclusions

- **In patients with metastatic PDAC, combining ibrutinib with nab-paclitaxel + gemcitabine did not provide any additional survival benefit**
- **The safety profile was comparable with that of the known profiles for each agent**

Tempero M, et al. Ann Oncol 2019;30(suppl):abstr O-002

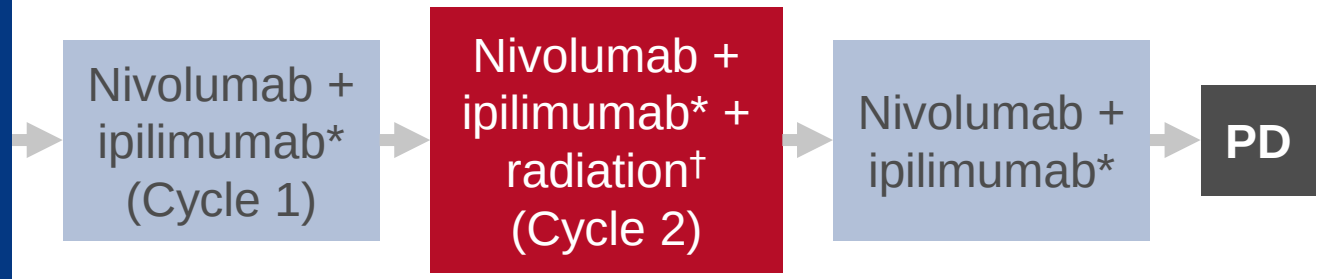
O-008: Proof of concept of the abscopal effect in MSS GI cancers: A phase 2 study of ipilimumab and nivolumab with radiation in metastatic pancreatic and colorectal adenocarcinoma – Parikh A, et al

Study objective

- To investigate the efficacy and safety of nivolumab + ipilimumab with radiation in patients with metastatic pancreatic and colorectal adenocarcinoma

Key patient inclusion criteria

- Metastatic CRC (n=40)
  - Progressed on 5FU, oxaliplatin or irinotecan
- Metastatic pancreatic (n=25)
  - >1 prior therapy
- MSS by IHC
- ECOG PS 0–1



PRIMARY ENDPOINT

- DCR (MSS colon)

SECONDARY ENDPOINTS

- ORR, DCR (PDAC and MSI), PFS, OS, safety

*Nivolumab 240 mg q2w x3, ipilimumab 1 mg/kg q6w x1; †8 Gy to single lesion (liver, nodal, lung, pulmonary, soft tissue) start D1

Parikh A, et al. Ann Oncol 2019;30(suppl):abstr O-008

O-008: Proof of concept of the abscopal effect in MSS GI cancers: A phase 2 study of ipilimumab and nivolumab with radiation in metastatic pancreatic and colorectal adenocarcinoma – Parikh A, et al

Key results

- In the MSS colon arm 13 patients and in the PDAC arm 8 patients discontinued prior to receiving radiotherapy

Outcome	MSS colon		PDAC	
	ITT (n=40)	mITT (n=27)	ITT (n=25)	mITT (n=17)
ORR, n (%)	4 (10)	4 (15)	3 (12)	3 (18)
DCR, n (%)	10 (25)	10 (37)	5 (20)	5 (29)
Discontinued due to toxicity, n (%)	4 (10)	1 (4)	1 (4)	1 (6)
DCR, months	2.4	2.5	2.5	2.7
Patients with CR/PR/SD	5.2	5.2	5.4	5.4
Patients without CR/PR/SD	2.0	2.4	2.1	2.5
OS, months	7.6	13.3	4.2	6.1
Patients with CR/PR/SD	15.8	15.8	12.4	12.4
Patients without CR/PR/SD	4.8	8.9	3.8	4.4

Parikh A, et al. Ann Oncol 2019;30(suppl):abstr O-008

O-008: Proof of concept of the abscopal effect in MSS GI cancers: A phase 2 study of ipilimumab and nivolumab with radiation in metastatic pancreatic and colorectal adenocarcinoma – Parikh A, et al

Key results (cont.)

Grade ≥3 AEs, n (%)			
MSS colon		**PDAC**	
Lymphocyte count decreased	10 (25.0)	Lymphocyte count decreased	5 (20.0)
Anaemia	5 (12.5)	Fatigue	2 (8.0)
Hyponatremia	4 (10.0)	Hyperglycaemia	2 (8.0)
Fatigue	4 (10.0)	Mucositis	2 (8.0)

Conclusion

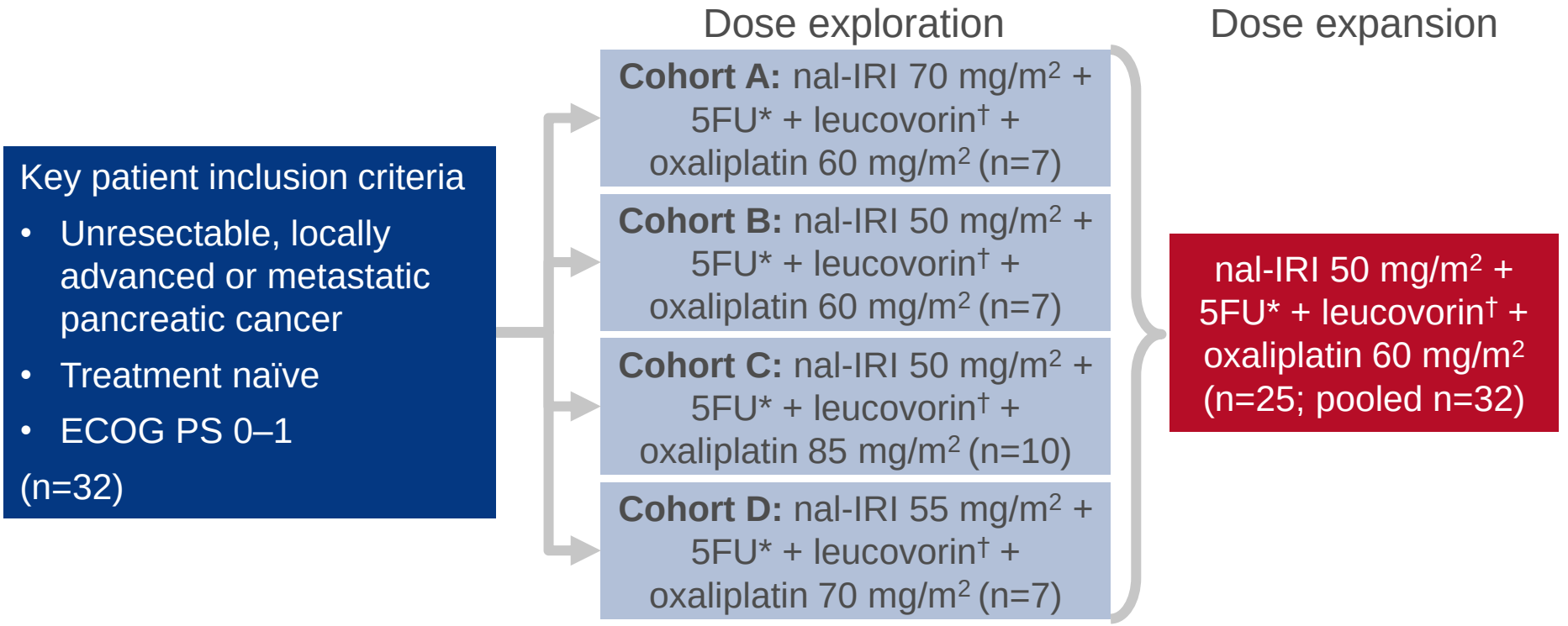
- **In patients with metastatic colorectal or pancreatic adenocarcinoma, combining nivolumab + ipilimumab with radiotherapy demonstrated some activity in certain subsets of patients**

Parikh A, et al. Ann Oncol 2019;30(suppl):abstr O-008

SO-005: A phase 1/2, open-label, dose-expansion study of liposomal irinotecan (nal-IRI) plus 5- fluorouracil/leucovorin (5-FU/LV) and oxaliplatin (OX) in patients with previously untreated metastatic pancreatic cancer (mPAC) – Wainberg Z, et al

Study objective

- To investigate the efficacy and safety of liposomal irinotecan (nal-IRI) + 5FU + leucovorin + oxaliplatin in patients with previously untreated metastatic pancreatic cancer



PRIMARY ENDPOINT

- Safety

SECONDARY ENDPOINTS

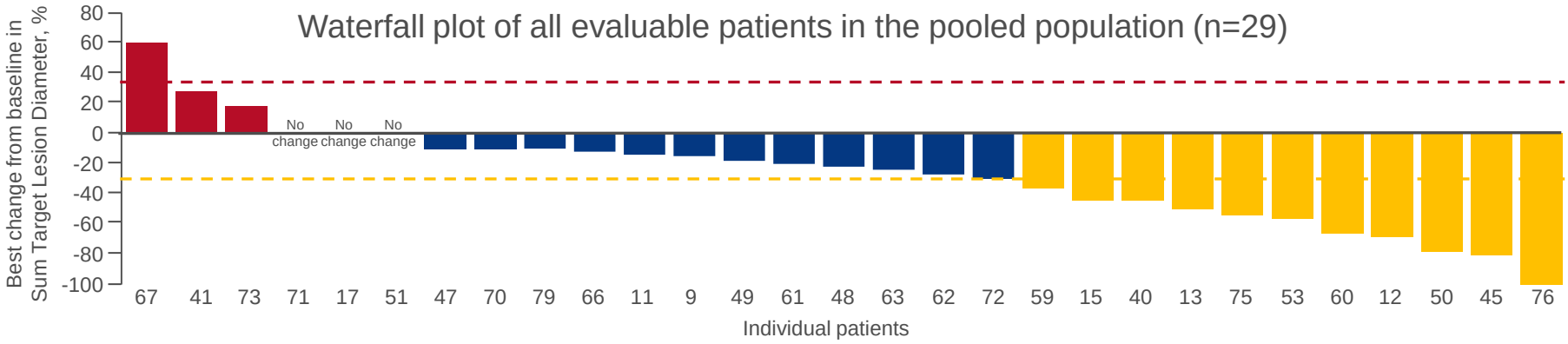
- ORR, DCR, BOR, PFS, OS

*2400 mg/m^2; †400 mg/m^2

Wainberg Z, et al. Ann Oncol 2019;30(suppl):abstr SO-005

SO-005: A phase 1/2, open-label, dose-expansion study of liposomal irinotecan (nal-IRI) plus 5- fluorouracil/leucovorin (5-FU/LV) and oxaliplatin (OX) in patients with previously untreated metastatic pancreatic cancer (mPAC) – Wainberg Z, et al

Key results



Response, n (%) [unless otherwise stated]	Dose expansion (n=25)	Pooled population (n=32)
BOR at any time (CR + PR + SD)	20 (80.0)	26 (81.3)
CR	1 (4.0)	1 (3.1)
PR	7 (28.0)	10 (31.3)
SD	12 (48.0)	15 (46.9)
DCR at Week 16, % (95%CI)	72.0 (50.6, 87.9)	71.9 (53.3, 86.3)
CR	1 (4.0)	1 (3.1)
PR	5 (20.0)	8 (25.0)
SD	12 (48.0)	14 (43.8)

Wainberg Z, et al. Ann Oncol 2019;30(suppl):abstr SO-005

SO-005: A phase 1/2, open-label, dose-expansion study of liposomal irinotecan (nal-IRI) plus 5- fluorouracil/leucovorin (5-FU/LV) and oxaliplatin (OX) in patients with previously untreated metastatic pancreatic cancer (mPAC) – Wainberg Z, et al

Key results (cont.)

Grade ≥3 TRAEs, n (%)	Dose-expansion (n=25)	Pooled population (n=32)
Any	16 (64.0)	20 (62.5)
Neutropenia	7 (28.0)	9 (28.1)
Febrile neutropenia	3 (12.0)	4 (12.5)
Anaemia	1 (4.0)	2 (6.3)
Diarrhoea	2 (8.0)	3 (9.4)
Vomiting	2 (8.0)	2 (6.3)
Nausea	3 (12.0)	3 (9.4)
Colitis	1 (4.0)	1 (3.1)
Hypokalemia	2 (8.0)	4 (12.5)
Decreased appetite	1 (4.0)	1 (3.1)

Conclusion

- **In patients with metastatic pancreatic cancer, the combination of nal-IRI + 5FU + leucovorin + oxaliplatin as a 1L treatment option demonstrated encouraging antitumor activity and had a manageable safety profile**

Wainberg Z, et al. Ann Oncol 2019;30(suppl):abstr SO-005

Cancers of the pancreas, small bowel and hepatobiliary tract

SMALL BOWEL

O-007: ZEBRA: An ACCRU/IRCI multicenter phase II study of pembrolizumab in patients with advanced small bowel adenocarcinoma (SBA) – Pedersen K, et al

Study objective

- To investigate the efficacy and safety of pembrolizumab in patients with advanced small bowel adenocarcinoma

Key patient inclusion criteria

- Advanced small bowel adenocarcinoma (duodenum, jejunum or ileum)
- >1 prior line of chemotherapy

(n=40)

→ Pembrolizumab 200 mg IV q3w (up to 35 cycles)

PRIMARY ENDPOINT

- ORR (RECIST v1.1)

SECONDARY ENDPOINTS

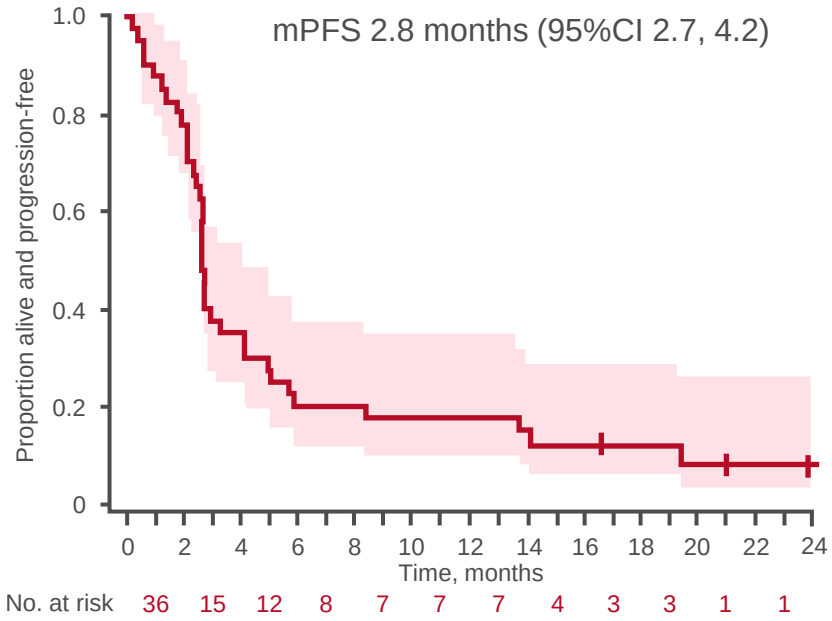
- PFS, OS, safety

Pedersen K, et al. Ann Oncol 2019;30(suppl):abstr O-007

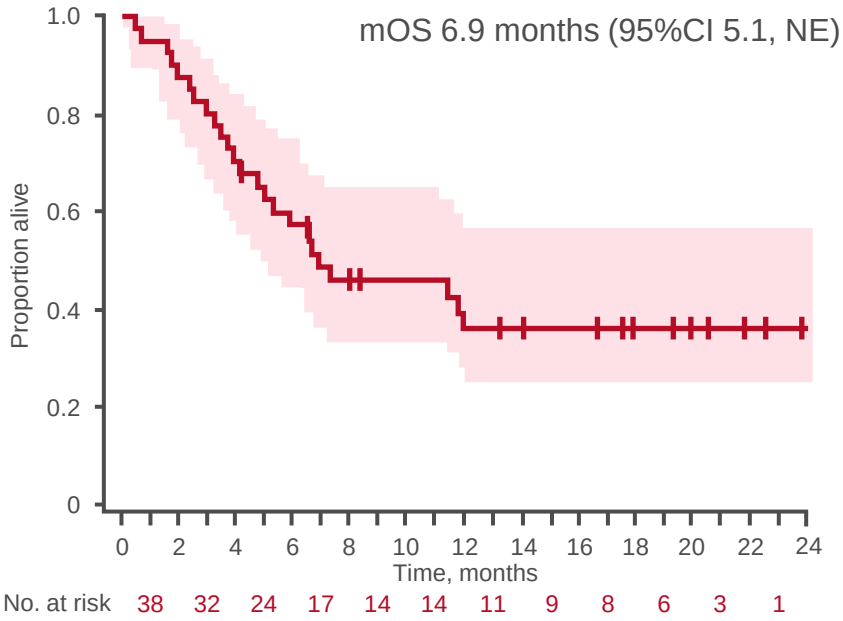
O-007: ZEBRA: An ACCRU/IRCI multicenter phase II study of pembrolizumab in patients with advanced small bowel adenocarcinoma (SBA) – Pedersen K, et al

Key results

PFS



OS



Pedersen K, et al. Ann Oncol 2019;30(suppl):abstr O-007

O-007: ZEBRA: An ACCRU/IRCI multicenter phase II study of pembrolizumab in patients with advanced small bowel adenocarcinoma (SBA) – Pedersen K, et al

Key results (cont.)

Response, n (%)	n=40
Confirmed ORR, n (%) [95%CI]	3 (8) [2, 20]
Unconfirmed ORR	1 (3)
CR	0
PR	4 (10)
SD	11 (28)
PD	19 (48)
NE	5 (13)
DCR	15 (38)

Grade 3–5 AEs, occurring in ≥5%, %	n=40
Alkaline phosphatase increased	13
AST increased	5
Hyperbilirubinemia	10
Abdominal pain	8
Sepsis	8
Disease progression	8
Anaemia	5

Conclusion

- **In patients with advanced small bowel adenocarcinoma, pembrolizumab failed to meet the pre-specified primary endpoint of an ORR of 20%**

Pedersen K, et al. Ann Oncol 2019;30(suppl):abstr O-007

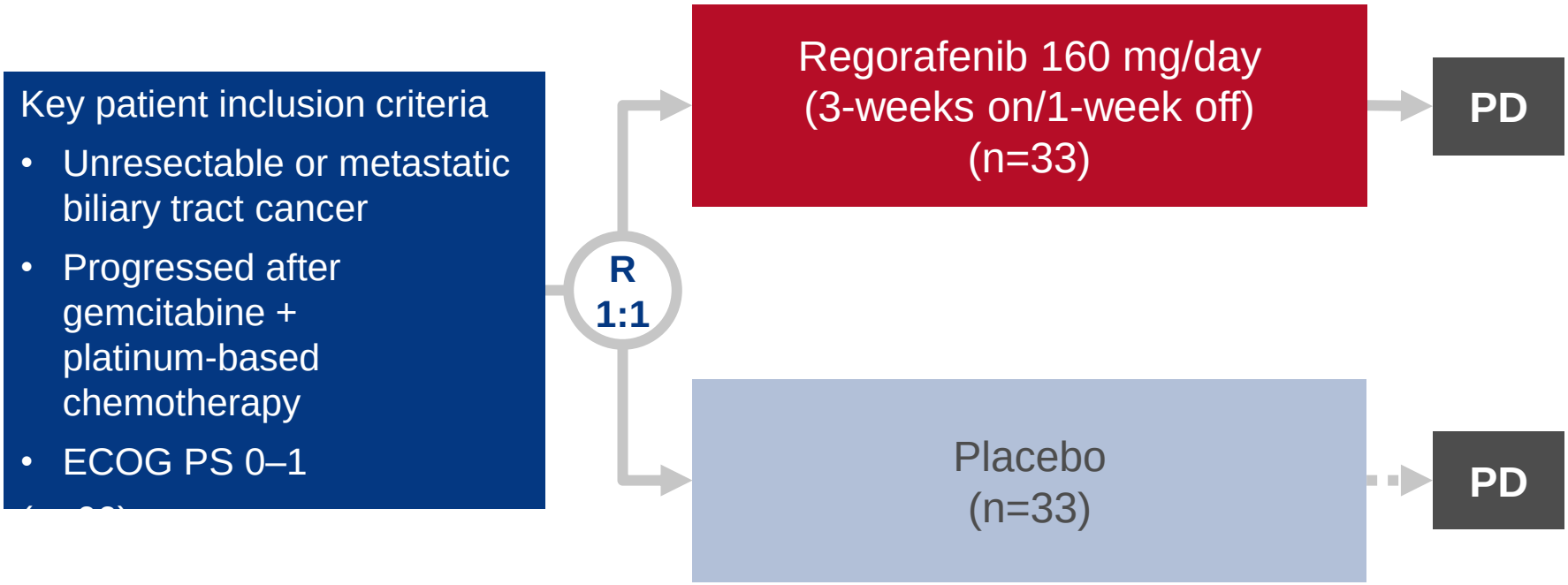
Cancers of the pancreas, small bowel and hepatobiliary tract

BILIARY TRACT CANCER

O-003: Exploratory analysis based on tumor location of REACHIN, a randomized double-blinded placebo-controlled phase II trial of regorafenib after failure of gemcitabine and platinum-based chemotherapy for advanced/metastatic biliary tract tumors – Demols A, et al

Study objective

- To investigate the efficacy and safety of regorafenib after failure of gemcitabine and platinum-based chemotherapy in patients with biliary tract tumours



PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

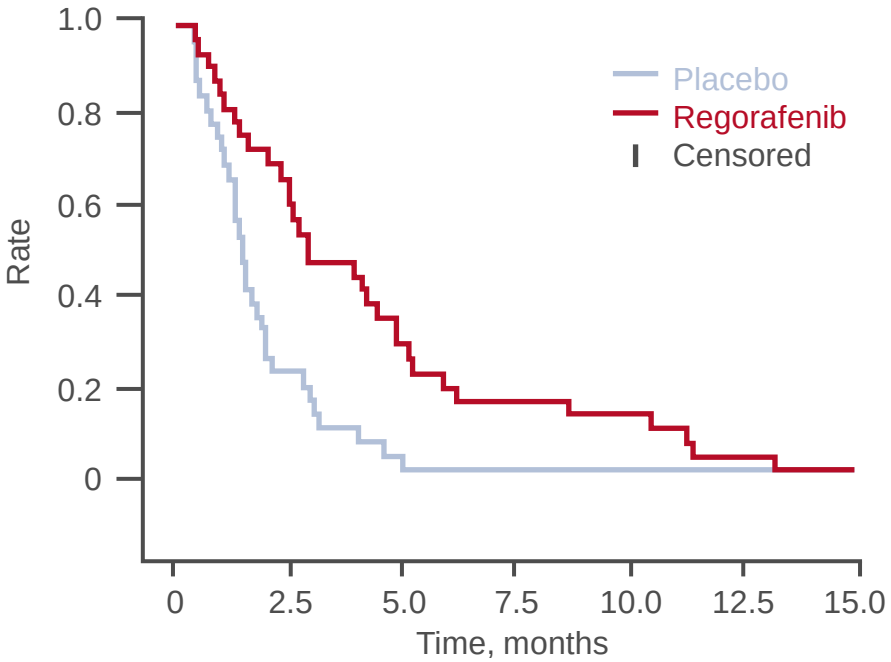
- Response rate, OS, safety

Demols A, et al. Ann Oncol 2019;30(suppl):abstr O-003

O-003: Exploratory analysis based on tumor location of REACHIN, a randomized double-blinded placebo-controlled phase II trial of regorafenib after failure of gemcitabine and platinum-based chemotherapy for advanced/metastatic biliary tract tumors – Demols A, et al

Key results

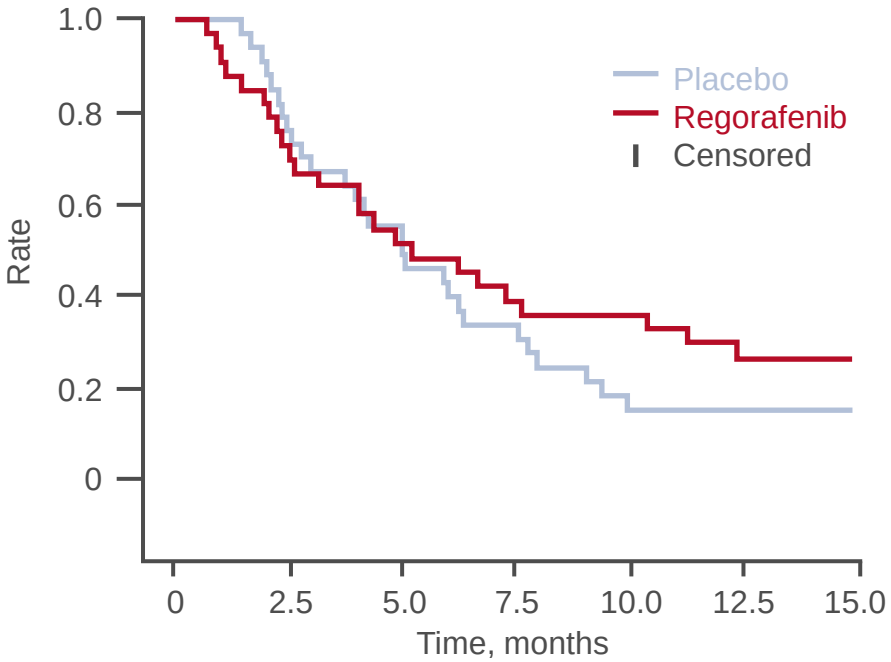
PFS



No. at risk							
Placebo	33	8	2	1	1	1	1
Regorafenib	33	22	10	6	5	2	1

mPFS 3.0 vs. 1.5 months
HR 0.49 (95%CI 0.29, 0.81); p=0.004

OS



Placebo	33	25	18	11	6	4	3
Regorafenib	33	24	17	13	12	8	7

mOS 5.3 vs. 5.1 months
HR 0.77 (95%CI 0.45, 1.31); p=0.28

Demols A, et al. Ann Oncol 2019;30(suppl):abstr O-003

O-003: Exploratory analysis based on tumor location of REACHIN, a randomized double-blinded placebo-controlled phase II trial of regorafenib after failure of gemcitabine and platinum-based chemotherapy for advanced/metastatic biliary tract tumors – Demols A, et al

Key results (cont.)

Grade ≥3 AEs, n	Regorafenib + BSC (n=33)	Placebo + BSC (n=33)
Nausea/vomiting	2 (G4, n=1)	2
Fatigue	6	3
Diarrhoea/constipation	1	0
Hypophosphatemia	1	0
Cutaneous toxicity/mucositis	2 (G4, n=1)	0
Anorexia	1	1

Conclusions

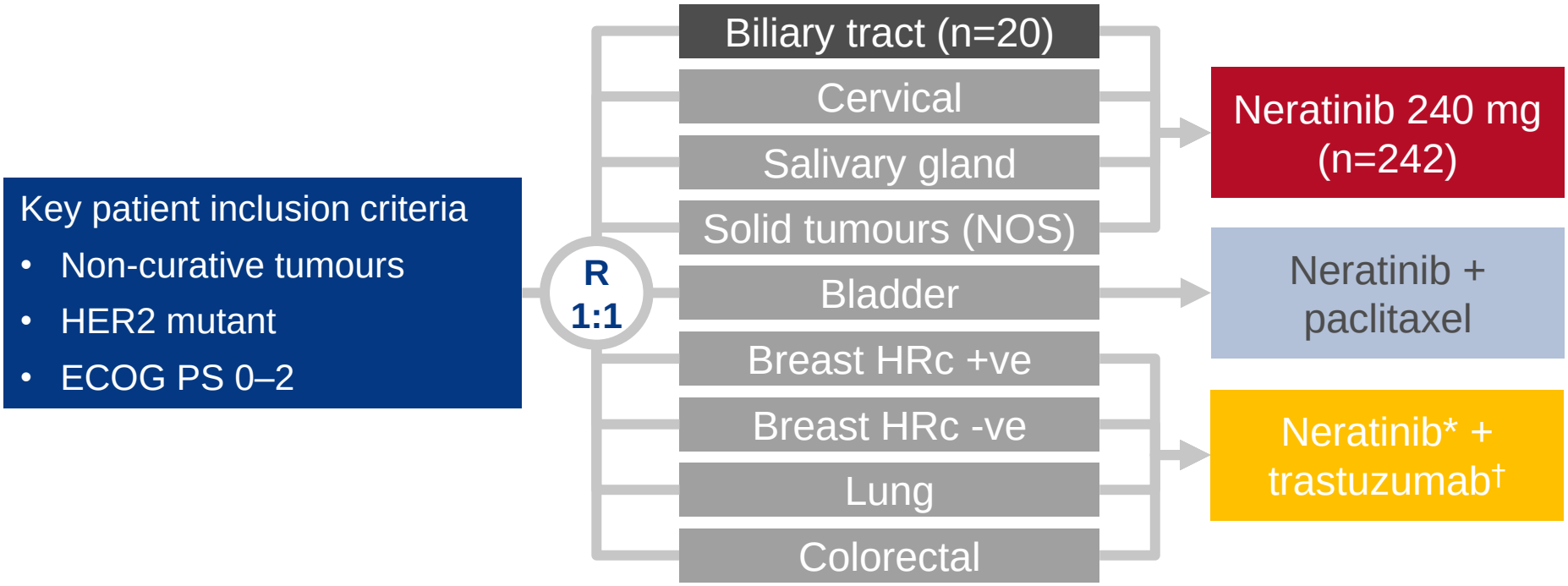
- **In previously treated patients with unresectable or advanced biliary tract cancer, regorafenib demonstrated a significant improvement in PFS, but not OS**
- **Regorafenib had a manageable safety profile**

Demols A, et al. Ann Oncol 2019;30(suppl):abstr O-003

O-005: Treating HER2-mutant advanced biliary tract cancer with neratinib: benefits of HER2-directed targeted therapy in the phase 2 SUMMIT 'basket' trial – Harding J, et al

Study objective

- To investigate the efficacy and safety of neratinib in patients with biliary tract cancer in the SUMMIT basket trial



PRIMARY ENDPOINT

- ORR

SECONDARY ENDPOINTS

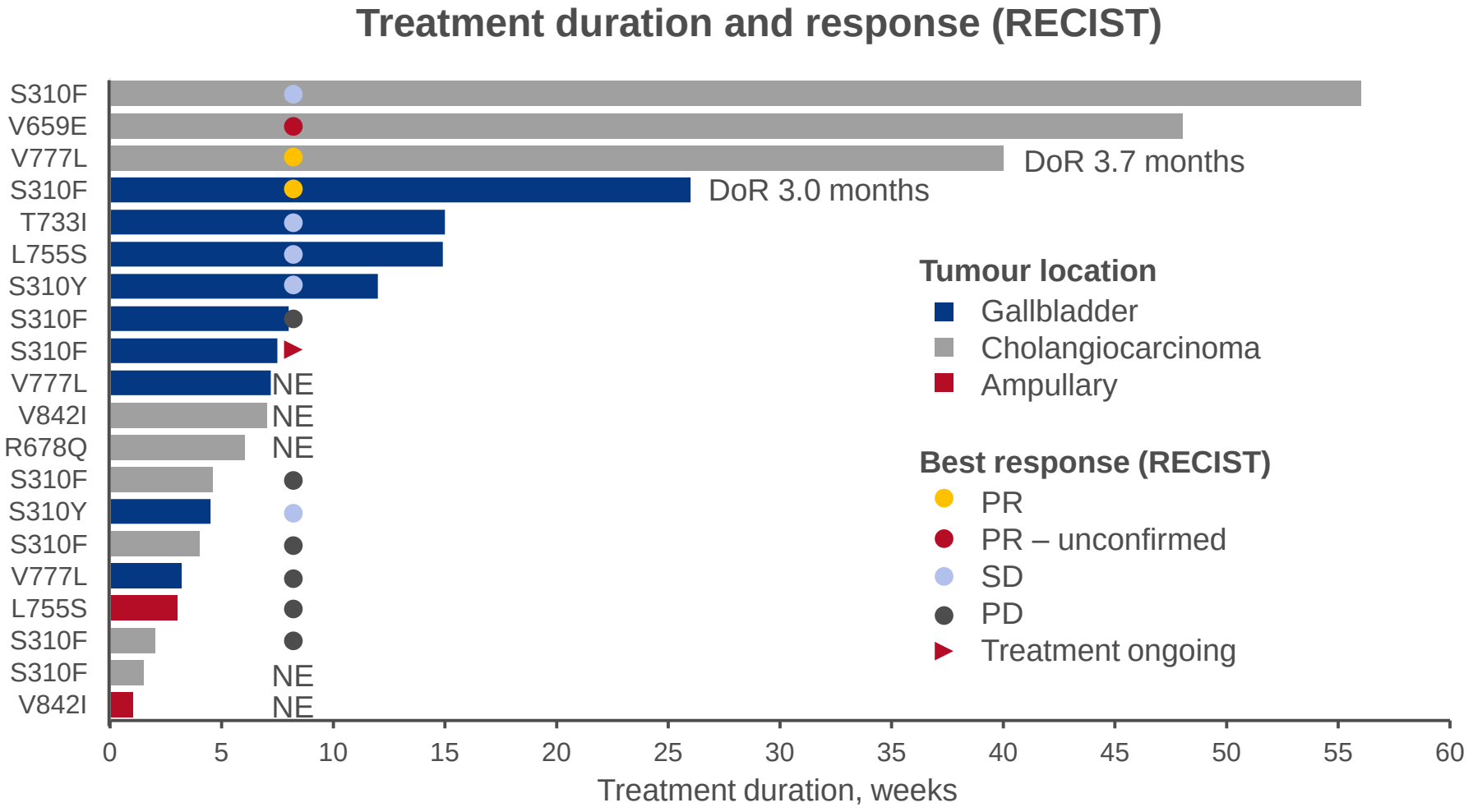
- CBR, PFS, safety

*Plus fulvestrant for HRc +ve breast cancer; †biosimilar if available

Harding J, et al. Ann Oncol 2019;30(suppl):abstr O-005

O-005: Treating HER2-mutant advanced biliary tract cancer with neratinib: benefits of HER2-directed targeted therapy in the phase 2 SUMMIT 'basket' trial – Harding J, et al

Key results



Harding J, et al. Ann Oncol 2019;30(suppl):abstr O-005

O-005: Treating HER2-mutant advanced biliary tract cancer with neratinib: benefits of HER2-directed targeted therapy in the phase 2 SUMMIT 'basket' trial – Harding J, et al

Key results (cont.)

Grade 3/4 AEs, n (%)	HER2-mutant biliary tract cancer (n=20)	HER2-mutant monotherapy (n=242)
Vomiting	1 (5.0)	7 (2.9)
Diarrhoea	4 (20.0)*	45 (18.6)
Abdominal pain	2 (10.0)	10 (4.1)
Ascites	1 (5.0)	2 (0.8)
Asthenia	1 (5.0)	2 (0.8)
Dehydration	2 (10.0)	10 (4.1)

Conclusion

- **In patients with HER2-mutant biliary tract cancers, neratinib demonstrated antitumor activity particularly in those with cholangiocarcinoma and gallbladder cancer and was generally well tolerated**

*No grade 4 events reported

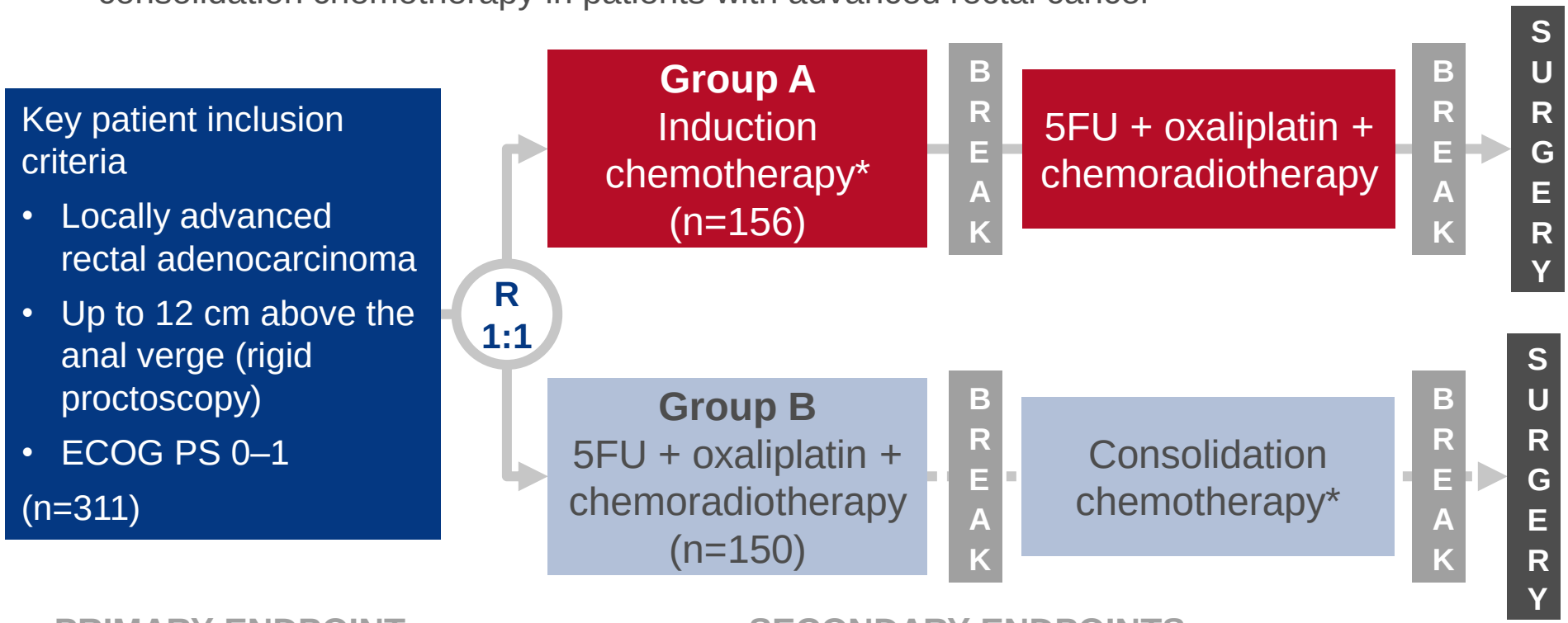
Harding J, et al. Ann Oncol 2019;30(suppl):abstr O-005

CANCERS OF THE COLON, RECTUM AND ANUS

O-011: Randomized phase II trial of chemoradiotherapy plus induction or consolidation chemotherapy as total neoadjuvant therapy for locally advanced rectal cancer: CAO/ARO/AIO-12 – Hofheinz R-D, et al

Study objective

- To investigate the efficacy and safety of neoadjuvant chemoradiotherapy + induction consolidation chemotherapy in patients with advanced rectal cancer



PRIMARY ENDPOINT

- pCR

SECONDARY ENDPOINTS

- Pathological staging, R0 rates, recurrence, OS, safety

*FOLFOX (3 cycles)

Hofheinz R-D, et al. Ann Oncol 2019;30(suppl):abstr O-011

O-011: Randomized phase II trial of chemoradiotherapy plus induction or consolidation chemotherapy as total neoadjuvant therapy for locally advanced rectal cancer: CAO/ARO/AIO-12 – Hofheinz R-D, et al

Key results

Pathology, %	Group A (n=142)	Group B (n=142)
Abdominoperineal resection	28	23
R0 resection	92	90
CRM ≤1 mm	10	7
pCR* (ITT, n=306)	17 p=0.210	25 p=0.0002
pCR + confirmed CR	21	28
TRG4	20	27
NAR score Low Intermediate High	 26 50 23	 35 44 18

Postoperative morbidity, %	Group A (n=142)	Group B (n=142)
Clavien-Dindo classification None Grade 1–2 Grade 3–5 Missing	 54 25 17 4	 66 18 16 1
NCI classification Grade 1–2 Grade 3–5	 38 18	 32 18
Death within 60 days of surgery	1	1

*For the statistical analysis: each group vs. 15% expected after standard chemoradiotherapy

Hofheinz R-D, et al. Ann Oncol 2019;30(suppl):abstr O-011

O-011: Randomized phase II trial of chemoradiotherapy plus induction or consolidation chemotherapy as total neoadjuvant therapy for locally advanced rectal cancer: CAO/ARO/AIO-12 – Hofheinz R-D, et al

Key results (cont.)

Toxicity, %	Group A (n=156)				Group B (n=150)			
	G1–2	G3	G4	G5	G1–2	G3	G4	G5
Chemoradiotherapy	62	34	3	1	72	24	3	1
Chemotherapy	75	21	1	0	80	18	4	0

Conclusion

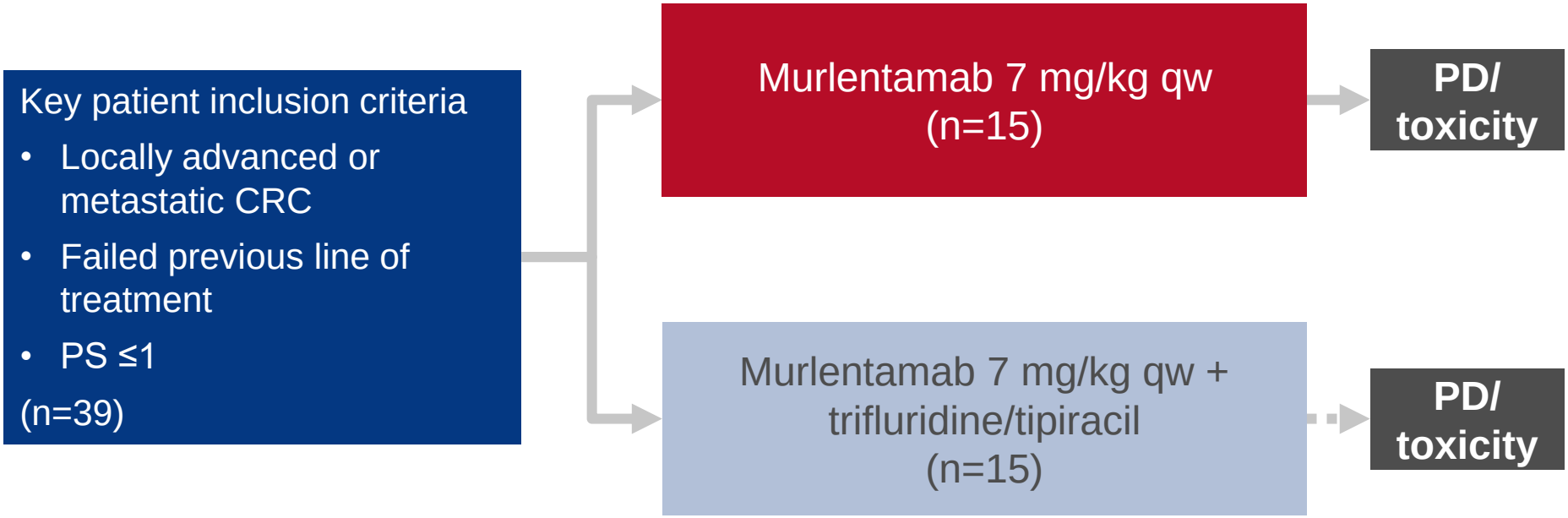
- **In patients with locally advanced rectal cancer, using chemoradiotherapy followed by consolidation chemotherapy demonstrated a reduction in chemoradiotherapy toxicity and was not associated with any increases in surgical morbidity**

Hofheinz R-D, et al. Ann Oncol 2019;30(suppl):abstr O-011

LBA-004: Phase 2 study results of murlentamab, a monoclonal antibody targeting the anti-Mullerian-hormone-receptor II (AMHRII), acting through tumor associated macrophage engagement in advanced/metastatic colorectal cancers – Van Cutsem E, et al

Study objective

- To investigate the efficacy and safety of murlentamab, a mAb targeting anti-Müllerian hormone receptor, in patients with locally advanced or metastatic CRC



PRIMARY ENDPOINT

- ORR

SECONDARY ENDPOINTS

- PFS, pharmacodynamics, safety

Van Cutsem E, et al. Ann Oncol 2019;30(suppl):abstr LBA-004

LBA-004: Phase 2 study results of murlentamab, a monoclonal antibody targeting the anti-Mullerian-hormone-receptor II (AMHRII), acting through tumor associated macrophage engagement in advanced/metastatic colorectal cancers – Van Cutsem E, et al

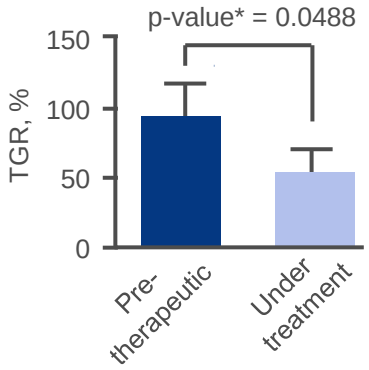
Key results

Response, % (n/N)	Murlentamab	Murlentamab + trifluridine/tipiracil
ORR	0	0
SD		
At 2 months	21.4 (3/14)	53.3 (8/15)
At 4 months	7.1 (1/14)	40.0 (6/15)
At 6 months		30.8 (4/13)
At 8 months		8.3 (1/12)

Tumour growth rate (TGR)

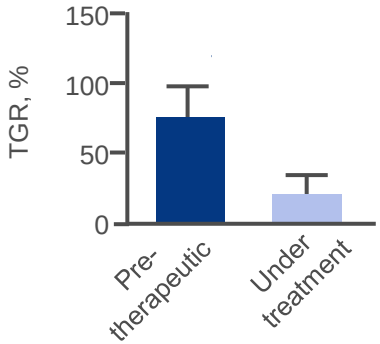
Murlentamab

1.7-fold TGR decrease



Murlentamab + trifluridine/tipiracil

3.6-fold TGR decrease



*Wilcoxon matched-pairs nonparametric test, one-sided, α=5%

Van Cutsem E, et al. Ann Oncol 2019;30(suppl):abstr LBA-004

LBA-004: Phase 2 study results of murlentamab, a monoclonal antibody targeting the anti-Mullerian-hormone-receptor II (AMHRII), acting through tumor associated macrophage engagement in advanced/metastatic colorectal cancers – Van Cutsem E, et al

Key results (cont.)

- In 5/7 and 7/10 paired biopsies, increases were observed in granzymeB/CD16 and CD86, respectively
- Increases in CD86 and CD8 staining in 2 patients receiving the combination treatment for ≥4 months reflected early macrophage activation and T cell activation, respectively
- Increases were also observed in CD64+ and CD69+ reflecting neutrophil and monocyte activation, respectively, while there were decreases in the number of CD16+ receptors indicative of NK cell engagement and long-term decreases in CD69 in Treg population
- The most common AEs included decreased appetite (9 events), vomiting, nausea, constipation and asthenia (3 events each)

Conclusion

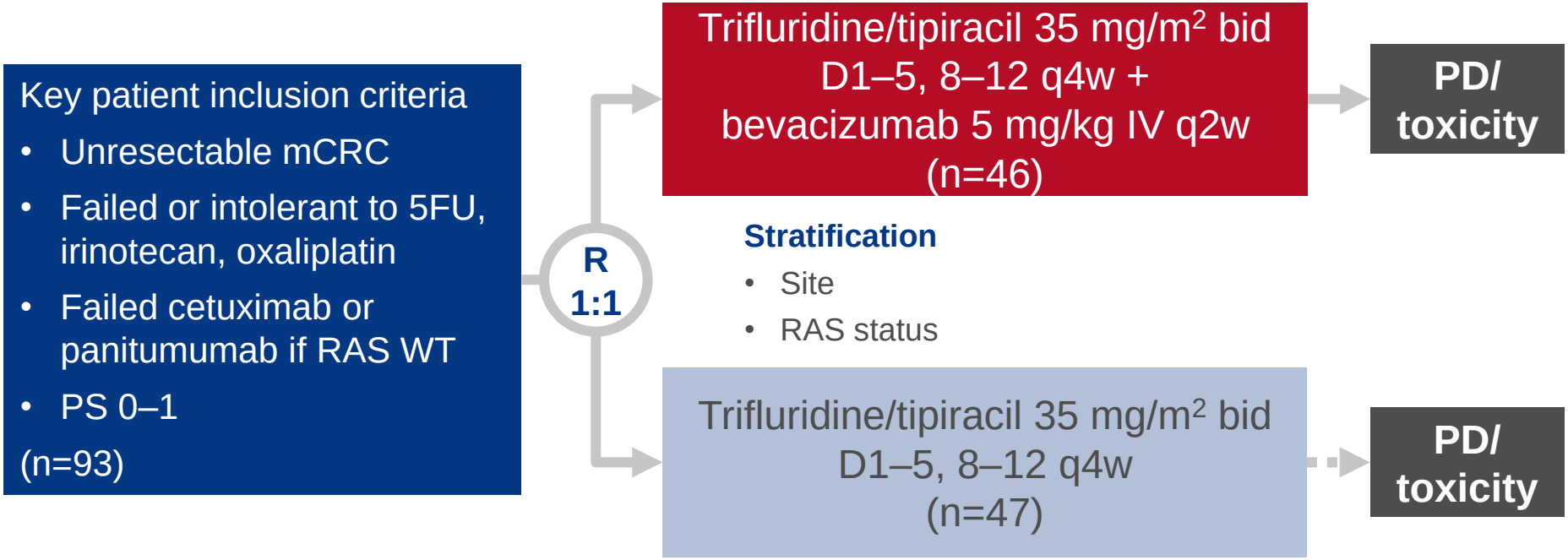
- **In patients with locally advanced or metastatic CRC, murlentamab + trifluridine/tipiracil provided disease stabilisation and reduced tumour growth rates**

Van Cutsem E, et al. Ann Oncol 2019;30(suppl):abstr LBA-004

O-014: Bevacizumab improves efficacy of trifluridine/tipiracil (TAS-102) in patients with chemorefractory metastatic colorectal cancer (mCRC). A Danish randomized trial – Pfeiffer P, et al

Study objective

- To investigate the efficacy and safety of trifluridine/tipiracil combined with bevacizumab in patients with chemorefractory mCRC



PRIMARY ENDPOINT

- PFS

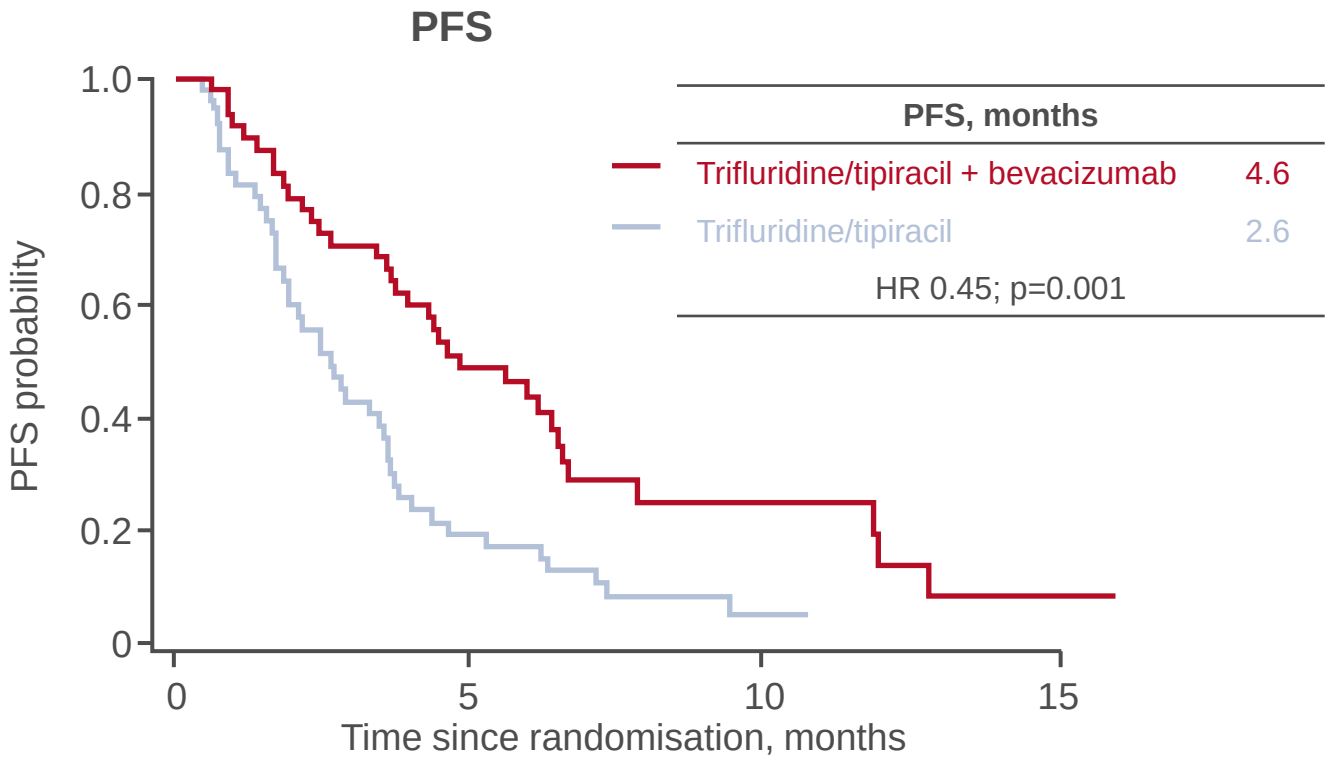
SECONDARY ENDPOINTS

- OS, safety

Pfeiffer P, et al. Ann Oncol 2019;30(suppl):abstr O-014

O-014: Bevacizumab improves efficacy of trifluridine/tipiracil (TAS-102) in patients with chemorefractory metastatic colorectal cancer (mCRC). A Danish randomized trial – Pfeiffer P, et al

Key results

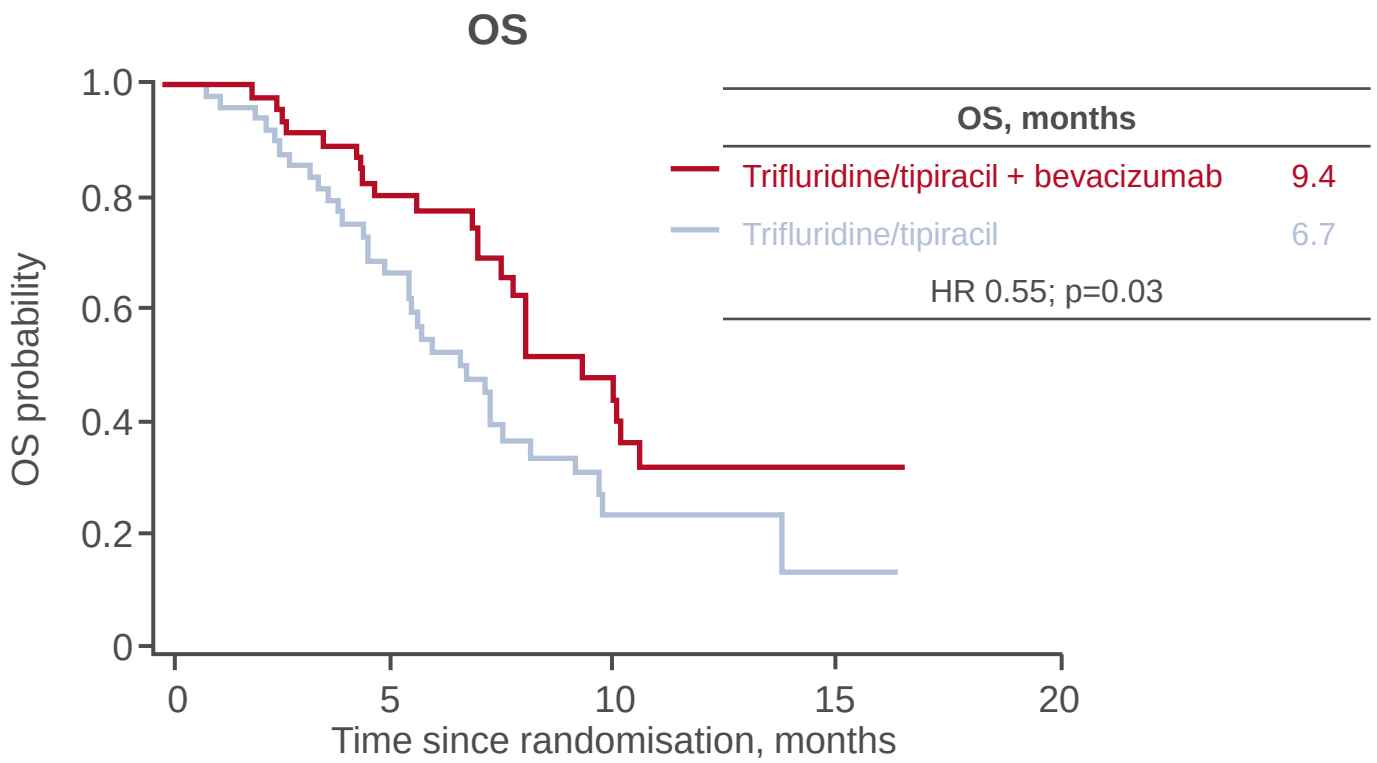


No. at risk							
Trifluridine/tipiracil	47	(38)	8	(6)	1	(0)	0
Trifluridine/tipiracil + bevacizumab	46	(24)	20	(8)	5	(3)	1

Pfeiffer P, et al. Ann Oncol 2019;30(suppl):abstr O-014

O-014: Bevacizumab improves efficacy of trifluridine/tipiracil (TAS-102) in patients with chemorefractory metastatic colorectal cancer (mCRC). A Danish randomized trial – Pfeiffer P, et al

Key results (cont.)



No. at risk									
Trifluridine/tipiracil	47	(16)	29	(16)	6	(1)	1	(0)	0
Trifluridine/tipiracil + bevacizumab	46	(9)	34	(10)	12	(4)	2	(0)	0

Pfeiffer P, et al. Ann Oncol 2019;30(suppl):abstr O-014

O-014: Bevacizumab improves efficacy of trifluridine/tipiracil (TAS-102) in patients with chemorefractory metastatic colorectal cancer (mCRC). A Danish randomized trial – Pfeiffer P, et al

Key results (cont.)

Grade 3–4 AEs occurring in ≥5%, n (%)	Trifluridine/tipiracil + bevacizumab	Trifluridine/tipiracil
Neutropenia	31 (67)	18 (38)
Anaemia	2 (4)	8 (17)
Nausea	1 (2)	3 (6)
Diarrhoea	4 (9)	0 (0)
Fatigue	3 (7)	5 (11)
Febrile neutropenia	3 (7)	1 (2)

Conclusion

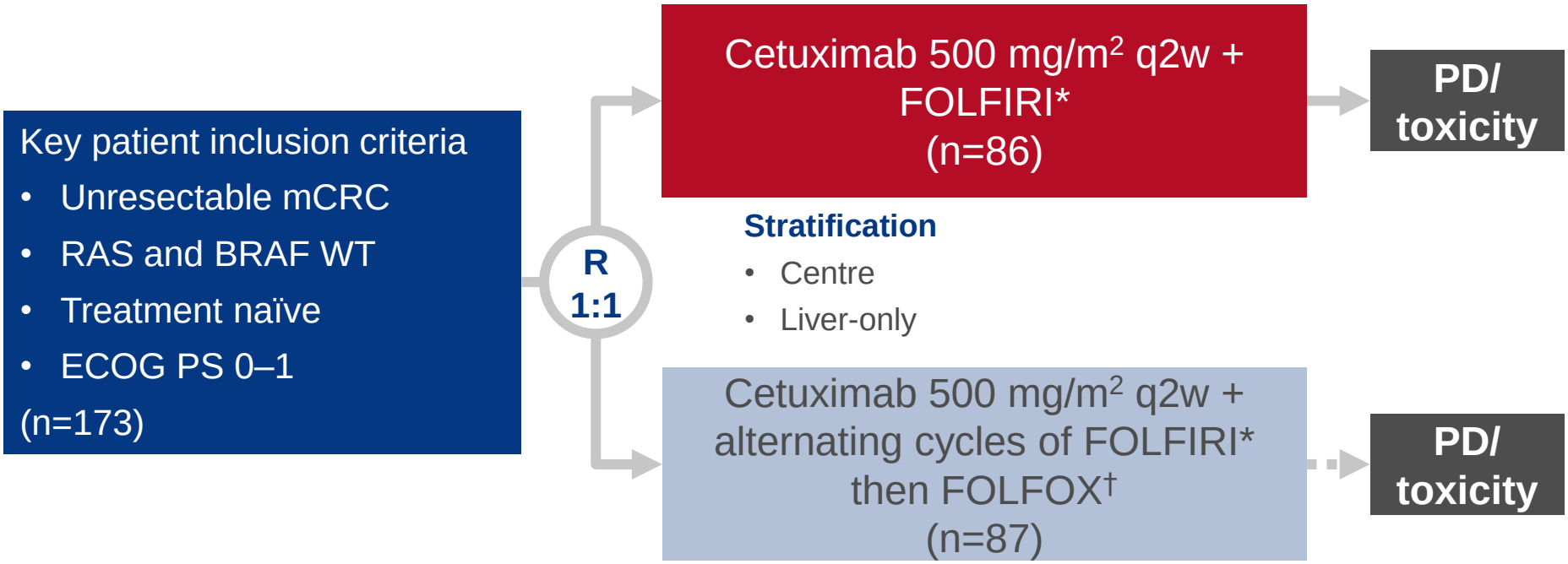
- **In patients with mCRC, the addition of bevacizumab to trifluridine/tipiracil demonstrated significant improvements in survival regardless of prior bevacizumab treatment**

Pfeiffer P, et al. Ann Oncol 2019;30(suppl):abstr O-014

O-015: Randomised trial of cetuximab every 2 weeks with FOLFIRI or cetuximab with alternating FOLFIRI/FOLFOX in patients with RAS and BRAF wild type metastatic colorectal cancer: Nordic 8 results – Pfeiffer P, et al

Study objective

- To investigate the efficacy and safety of cetuximab with FOLFIRI or alternating cycles of FOLFIRI then FOLFOX in patients with unresectable mCRC



PRIMARY ENDPOINT

- Response rate

SECONDARY ENDPOINTS

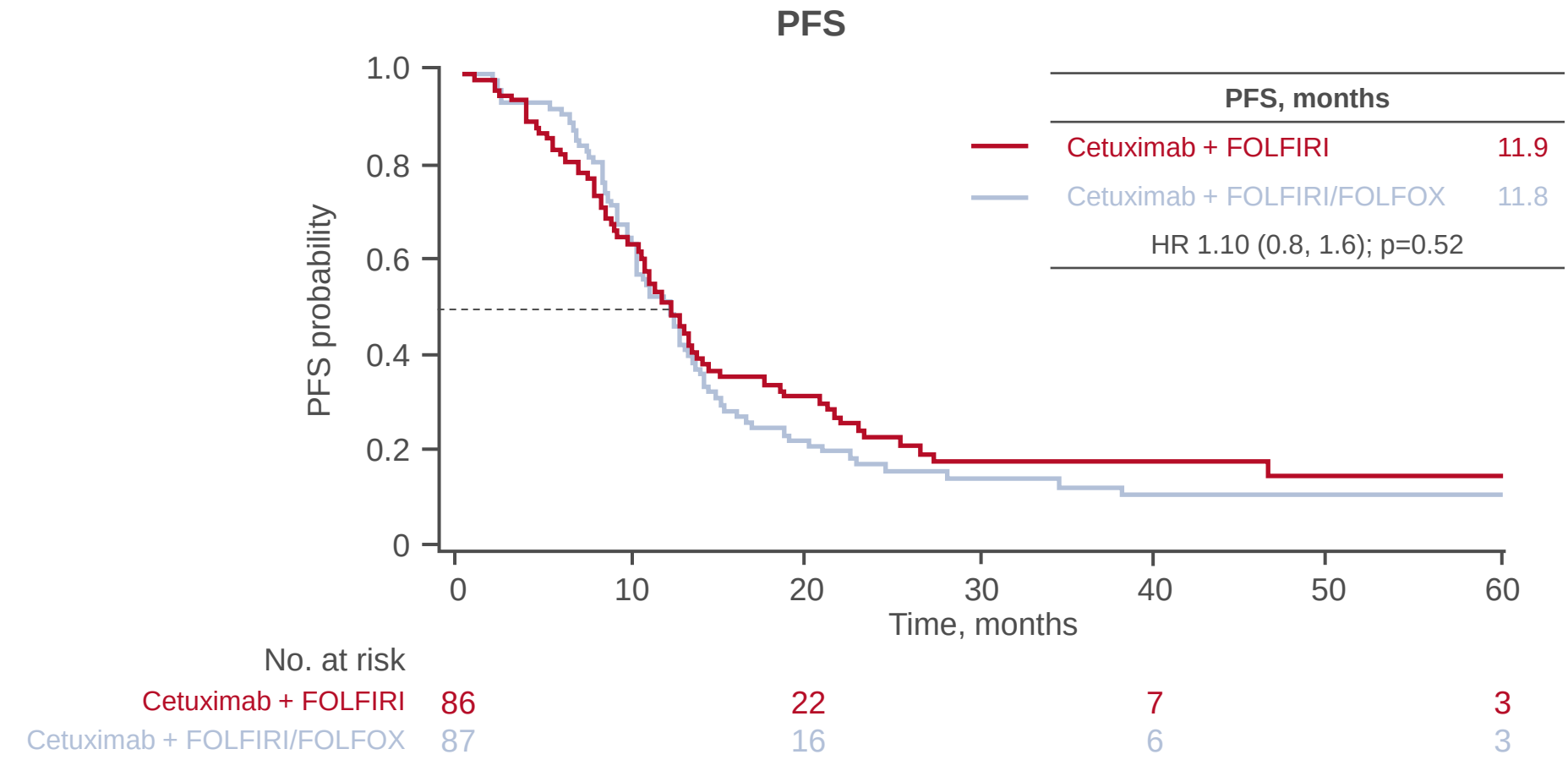
- PFS, OS, safety

*Folinic acid 400 mg/m², 5FU 400 mg/m² bolus then 2400 mg/m², irinotecan 180 mg/m²; †folinic acid 400 mg/m², 5FU 400 mg/m² bolus then 2400 mg/m², oxaliplatin 85 mg/m²

Pfeiffer P, et al. Ann Oncol 2019;30(suppl):abstr O-015

O-015: Randomised trial of cetuximab every 2 weeks with FOLFIRI or cetuximab with alternating FOLFIRI/FOLFOX in patients with RAS and BRAF wild type metastatic colorectal cancer: Nordic 8 results – Pfeiffer P, et al

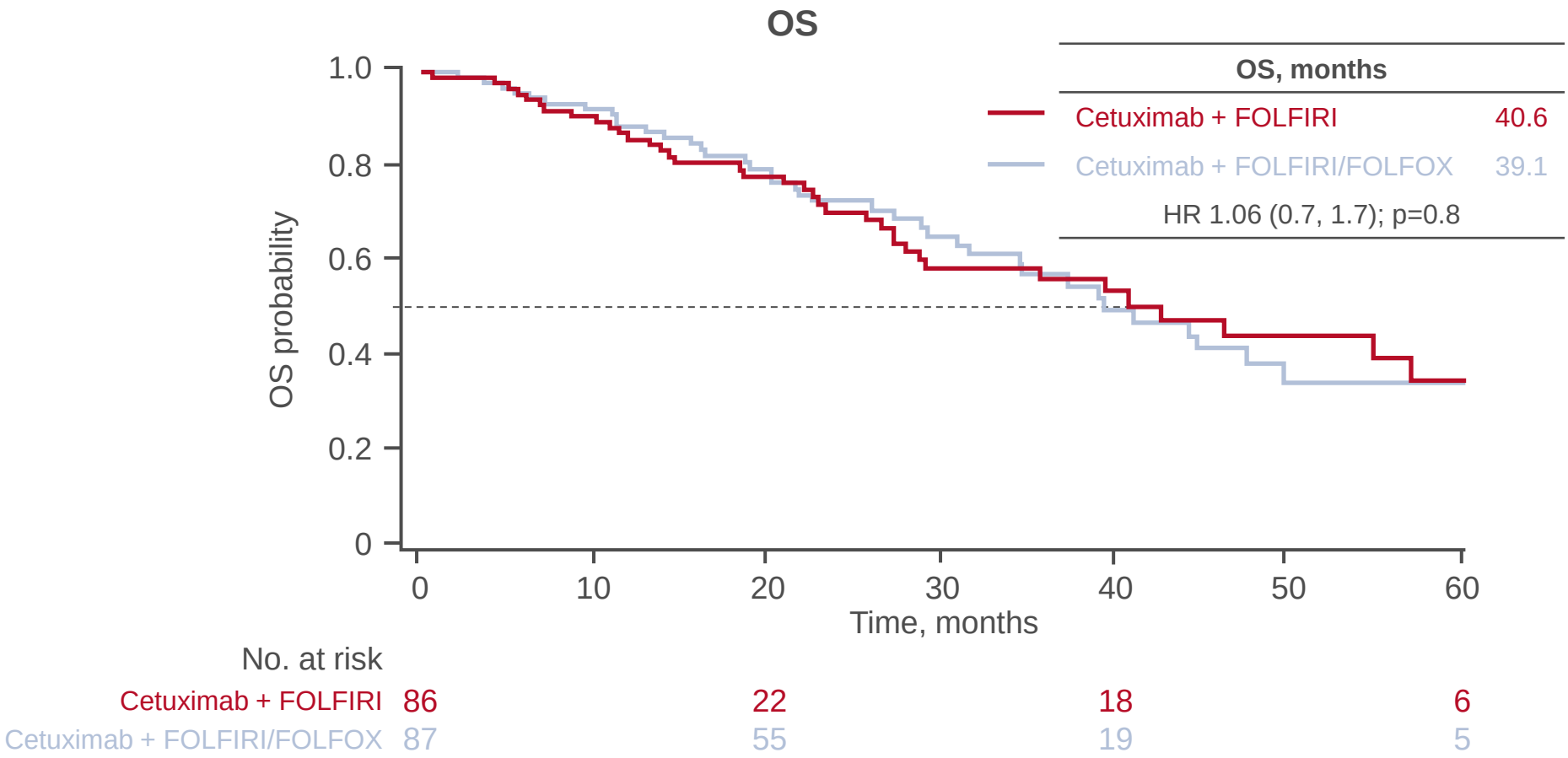
Key results



Pfeiffer P, et al. Ann Oncol 2019;30(suppl):abstr O-015

O-015: Randomised trial of cetuximab every 2 weeks with FOLFIRI or cetuximab with alternating FOLFIRI/FOLFOX in patients with RAS and BRAF wild type metastatic colorectal cancer: Nordic 8 results – Pfeiffer P, et al

Key results (cont.)

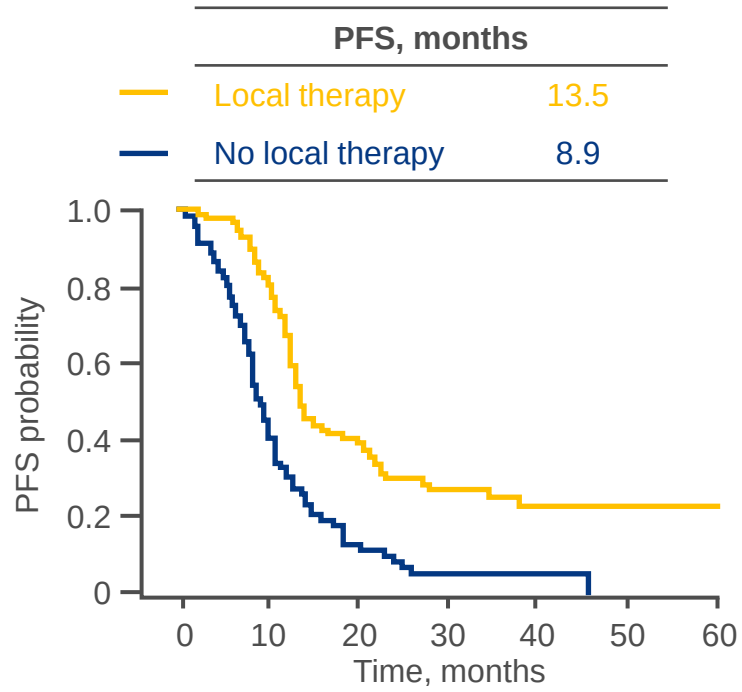


Pfeiffer P, et al. Ann Oncol 2019;30(suppl):abstr O-015

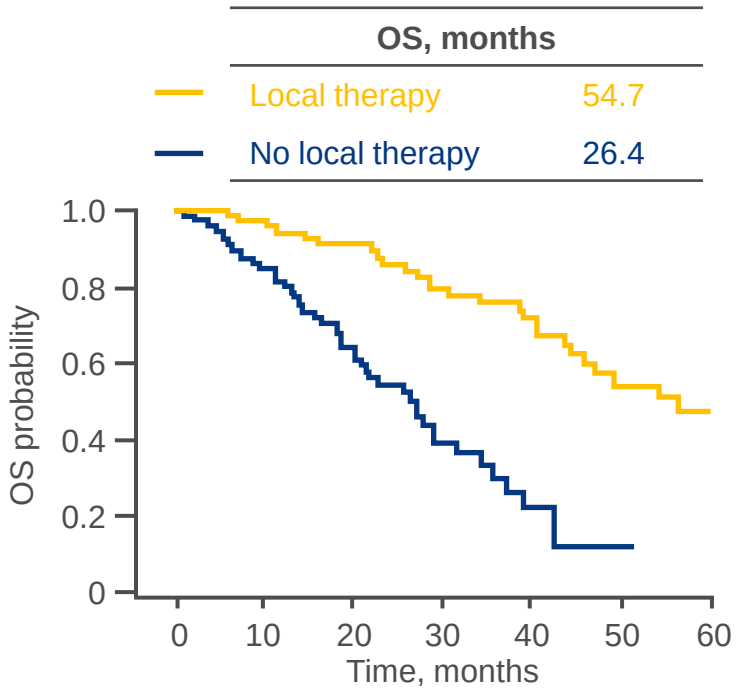
O-015: Randomised trial of cetuximab every 2 weeks with FOLFIRI or cetuximab with alternating FOLFIRI/FOLFOX in patients with RAS and BRAF wild type metastatic colorectal cancer: Nordic 8 results – Pfeiffer P, et al

Key results (cont.)

Local therapy, PFS and OS



No. at risk				
No local therapy	86	8	2	0
Local therapy	87	30	11	6



No. at risk				
No local therapy	86	39	5	0
Local therapy	87	68	32	11

Pfeiffer P, et al. Ann Oncol 2019;30(suppl):abstr O-015

O-015: Randomised trial of cetuximab every 2 weeks with FOLFIRI or cetuximab with alternating FOLFIRI/FOLFOX in patients with RAS and BRAF wild type metastatic colorectal cancer: Nordic 8 results – Pfeiffer P, et al

Key results (cont.)

Response, n (%)	Cetuximab + FOLFIRI (n=86)	Cetuximab + FOLFIRI/ FOLFOX (n=87)
Response rate	59 (68)	68 (78)
CR	2 (2)	2 (2)
PR	57 (66)	66 (76)
SD	21 (25)	12 (14)
PD	4 (5)	3 (3)
NE	2 (2)	4 (5)

Grade ≥3 AEs occurring in ≥5%, n (%)	Cetuximab + FOLFIRI (n=86)	Cetuximab + FOLFIRI/ FOLFOX (n=87)
Neutrophil count ↓	13 (15)	15 (17)
Nausea	1 (1)	5 (6)
Diarrhoea	6 (7)	10 (11)
Fatigue	6 (7)	6 (7)
Skin rash	8 (9)	13 (15)

Conclusions

- **In patients with RAS and BRAF WT mCRC, there were no survival differences between using cetuximab + FOLFIRI or cetuximab with alternating FOLFIRI/FOLFOX**
- **Both treatment regimens were well tolerated**
- **In clinical practice, the use of cetuximab with alternating FOLFIRI/FOLFOX is not recommended**

Pfeiffer P, et al. Ann Oncol 2019;30(suppl):abstr O-015

O-016: Serial assessment of cell-free circulating tumor DNA (ctDNA) to assess treatment effect and minimal residual disease during neoadjuvant and adjuvant therapy in colorectal cancer – Parikh A, et al

Study objective

- To investigate whether ctDNA can be used to assess outcomes in patients with colorectal cancer receiving neoadjuvant and adjuvant therapy

Methods

- Patients with resectable colon cancer (n=43) who received neoadjuvant therapy followed by surgery (n=42) then adjuvant therapy (n=16) had serial plasma samples collected approximately 1 month after the completion of each intervention to be analysed for ctDNA
- Patients were grouped into those with persistent ctDNA (defined as ctDNA detected following completion of therapy), cleared ctDNA (defined as ctDNA detected followed by not detected after completion of therapy) and negative ctDNA (ctDNA not detected at any timepoint)

Parikh A, et al. Ann Oncol 2019;30(suppl):abstr O-016

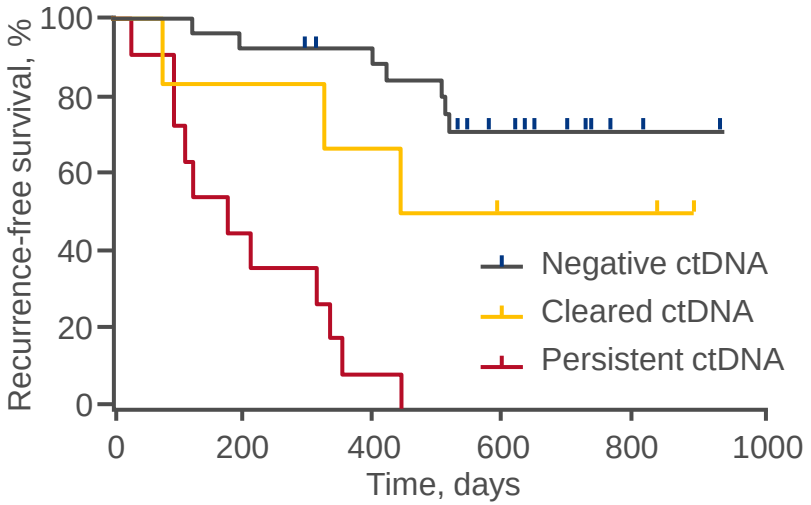
O-016: Serial assessment of cell-free circulating tumor DNA (ctDNA) to assess treatment effect and minimal residual disease during neoadjuvant and adjuvant therapy in colorectal cancer – Parikh A, et al

Key results

ctDNA persistence following therapeutic intervention

	Recurred	Recurrence free	Median time to recurrence, days
Persistent ctDNA	11	0	182
Cleared ctDNA	3	3	333
Negative ctDNA	7	19	NR*

*Median follow-up: 580 days



Conclusions

- In patients with CRC, disease recurrence is more likely to occur earlier in those who have persistent detection of ctDNA after completing therapy
- ctDNA status may help to understand which patients will require additional treatment

Parikh A, et al. Ann Oncol 2019;30(suppl):abstr O-016

O-018: Microsatellite instability and survival after adjuvant chemotherapy among stage II and III colon cancer patients: results from a population-based study – Alwers E, et al

Study objective

- To investigate the association between MSI and survival in patients with stage II and II colon cancer after adjuvant chemotherapy

Methods

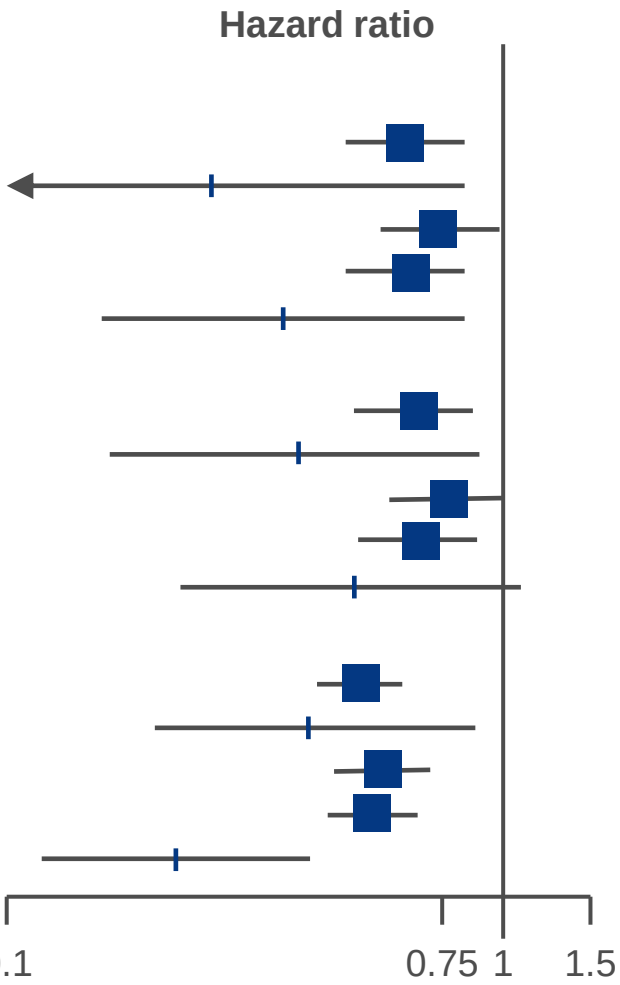
- In this population-based cohort study, data were collected from patients with resected stage II or II colon cancer who were recruited between 2003 and 2010
- Tumour tissue samples were tested for MSI using a mononucleotide marker panel (BAT25, BAT26 and CAT25)
- A propensity score weighted Cox model was used for cancer-specific, relapse-free and overall survival

Alwers E, et al. Ann Oncol 2019;30(suppl):abstr O-018

O-018: Microsatellite instability and survival after adjuvant chemotherapy among stage II and III colon cancer patients: results from a population-based study – Alwers E, et al

Key results

Population	Events	N	HR	95%CI
Cancer-specific survival				
Overall	94	414	0.65	(0.49, 0.86)
Stage II	4	48	0.26	(0.08, 0.81)
Stage III	90	366	0.74	(0.55, 0.99)
MSS	88	345	0.65	(0.48, 0.87)
MSI	8	69	0.36	(0.15, 0.82)
Relapse-free survival				
Overall	113	411	0.67	(0.52, 0.87)
Stage II	8	48	0.38	(0.16, 0.89)
Stage III	105	363	0.78	(0.60, 1.02)
MSS	102	342	0.68	(0.52, 0.88)
MSI	11	69	0.49	(0.22, 1.06)
Overall survival				
Overall	160	414	0.52	(0.43, 0.65)
Stage II	11	48	0.42	(0.20, 0.88)
Stage III	149	366	0.58	(0.47, 0.73)
MSS	145	345	0.55	(0.45, 0.69)
MSI	15	69	0.22	(0.12, 0.41)



Alwers E, et al. Ann Oncol 2019;30(suppl):abstr O-018

O-018: Microsatellite instability and survival after adjuvant chemotherapy among stage II and III colon cancer patients: results from a population-based study – Alwers E, et al

Key results (cont.)

	N	Cancer-specific deaths		Relapse event		Death from any cause	
		n (%)	5-year survival	n (%)	5-year survival	n (%)	5-year survival
Stage II MSS	416						
No CT	381	53 (13.9)	89.1	69 (18.3)	83.6	153 (40.2)	77.6
Adjuvant CT	35	**4** (11.4)	**91.3**	**6** (17.1)	**82.7**	10 (28.6)	**85.5**
Stage II MSI-H	133						
No CT	120	7 (5.8)	94.6	12 (10.0)	90.2	43 (35.8)	79.6
Adjuvant CT	13	**0** (0)	**100**	**2** (15.4)	**92.3**	**1** (7.7)	**100**
Stage III MSS	388						
No CT	78	25 (32.1)	68.0	32 (41.0)	55.6	59 (75.6)	42.9
Adjuvant CT	310	82 (26.5)	**80.7**	96 (31.3)	**70.0**	135 (43.5)	**74.4**
Stage III MSI-H	73						
No CT	17	4 (23.5)	76.5	3 (18.8)	81.3	14 (82.4)	37.8
Adjuvant CT	56	8 (14.3)	**85.3**	9 (16.1)	**85.5**	14 (25.0)	**80.4**

Conclusions

- **In patients with stage II colon cancer and MSI, the use of adjuvant treatment seems to provide some benefit**
- **In patients with stage II high-risk colon cancer, the presence of MSI-H does not provide clear evidence for the use of CT**

Alwers E, et al. Ann Oncol 2019;30(suppl):abstr O-018

O-023: Significant differences in outcome between Immunoscore categories in stage I colon cancer patients – Galon J, et al

Study objective

- To investigate the correlation between Immunoscore (I) and outcomes in patients with stage I colon cancer

Methods

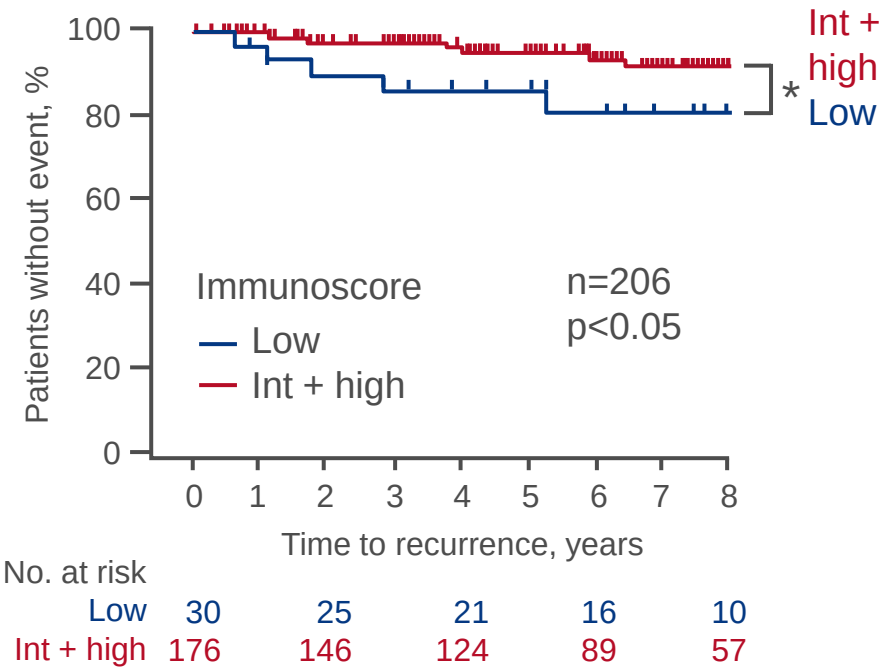
- Data were collected for patients with stage I colon cancer from a worldwide consortium involving 17 countries
- Digital pathology is used to quantify the densities of CD3+ and cytotoxic CD8+ T cells in core tumour and invasive margin and converted to predefined cut-offs and grouped as either low, intermediate or high or as low or intermediate + high or as a continuous score

Galon J, et al. Ann Oncol 2019;30(suppl):abstr O-023

O-023: Significant differences in outcome between Immunoscore categories in stage I colon cancer patients – Galon J, et al

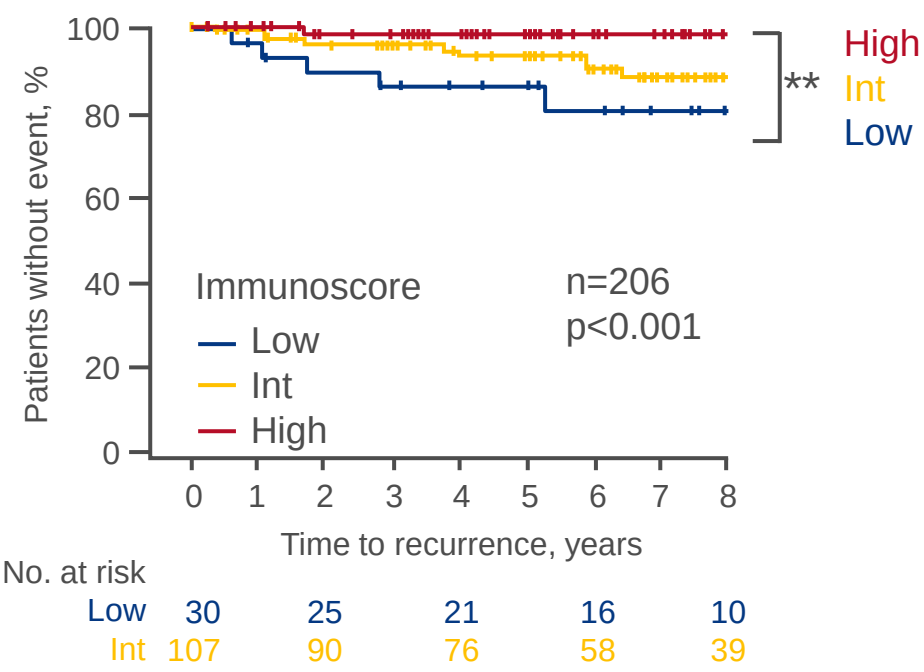
Key results

- In patients with MSS stage I colon cancer, a lower Immunoscore is associated with a higher risk of recurrence



No. at risk

Low	30	25	21	16	10
Int + high	176	146	124	89	57



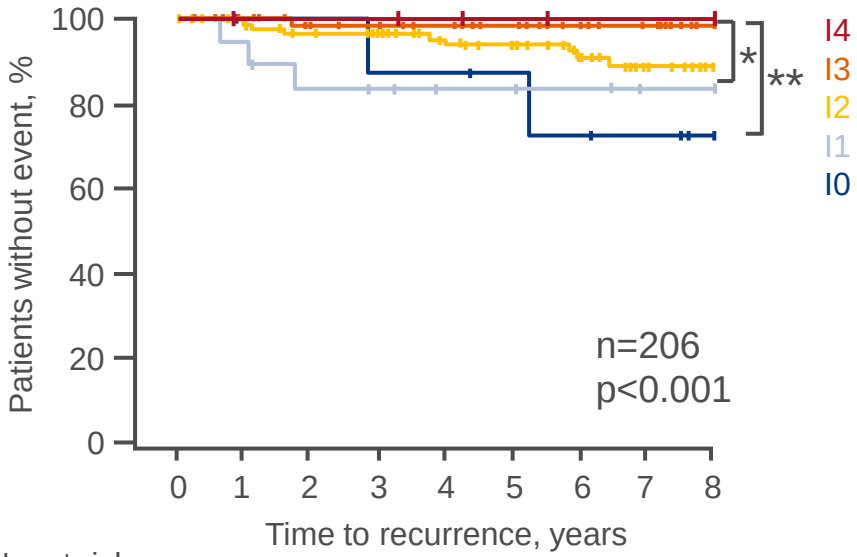
No. at risk

Low	30	25	21	16	10
Int	107	90	76	58	39
High	69	56	48	31	18

Galon J, et al. Ann Oncol 2019;30(suppl):abstr O-023

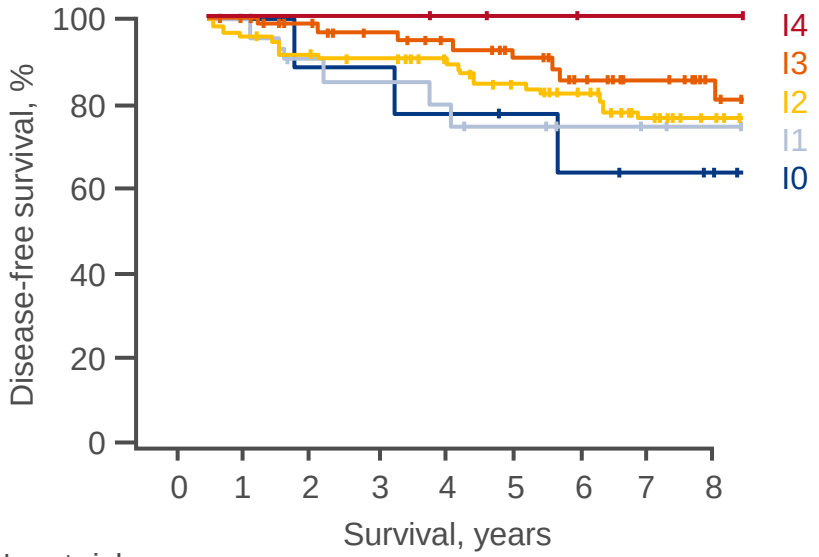
O-023: Significant differences in outcome between Immunoscore categories in stage I colon cancer patients – Galon J, et al

Key results (cont.)



No. at risk

I0	9	8	7	5	1
I1	21	17	14	11	9
I2	107	90	76	58	39
I3	63	50	43	28	15
I4	6	6	5	3	3



No. at risk

I0	9	8	7	5	1
I1	21	17	14	11	9
I2	107	90	77	58	39
I3	63	50	44	28	16
I4	6	6	5	3	3

Conclusion

- **In patients with stage I colon cancer, the Immunoscore is a reliable prognostic indicator for the risk of recurrence and can identify patients who would require more intensive follow-up after surgery because of their increased risk of relapse**

Galon J, et al. Ann Oncol 2019;30(suppl):abstr O-023

LBA-006: BEACON CRC: A randomized, 3-arm, phase-3 study of encorafenib and cetuximab with or without binimetinib vs. choice of either irinotecan or FOLFIRI plus cetuximab in BRAF V600E–mutant metastatic colorectal cancer – Kopetz S, et al

Study objective

- To investigate the efficacy and safety of cetuximab + encorafenib ± binimetinib vs. cetuximab + irinotecan or FOLFIRI in patients with BRAF V600E-mutant mCRC

Key patient inclusion criteria

- mCRC
- BRAF V600E mutant
- Progression after 1 or 2 prior regimens
- No prior RAF, MEK or EGFR inhibitors
- ECOG PS 0–1

(n=665)

R 1:1:1

- **Triplet:** Encorafenib 300 mg/day + binimetinib 45 mg bid + cetuximab* (n=224)
- **Doublet:** Encorafenib 300 mg/day + cetuximab* (n=220)
- **Control:** FOLFIRI or irinotecan + cetuximab* (n=221)

Stratification

- ECOG PS (0 vs. 1), prior irinotecan use (yes vs. no), cetuximab source (US licensed vs. EU approved)

PRIMARY ENDPOINTS

- OS, ORR (BICR) for triplet vs. control

SECONDARY ENDPOINTS

- OS, ORR for doublet vs. control, PFS, safety

*Standard weekly dosing

Kopetz S, et al. Ann Oncol 2019;30(suppl):abstr LBA-006

LBA-006: BEACON CRC: A randomized, 3-arm, phase-3 study of encorafenib and cetuximab with or without binimetinib vs. choice of either irinotecan or FOLFIRI plus cetuximab in BRAF V600E–mutant metastatic colorectal cancer – Kopetz S, et al

Key results

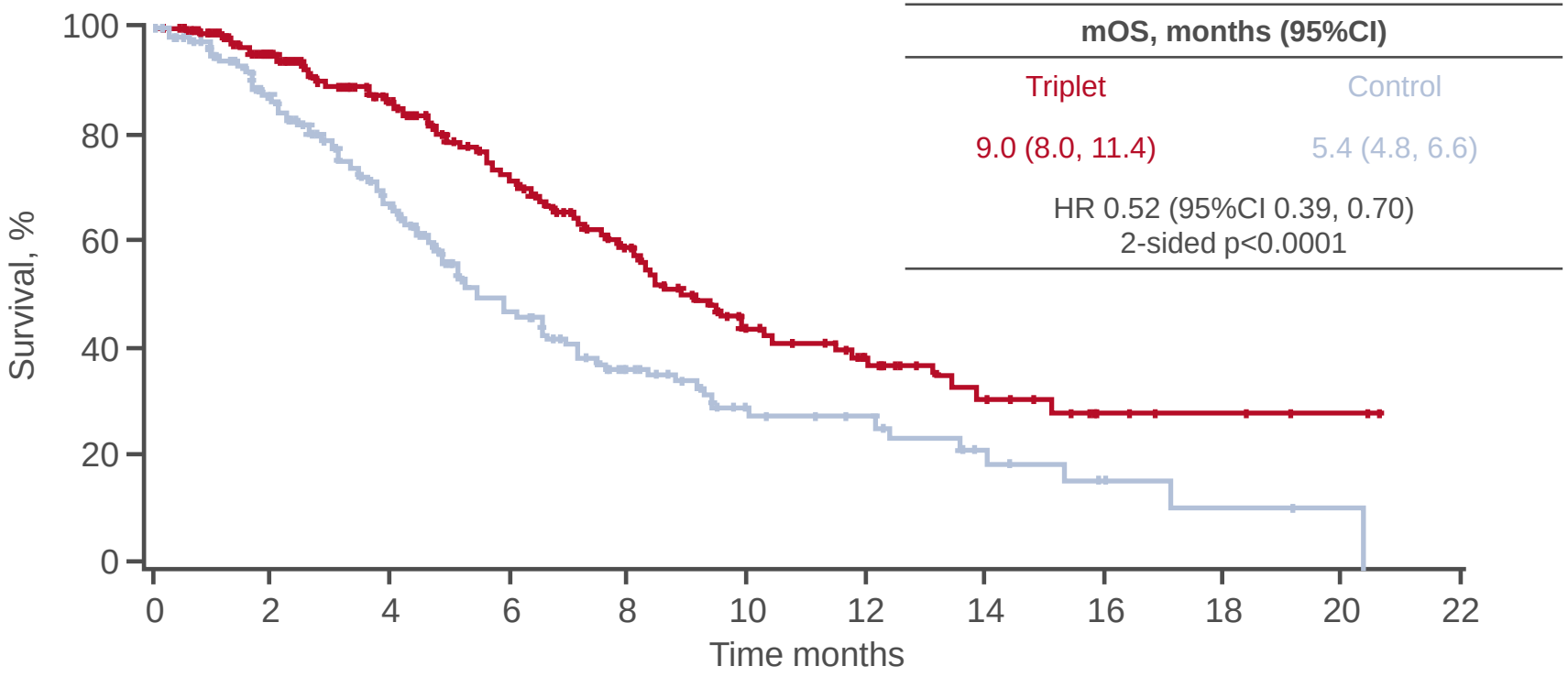
Characteristic, % [unless otherwise stated]	Triplet (n=224)	Doublet (n=220)	Control (n=221)
Median age, years (range)	62 (26–85)	61 (30–91)	60 (27–91)
Female	53	48	57
ECOG PS 0	52	51	49
Location of primary tumour			
Left colon (includes rectum)	35	38	31
Right colon	56	50	54
≥3 organs involved	49	47	44
Presence of liver metastases	64	61	58
Prior lines of therapy			
1	65	66	66
>1	35	34	34
MSI-H	10	9	5
Baseline CEA >5 µg/L	80	70	81
Baseline CRP >10 mg/L	42	37	41

Kopetz S, et al. Ann Oncol 2019;30(suppl):abstr LBA-006

LBA-006: BEACON CRC: A randomized, 3-arm, phase-3 study of encorafenib and cetuximab with or without binimetinib vs. choice of either irinotecan or FOLFIRI plus cetuximab in BRAF V600E–mutant metastatic colorectal cancer – Kopetz S, et al

Key results (cont.)

OS for triplet vs. control



No. at risk

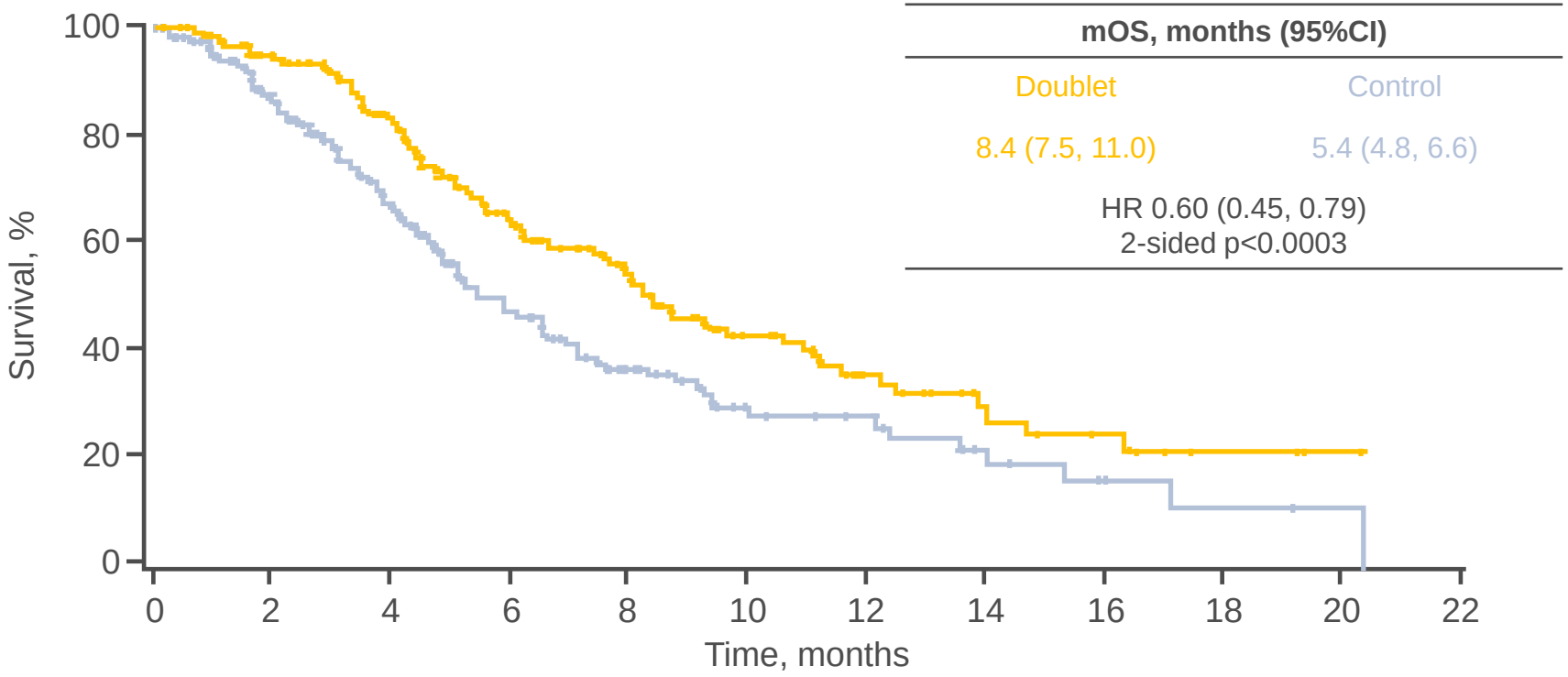
Triplet	224	186	141	103	69	37	24	14	6	4	2	0
Control	221	158	102	60	34	18	15	7	4	2	1	1

Kopetz S, et al. Ann Oncol 2019;30(suppl):abstr LBA-006

LBA-006: BEACON CRC: A randomized, 3-arm, phase-3 study of encorafenib and cetuximab with or without binimetinib vs. choice of either irinotecan or FOLFIRI plus cetuximab in BRAF V600E–mutant metastatic colorectal cancer – Kopetz S, et al

Key results (cont.)

OS for doublet vs. control



No. at risk

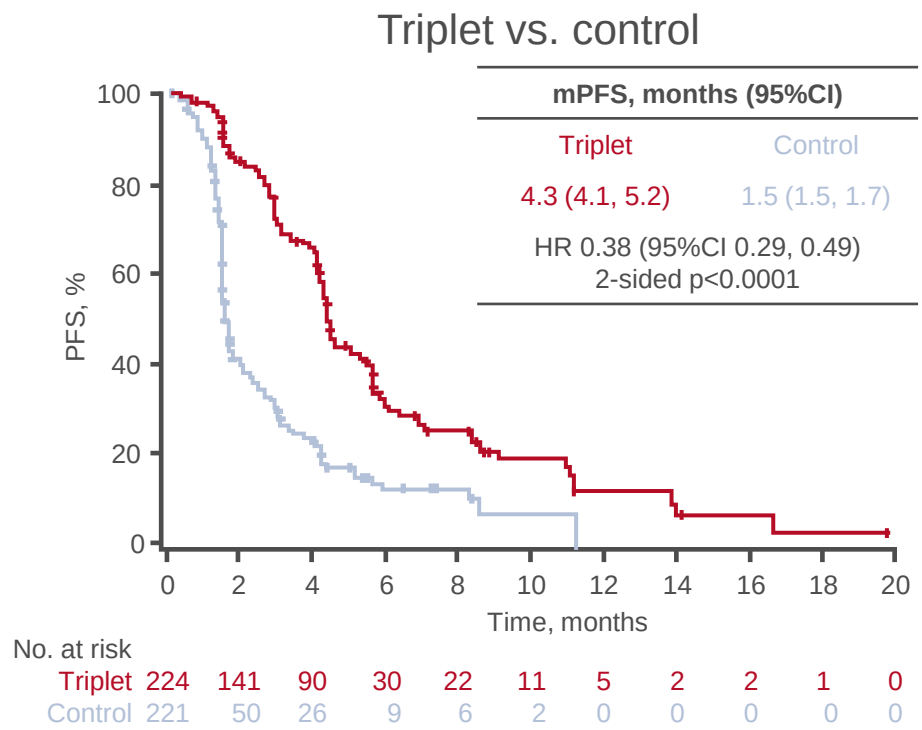
Doublet	220	184	133	87	57	33	21	12	8	3	1	0
Control	221	158	102	60	34	18	15	7	4	2	1	1

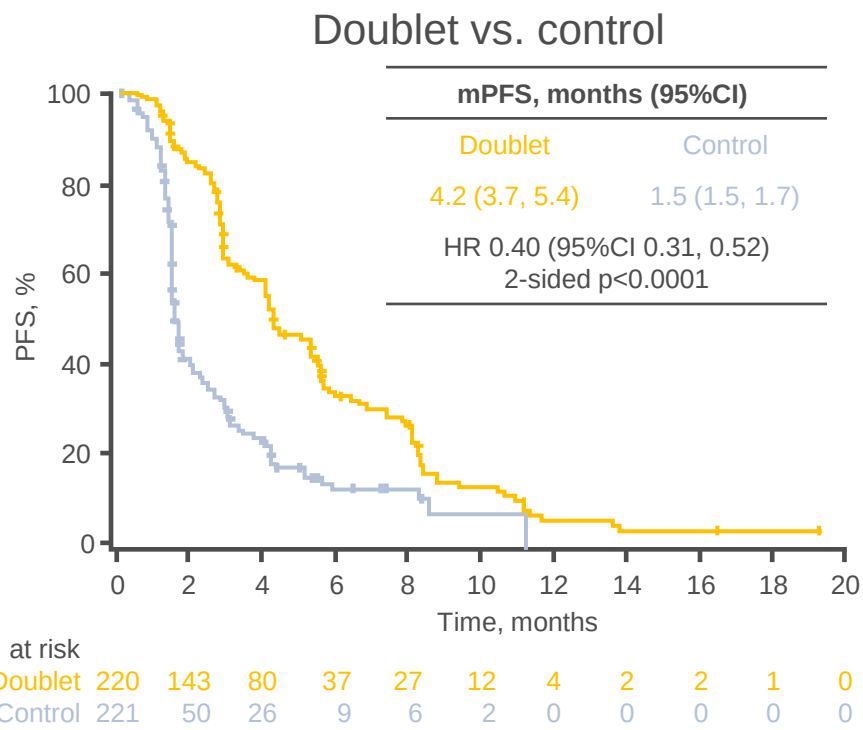
Kopetz S, et al. Ann Oncol 2019;30(suppl):abstr LBA-006

LBA-006: BEACON CRC: A randomized, 3-arm, phase-3 study of encorafenib and cetuximab with or without binimetinib vs. choice of either irinotecan or FOLFIRI plus cetuximab in BRAF V600E–mutant metastatic colorectal cancer – Kopetz S, et al

Key results (cont.)

PFS





Kopetz S, et al. Ann Oncol 2019;30(suppl):abstr LBA-006

LBA-006: BEACON CRC: A randomized, 3-arm, phase-3 study of encorafenib and cetuximab with or without binimetinib vs. choice of either irinotecan or FOLFIRI plus cetuximab in BRAF V600E–mutant metastatic colorectal cancer – Kopetz S, et al

Key results (cont.)

Response	Triplet (n=111)	Doublet (n=113)	Control (n=107)
ORR, %	26	20	2
(95%CI)	(18, 35)	(13, 29)	(<1, 7)
p-value	<0.0001	<0.0001	-
1 prior line, %	34	22	2
>1 prior line, %	14	16	2
BOR, %			
CR	4	5	0
PR	23	15	2
SD	42	54	29
PD	10	7	34
NE	22	17	36

Grade ≥3 AEs occurring in ≥3%, %	Triplet (n=222)	Doublet (n=216)	Control (n=193)
Diarrhoea	10	2	10
Abdominal pain	6	2	5
Nausea	5	<1	1
Vomiting	4	1	3
Pulmonary embolism	4	1	4
Intestinal obstruction	3	4	3
Asthenia	3	3	5
Acute kidney injury	3	2	<1
Fatigue	2	4	4
Dermatitis acneiform	2	<1	3

Conclusion

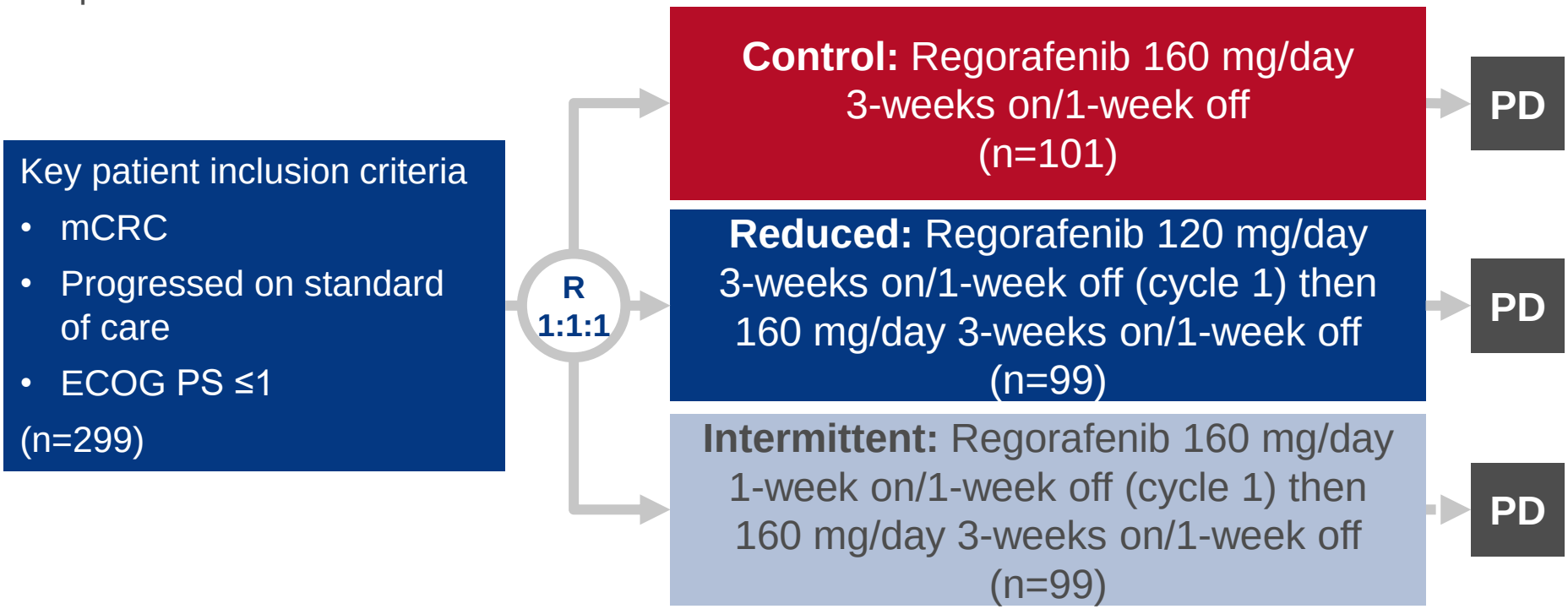
- **In patients with BRAF V600E-mutant mCRC using the triplet combination of encorafenib + binimetinib + cetuximab or doublet of encorafenib + cetuximab provided significant improvements in survival and response compared with FOLFIRI or irinotecan + cetuximab (control) and both regimens were generally well tolerated**

Kopetz S, et al. Ann Oncol 2019;30(suppl):abstr LBA-006

O-026: Results of REARRANGE trial: A randomized phase 2 study comparing different dosing approaches for regorafenib (REG) during the first cycle of treatment in patients (pts) with metastatic colorectal cancer (mCRC) – Argiles G, et al

Study objective

- To investigate the efficacy and safety of different dosing regimens for regorafenib in patients with mCRC



PRIMARY ENDPOINT

- Safety – proportion of patients with grade 3/4 TRAEs

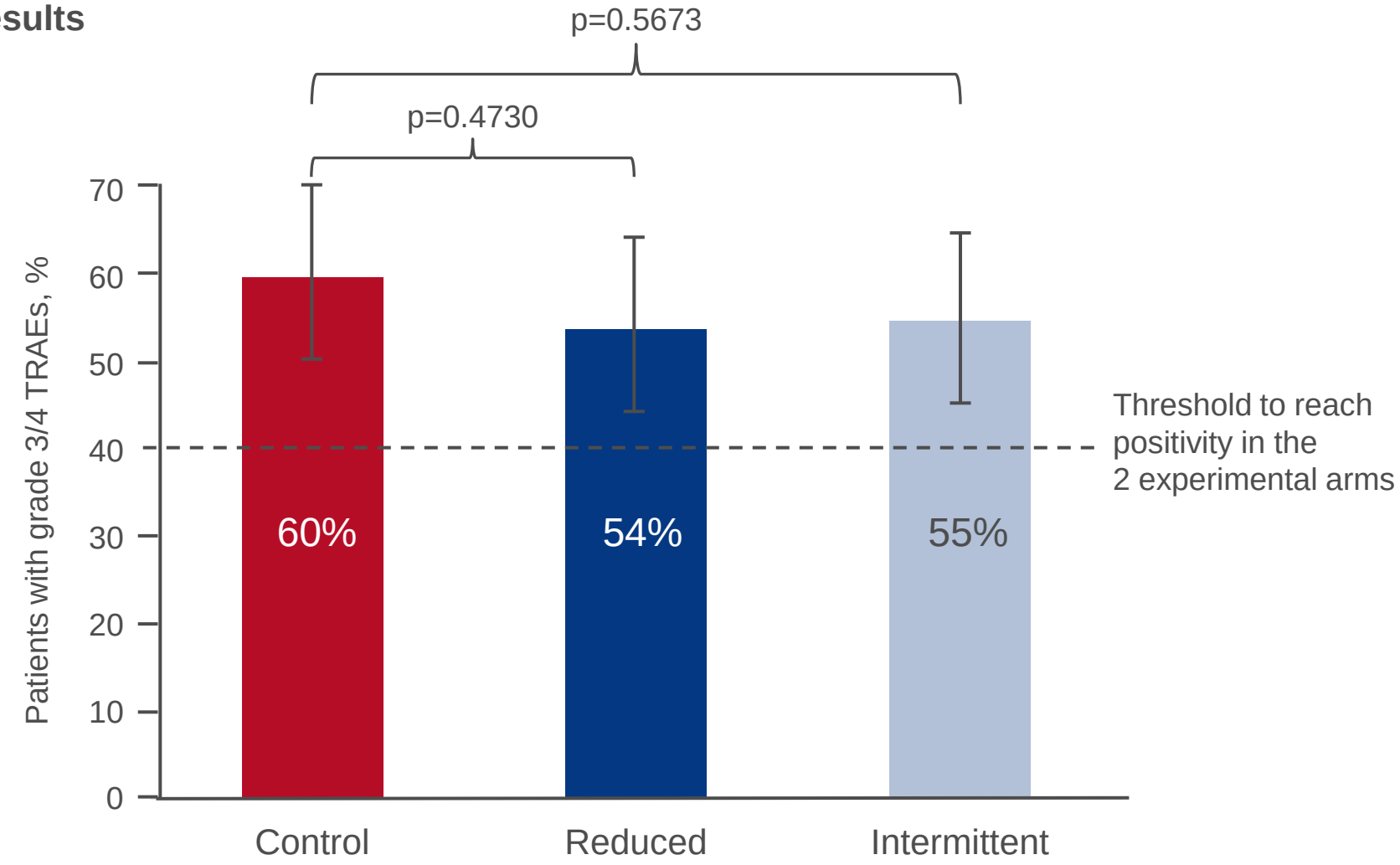
SECONDARY ENDPOINTS

- OS, PFS, DCR

Argiles G, et al. Ann Oncol 2019;30(suppl):abstr O-026

O-026: Results of REARRANGE trial: A randomized phase 2 study comparing different dosing approaches for regorafenib (REG) during the first cycle of treatment in patients (pts) with metastatic colorectal cancer (mCRC) – Argiles G, et al

Key results



Argiles G, et al. Ann Oncol 2019;30(suppl):abstr O-026

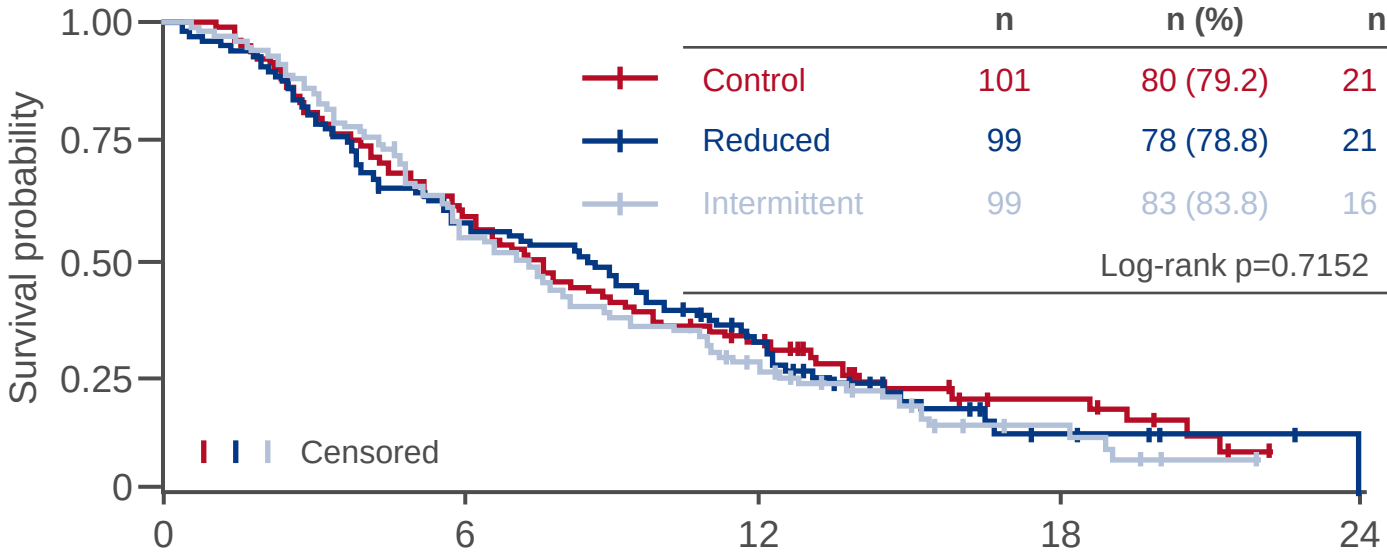
O-026: Results of REARRANGE trial: A randomized phase 2 study comparing different dosing approaches for regorafenib (REG) during the first cycle of treatment in patients (pts) with metastatic colorectal cancer (mCRC) – Argiles G, et al

Key results (cont.)

OS by treatment arm

	Subjects, n	Event, n (%)	Censored, n (%)	Median, months (95%CI)
Control	101	80 (79.2)	21 (20.8)	7.4 (6.0, 9.3)
Reduced	99	78 (78.8)	21 (21.2)	8.6 (5.8, 10.1)
Intermittent	99	83 (83.8)	16 (16.2)	7.1 (5.8, 8.2)

Log-rank p=0.7152



No. at risk					
Control	101	59	30	9	0
Reduced	99	55	27	5	1
Intermittent	99	53	24	6	0

OS rate, %	Control	Reduced	Intermittent
12 months	32.4	32.3	27.8

Argiles G, et al. Ann Oncol 2019;30(suppl):abstr O-026

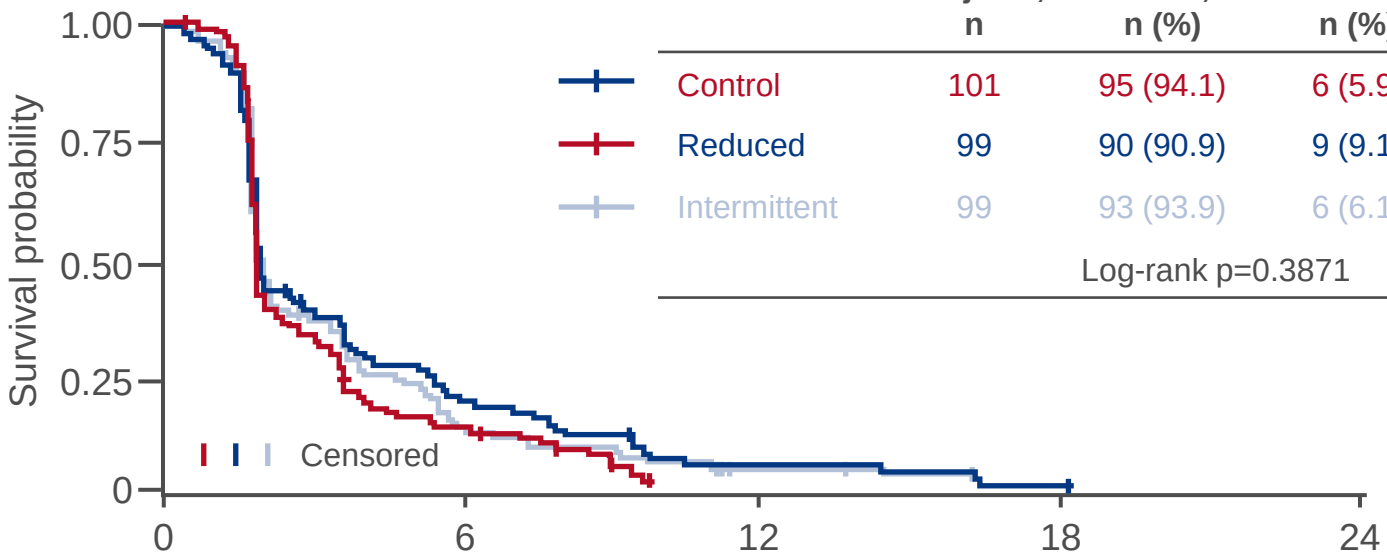
O-026: Results of REARRANGE trial: A randomized phase 2 study comparing different dosing approaches for regorafenib (REG) during the first cycle of treatment in patients (pts) with metastatic colorectal cancer (mCRC) – Argiles G, et al

Key results (cont.)

PFS by treatment arm

	Subjects, n	Event, n (%)	Censored, n (%)	Median, months (95% CI)
Control	101	95 (94.1)	6 (5.9)	1.9 (1.8, 2.1)
Reduced	99	90 (90.9)	9 (9.1)	2.0 (1.9, 2.9)
Intermittent	99	93 (93.9)	6 (6.1)	2.0 (1.9, 2.2)

Log-rank p=0.3871



No. at risk				
Control	101	13	0	0	0
Reduced	99	17	4	1	0
Intermittent	99	14	2	0	0

PFS rate, %	Control	Reduced	Intermittent
6 months	13.6	20.5	14.5

Argiles G, et al. Ann Oncol 2019;30(suppl):abstr O-026

O-026: Results of REARRANGE trial: A randomized phase 2 study comparing different dosing approaches for regorafenib (REG) during the first cycle of treatment in patients (pts) with metastatic colorectal cancer (mCRC) – Argiles G, et al

Key results (cont.)

Grade 3/4 AEs occurring in >4%, %	Control	Reduced	Intermittent
Total	61	57	55
Asthenia + fatigue	20	14	15
Hypertension	19	12	20
Hypokalemia	11	7	10
Hand–foot skin reaction	8	7	3
GGT	2	7	2
Proteinuria	6	3	1
Rash	1	4	2
AST increased	1	4	1
Decreased appetite	2	4	2

Conclusion

- **In patients with mCRC, using a reduced or intermittent dosing regimen for regorafenib did not provide any significant improvement in tolerability compared with standard dosing**

Argiles G, et al. Ann Oncol 2019;30(suppl):abstr O-026

SO-009: Phase 1 studies assessing the safety and clinical activity of autologous and allogeneic NKG2D-based CAR-T therapy in metastatic colorectal cancer – Van Cutsem E, et al

Study objective

- To investigate the efficacy and safety of autologous (CYAD-01) and allogeneic (CYAD-101) NKG2D-CD3ζ CAR T-cell therapy in patients with mCRC

Key patient inclusion criteria (SHRINK study)
- Unresectable mCRC
  - Recurrence/progression after ≥1 line therapy
  - Due to receive re-challenge with FOLFOX
- mCRC with resectable liver metastases
  - Due to receive 1L neoadjuvant FOLFOX

→ Apheresis at D21 to produce CAR T-cells
Concurrent FOLFOX (6 cycles)
3x CYAD-01 infusions* q2w D3 of FOLFOX cycles 2, 3 + 4
Potential consolidation cycle 3x CYAD-01 infusions ± concurrent FOLFOX if no PD after cycle 1 (n=9)

Key patient inclusion criteria (ALLOSHRINK study)
- Unresectable mCRC
  - Recurrence/progression after ≥1 line therapy
  - Due to receive re-challenge with FOLFOX

→ No apheresis
Concurrent FOLFOX (6 cycles)
3x CYAD-101 infusions* q2w D3 of FOLFOX cycles 1, 2 + 3 (n=6)

PRIMARY ENDPOINT

- Safety

SECONDARY ENDPOINT

- BOR

*3+3 design, dose escalation $1x10^8$, $3x10^8$ and $1x10^9$

Van Cutsem E, et al. Ann Oncol 2019;30(suppl):abstr SO-009

SO-009: Phase 1 studies assessing the safety and clinical activity of autologous and allogeneic NKG2D-based CAR-T therapy in metastatic colorectal cancer – Van Cutsem E, et al

Key results

SHRINK (n=9) – 36 infusions

AEs, n	G1	G2	G3
Cytokine release syndrome	2	-	-
Anaemia	-	-	1
Infusion site reaction	1	-	-
Pyrexia	3	-	-
INR increase	-	1	-
Fatigue	1	-	-
Atrial tachycardia	1	-	-

BOR, n	$1x10^8$/inf (n=3)	$3x10^8$/inf (n=3)	$1x10^9$/inf (n=3)
CR	0	0	0
PR	1*	0	0
SD ≥3 months	2*	2	2
PD	0	1	1*

ALLOSHRINK (n=6) – 17 infusions

AEs, n	G1	G2	G3
Abdominal pain	1	-	-
Diarrhoea	1	-	-
Decreased appetite	1	-	-

BOR, n	$1x10^8$/inf (n=3)	$3x10^8$/inf (n=3)
CR	0	0
PR	1	0
SD ≥3 months	0	3
PD	2	0

*Neoadjuvant

Van Cutsem E, et al. Ann Oncol 2019;30(suppl):abstr SO-009

SO-009: Phase 1 studies assessing the safety and clinical activity of autologous and allogeneic NKG2D-based CAR-T therapy in metastatic colorectal cancer – Van Cutsem E, et al

Conclusion

- **In patients with mCRC, using autologous and allogeneic NKG2D-CD3ζ CAR T-cells with concurrent FOLFOX demonstrated some evidence of antitumoral activity and had a manageable safety profile**

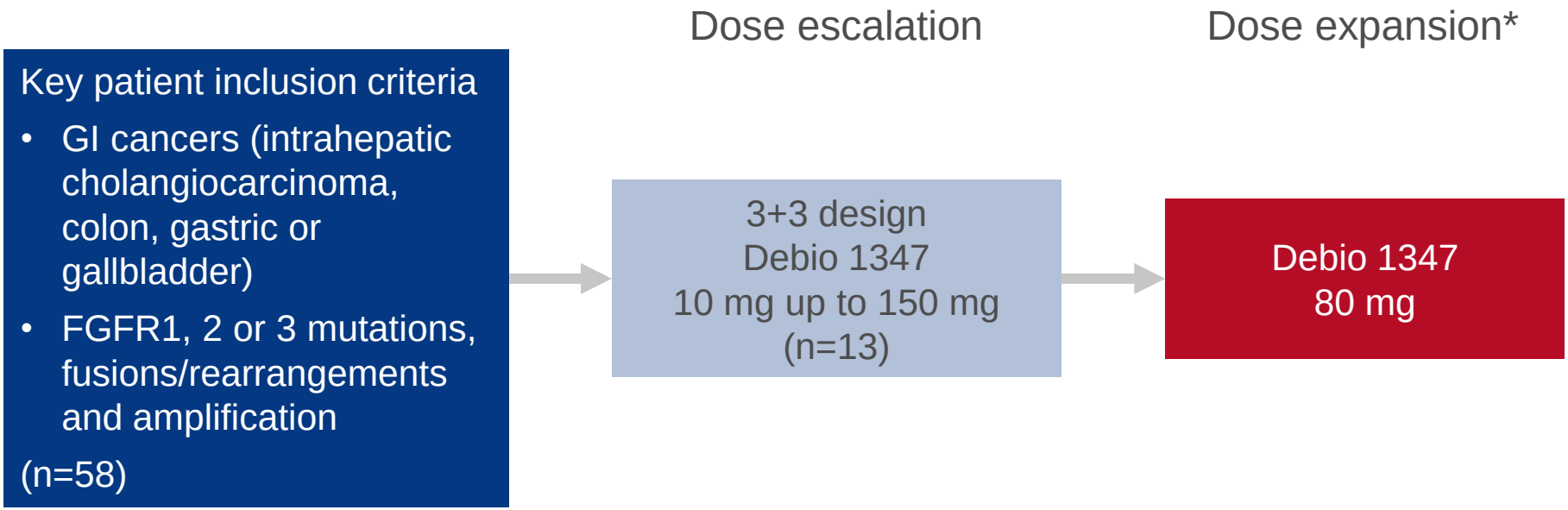
Van Cutsem E, et al. Ann Oncol 2019;30(suppl):abstr SO-009

GASTROINTESTINAL CANCER

SO-003: Debio 1347 in patients with gastrointestinal cancers harboring an FGFR gene fusion: Preliminary results – Matos I, et al

Study objective

- To investigate the efficacy and safety of Debio 1347, an ATP-competitive inhibitor of FGFR1–3, in patients with GI cancers and FGFR gene fusion mutations



PRIMARY ENDPOINTS

- Safety, recommended dose

SECONDARY ENDPOINT

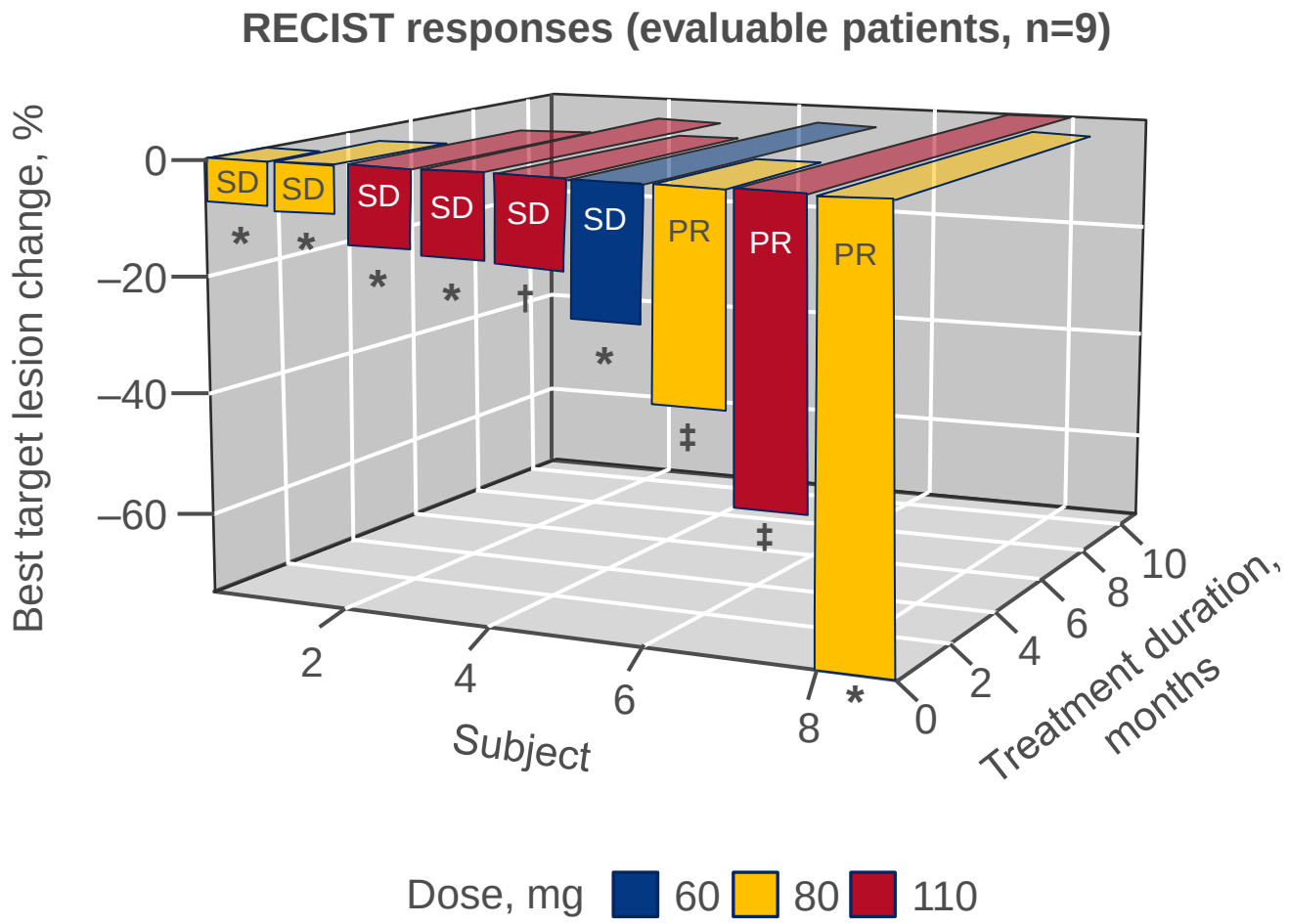
- Clinical activity

*This part is recruiting

Matos I, et al. Ann Oncol 2019;30(suppl):abstr SO-003

SO-003: Debio 1347 in patients with gastrointestinal cancers harboring an FGFR gene fusion: Preliminary results – Matos I, et al

Key results



Cut-off: April 18, 2019

*Cholangiocarcinoma, †gallbladder cancer, ‡colon cancer

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SO-003: Debio 1347 in patients with gastrointestinal cancers harboring an FGFR gene fusion: Preliminary results – Matos I, et al

Key results (cont.)

AEs occurring in ≥40% of patients, %	All grades	Grade 3–4
Hyperphosphatemia	69	31
Nausea	61	
Constipation	54	
Fatigue	54	
Alopecia	46	
Nail changes	46	

Conclusion

- **In patients with GI cancers and FGFR1–3 fusions, Debio 1347 showed encouraging antitumor activity and had a manageable initial safety profile**

Matos I, et al. Ann Oncol 2019;30(suppl):abstr SO-003

O-024: Entrectinib in NTRK-fusion positive gastrointestinal cancers: Integrated analysis of patients enrolled in three trials (STARTRK-2, STARTRK-1 and ALKA-372-001) – Siena S, et al

Study objective

- To investigate the efficacy and safety of entrectinib in patients with NTRK fusion-positive GI cancers

Key patient inclusion criteria

- Solid tumours including GI cancers*
- NTRK fusion positive
- Data collected from 3 trials: ALKA-372-001, STARTRK-1, STARTRK-2

(n=54)

→ Entrectinib dose escalation (n=4) or entrectinib 600 mg/day q4w (n=51)

PRIMARY ENDPOINTS

- ORR, DoR

SECONDARY ENDPOINTS

- PFS, OS, intracranial ORR and DoR, safety

*CRC (n=4), pancreatic (n=3) or cholangiocarcinoma (n=1)

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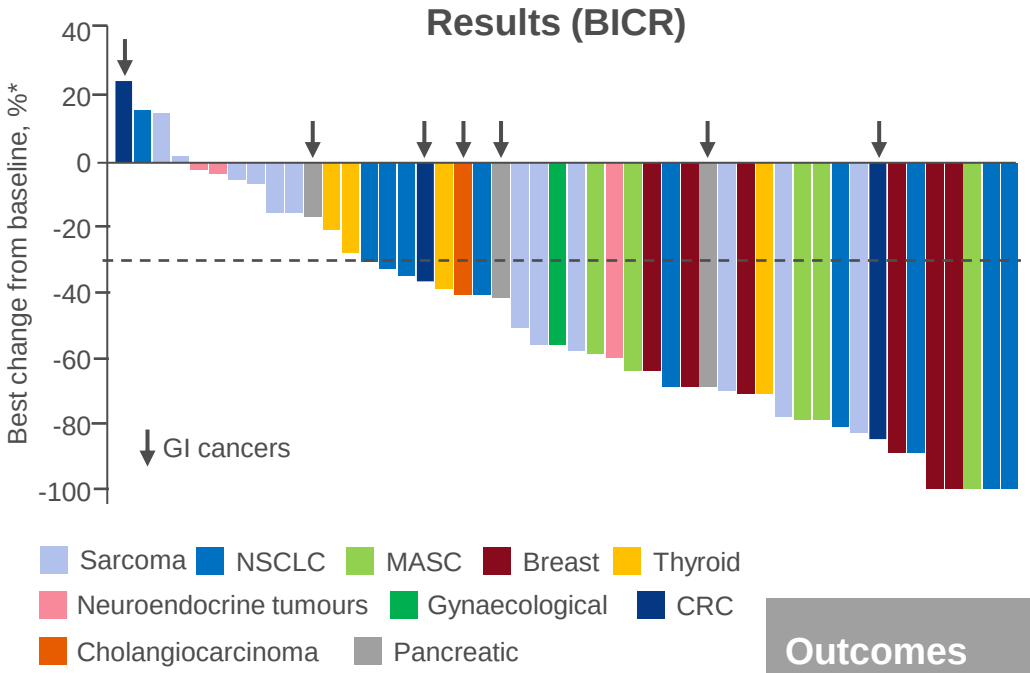
Key results



Note: patients (n=6) without matched pre/post therapy scans were excluded from the plot

Efficacy outcomes (BICR)	NTRK+ patients (n=54)
ORR,† % (95%CI)	**57.4 (43.2, 70.8)**
CR, n (%)	4 (7.4)
mDoR, months (95%CI)	10.4 (7.1, NR)
mPFS, months (95%CI)	11.2 (8.0, 14.9)
mOS, months (95%CI)	20.9 (14.9, NR)

NTRK+ patients with CNS mets (n=11)	
Intracranial ORR, %	**54.5**
CR, %	27.3
Intracranial mPFS, months	14.3

Outcomes	CRC (n=4)	Pancreatic (n=3)	Cholangiocarcinoma (n=1)
ORR, %	25.0	66.7	100
PR, n	1	2	1
DoR, months	4.8	7.1, 12.9	9.3
PFS, months	0.6–5.7	6.2–17.5	12.0
OS, months	0.6–23.4	9.1–20.3	17.1

*Best change at any single timepoint;
†confirmed responses only

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O-024: Entrectinib in NTRK-fusion positive gastrointestinal cancers: Integrated analysis of patients enrolled in three trials (STARTRK-2, STARTRK-1 and ALKA-372-001) – Siena S, et al

Key results (cont.)

Grade 3 AEs, n (%)	NTRK fusion-positive (n=68)
Fatigue	5 (7.4)
Diarrhoea	1 (1.5)
Peripheral oedema	1 (1.5)
Dizziness	1 (1.5)
Blood creatinine increased	1 (1.5)
AST increased	7 (10.3)
Anaemia	8 (11.8)

Conclusion

- **In patients with NTRK fusion-positive GI cancers, entrectinib demonstrated clinically meaningful responses comparable with the overall NTRK fusion-positive population and was generally well tolerated**

Siena S, et al. Ann Oncol 2019;30(suppl):abstr O-024