GI SLIDE DECK 2018

Selected abstracts from:

20th World Congress on Gastrointestinal Cancer

20–23 June 2018 | 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 2018. This slide set specifically focuses on the **20th World Congress on Gastrointestinal Cancer** and is available in English, French, Japanese and Chinese.

The area of clinical research in oncology is a challenging and ever changing environment. Within this environment, we all value access to scientific data and research which helps to educate and inspire further advancements in our roles as scientists, clinicians and educators. I hope you find this review of the latest developments in digestive cancers of benefit to you in your practice. If you would like to share your thoughts with us we would welcome your comments. Please send any correspondence to info@esdo.eu.

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

Yours sincerely,

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ESDO Medical Oncology Slide Deck
Editors 2018

COLORECTAL CANCERS




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PANCREATIC CANCER AND HEPATOBILIARY TUMOURS



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GASTRO-OESOPHAGEAL AND NEUROENDOCRINE TUMOURS


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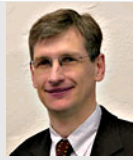
BIOMARKERS

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

Glossary

1/2/3L	first/second/third line
5FU	5-fluorouracil
AE	adverse event
AFP	alpha-fetoprotein
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BCLC	Barcelona clinic liver cancer
BICR	blinded-independent central review
bid	twice daily
BOR	best overall response
BSC	best supportive care
CI	confidence interval
CPS	combined positive score
CR	complete response
CRC	colorectal cancer
CT	chemotherapy
ctDNA	circulating tumour DNA
DCR	disease control rate
DFS	disease-free survival
dMMR	deficient mismatch repair
(m)DoR	(median) duration of response
ECOG	Eastern Cooperative Oncology Group
EGFR	epidermal growth factor receptor
ESCC	oesophageal squamous cell cancer
ESMO	European Society of Medical Oncology
FAS	full analysis set
FOLFIRINOX	leucovorin + 5-fluorouracil + irinotecan + oxaliplatin
FOLFOX	leucovorin + 5-fluorouracil + oxaliplatin
(m)FOLFOXIRI	(modified) leucovorin + 5-fluorouracil + oxaliplatin + irinotecan
GEJ	gastro-oesophageal junction
GI	gastrointestinal
GIST	gastrointestinal stromal tumour
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HIF-1α	hypoxia-inducible factor-1α
HR	hazard ratio
IHC	immunohistochemistry
IQR	interquartile range
ITT	intent-to-treat
iv	intravenous
KM	Kaplan-Meier
LV	leucovorin
mAb	monoclonal antibody
mCRC	metastatic colorectal cancer
met	metastasis
mPDAC	metastatic pancreatic ductal adenocarcinoma
MSI(-H)	(high) microsatellite instability
Mut	mutant
NA	not available
NE	not evaluable
NR	not reached
OR	odds ratio
ORR	overall/objective response rate
(m)OS	(median) overall survival
PCR	polymerase chain reaction
PD	progressive disease
PD-L1	programmed death-ligand 1
PI3KCA	phosphatidylinositol 3-kinase
(m)PFS	(median) progression-free survival
PPES	palmar-plantar erythrodysesthesia syndrome
PR	partial response
PS	performance status
q(2/3/4/6)w	every (2/3/4/6) week(s)
QoL	quality of life
R	randomised
RCT	randomised controlled trial
RECIST	Response Evaluation Criteria In Solid Tumors
RT	radiotherapy
SAE	serious adverse event
SD	stable disease
Tid	three times daily
TRAE	treatment-related adverse event
TRK	tropomyosin receptor kinase
TRR	tumour resection rate
TTP	time-to-progression
(m)TTR	(median) time-to-response
tx	treatment
VEGF	vascular endothelial growth factor
WT	wild-type

Contents

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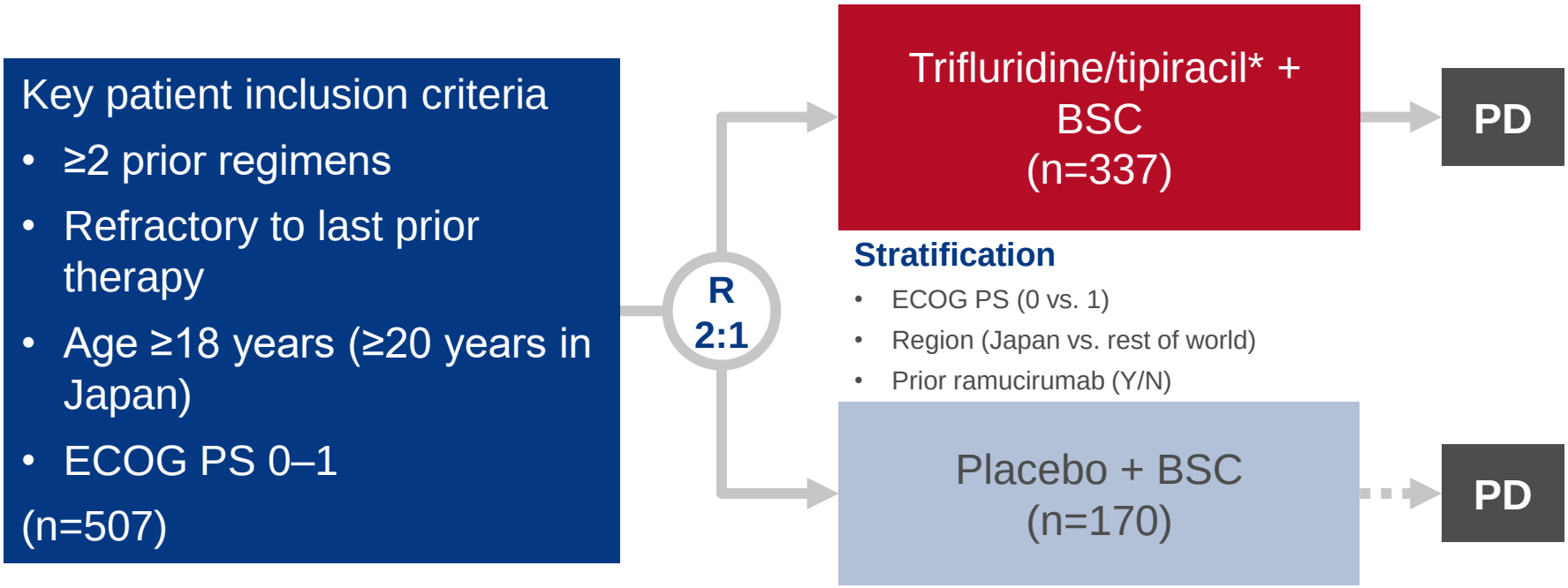
CANCERS OF THE OESOPHAGUS AND STOMACH

LBA-002: Overall survival results from a phase III trial of trifluridine/tipiracil vs. placebo in patients with metastatic gastric cancer refractory to standard therapies (TAGS) – Tabernero J, et al

Study objective

- To assess the efficacy and safety of trifluridine/tipiracil vs. placebo in patients with metastatic gastric cancer refractory to standard therapies (TAS-102 trial)



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR, DCR, QoL, time to ECOG PS ≥2, safety

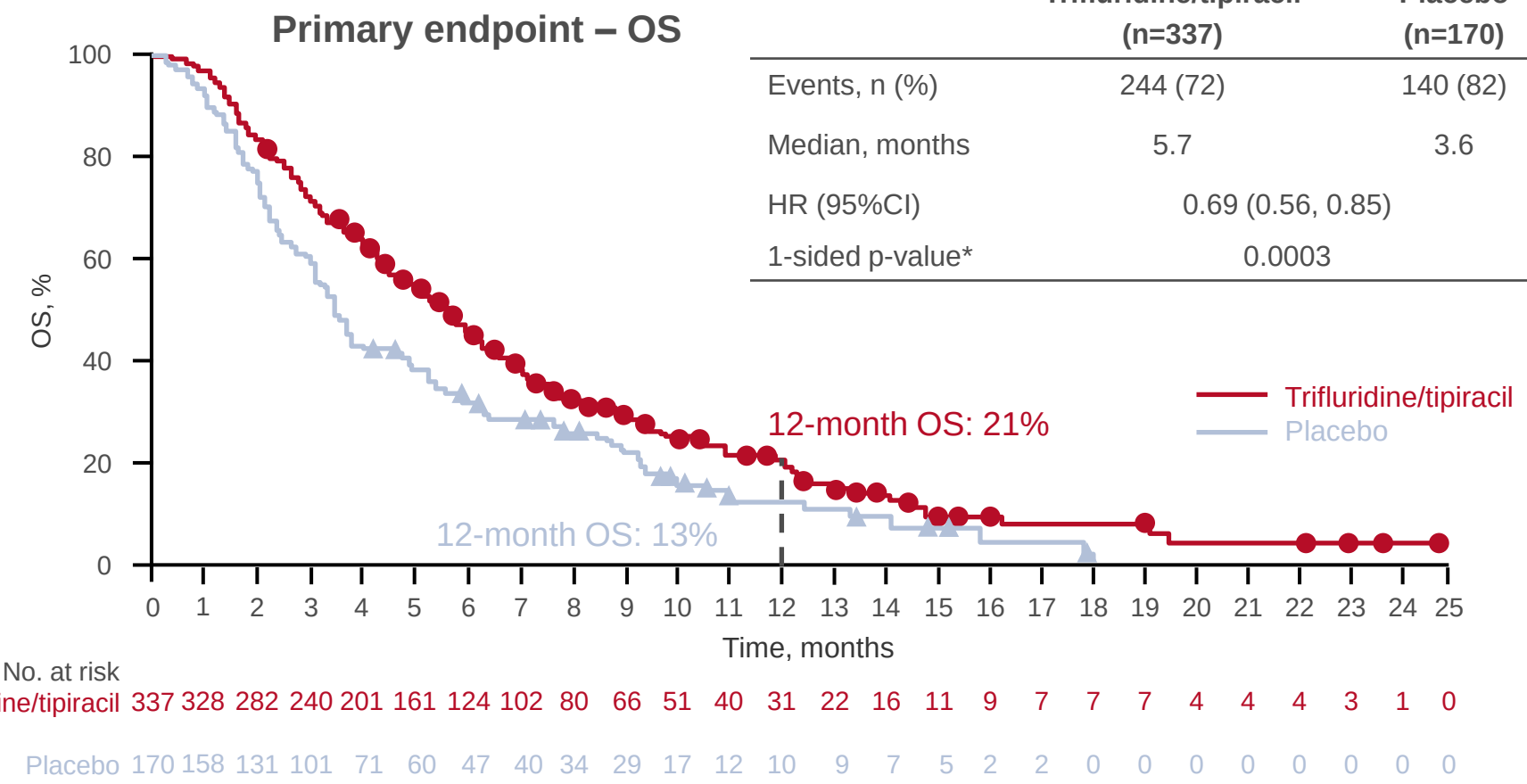
*35 mg/m^2 bid orally D1–5, 8–12 of each 28-day cycle

Tabernero J, et al. Ann Oncol 2018;29(suppl 5):abstr LBA-002

LBA-002: Overall survival results from a phase III trial of trifluridine/tipiracil vs. placebo in patients with metastatic gastric cancer refractory to standard therapies (TAGS) – Tabernero J, et al

Key results

	Trifluridine/tipiracil (n=337)	Placebo (n=170)
Events, n (%)	244 (72)	140 (82)
Median, months	5.7	3.6
HR (95%CI)	0.69 (0.56, 0.85)	
1-sided p-value*	0.0003	



*Stratified log-rank test

Tabernero J, et al. Ann Oncol 2018;29(suppl 5):abstr LBA-002

LBA-002: Overall survival results from a phase III trial of trifluridine/tipiracil vs. placebo in patients with metastatic gastric cancer refractory to standard therapies (TAGS) – Tabernero J, et al

Key results (cont.)

AEs, %	Trifluridine/tipiracil (n=355)	Placebo (n=168)
Any AE	97	93
Grade ≥3 AEs	80	58
AEs leading to discontinuation	13	17
TRAEs	81	57
Treatment-related death	0.3	0.6

- The most common haematological laboratory abnormality observed in patients treated with trifluridine/tipiracil (n=328)* was grade 3/4 neutropenia (38%) compared with none in the placebo arm
  - In 2% of patients treated with trifluridine/tipiracil, grade ≥3 febrile neutropenia was reported

*Treated patients with ≥1 baseline measurement

Tabernero J, et al. Ann Oncol 2018;29(suppl 5):abstr LBA-002

LBA-002: Overall survival results from a phase III trial of trifluridine/tipiracil vs. placebo in patients with metastatic gastric cancer refractory to standard therapies (TAGS) – Tabernero J, et al

Conclusions

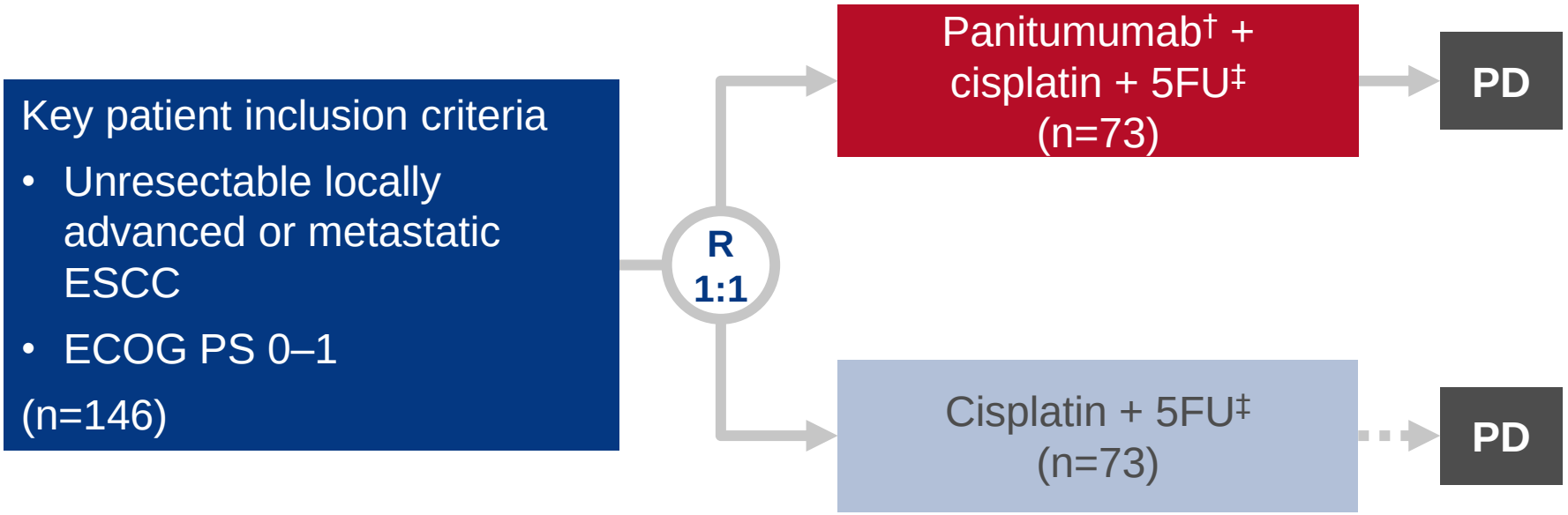
- **In heavily pre-treated patients with metastatic gastric cancer, trifluridine/tipiracil was associated with a clinically meaningful and statistically significant improvement in survival vs. placebo**
- **No new safety signals were noted and the safety profile was consistent with that previously seen in other patient populations**

Tabernero J, et al. Ann Oncol 2018;29(suppl 5):abstr LBA-002

O-010: Cisplatin/5-fluorouracil +/- panitumumab for patients with non-resectable, advanced or metastatic esophageal squamous cell cancer: A randomized phase III AIO/EORTC trial with an extensive biomarker program – Moehler M, et al

Study objective

- To assess the efficacy and safety of cisplatin + 5FU with or without panitumumab in patients with ESCC in an AIO/EORTC study*



ENDPOINTS

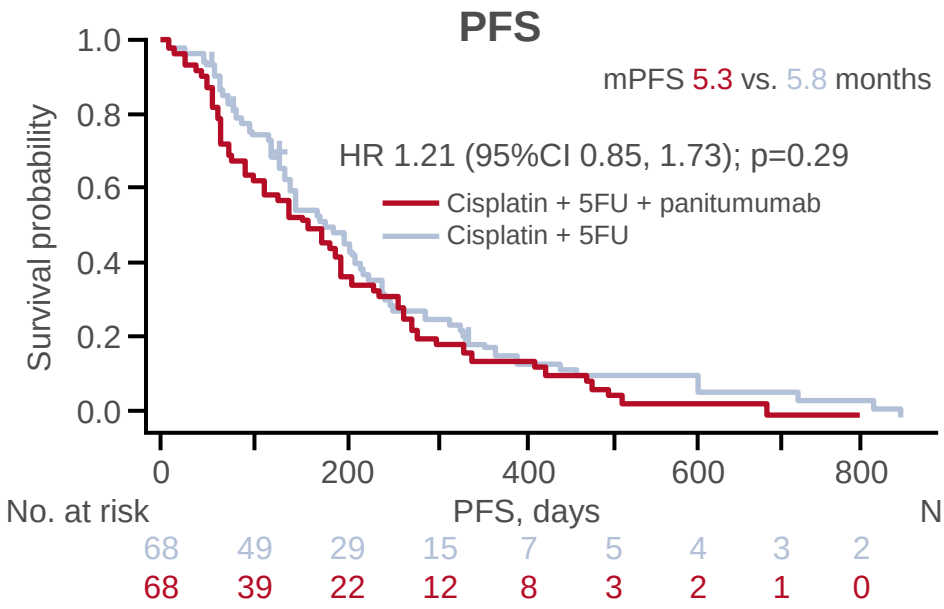
- BOR, OS, PFS and safety

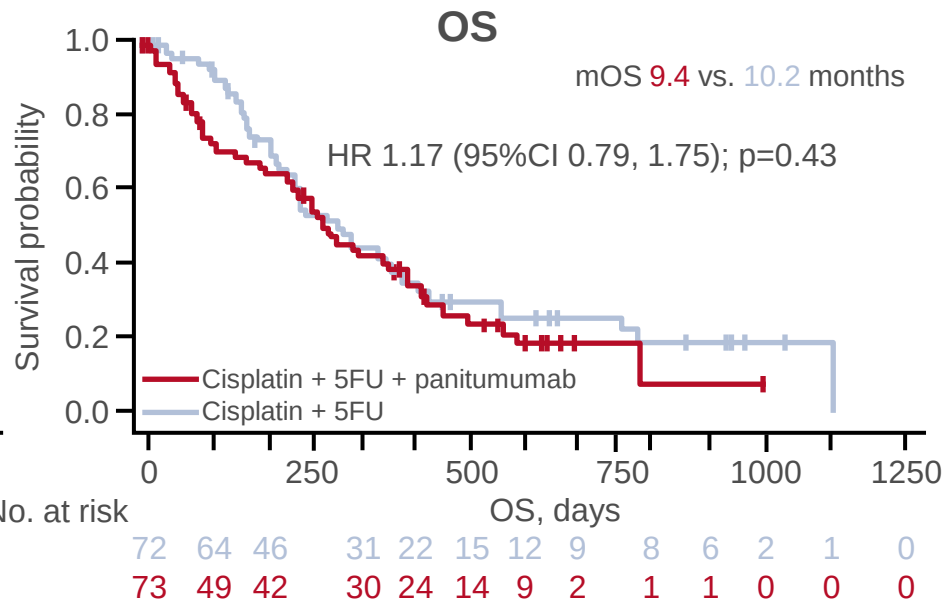
*Study stopped early due to futility and potential safety concerns; †panitumumab 9 mg/kg D1 of each cycle prior to CT q3w; ‡cisplatin 100 mg/m^2 iv infusion over 2 hours D1 + 5FU 1000 mg/m^2 iv infusion over 24 hours D1–4 q3w

Moehler M, et al. Ann Oncol 2018;29(suppl 5):abstr O-010

O-010: Cisplatin/5-fluorouracil +/- panitumumab for patients with non-resectable, advanced or metastatic esophageal squamous cell cancer: A randomized phase III AIO/EORTC trial with an extensive biomarker program – Moehler M, et al

Key results



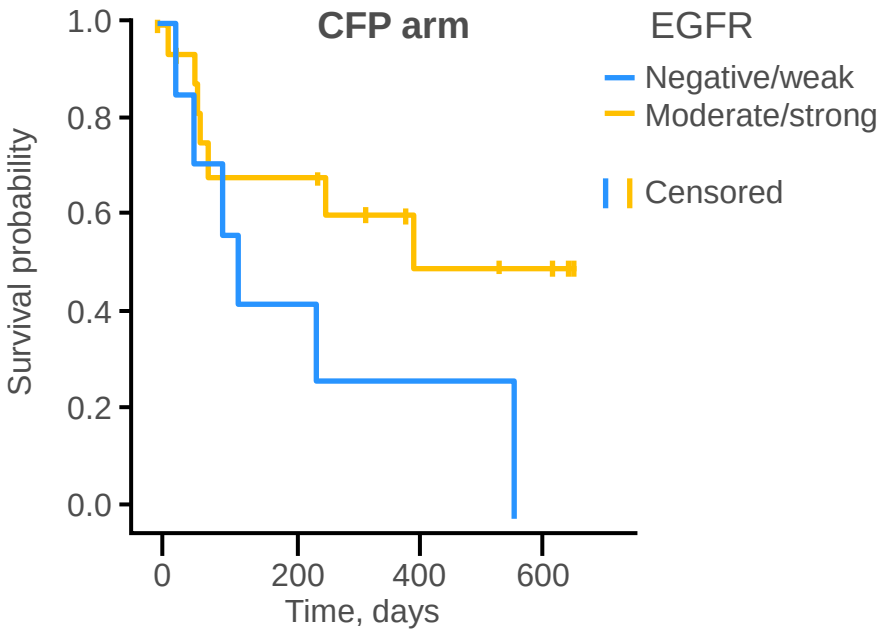


Moehler M, et al. Ann Oncol 2018;29(suppl 5):abstr O-010

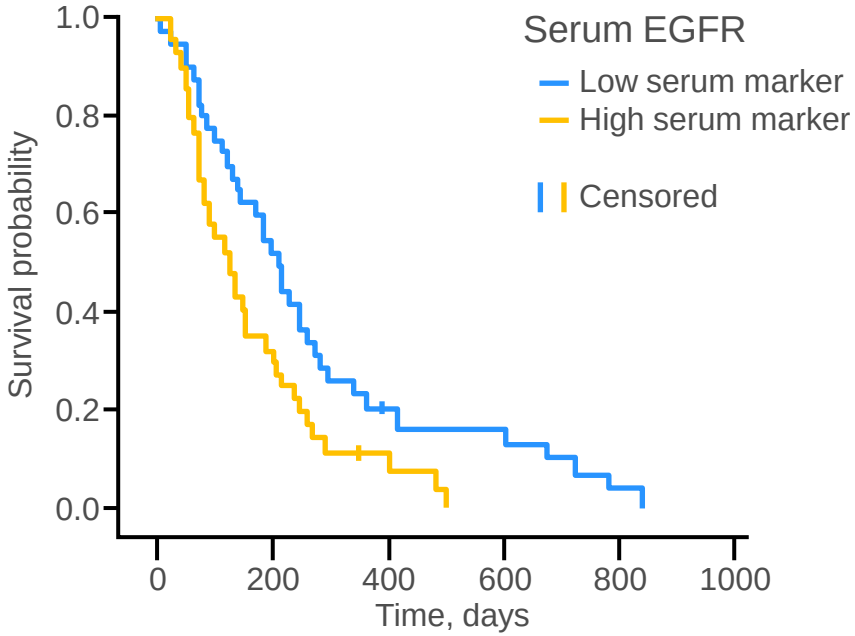
O-010: Cisplatin/5-fluorouracil +/- panitumumab for patients with non-resectable, advanced or metastatic esophageal squamous cell cancer: A randomized phase III AIO/EORTC trial with an extensive biomarker program – Moehler M, et al

Key results (cont.)

OS



PFS



- Panitumumab + cisplatin + 5FU demonstrated a trend for improved OS in patients who were EGFR-positive compared with cisplatin + 5FU alone
- An improved PFS was observed in patients with low vs. high serum EGFR or HIF-1α (p=0.014 and p=0.109, respectively)

Moehler M, et al. Ann Oncol 2018;29(suppl 5):abstr O-010

O-010: Cisplatin/5-fluorouracil +/- panitumumab for patients with non-resectable, advanced or metastatic esophageal squamous cell cancer: A randomized phase III AIO/EORTC trial with an extensive biomarker program – Moehler M, et al

Key results (cont.)

- At least one SAE was observed in 83.3% vs. 78.6% of patients in the panitumumab + cisplatin + 5FU vs. cisplatin + 5FU arms, respectively
- The most common grade ≥3 AEs were low neutrophils (21% vs. 24%) and anaemia (13% vs. 16%) in panitumumab + cisplatin + 5FU vs. cisplatin + 5FU arms, respectively

Conclusions

- **In patients with locally advanced or metastatic ESCC, the addition of panitumumab to cisplatin and 5FU was not associated with improved OS compared with cisplatin + 5FU alone**
- **EGFR-1, HIF-1α and serum EGFR under EGFR-1 inhibition may be potential biomarkers in locally advanced or metastatic ESCC**

Moehler M, et al. Ann Oncol 2018;29(suppl 5):abstr O-010

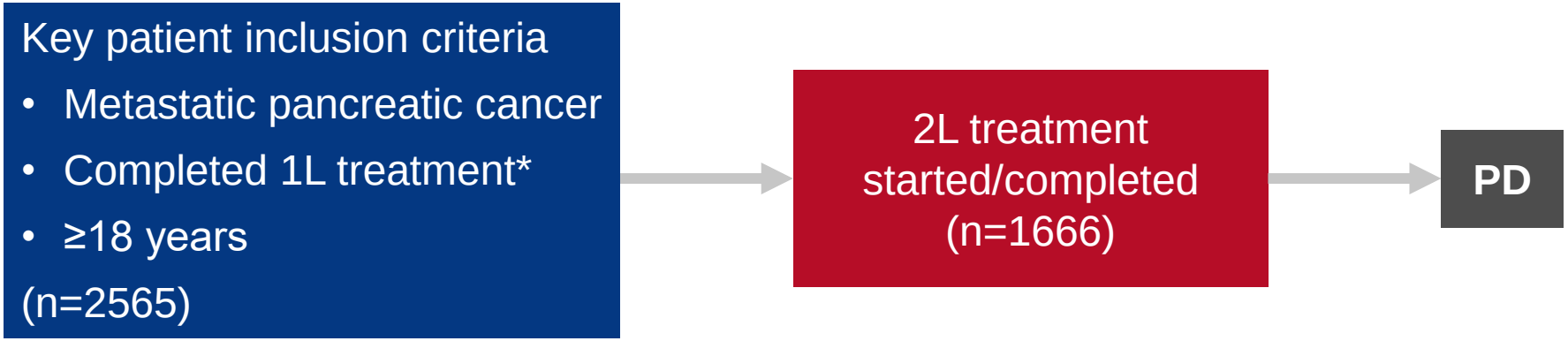
CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

PANCREATIC CANCER

O-002: Geographic variation in systemic treatment of metastatic pancreatic adenocarcinoma (mPAC) patients in real world across Europe – Taieb J, et al

Study objective

- To investigate the geographical variations in treatment selection in European patients from 9 different countries who completed 1L treatment for metastatic pancreatic cancer



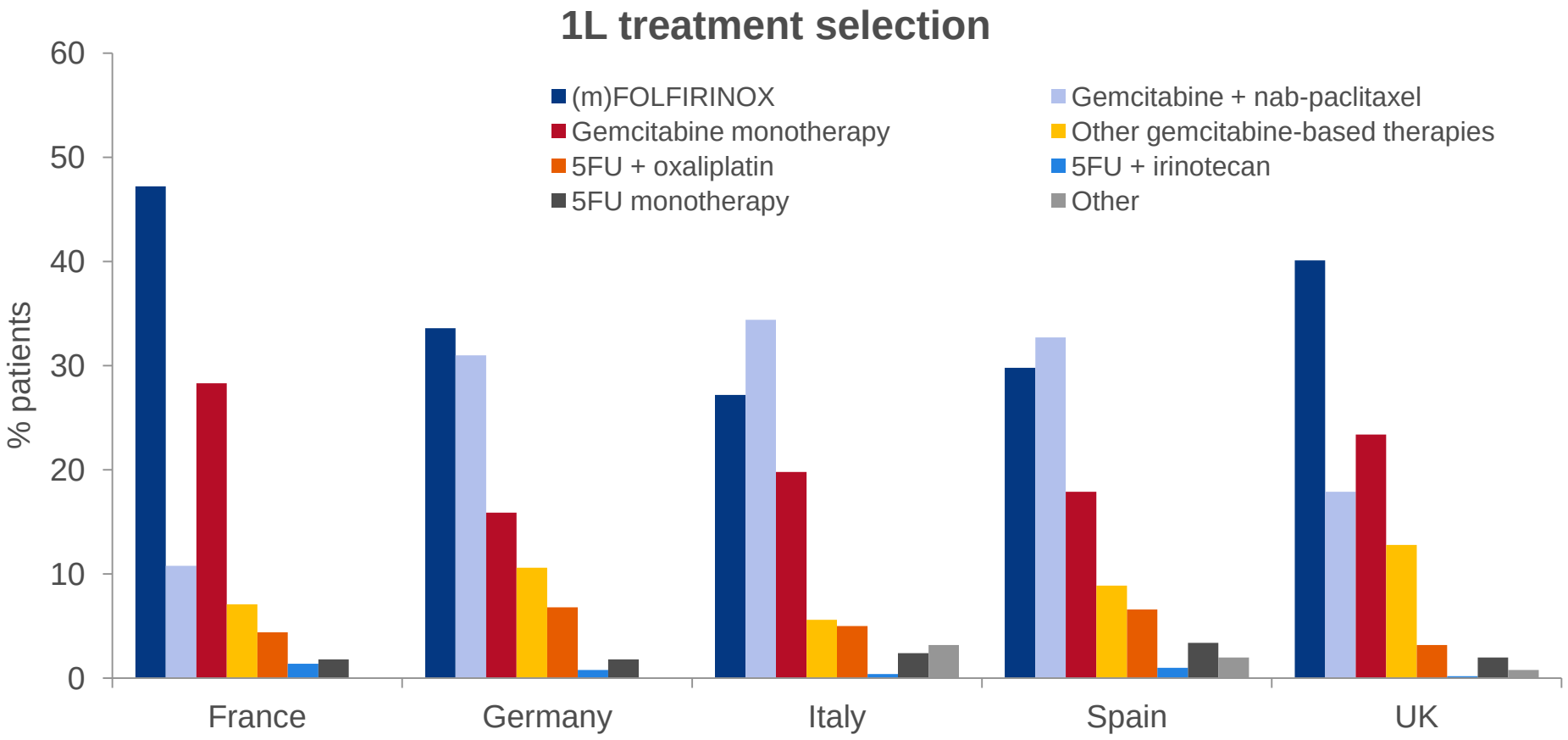
- A retrospective electronic chart review based on data gathered from patient records
- The following information was obtained:
  - General disease information and patient characteristics
  - Disease characteristics at diagnosis
  - Initial treatment for pancreatic cancer
  - Details of 1L, 2L and 3L treatment

*Between July 2014 and January 2016

Taieb J, et al. Ann Oncol 2018;29(suppl 5):abstr O-002

O-002: Geographic variation in systemic treatment of metastatic pancreatic adenocarcinoma (mPAC) patients in real world across Europe – Taieb J, et al

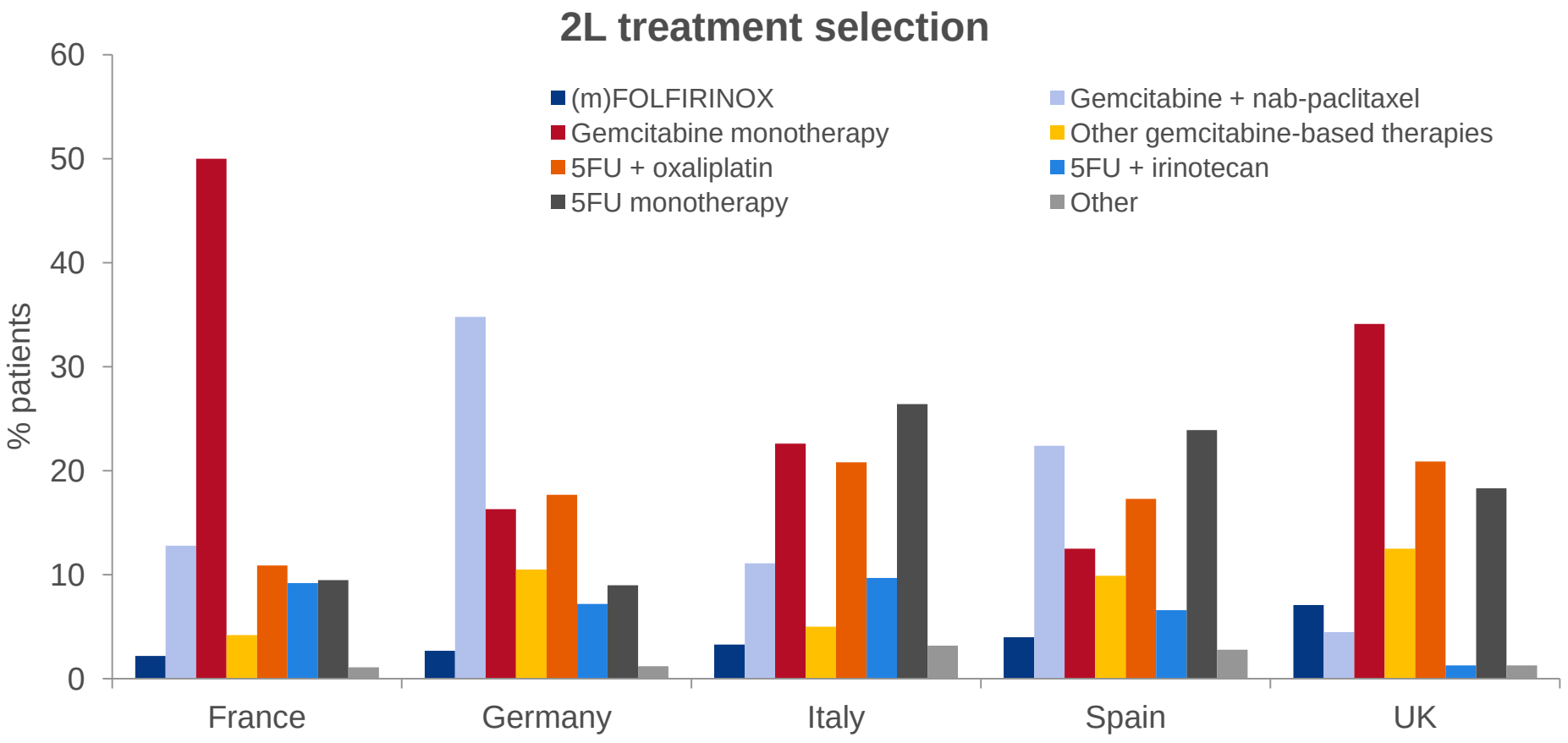
Key results



Taieb J, et al. Ann Oncol 2018;29(suppl 5):abstr O-002

O-002: Geographic variation in systemic treatment of metastatic pancreatic adenocarcinoma (mPAC) patients in real world across Europe – Taieb J, et al

Key results (cont.)



Taieb J, et al. Ann Oncol 2018;29(suppl 5):abstr O-002

O-002: Geographic variation in systemic treatment of metastatic pancreatic adenocarcinoma (mPAC) patients in real world across Europe – Taieb J, et al

Conclusions

- In European patients with metastatic pancreatic cancer the 1L treatment selection was broadly consistent with ESMO recommendations
  - There was variation between countries in the relative proportion of different treatments used
  - 1L treatment choice depended on local reimbursement status and the patient's condition
- 2L treatment selection varied widely between countries
  - 2L choice was dependent on 1L treatment and local reimbursement policies
- At the time of the study, there were no approved 2L treatments for patients with metastatic pancreatic cancer

Taieb J, et al. Ann Oncol 2018;29(suppl 5):abstr O-002

HEPATOCELLULAR CARCINOMA

LBA-001: Ramucirumab as second-line treatment in patients with advanced hepatocellular carcinoma (HCC) and elevated alpha-fetoprotein (AFP) following first-line sorafenib: Pooled efficacy and safety across two global randomized phase 3 studies (REACH-2 and REACH) – Zhu A, et al

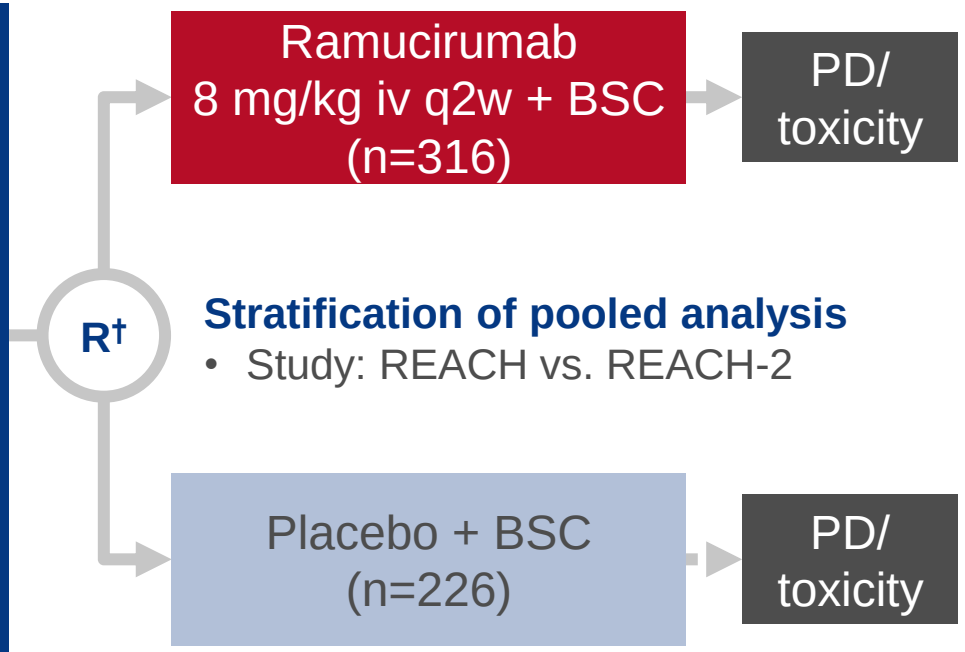
Study objective

- To assess the benefit of ramucirumab in patients with advanced HCC and baseline AFP ≥400 ng/mL in a pooled analysis of the phase III REACH and REACH-2 studies

Key patient inclusion criteria for REACH and REACH-2 studies

- Advanced HCC
- BCLC stage B or C
- Prior sorafenib
- Child-Pugh A
- ECOG PS 0–1
- REACH-2: Baseline AFP* ≥400 ng/mL

(n=542)



PRIMARY ENDPOINT (BOTH STUDIES)

- OS

SECONDARY ENDPOINTS (BOTH STUDIES)

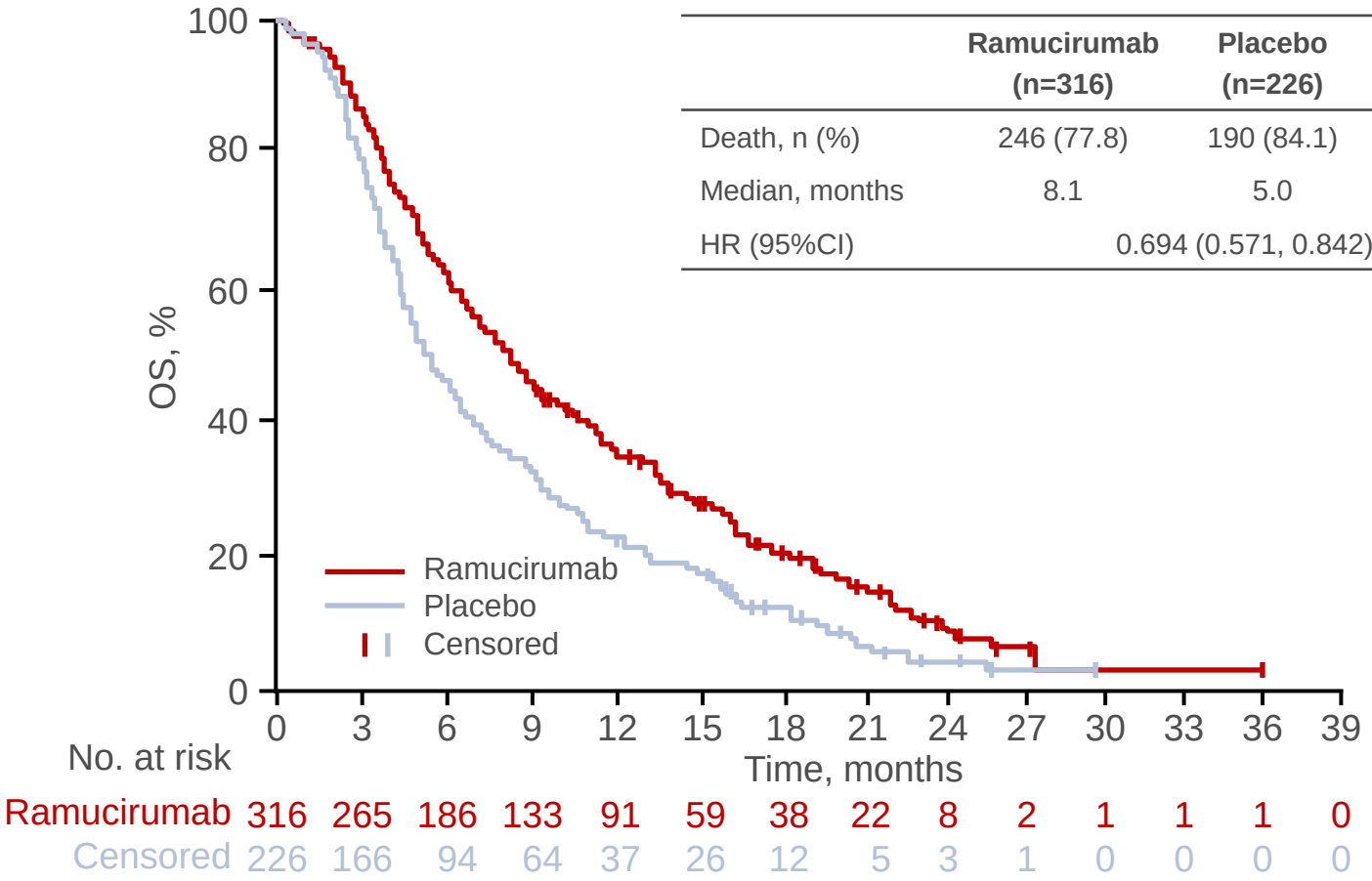
- PFS, ORR, safety, patient-reported outcomes

*Patients with AFP ≥400 ng/mL selected for both studies in the pooled analysis; †1:1 (REACH) or 2:1 (REACH-2)

Zhu A, et al. Ann Oncol 2018;29(suppl 5):abstr LBA-001

LBA-001: Ramucirumab as second-line treatment in patients with advanced hepatocellular carcinoma (HCC) and elevated alpha-fetoprotein (AFP) following first-line sorafenib: Pooled efficacy and safety across two global randomized phase 3 studies (REACH-2 and REACH) – Zhu A, et al

Key results



	Ramucirumab (n=316)	Placebo (n=226)	Difference	p-value
Death, n (%)	246 (77.8)	190 (84.1)		
Median, months	8.1	5.0	3.1	
HR (95%CI)	0.694 (0.571, 0.842)			0.0002

No heterogeneity in treatment effect observed across both studies

A random effect frailty model after adjusting for study (as random effect) produced a similar treatment result (HR 0.689; p=0.0002)

Zhu A, et al. Ann Oncol 2018;29(suppl 5):abstr LBA-001

LBA-001: Ramucirumab as second-line treatment in patients with advanced hepatocellular carcinoma (HCC) and elevated alpha-fetoprotein (AFP) following first-line sorafenib: Pooled efficacy and safety across two global randomized phase 3 studies (REACH-2 and REACH) – Zhu A, et al

Key results (cont.)

	Ramucirumab (n=316)	Placebo (n=226)	p-value
PFS			
Median, months	2.8	1.5	
HR (95%CI)	0.572 (0.472, 0.694)		<0.0001
ORR, n (%) [95%CI]	17 (5.4) [2.9, 7.9]	2 (0.9) [0.0, 2.1]	0.0064
DCR, n (%) [95%CI]	178 (56.3) [50.9, 61.8]	84 (37.2) [30.9, 43.5]	<0.001

Zhu A, et al. Ann Oncol 2018;29(suppl 5):abstr LBA-001

LBA-001: Ramucirumab as second-line treatment in patients with advanced hepatocellular carcinoma (HCC) and elevated alpha-fetoprotein (AFP) following first-line sorafenib: Pooled efficacy and safety across two global randomized phase 3 studies (REACH-2 and REACH) – Zhu A, et al

Key results (cont.)

Grade >3 AEs of special interest occurring in ≥3% of patients, n (%)	Ramucirumab (n=316)	Placebo (n=223)
Liver injury/failure	63 (19.9)	59 (26.5)
Ascites	15 (4.7)	9 (4.0)
Bleeding/haemorrhage events	15 (4.7)	15 (6.7)
GI haemorrhage events	11 (3.5)	12 (5.4)
Hypertension	40 (12.7)	8 (3.6)

Conclusions

- **In patients with advanced HCC and baseline AFP ≥400 ng/mL, ramucirumab improved OS vs. placebo in a pooled analysis of the REACH and REACH-2 studies**
- **Ramucirumab was well tolerated, with a safety profile consistent with other ramucirumab monotherapy studies**
- **In patients with HCC and elevated AFP who have received prior sorafenib treatment, ramucirumab is potentially an important new treatment option**

Zhu A, et al. Ann Oncol 2018;29(suppl 5):abstr LBA-001

O-011: Assessment of tumor response, AFP response, and time to progression in the phase 3 CELESTIAL trial of cabozantinib versus placebo in advanced hepatocellular carcinoma (HCC) – Merle P, et al

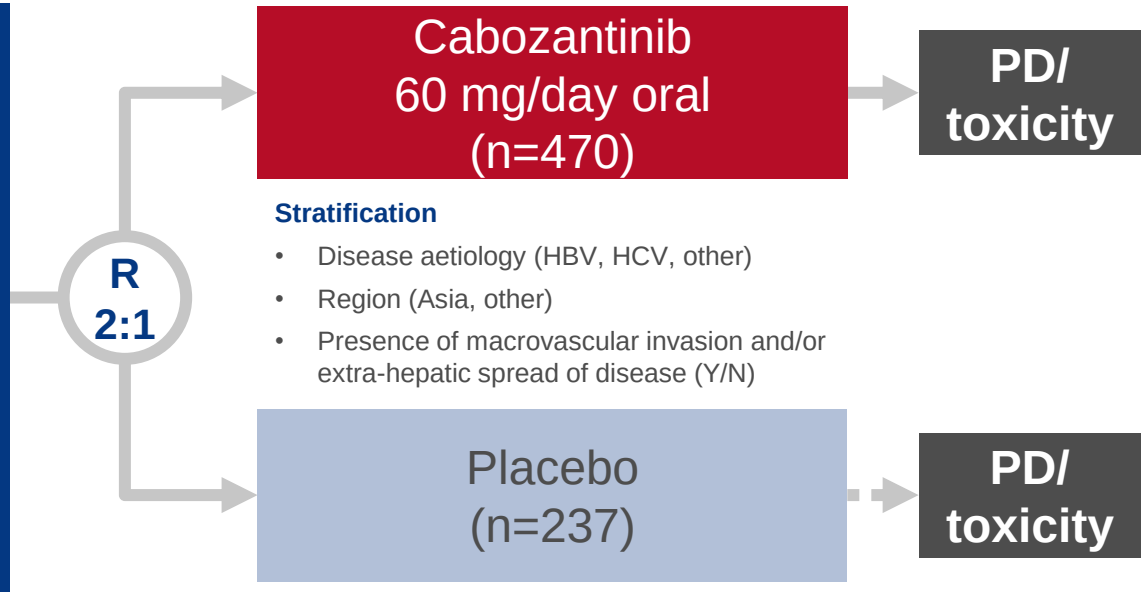
Study objective

- To assess the tumour response, AFP response and TTP in patients with advanced HCC receiving cabozantinib vs. placebo in the CELESTIAL trial

Key patient inclusion criteria

- Advanced HCC
- Child-Pugh A
- Prior sorafenib
- ≤2 systemic regimens and progressed following ≥1
- ECOG PS ≤1

(n=760)



EXPLORATORY ENDPOINTS*

- Tumour response, AFP response, TTP

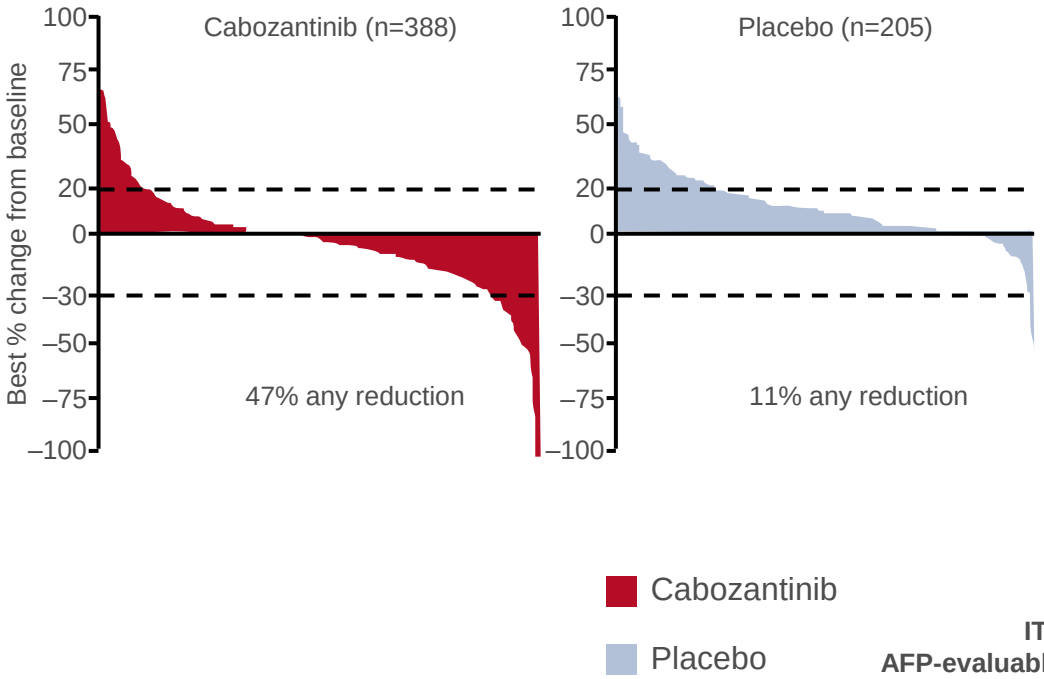
*Primary (OS) and secondary (PFS, ORR and safety) endpoints presented previously

Merle P, et al. Ann Oncol 2018;29(suppl 5):abstr O-011

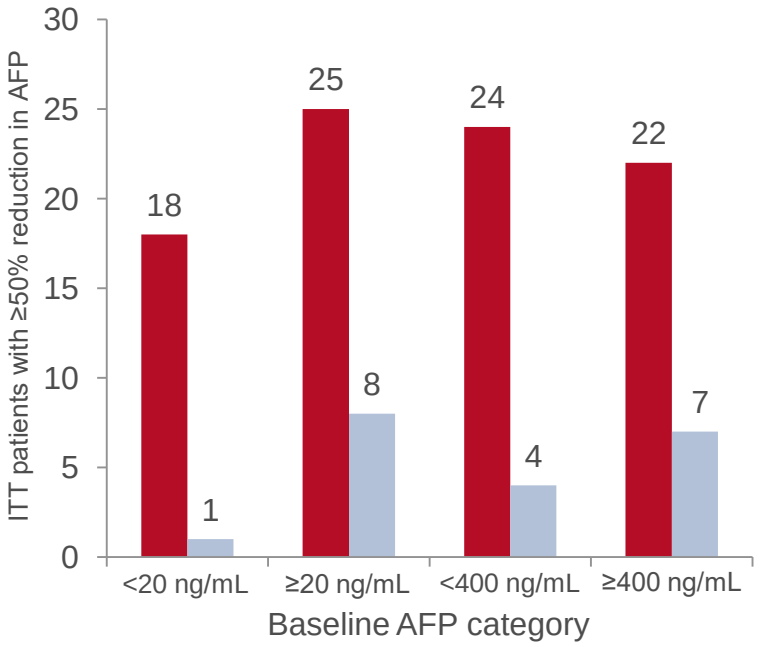
O-011: Assessment of tumor response, AFP response, and time to progression in the phase 3 CELESTIAL trial of cabozantinib versus placebo in advanced hepatocellular carcinoma (HCC) – Merle P, et al

Key results

Best % change from baseline in sum of diameters



AFP response

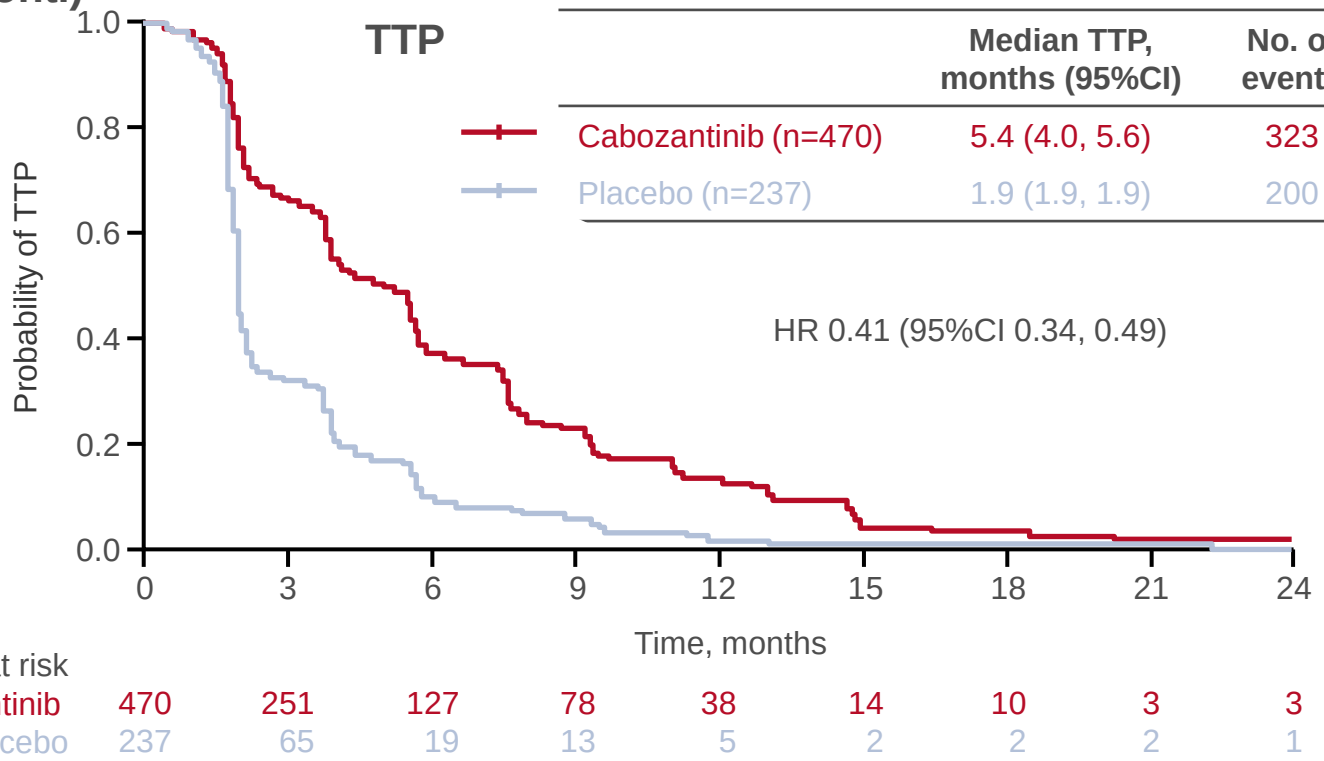


ITT patients, n	139	77	331	160	278	136	192	101
AFP-evaluable patients, n	112	66	261	126	221	119	152	73

Merle P, et al. Ann Oncol 2018;29(suppl 5):abstr O-011

O-011: Assessment of tumor response, AFP response, and time to progression in the phase 3 CELESTIAL trial of cabozantinib versus placebo in advanced hepatocellular carcinoma (HCC) – Merle P, et al

Key results (cont.)



	Median TTP, months (95%CI)	No. of events
Cabozantinib (n=470)	5.4 (4.0, 5.6)	323
Placebo (n=237)	1.9 (1.9, 1.9)	200

- Dose reductions occurred in 62% and 13% of patients in the cabozantinib and placebo arms, respectively
- Discontinuations due to TRAEs occurred in 16% and 3% of patients in the cabozantinib and placebo arms, respectively

Merle P, et al. Ann Oncol 2018;29(suppl 5):abstr O-011

O-011: Assessment of tumor response, AFP response, and time to progression in the phase 3 CELESTIAL trial of cabozantinib versus placebo in advanced hepatocellular carcinoma (HCC) – Merle P, et al

Results (cont.)

Grade 3 AEs occurring in ≥5% in cabozantinib arm, %	Cabozantinib (n=467)	Placebo (n=237)
Diarrhoea	10	2
Decreased appetite	6	<1
Hand-foot syndrome	17	0
Fatigue	10	4
Hypertension	16	2
AST increased	11	6
Asthenia	7	2

Conclusions

- **In patients with advanced HCC, cabozantinib demonstrated greater reductions in target lesions than placebo**
- **In patients with elevated AFP at baseline, reductions of ≥50% in AFP were observed in a quarter of those in the cabozantinib arm**
- **Cabozantinib was also associated with improved TTP compared with placebo**

Merle P, et al. Ann Oncol 2018;29(suppl 5):abstr O-011

CANCERS OF THE COLON, RECTUM AND ANUS

LBA-004: Efficacy and safety results from IMblaze370, a randomized phase III study comparing atezolizumab plus cobimetinib and atezolizumab monotherapy vs. regorafenib in chemotherapy-refractory metastatic colorectal cancer – Bendell J, et al

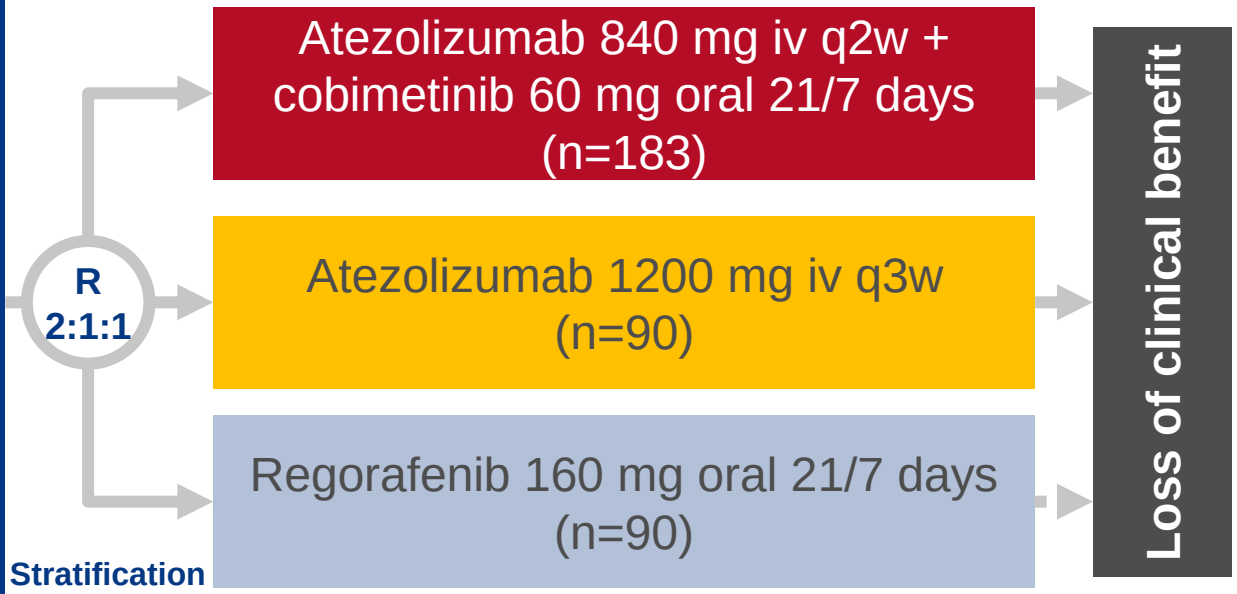
Study objective

- To assess the efficacy and safety of atezolizumab + cobimetinib vs. atezolizumab alone vs. regorafenib in patients with chemotherapy refractory mCRC in the IMblaze370 study

Key patient inclusion criteria

- Unresectable locally advanced or metastatic CRC
- ≥2 prior regimens of cytotoxic chemotherapy
- MSI-H capped at 5%
- ECOG PS 0–1

(n=363)



Stratification

- Extended RAS mutation status (≥50% of patients in each arm)
- Time since diagnosis of first metastasis (<18 vs. ≥18 months)

PRIMARY ENDPOINT

- OS for atezolizumab + cobimetinib or atezolizumab vs. regorafenib

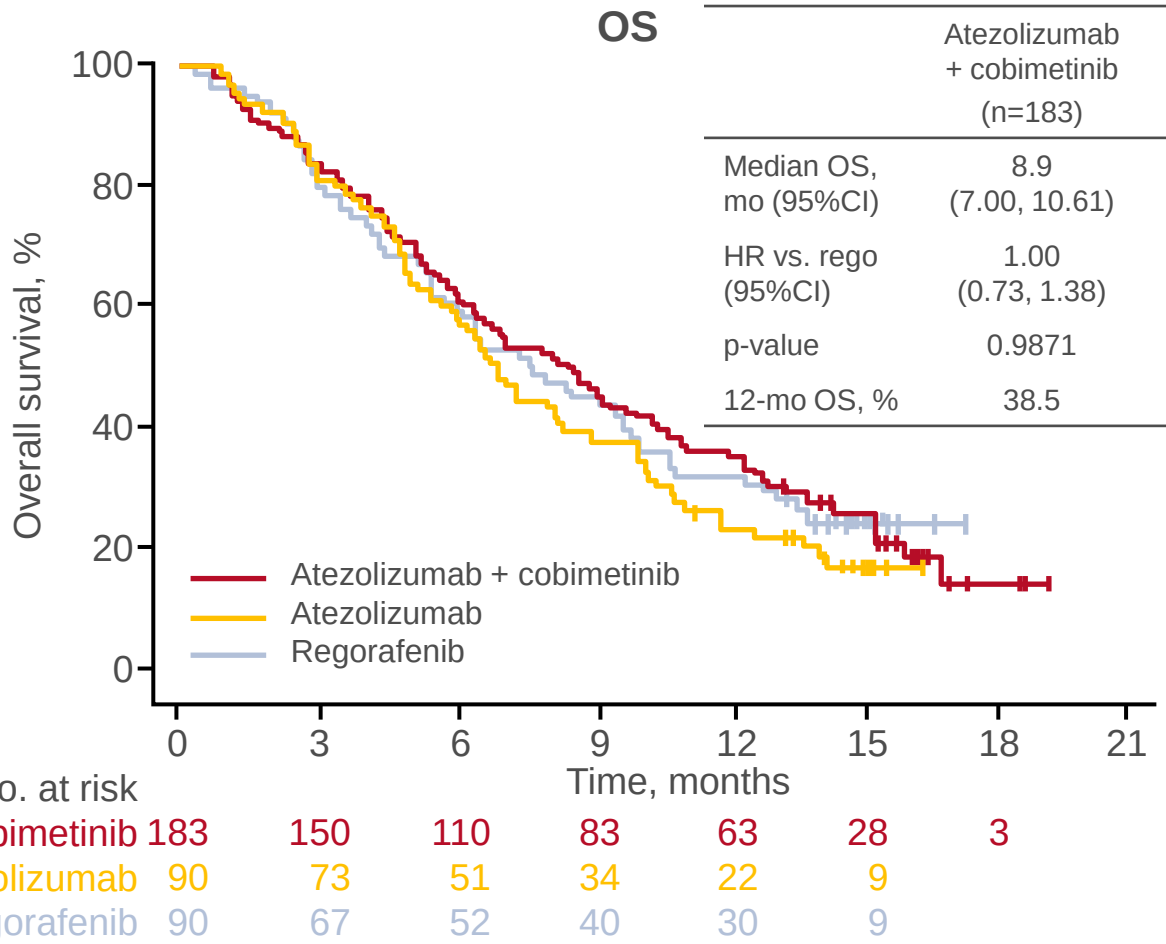
SECONDARY ENDPOINTS

- PFS, ORR, DoR

Bendell J, et al. Ann Oncol 2018;29(suppl 5):abstr LBA-004

LBA-004: Efficacy and safety results from IMblaze370, a randomized phase III study comparing atezolizumab plus cobimetinib and atezolizumab monotherapy vs. regorafenib in chemotherapy-refractory metastatic colorectal cancer – Bendell J, et al

Key results



	Atezolizumab + cobimetinib (n=183)	Atezolizumab (n=90)	Regorafenib (n=90)
Median OS, mo (95%CI)	8.9 (7.00, 10.61)	7.1 (6.05, 10.05)	8.5 (6.41, 10.71)
HR vs. rego (95%CI)	1.00 (0.73, 1.38)	1.19 (0.83, 1.71)	NA
p-value	0.9871	0.3360*	NA
12-mo OS, %	38.5	27.2	36.6

HRs are from stratified log-rank tests. Data cut-off: March 9, 2018. *For descriptive purposes only

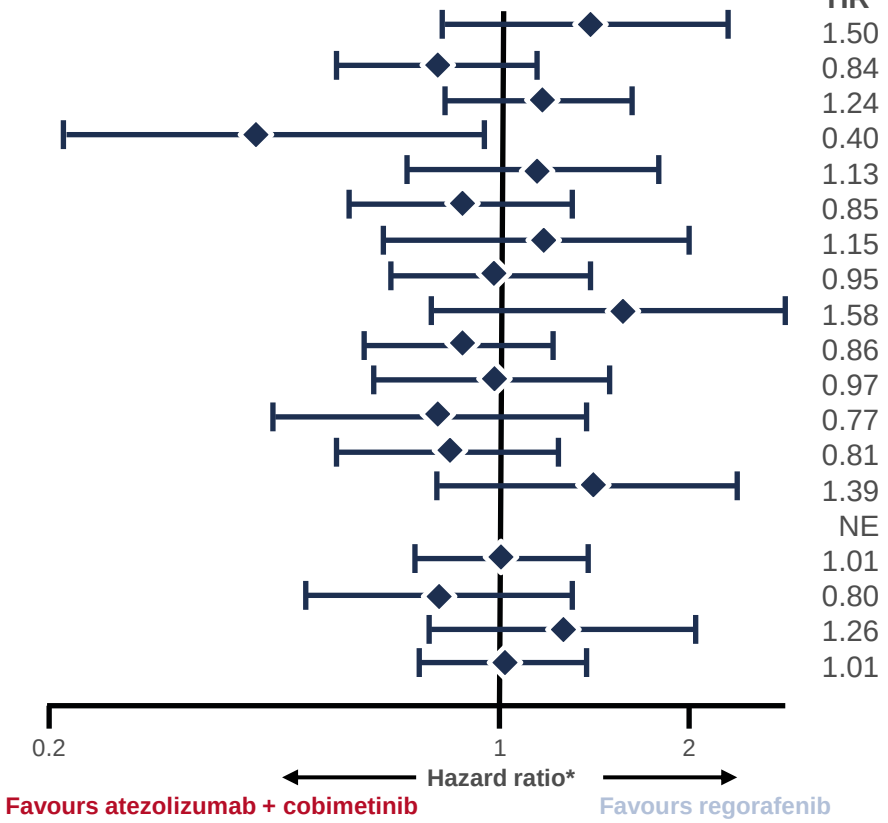
Bendell J, et al. Ann Oncol 2018;29(suppl 5):abstr LBA-004

LBA-004: Efficacy and safety results from IMblaze370, a randomized phase III study comparing atezolizumab plus cobimetinib and atezolizumab monotherapy vs. regorafenib in chemotherapy-refractory metastatic colorectal cancer – Bendell J, et al

Key results (cont.)

OS in key subgroups

Subgroup	n	HR
≥65 years	86	1.50
<65 years	187	0.84
White	223	1.24
Non-white	39	0.40
ECOG PS 0	133	1.13
ECOG PS 1	140	0.85
<18 mo since 1st met diagnosis	83	1.15
≥18 mo since 1st met diagnosis	190	0.95
>3 prior tx in met setting	70	1.58
≤3 prior tx in met setting	203	0.86
Left sided tumour	148	0.97
Right sided tumour	72	0.77
RAS mutant	148	0.81
RAS wild-type	104	1.39
MSI high	3	NE
MSI stable/low	250	1.01
PD-L1 high	110	0.80
PD-L1 low	124	1.26
ITT	273	1.01



*Unstratified

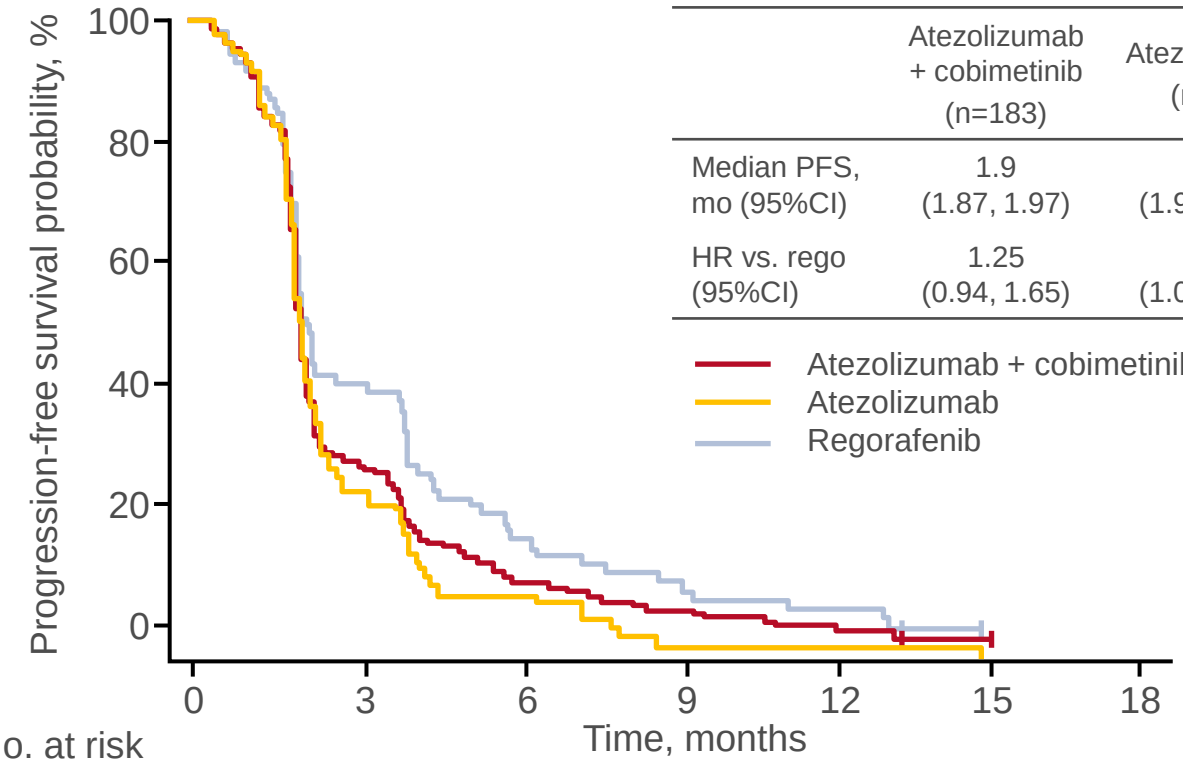
Bendell J, et al. Ann Oncol 2018;29(suppl 5):abstr LBA-004

LBA-004: Efficacy and safety results from IMblaze370, a randomized phase III study comparing atezolizumab plus cobimetinib and atezolizumab monotherapy vs. regorafenib in chemotherapy-refractory metastatic colorectal cancer – Bendell J, et al

Key results (cont.)

PFS

	Atezolizumab + cobimetinib (n=183)	Atezolizumab (n=90)	Regorafenib (n=90)
Median PFS, mo (95%CI)	1.9 (1.87, 1.97)	1.9 (1.91, 2.10)	2.0 (1.87, 3.61)
HR vs. rego (95%CI)	1.25 (0.94, 1.65)	1.39 (1.00, 1.94)	NA



No. at risk						
Atezolizumab + cobimetinib	183	49	18	11	6	1
Atezolizumab	90	22	7	1	1	
Regorafenib	90	33	13	7	5	

Bendell J, et al. Ann Oncol 2018;29(suppl 5):abstr LBA-004

LBA-004: Efficacy and safety results from IMblaze370, a randomized phase III study comparing atezolizumab plus cobimetinib and atezolizumab monotherapy vs. regorafenib in chemotherapy-refractory metastatic colorectal cancer – Bendell J, et al

Key results (cont.)

AEs, n (%)	Atezolizumab + cobimetinib (n=179)	Atezolizumab (n=90)	Regorafenib (n=80)
TRAEs Grade 3–4 Grade 5	170 (95) 80 (45) 2 (1)	49 (54) 9 (10) 0	77 (96) 39 (49) 1 (1)
SAEs Treatment related	71 (40) 46 (26)	15 (17) 7 (8)	18 (23) 9 (11)
Leading to withdrawal	37 (21)	4 (4)	7 (9)
Leading to dose interruption or modification	109 (61)	18 (20)	55 (69)

Conclusions

- **In patients with chemotherapy refractory mCRC neither atezolizumab + cobimetinib or atezolizumab alone improved OS compared with regorafenib**
- **The safety profile of atezolizumab + cobimetinib was similar to the safety profiles of the individual agents**

Bendell J, et al. Ann Oncol 2018;29(suppl 5):abstr LBA-004

O-012: Safety and effectiveness of regorafenib in patients with metastatic colorectal cancer (mCRC) in routine clinical practice: Final analysis from prospective, observational CORRELATE study – Ducreux M, et al

Study objectives

- To assess the efficacy and safety of regorafenib in patients with mCRC in the real-world CORRELATE study

Key patient inclusion criteria

- mCRC
- Previously treated with other approved therapies
- Physician's decision to treat with regorafenib

(n=1037)

PRIMARY ENDPOINT

- Safety

SECONDARY ENDPOINTS

- OS, PFS

Ducreux M, et al. Ann Oncol 2018;29(suppl 5):abstr O-012

O-012: Safety and effectiveness of regorafenib in patients with metastatic colorectal cancer (mCRC) in routine clinical practice: Final analysis from prospective, observational CORRELATE study – Ducreux M, et al

Key results

AE, n (%)	Regardless of relation to drug	Drug related
Any	990 (95)	830 (80)
Grade 3	426 (41)	338 (33)
Grade 4	41 (4)	22 (2)
Grade 5	175 (17)	10 (1)
SAEs	443 (43)	116 (11)
Leading to treatment discontinuation	330 (32)	163 (16)
Leading to dose reduction	266 (26)	251 (24)
Leading to treatment interruption	439 (42)	319 (31)

- Drug-related grade ≥3 AEs occurring >5% of patients in included: fatigue (9%), hand-foot skin reaction (7%) and hypertension (6%)

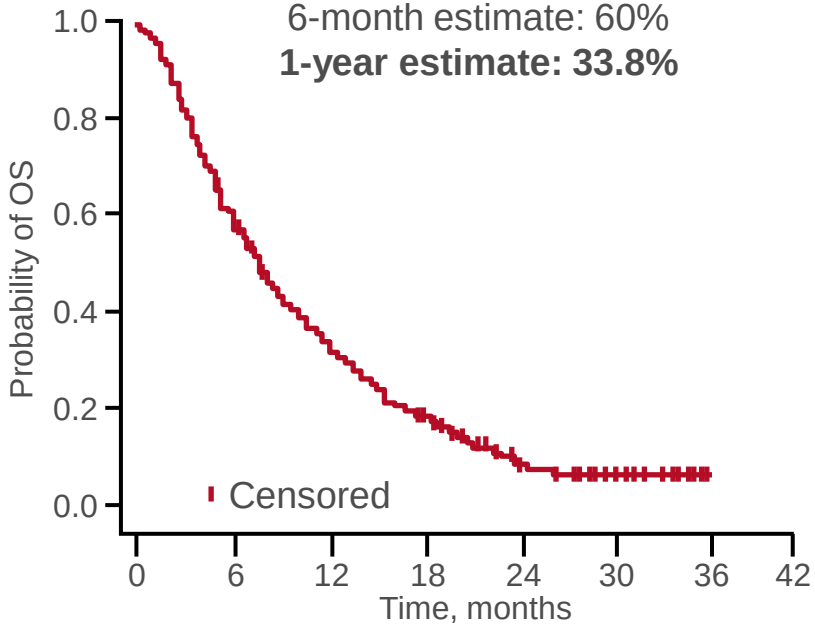
Ducreux M, et al. Ann Oncol 2018;29(suppl 5):abstr O-012

O-012: Safety and effectiveness of regorafenib in patients with metastatic colorectal cancer (mCRC) in routine clinical practice: Final analysis from prospective, observational CORRELATE study – Ducreux M, et al

Key results (cont.)

Overall survival

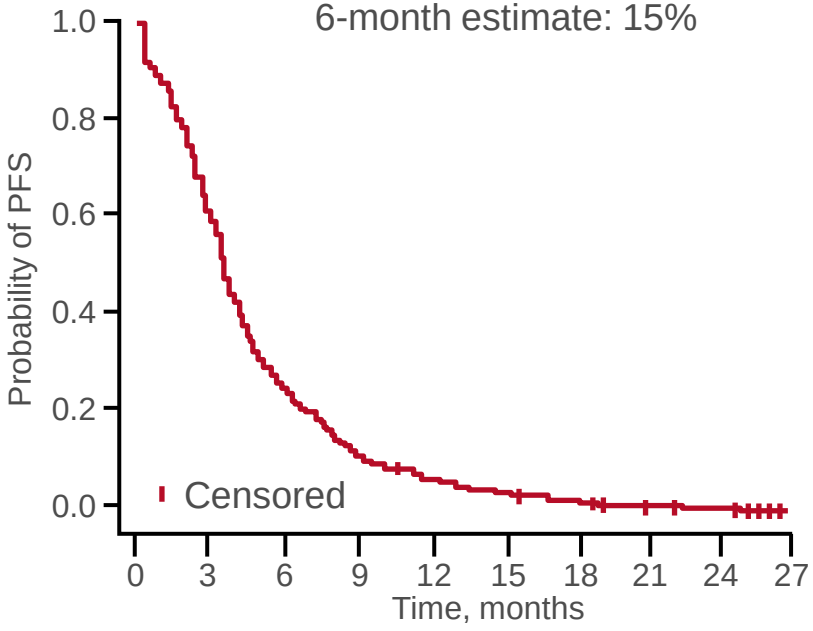
Median 7.6 months (95%CI 7.1, 8.2)
3-month estimate: 82%
6-month estimate: 60%
1-year estimate: 33.8%



No. at risk	1037	586	210	50	18	5	2

Progression-free survival

Median 2.8 months (95%CI 2.6, 2.8)
3-month estimate: 43%
6-month estimate: 15%



No. at risk	1037	417	167	59	31	12	4	2	1

Ducreux M, et al. Ann Oncol 2018;29(suppl 5):abstr O-012

O-012: Safety and effectiveness of regorafenib in patients with metastatic colorectal cancer (mCRC) in routine clinical practice: Final analysis from prospective, observational CORRELATE study – Ducreux M, et al

Conclusions

- **In patients with mCRC, regorafenib demonstrated a safety profile that was similar to previous findings**
- **Nearly 50% of the patients initiated regorafenib at a lower dose than the recommended 160 mg/day**
- **Survival rates with regorafenib were comparable to those seen in previous phase III clinical trials even with flexible dosing**

Ducreux M, et al. Ann Oncol 2018;29(suppl 5):abstr O-012

O-013: Safety and efficacy of trifluridine/tipiracil in previously treated metastatic colorectal cancer (mCRC): Preliminary results from the phase IIIb, international, open-label, early-access PRECONNECT study – Falcone A, et al

Study objective

- To assess the efficacy and safety of trifluridine/tipiracil in previously treated patients with mCRC in the open-label, early access PRECONNECT study (preliminary data reported)

Key patient inclusion criteria

- mCRC
- ≥2 prior chemotherapy regimens
- Refractory, intolerant or unsuitable for fluoropyrimidine, irinotecan, oxaliplatin, anti-VEGF or anti-EGFR for RAS WT
- ECOG PS 0–1

(n=462)

→ Trifluridine/tipiracil 35 mg/m^2 oral bid D1–5, 8–12 of 28-day cycle → **PD/ toxicity**

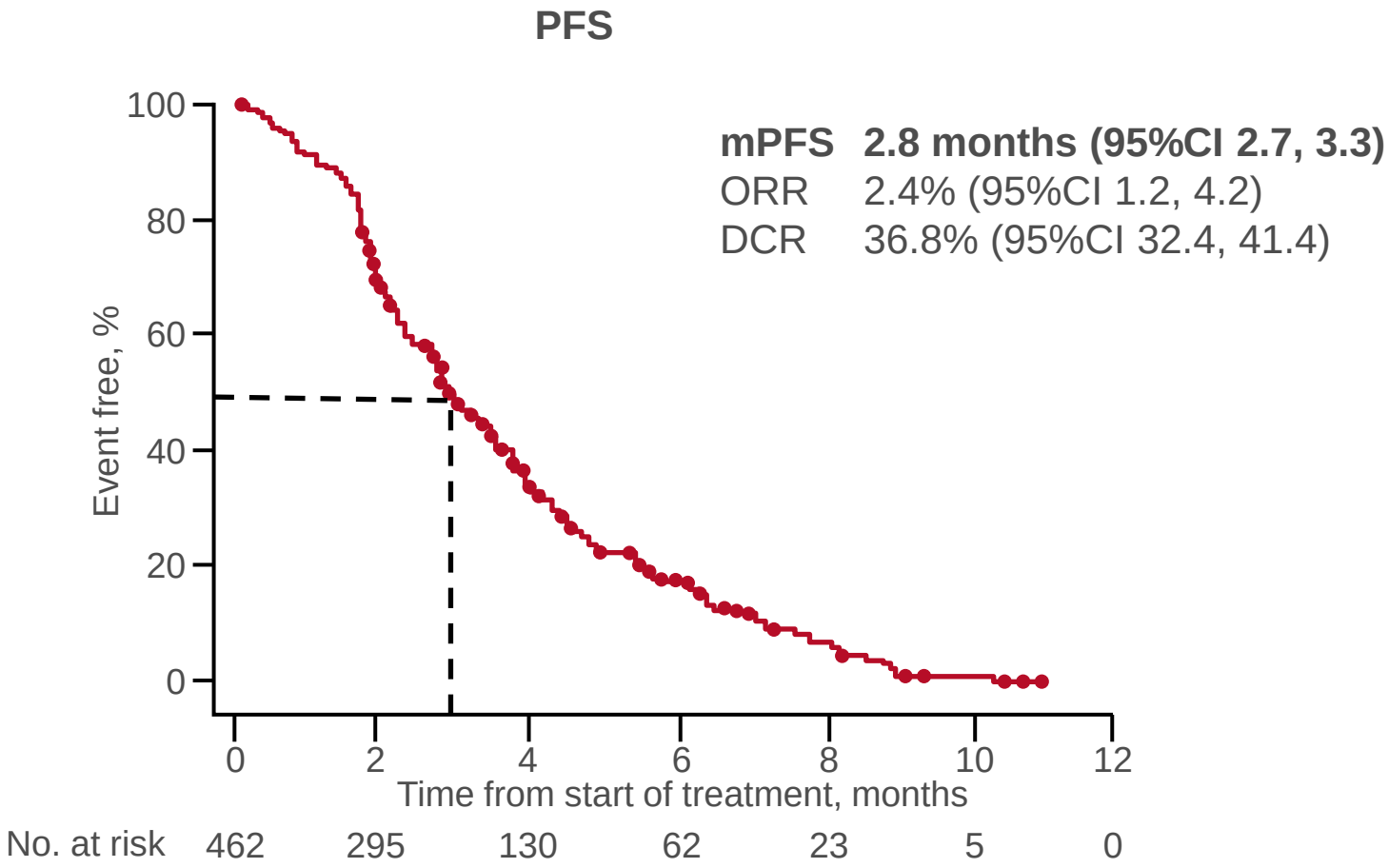
ENDPOINTS

- Safety, PFS, ORR, DCR, time to deterioration to ECOG PS ≥2, QoL

Falcone A, et al. Ann Oncol 2018;29(suppl 5):abstr O-013

O-013: Safety and efficacy of trifluridine/tipiracil in previously treated metastatic colorectal cancer (mCRC): Preliminary results from the phase IIIb, international, open-label, early-access PRECONNECT study – Falcone A, et al

Key results

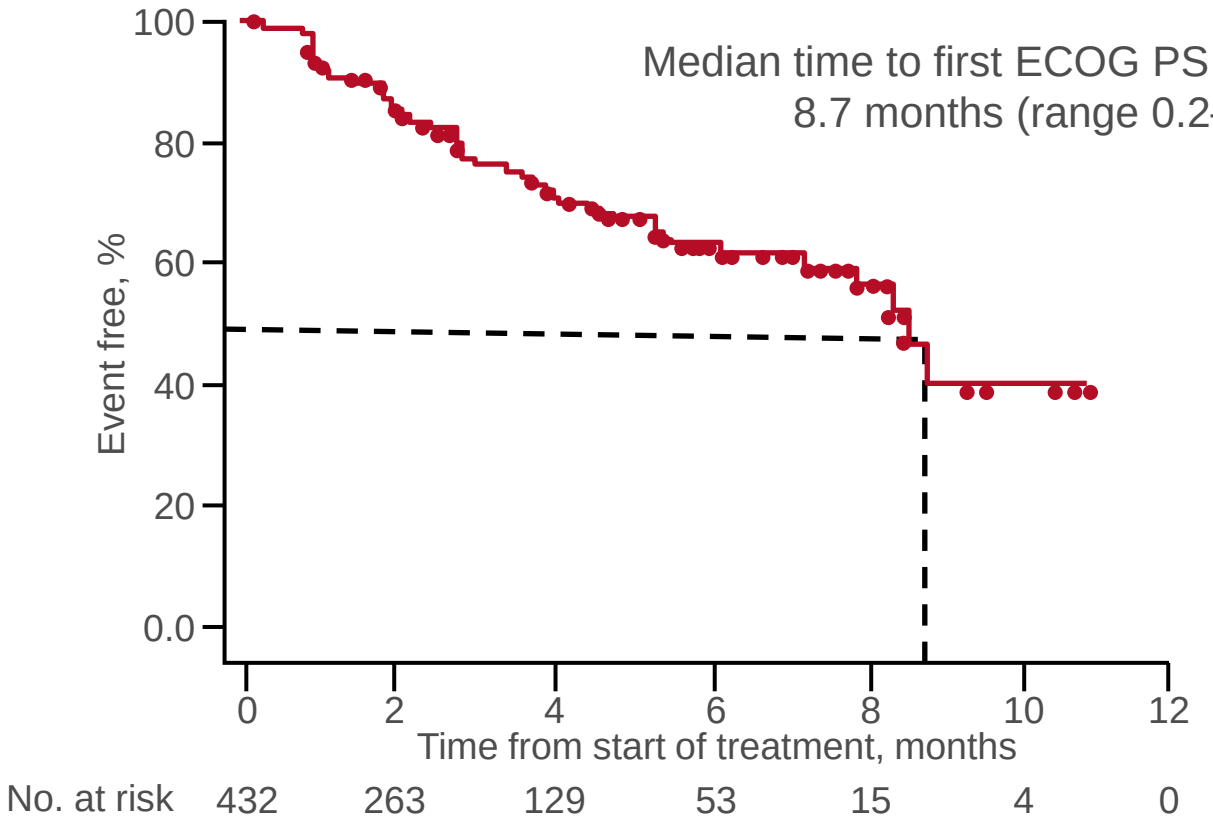


Falcone A, et al. Ann Oncol 2018;29(suppl 5):abstr O-013

O-013: Safety and efficacy of trifluridine/tipiracil in previously treated metastatic colorectal cancer (mCRC): Preliminary results from the phase IIIb, international, open-label, early-access PRECONNECT study – Falcone A, et al

Key results (cont.)

Deterioration in ECOG PS – time to ECOG PS ≥2



Falcone A, et al. Ann Oncol 2018;29(suppl 5):abstr O-013

O-013: Safety and efficacy of trifluridine/tipiracil in previously treated metastatic colorectal cancer (mCRC): Preliminary results from the phase IIIb, international, open-label, early-access PRECONNECT study – Falcone A, et al

Key results (cont.)

Grade ≥3 AEs occurring in >2%, n (%)	Regardless of relation to drug
Haematological	
Neutropenia	182 (39.3)
Anaemia	55 (11.8)
Non-haematological	
Diarrhoea	24 (5.2)
Fatigue	15 (3.2)
Asthenia	12 (2.6)

Conclusion

- **In previously treated patients with mCRC, this preliminary data demonstrated that trifluridine/tipiracil had a safety profile similar to previous findings and was efficacious with improvements in time to deterioration of ECOG PS and PFS**

Falcone A, et al. Ann Oncol 2018;29(suppl 5):abstr O-013

O-014: Regorafenib dose optimization study (reDOS): Randomized phase II trial to evaluate escalating dosing strategy and pre-emptive topical steroids for regorafenib in refractory metastatic colorectal cancer (mCRC) – An ACCRU network study – Bekaii-Saab T, et al

Study objective

- To determine the optimal dose of regorafenib to enable maintenance of benefits and improve tolerability in patients with refractory mCRC in the ReDOS study

Key patient inclusion criteria

- Refractory mCRC
- Failure of all standard iv regimens including appropriate biologics
- No prior regorafenib
- ECOG PS 0–1

(n=363)

R
1:1:1:1

- **Arm A1**: Regorafenib start low* + pre-emptive strategy for PPES
- **Arm A2**: Regorafenib start low* + reactive strategy for PPES
- **Arm B1**: Regorafenib 160 mg/day oral 21 days + pre-emptive strategy for PPES
- **Arm B2**: Regorafenib 160 mg/day oral 21 days + reactive strategy for PPES

PRIMARY ENDPOINT

- Proportion of patients who completed 2 cycles and cold initiate cycle 3

SECONDARY ENDPOINTS

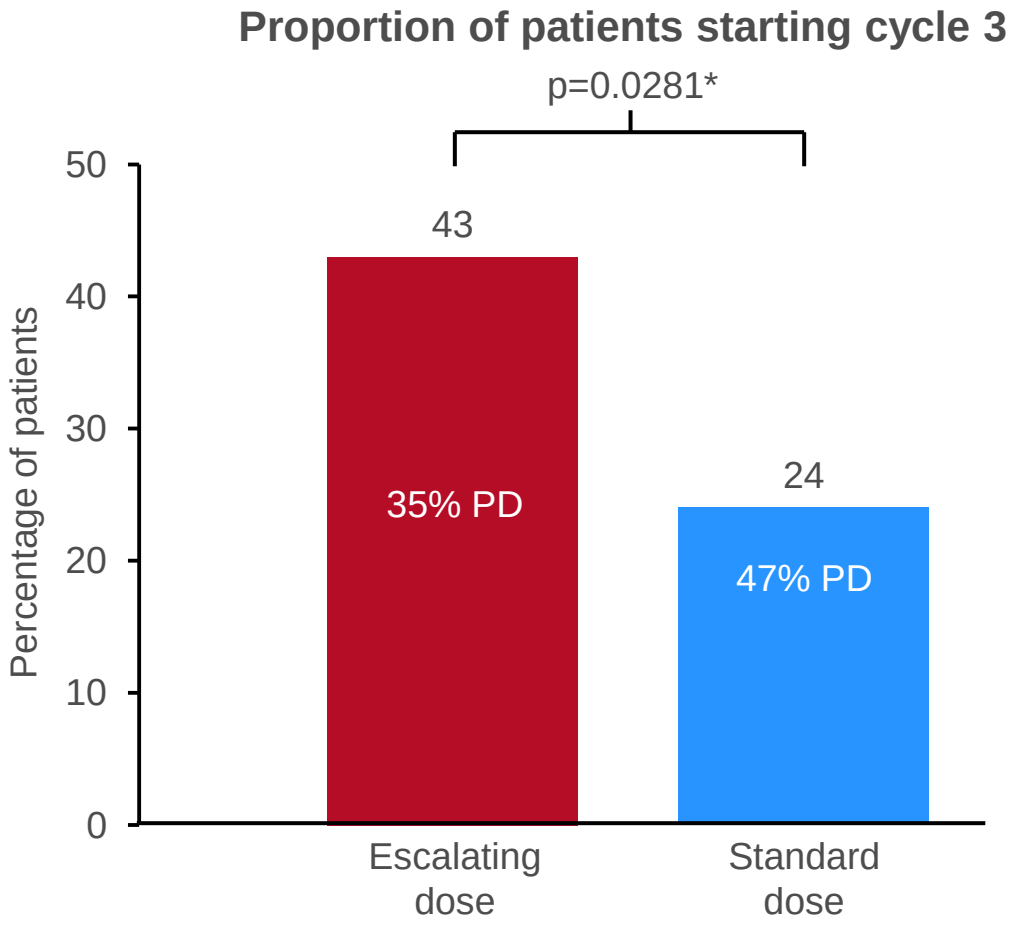
- OS, PFS, TTP

*Cycle 1 week 1 80 mg, week 2 120 mg and week 3 160 mg

Bekaii-Saab T, et al. Ann Oncol 2018;29(suppl 5):abstr O-014

O-014: Regorafenib dose optimization study (reDOS): Randomized phase II trial to evaluate escalating dosing strategy and pre-emptive topical steroids for regorafenib in refractory metastatic colorectal cancer (mCRC) – An ACCRU network study – Bekaii-Saab T, et al

Key results



*Fisher's exact test (1-sided)

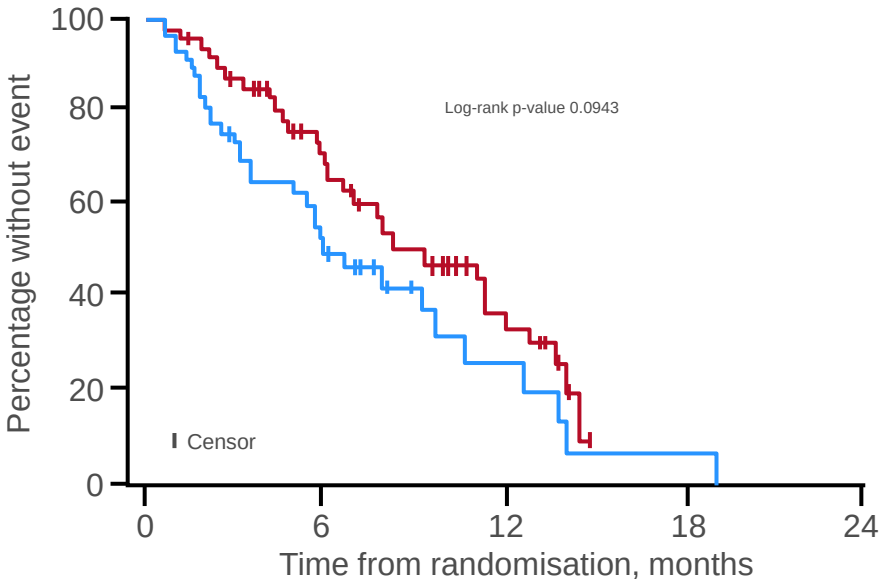
Bekaii-Saab T, et al. Ann Oncol 2018;29(suppl 5):abstr O-014

O-014: Regorafenib dose optimization study (reDOS): Randomized phase II trial to evaluate escalating dosing strategy and pre-emptive topical steroids for regorafenib in refractory metastatic colorectal cancer (mCRC) – An ACCRU network study – Bekaii-Saab T, et al

Key results (cont.)

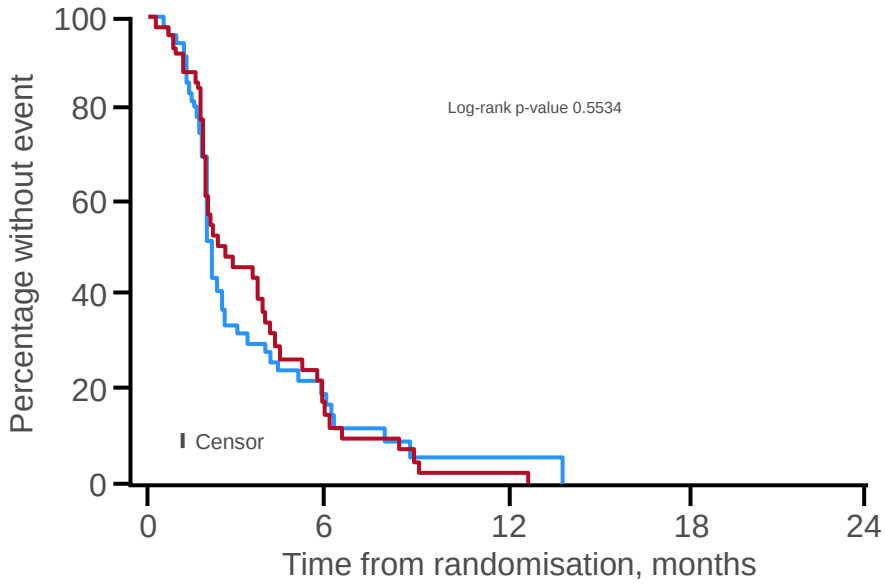
OS

	Events/ total	Median (95%CI)	Time period	KM estimate (95%CI)	HR (95%CI)
Arm A	29/54	9.0 (6.8, 13.4)	6 months 12 months	66.5 (53.8, 82.2) 34.4 (21.5, 55.2)	0.65 (0.39, 1.08)
Arm B	34/62	5.9 (5.3, 12.4)	6 months 12 months	49.8 (37.2, 66.8) 26.7 (14.0, 51.1)	Reference



PFS

	Events/ total	Median (95%CI)	Time period	KM estimate (95%CI)	HR (95%CI)
Arm A	45/54	2.5 (1.9, 4.0)	6 months 12 months	12.2 (5.4, 27.5) 2.4 (0.4, 16.9)	0.89 (0.59, 1.33)
Arm B	50/62	2.0 (1.8, 2.4)	6 months 12 months	11.8 (5.2, 26.6) 5.9 (1.6, 21.0)	Reference



Bekaii-Saab T, et al. Ann Oncol 2018;29(suppl 5):abstr O-014

O-014: Regorafenib dose optimization study (reDOS): Randomized phase II trial to evaluate escalating dosing strategy and pre-emptive topical steroids for regorafenib in refractory metastatic colorectal cancer (mCRC) – An ACCRU network study – Bekaii-Saab T, et al

Key results (cont.)

AEs occurring in ≥5%, n (%)	Escalating dose (n=54)		Standard dose (n=82)	
	Grade 3	Grade 4	Grade 3	Grade 4
Fatigue	7 (13.0)	0	11 (17.7)	0
PPES	8 (14.8)	0	10 (16.1)	0
Abdominal pain	9 (16.7)	0	4 (6.5)	0
Hypertension	4 (7.4)	0	9 (14.5)	0
Hyponatremia	2 (3.7)	1 (1.9)	4 (6.5)	1 (1.6)
Bilirubin increased	2 (3.7)	0	5 (8.1)	0
ALP increased	3 (5.6)	0	1 (1.6)	1 (1.6)
AST increased	1 (1.9)	0	4 (6.5)	0
Dehydration	0	0	5 (8.1)	0
Lymphocyte count decreased	4 (7.4)	0	0	0

Conclusion

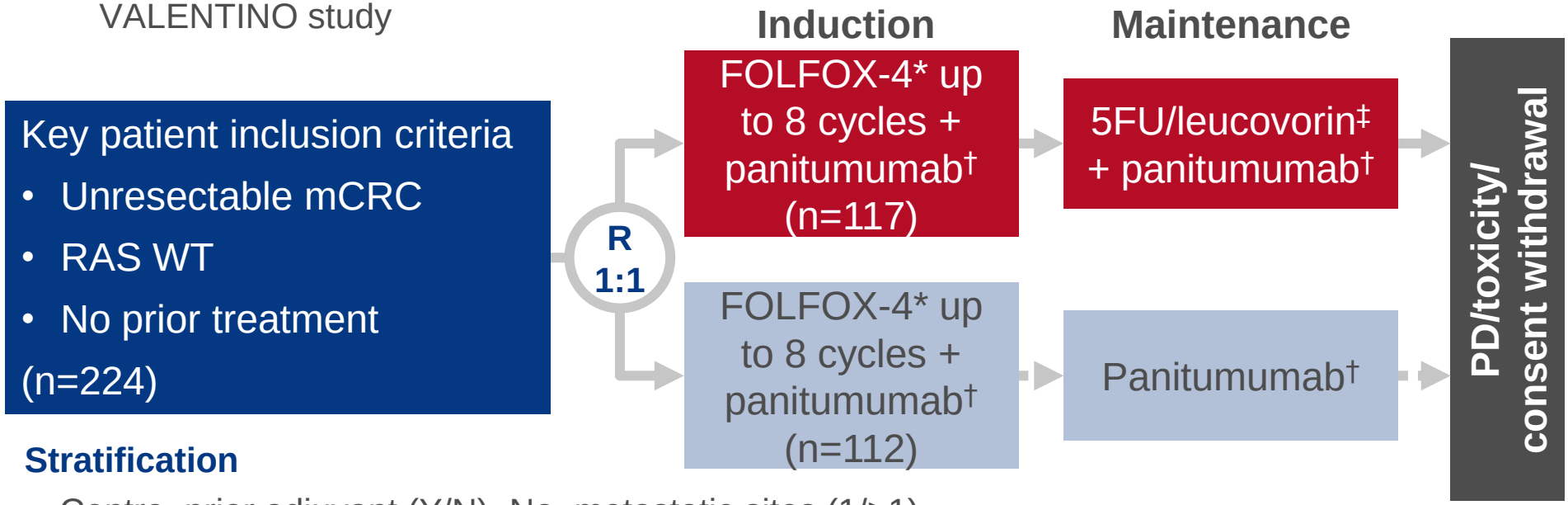
- **In patients with refractory mCRC, using an escalating dosing strategy for regorafenib was superior to the standard dosing strategy and may provide a new optimal dosing strategy**

Bekaii-Saab T, et al. Ann Oncol 2018;29(suppl 5):abstr O-014

O-016: First-line FOLFOX plus panitumumab followed by 5-FU/LV plus panitumumab or single-agent panitumumab as maintenance therapy in patients with RAS wild-type metastatic colorectal cancer (mCRC): The VALENTINO study – Pietrantonio F, et al

Study objective

- To assess the efficacy and safety of FOLFOX + panitumumab followed by 5FU/leucovorin + panitumumab as maintenance therapy in patients with RAS WT mCRC in the VALENTINO study



Stratification

- Centre, prior adjuvant (Y/N), No. metastatic sites (1/>1)

PRIMARY ENDPOINT

- 10-month PFS rate

SECONDARY ENDPOINTS

- Safety, PFS by tumour sidedness

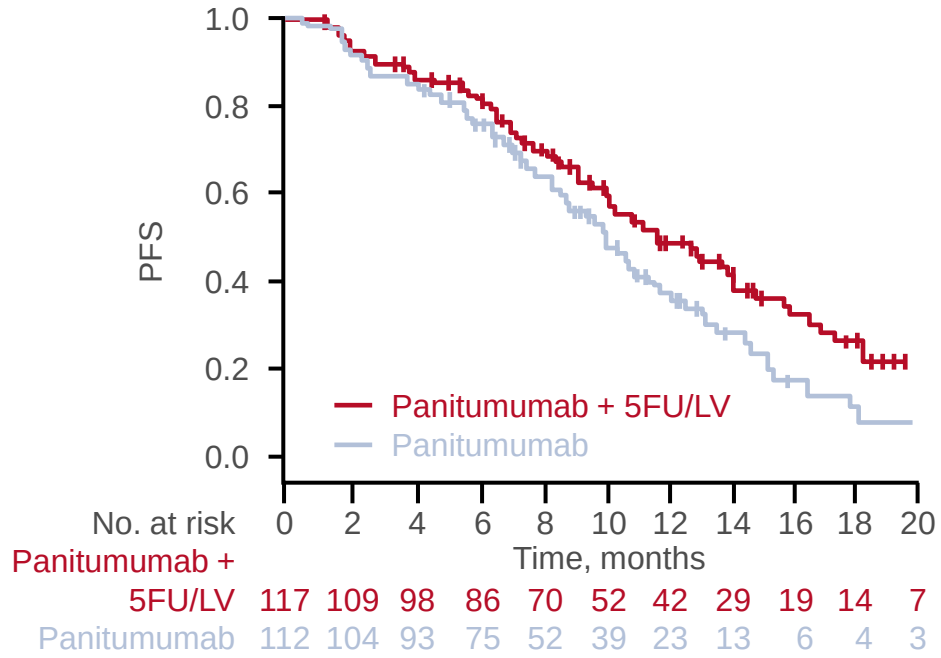
*Oxaliplatin 85 mg/m^2 D1 + LV 200 mg/m^2 D1,2 + 5FU bolus 400 mg/m^2 D1,2 + 5FU pvi 600 mg/m^2 D1,2 q14; †6 mg/kg D1 q14; ‡LV 200 mg/m^2 D1,2 + 5FU bolus 400 mg/m^2 D1,2 + 5FU pvi 600 mg/m^2 D1,2 q14

Pietrantonio F, et al. Ann Oncol 2018;29(suppl 5):abstr O-016

O-016: First-line FOLFOX plus panitumumab followed by 5-FU/LV plus panitumumab or single-agent panitumumab as maintenance therapy in patients with RAS wild-type metastatic colorectal cancer (mCRC): The VALENTINO study – Pietrantonio F, et al

Key results

PFS



Median follow-up 13.8 months (IQR 8.6–18.3)

HR 1.55 (95%CI 1.09, 2.20); p=0.011

	10-month PFS		Median PFS	
	Rate, %	95%CI	Mo	95%CI
Arm A (5FU/LV + panitumumab)	62.8	54.0, 73.1	13.0	10.5, 16.0
Arm B (panitumumab)	52.8	43.4, 64.3	10.2	8.9, 12.2

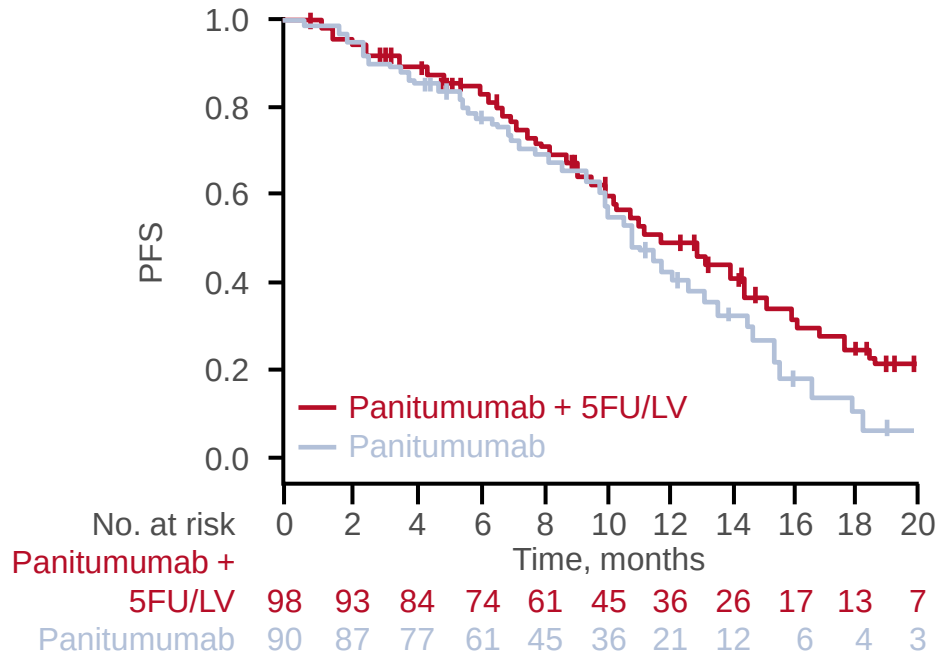
Pietrantonio F, et al. Ann Oncol 2018;29(suppl 5):abstr O-016

O-016: First-line FOLFOX plus panitumumab followed by 5-FU/LV plus panitumumab or single-agent panitumumab as maintenance therapy in patients with RAS wild-type metastatic colorectal cancer (mCRC): The VALENTINO study – Pietrantonio F, et al

Key results (cont.)

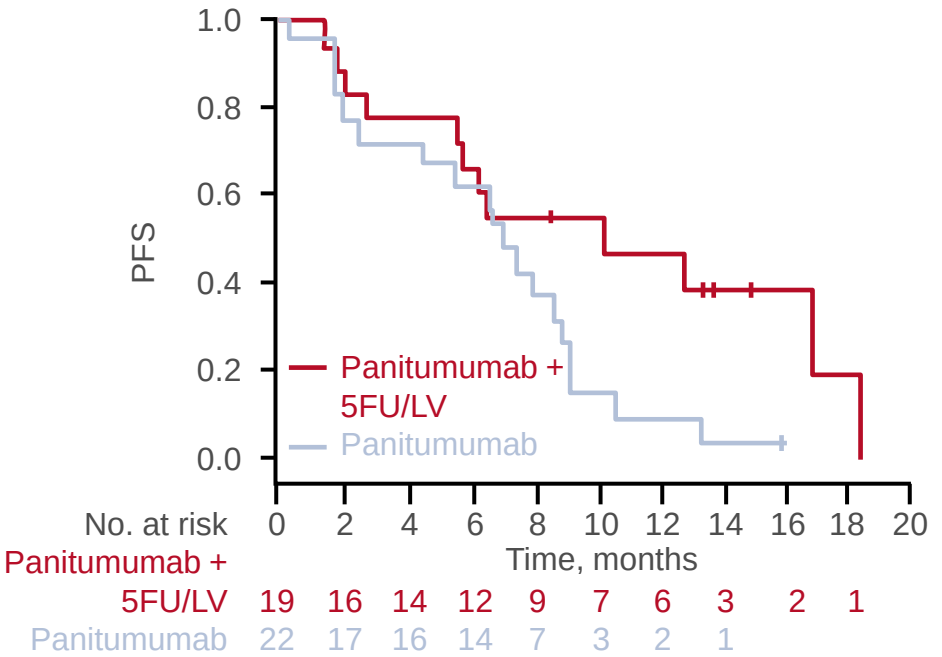
PFS left-sided primary tumours

		10-month PFS		Median PFS	
	n	Rate, %	95%CI	Months	95%CI
Arm A (5FU/LV + panitumumab)	98	64.5	55.0, 75.8	13.2	10.7, 16.0
Arm B (panitumumab)	90	63.0	52.7, 75.4	11.6	10.1, 14.5



PFS right-sided primary tumours

		10-month PFS		Median PFS	
	n	Rate, %	95%CI	Months	95%CI
Arm A (5-FU/LV + panitumumab)	19	55.6	37.0, 84.0	10.4	5.9, NA
Arm B (panitumumab)	22	16.2	6.0, 45.2	7.0	5.5, 8.9



Pietrantonio F, et al. Ann Oncol 2018;29(suppl 5):abstr O-016

O-016: First-line FOLFOX plus panitumumab followed by 5-FU/LV plus panitumumab or single-agent panitumumab as maintenance therapy in patients with RAS wild-type metastatic colorectal cancer (mCRC): The VALENTINO study – Pietrantonio F, et al

Key results (cont.)

AEs occurring in ≥10%, %	5FU/leucovorin + panitumumab (n= 81)		Panitumumab (n=71)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Stomatitis/oral mucositis	27	6	8	1
Diarrhoea	20	4	10	1
Hand-foot syndrome	14	5	10	1
Peripheral neuropathy	26	-	13	1
Neutropenia	11	3	1	-
Skin rash	54	22	46	14
Paronychia	14	1	6	-
Hypomagnesemia	16	1	17	1

Conclusions

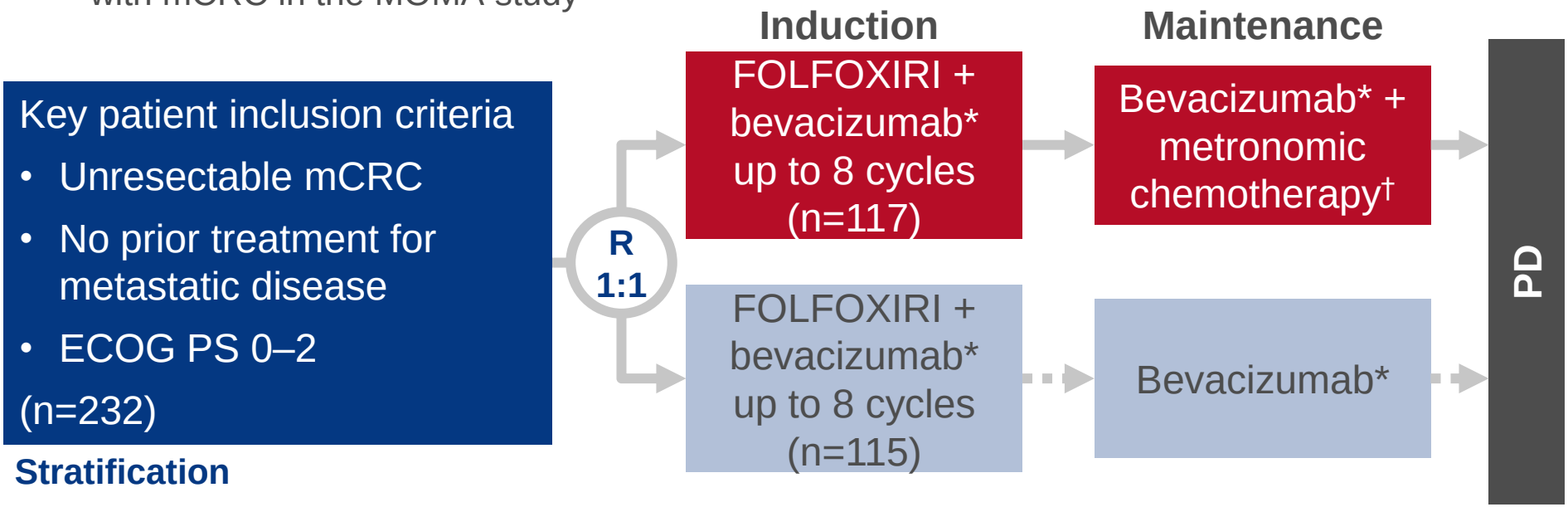
- **In patients with RAS WT mCRC who have received induction therapy with FOLFOX + panitumumab, maintenance treatment with 5FU/leucovorin + panitumumab appears to provide better PFS than maintenance with panitumumab alone**
- **PFS was poorer in those with right-sided tumours, particularly with maintenance with panitumumab alone**

Pietrantonio F, et al. Ann Oncol 2018;29(suppl 5):abstr O-016

O-017: FOLFOXIRI plus bevacizumab (bev) followed by maintenance with bev alone or bev plus metronomic chemotherapy (metroCT) in mCRC: final results of the phase II randomized MOMA trial by GONO – Marmorino F, et al

Study objective

- To assess the efficacy and safety of FOLFOXIRI + bevacizumab followed by bevacizumab alone or bevacizumab + metronomic chemotherapy as maintenance therapy in patients with mCRC in the MOMA study



Stratification

- ECOG PS (0 vs. 1, 2), previous adjuvant chemotherapy

PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

- Safety, PFS by tumour sidedness

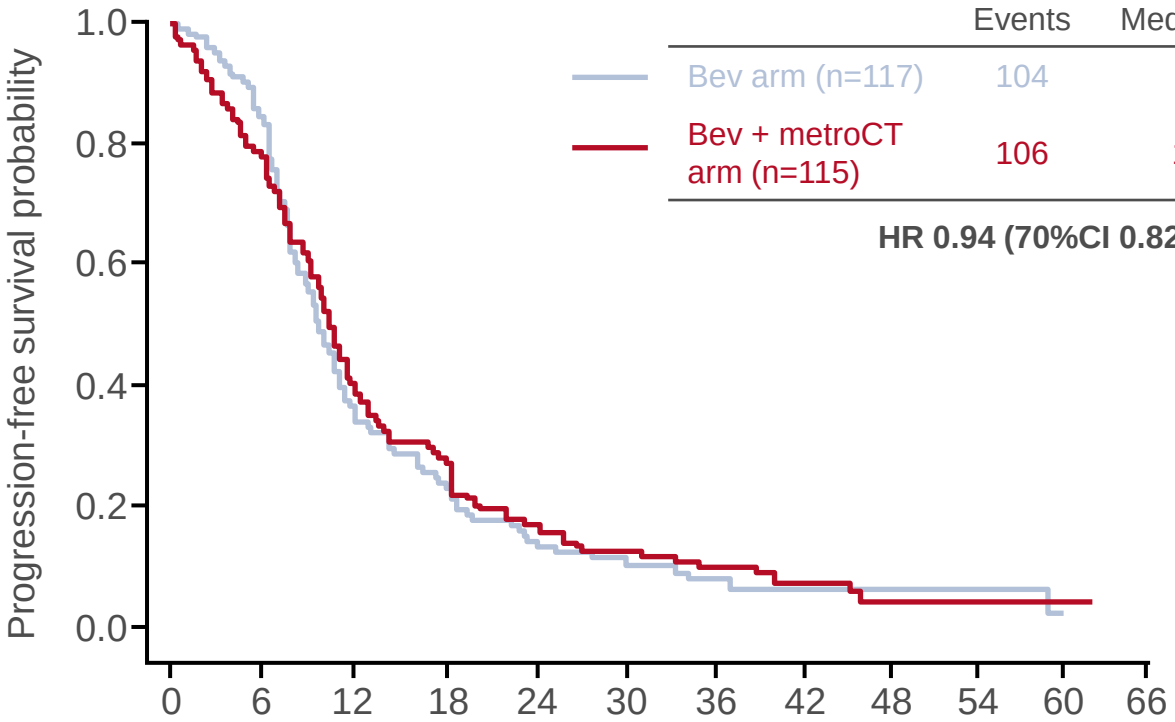
*7.5 m/day q3w; †capecitabine 500 mg tid + cyclophosphamide 50 mg/day

Marmorino F, et al. Ann Oncol 2018;29(suppl 5):abstr O-017

O-017: FOLFOXIRI plus bevacizumab (bev) followed by maintenance with bev alone or bev plus metronomic chemotherapy (metroCT) in mCRC: final results of the phase II randomized MOMA trial by GONO – Marmorino F, et al

Key results

PFS



	Events	Median, mo	70%CI
Bev arm (n=117)	104	9.4	8.3, 10.6
Bev + metroCT arm (n=115)	106	10.3	9.1, 11.6

HR 0.94 (70%CI 0.82, 1.09); p=0.680

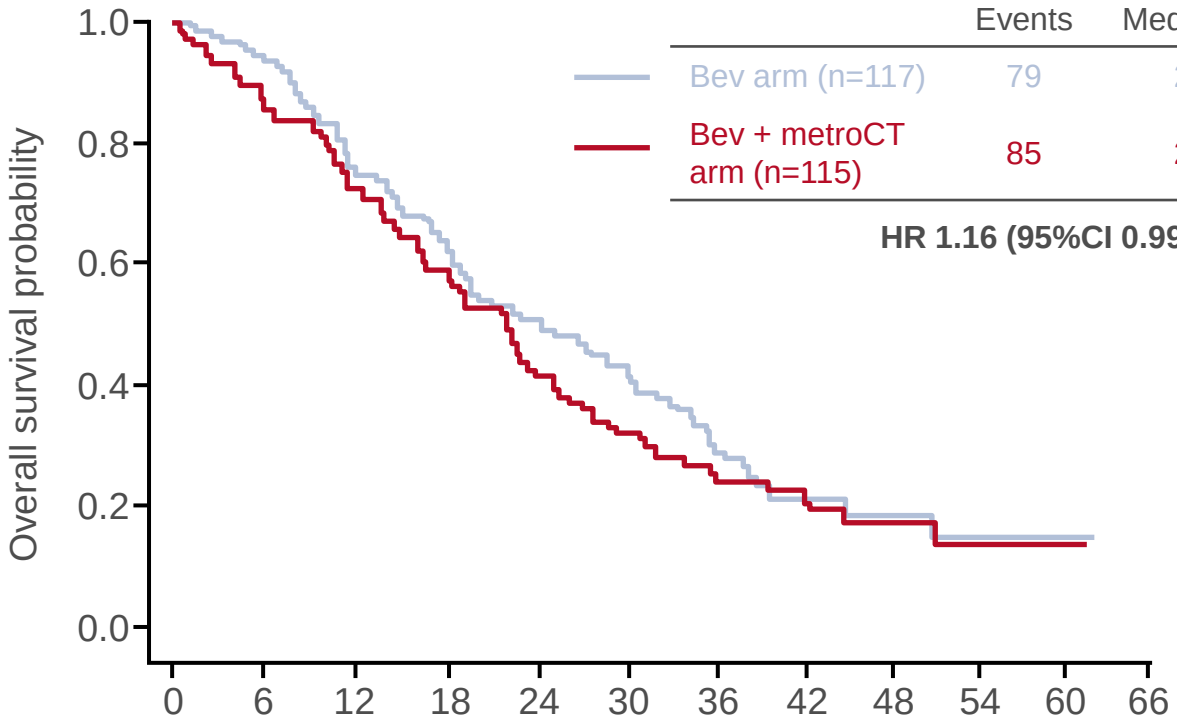
No. at risk												
Maintenance with bev	117	100	40	25	16	12	8	6	4	3	1	0
Maintenance with bev + metroCT	115	90	42	26	19	16	10	8	5	2	1	0

Marmorino F, et al. Ann Oncol 2018;29(suppl 5):abstr O-017

O-017: FOLFOXIRI plus bevacizumab (bev) followed by maintenance with bev alone or bev plus metronomic chemotherapy (metroCT) in mCRC: final results of the phase II randomized MOMA trial by GONO – Marmorino F, et al

Key results (cont.)

OS



	Events	Median, mo	95%CI
Bev arm (n=117)	79	28.0	20.0, 33.6
Bev + metroCT arm (n=115)	85	22.5	18.4, 25.8

HR 1.16 (95%CI 0.99, 1.37); p=0.336

No. at risk												
Maintenance with bev	117	111	89	75	60	50	29	16	10	6	3	0
Maintenance with bev + metroCT	115	101	84	69	51	40	27	18	12	7	1	0

Marmorino F, et al. Ann Oncol 2018;29(suppl 5):abstr O-017

O-017: FOLFOXIRI plus bevacizumab (bev) followed by maintenance with bev alone or bev plus metronomic chemotherapy (metroCT) in mCRC: final results of the phase II randomized MOMA trial by GONO – Marmorino F, et al

Key results (cont.)

Grade 3/4 AEs occurring in ≥5% in induction phase, %	Bev + metronomic CT (n=116)	Bev (n=115)
Vomiting	6.1	0.9
Diarrhoea	15.6	11.1
Neutropenia	50.4	59.5
Febrile neutropenia	8.7	13.8
Asthenia	8.7	12.9
Anorexia	6.1	4.3
Hypertension	1.7	5.2
Venous thrombosis	5.2	1.7

Grade 3/4 AEs in maintenance phase, %	Bev + metronomic CT (n=78)	Bev (n=88)
Neutropenia	3.9	0
Hand-foot syndrome	9.1	0
Hypertension	3.9	4.5

Conclusions

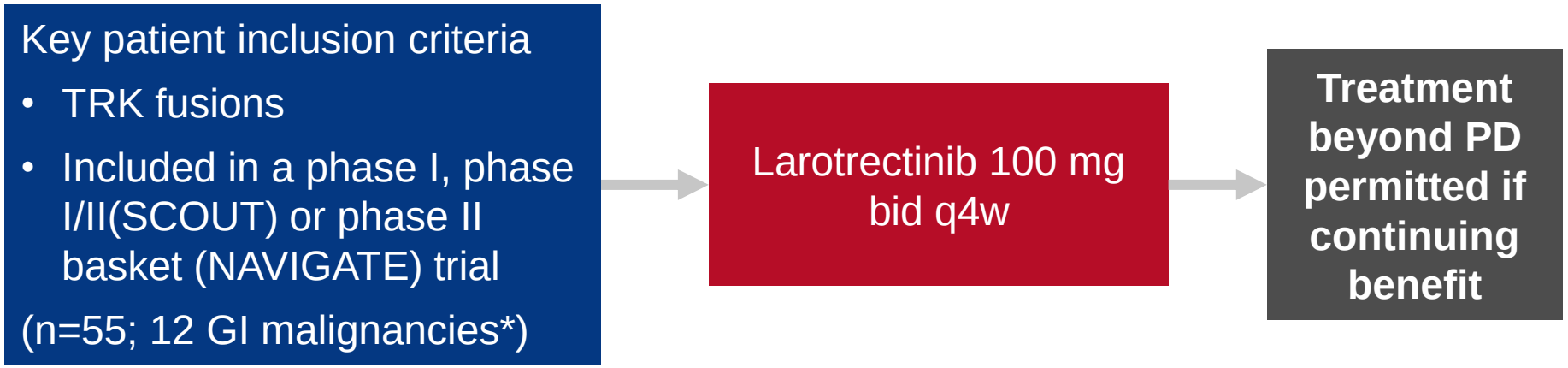
- **In patients with mCRC, after induction therapy with FOLFOXIRI + bevacizumab adding metronomic chemotherapy to bevacizumab as maintenance therapy did not improve PFS**
- **The best maintenance option after a 1L bevacizumab-containing regimen remains the standard of care fluoropyrimidine + bevacizumab**

Marmorino F, et al. Ann Oncol 2018;29(suppl 5):abstr O-017

O-020: Activity of larotrectinib in patients with TRK fusion GI malignancies – Nathenson M, et al

Study objective

- To assess the efficacy and safety of larotrectinib (a TRK inhibitor) in patients with TRK fusion gastrointestinal malignancies pooled data from three trials investigating larotrectinib in patients with solid tumours



PRIMARY ENDPOINT

- BOR (RECIST v1.1)

SECONDARY ENDPOINTS

- DoR, PFS, safety

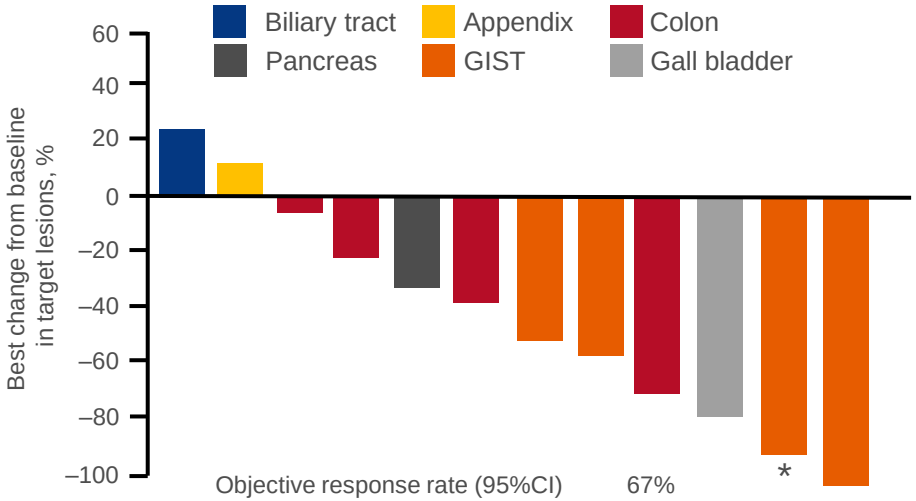
*Colon, GIST, gall bladder, biliary tract, appendix or pancreas

Nathenson M, et al. Ann Oncol 2018;29(suppl 5):abstr O-020

O-020: Activity of larotrectinib in patients with TRK fusion GI malignancies – Nathenson M, et al

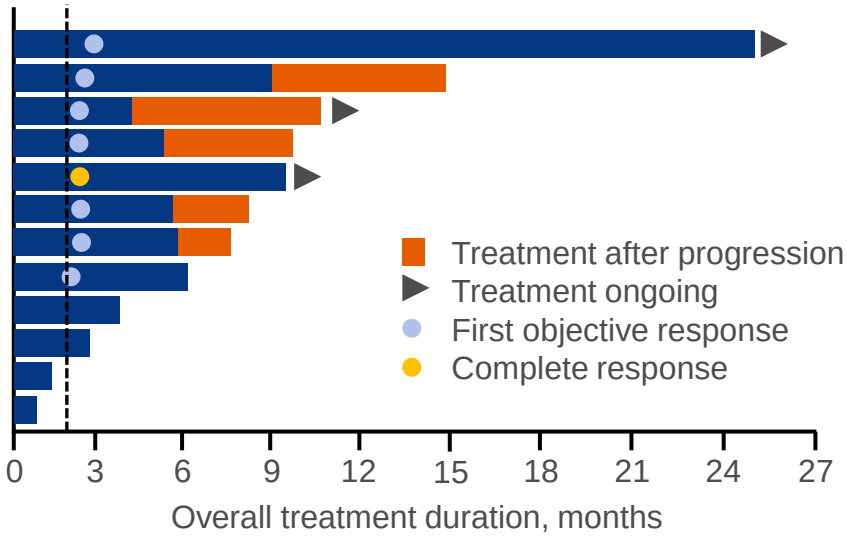
Key results

Best overall response



Objective response rate (95%CI)	67%
Partial response	7
Complete response	1
Stable disease	3
Progressive disease	1

Duration of response



Median time to response = 1.8 months

*One patient initially diagnosed with GIST was determined to have peri-rectal undifferentiated soft tissue sarcoma

Nathenson M, et al. Ann Oncol 2018;29(suppl 5):abstr O-020

O-020: Activity of larotrectinib in patients with TRK fusion GI malignancies – Nathenson M, et al

Key results (cont.)

Grade 3 TRAEs, %	
Increased ALT/AST	5
Dizziness	2
Nausea	2
Anaemia	2
Decreased neutrophil count	2

Conclusion

- **In patients with TRK fusion gastrointestinal malignancies, larotrectinib provided durable and clinically meaningful responses and was associated with minimal toxicity with prolonged treatment**

Nathenson M, et al. Ann Oncol 2018;29(suppl 5):abstr O-020

O-021: Safety and antitumor activity of pembrolizumab in patients with advanced microsatellite instability–high (MSI-H) colorectal cancer: KEYNOTE-164 – Le D, et al

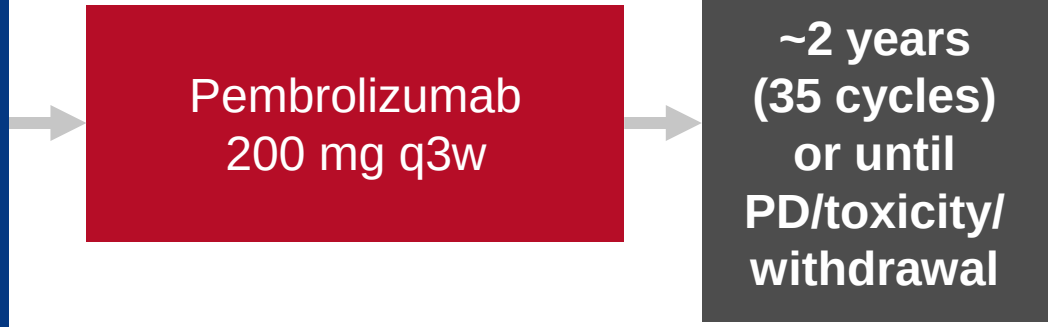
Study objective

- To assess the efficacy and safety of pembrolizumab in patients with advanced MSI-H CRC in the KEYNOTE-164 study

Key patient inclusion criteria

- Locally advanced, unresectable or metastatic CRC
- dMMR/MSI-H CRC by IHC/PCR
- ≥1 prior line of therapy
- ECOG PS 0–1

(n=63)



PRIMARY ENDPOINT

- ORR

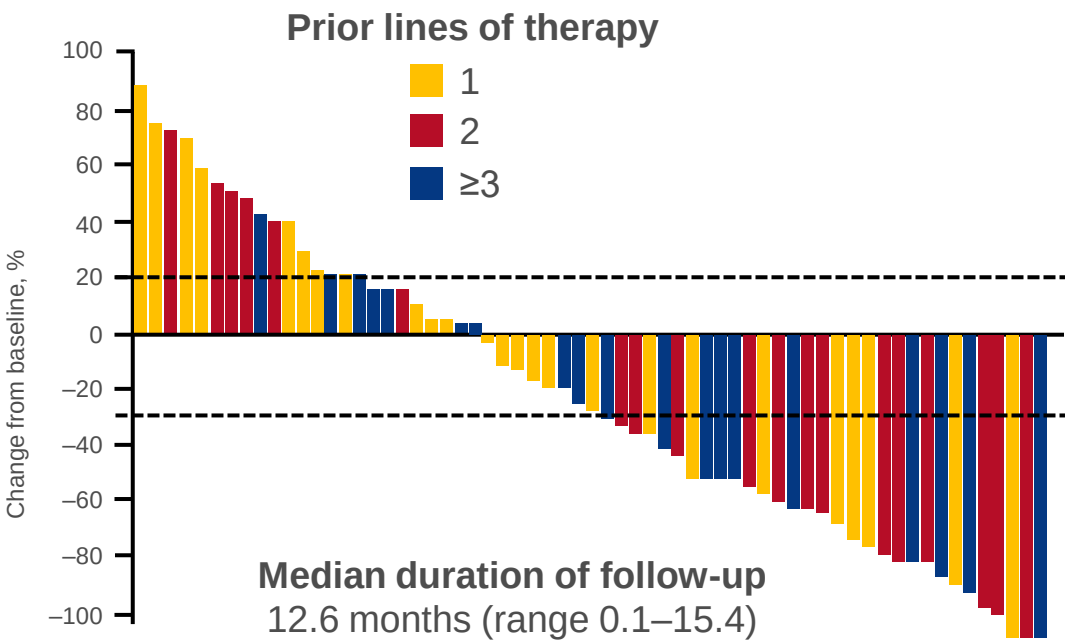
SECONDARY ENDPOINTS

- DoR, PFS, OS, safety

Le D, et al. Ann Oncol 2018;29(suppl 5):abstr O-021

O-021: Safety and antitumor activity of pembrolizumab in patients with advanced microsatellite instability–high (MSI-H) colorectal cancer: KEYNOTE-164 – Le D, et al

Key results



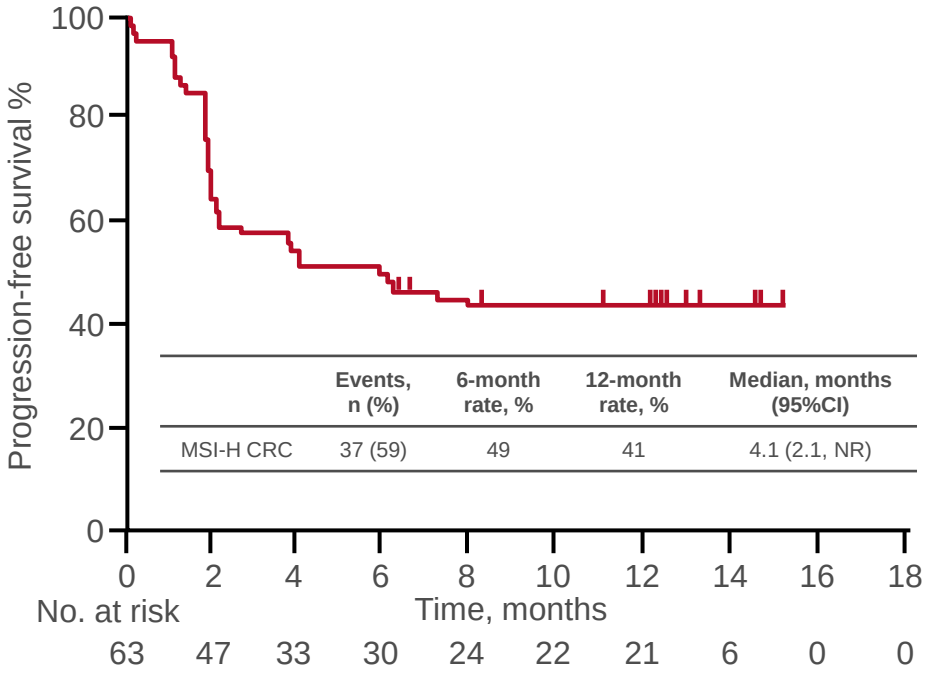
Pembrolizumab (n=63)	
ORR, n (%) [95%CI]	20 (32) [21, 45]
CR	2 (3) [0, 11]
PR	18 (29) [18,41]
SD	16 (25) [15, 38]
PD	25 (40) [28, 53]
DCR	36 (57) [44, 70]
mTTR, months (range)	3.9 (1.8–10.4)
mDoR, months (range)	NR (2.1+–13.2+)
ORR, n/N (%) BRAF mutated BRAF WT	 1/5 (20) 13/29 (45)
ORR, n/N (%) KRAS mutated KRAS WT	 8/22 (36) 11/34 (32)

Le D, et al. Ann Oncol 2018;29(suppl 5):abstr O-021

O-021: Safety and antitumor activity of pembrolizumab in patients with advanced microsatellite instability–high (MSI-H) colorectal cancer: KEYNOTE-164 – Le D, et al

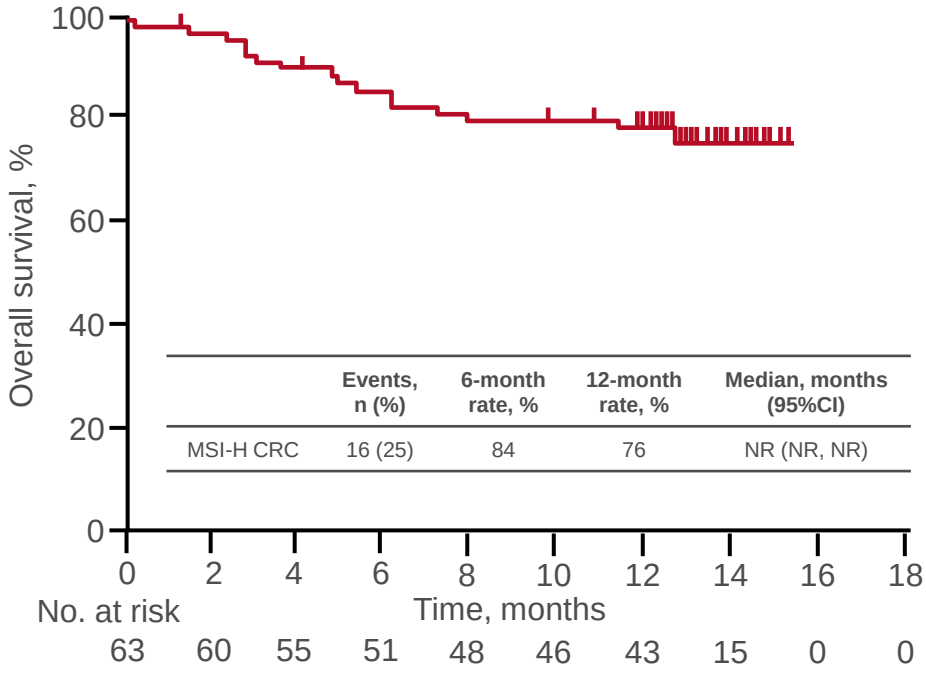
Key results (cont.)

PFS



	Events, n (%)	6-month rate, %	12-month rate, %	Median, months (95%CI)
MSI-H CRC	37 (59)	49	41	4.1 (2.1, NR)

OS



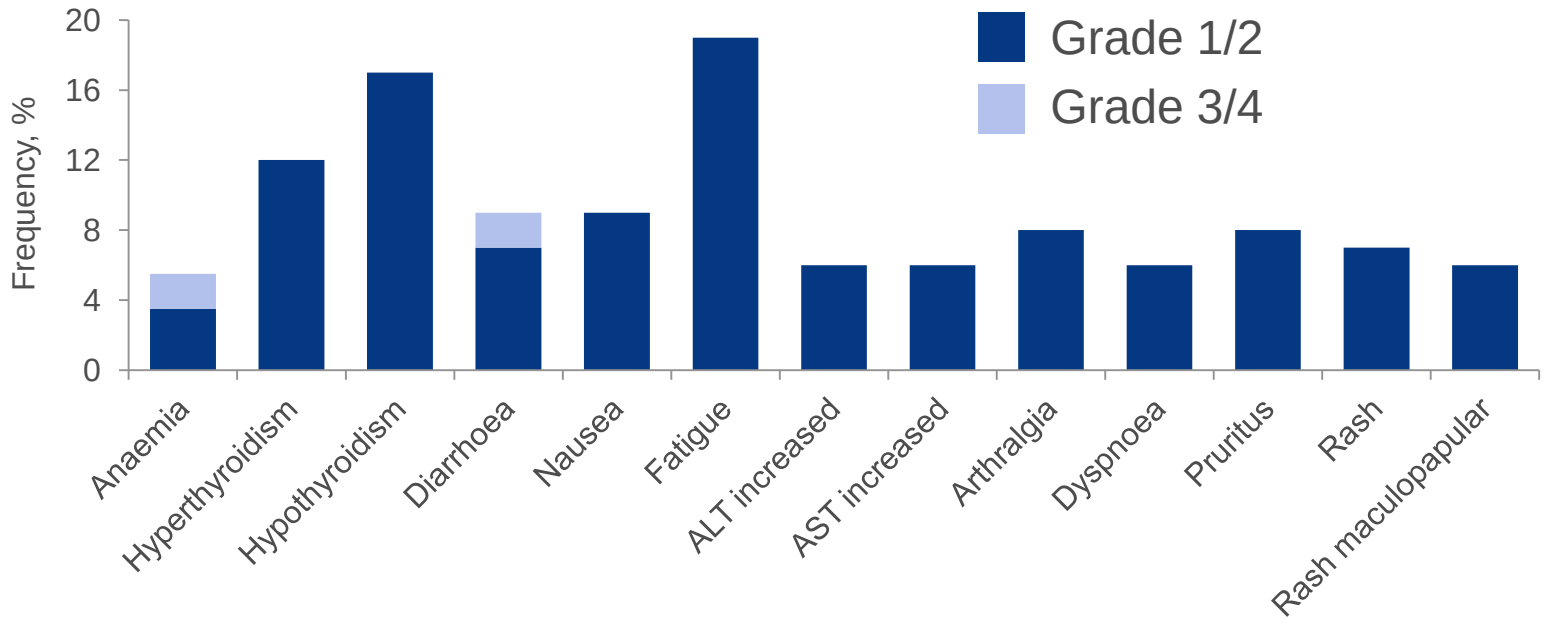
	Events, n (%)	6-month rate, %	12-month rate, %	Median, months (95%CI)
MSI-H CRC	16 (25)	84	76	NR (NR, NR)

Data cut-off: 12 September 2017

Le D, et al. Ann Oncol 2018;29(suppl 5):abstr O-021

O-021: Safety and antitumor activity of pembrolizumab in patients with advanced microsatellite instability–high (MSI-H) colorectal cancer: KEYNOTE-164 – Le D, et al

Key results (cont.)



Conclusion

- **In previously treated patients with advanced MSI-H CRC, pembrolizumab demonstrated durable responses and a safety profile comparable to previous studies in patients with solid tumours**

Le D, et al. Ann Oncol 2018;29(suppl 5):abstr O-021

O-022: Phase II study evaluating trifluridine/tipiracil+bevacizumab and capecitabine+bevacizumab in first-line unresectable metastatic colorectal cancer (mCRC) patients who are non-eligible for intensive therapy (TASCO1): results of the primary analysis – Van Cutsem E, et al

Study objective

- To assess the efficacy and safety of trifluridine/tipiracil + bevacizumab and capecitabine + bevacizumab as a 1L therapy for patients with unresectable mCRC who are not eligible for intensive therapy in the TASCO1 study

Key patient inclusion criteria

- mCRC
- No prior treatment for metastatic disease
- Not eligible for intensive therapy according to investigator's judgement
- ECOG PS 0–2

(n=153)

R

Trifluridine/tipiracil 35 mg bid D1–5, 8–12 + bevacizumab 5 mg/kg D1,15 q4w (n=77)

Capecitabine 1250 or 1000 mg/m^2 bid D1–14 + bevacizumab 7.5 mg/kg iv D1 q3w (n=76)

PD/ toxicity/ patient decision

PD/ toxicity/ patient decision

Stratification

- RAS status, ECOG PS, country

PRIMARY ENDPOINT

- PFS

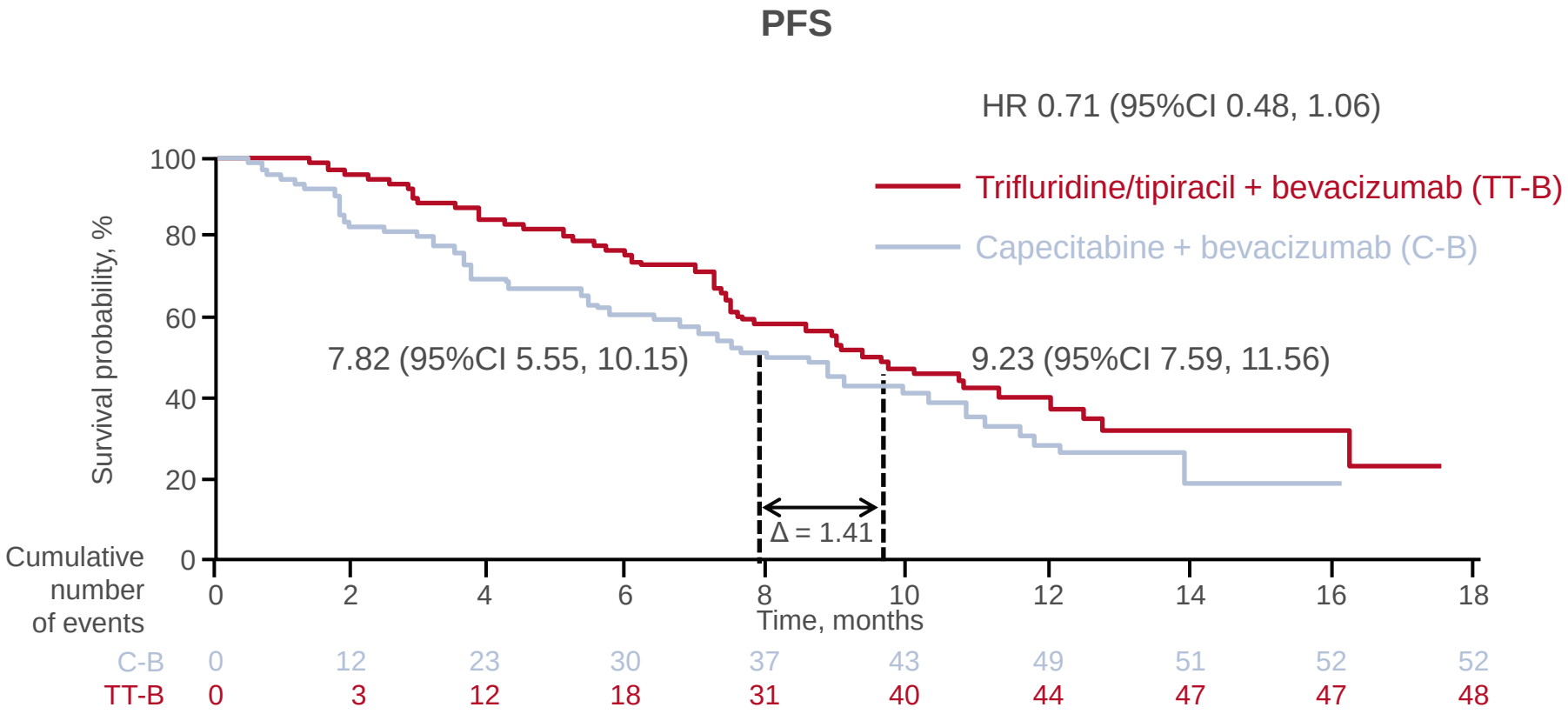
SECONDARY ENDPOINTS

- OS, ORR, DCR, safety, QoL

Van Cutsem E, et al. Ann Oncol 2018;29(suppl 5):abstr O-022

O-022: Phase II study evaluating trifluridine/tipiracil+bevacizumab and capecitabine+bevacizumab in first-line unresectable metastatic colorectal cancer (mCRC) patients who are non-eligible for intensive therapy (TASCO1): results of the primary analysis – Van Cutsem E, et al

Key results

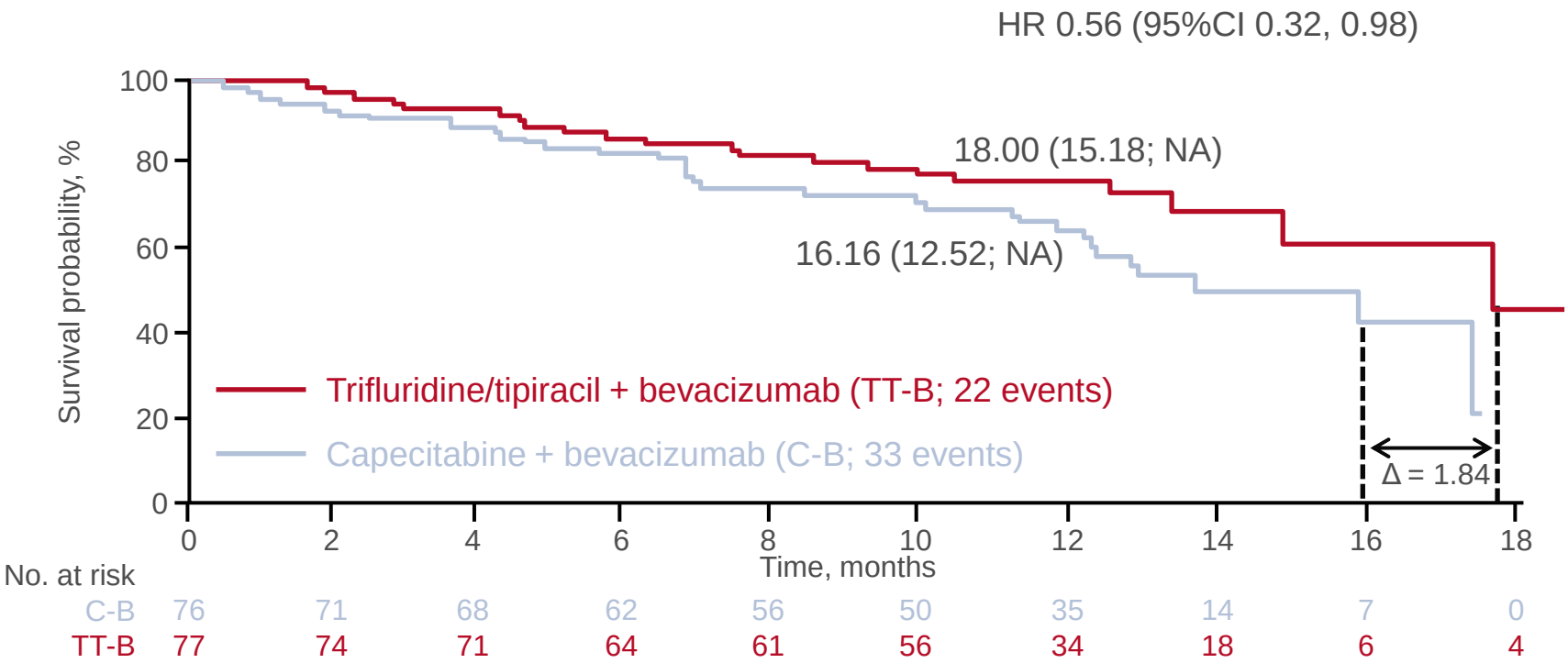


Van Cutsem E, et al. Ann Oncol 2018;29(suppl 5):abstr O-022

O-022: Phase II study evaluating trifluridine/tipiracil+bevacizumab and capecitabine+bevacizumab in first-line unresectable metastatic colorectal cancer (mCRC) patients who are non-eligible for intensive therapy (TASCO1): results of the primary analysis – Van Cutsem E, et al

Key results (cont.)

OS



Van Cutsem E, et al. Ann Oncol 2018;29(suppl 5):abstr O-022

O-022: Phase II study evaluating trifluridine/tipiracil+bevacizumab and capecitabine+bevacizumab in first-line unresectable metastatic colorectal cancer (mCRC) patients who are non-eligible for intensive therapy (TASCO1): results of the primary analysis – Van Cutsem E, et al

Key results (cont.)

AEs, n (%)	Trifluridine/tipiracil + bevacizumab (n=77)	Capecitabine + bevacizumab (n=76)
Any AE	77 (100)	74 (97.4)
SAEs	42 (54.5)	44 (57.9)
Grade ≥3 AEs	68 (88.3)	53 (69.7)
Any TRAEs	75 (97.4)	68 (89.5)
Grade ≥3 TRAEs	60 (77.9)	33 (43.4)
Serious TRAEs	25 (32.5)	17 (22.4)
Leading to withdrawal	31 (40.3)	28 (36.8)
Death during treatment period	4 (5.2)	9 (11.8)

Conclusions

- **In patients with mCRC who were not eligible for intensive therapy, trifluridine/tipiracil + bevacizumab demonstrated a mPFS of 9.2 months and had an acceptable safety profile**
- **Biomarker and QoL analyses are ongoing**

Van Cutsem E, et al. Ann Oncol 2018;29(suppl 5):abstr O-022

O-024: mFOLFOXIRI + panitumumab versus FOLFOXIRI as first-line treatment in patients with RAS wild- type metastatic colorectal cancer m(CRC): A randomized phase II VOLFI trial of the AIO (AIO-KRK0109) – Geissler M, et al

Study objective

- To assess the efficacy and safety of panitumumab + mFOLFOXIRI vs. FOLFOXIRI as 1L treatment in patients with mCRC

Key patient inclusion criteria

- Unresectable mCRC
- WT RAS
- 1L (1 cycle of FOLFIRINOX permitted prior to randomisation)
- ECOG PS 0–1

(n=96)

R 2:1

Panitumumab 6 mg/kg + mFOLFOXIRI q2w (n=63) → **PD/ resectability/ maximum 12 cycles***

FOLFOXIRI q2w (n=33) → **PD/ resectability/ maximum 12 cycles***

Stratification

- Cohort 1: Histologically confirmed and definitively inoperable/unresectable
- Cohort 2: Chance of secondary resection with curative intent (pre-treatment liver/tumour biopsy)

PRIMARY ENDPOINT

- ORR

SECONDARY ENDPOINTS

- TRR, time-to-relapse, PFS, OS, safety, QoL

*If resectable: surgery then protocol treatment for up to 12 cycles; if CR/PR/SD after 12 cycles: re-induction (same combination) recommended on PD

Geissler M, et al. Ann Oncol 2018;29(suppl 5):abstr O-024

O-024: mFOLFOXIRI + panitumumab versus FOLFOXIRI as first-line treatment in patients with RAS wild- type metastatic colorectal cancer m(CRC): A randomized phase II VOLFI trial of the AIO (AIO-KRK0109) – Geissler M, et al

Key results

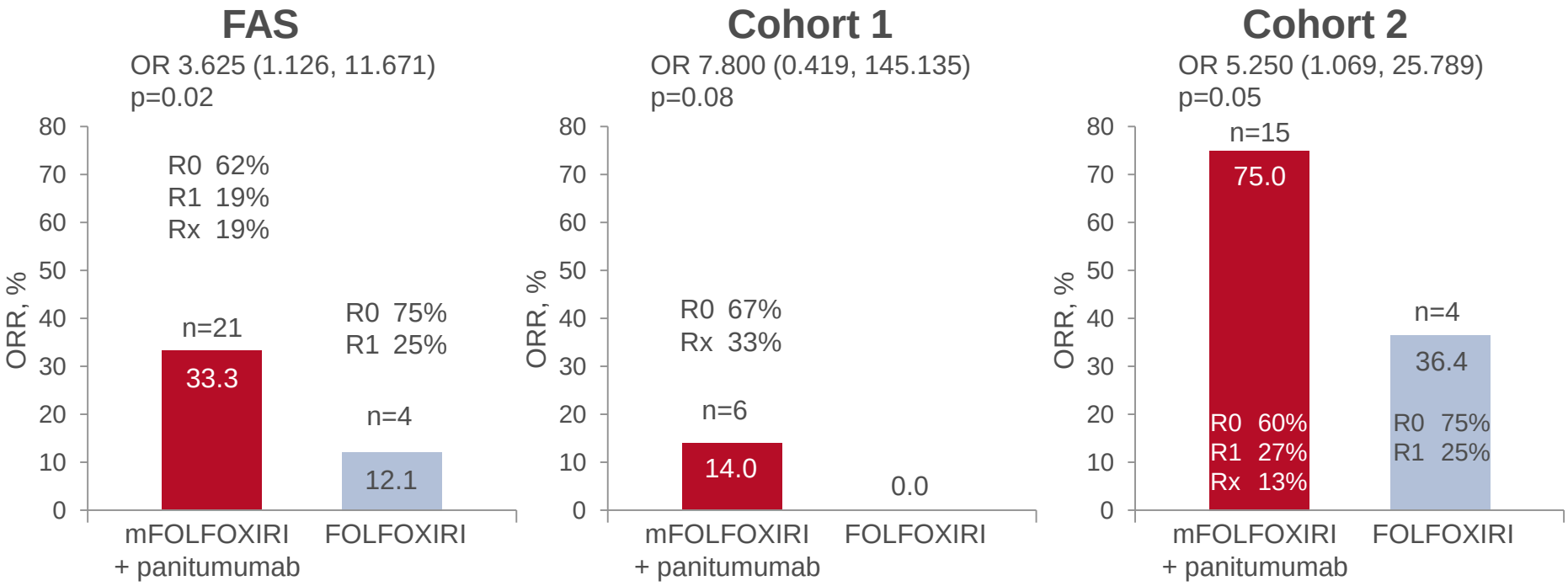
	Panitumumab + mFOLFOXIRI (n=63)	FOLFOXIRI alone (n=33)	OR (95%CI); p-value
ORR, % (95%CI)	87.3 (76.5, 94.4)	60.6 (42.1, 77.1)	4.469 (1.614, 12.376); 0.004

	Panitumumab + mFOLFOXIRI	FOLFOXIRI alone	OR (95%CI); p-value
ORR by tumour sidedness, %			
Left (n=78)	90.6	68.0	4.518 (1.298, 15.718); 0.02
Right (n=18)	70.0	37.5	3.889 (0.543, 27.886); 0.34
ORR by mutation status, %			
RAS/BRAF WT (n=60)	86.0	64.7	3.364 (0.902, 12.549); 0.08
BRAF mut (n=16)	85.7	22.2	21.000 (1.504, 293.25); 0.04

Geissler M, et al. Ann Oncol 2018;29(suppl 5):abstr O-024

O-024: mFOLFOXIRI + panitumumab versus FOLFOXIRI as first-line treatment in patients with RAS wild- type metastatic colorectal cancer m(CRC): A randomized phase II VOLFI trial of the AIO (AIO-KRK0109) – Geissler M, et al

Key results (cont.)



	Panitumumab + FOLFOXIRI (n=63)	FOLFOXIRI alone (n=33)	HR (95%CI); p-value
mPFS, months (95%CI)	9.7 (9.0, 11.7)	10.1 (7.8, 12.1)	0.920 (0.584, 1.451); 0.72

Geissler M, et al. Ann Oncol 2018;29(suppl 5):abstr O-024

O-024: mFOLFOXIRI + panitumumab versus FOLFOXIRI as first-line treatment in patients with RAS wild- type metastatic colorectal cancer m(CRC): A randomized phase II VOLFI trial of the AIO (AIO-KRK0109) – Geissler M, et al

Key results (cont.)

Non-haematological grade ≥3 AEs occurring in ≥5% patients, %	Panitumumab + mFOLFOXIRI (n=64)	FOLFOXIRI alone (n=33)
Nausea	9.4	-
Vomiting	9.4	3.0
Diarrhoea	25.0	12.1
Stomatitis	9.4	-
Fatigue	7.8	-
Pain	7.8	3.0
Infections	12.5	12.1

Conclusions

- **In patients with mCRC, 1L treatment with panitumumab + mFOLFOXIRI significantly improved ORR vs. FOLFOXIRI in the VOLFI trial**
- **Panitumumab + mFOLFOXIRI resulted in very high resection rates vs. mFOLFOXIRI, despite the fact that most patients had advanced disease**
- **Panitumumab + mFOLFOXIRI was associated with relevant, but manageable, GI toxicity and should only be used in patients with ECOG PS 0–1**

Geissler M, et al. Ann Oncol 2018;29(suppl 5):abstr O-024

O-027: BEACON CRC study safety lead-in: Assessment of the BRAF inhibitor encorafenib + MEK inhibitor binimetinib + EGFR inhibitor cetuximab for *BRAF^{V600E}* mCRC – Van Cutsem E, et al

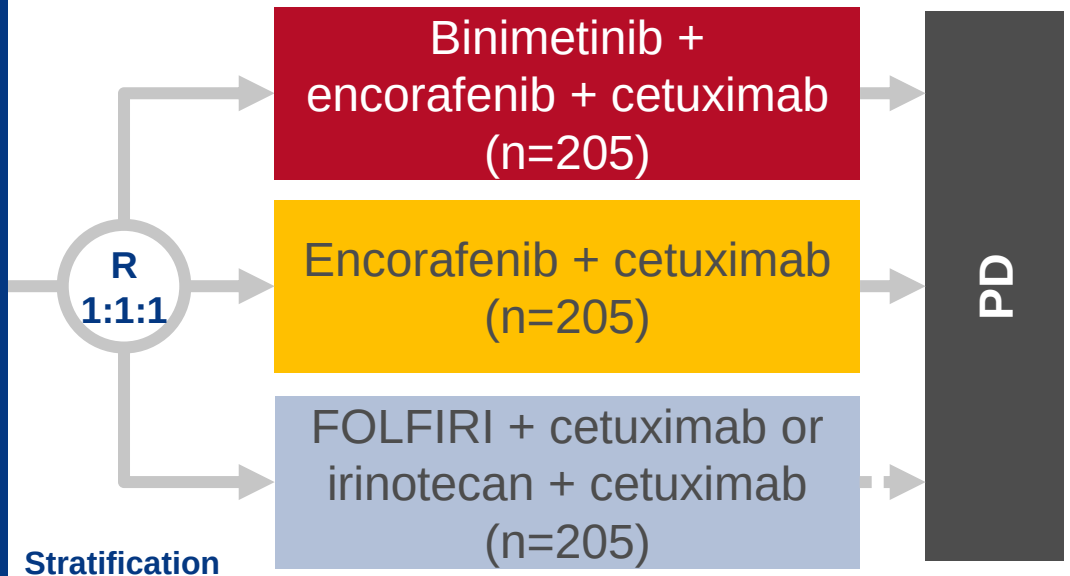
Study objective

- To assess the efficacy and safety of binimetinib + encorafenib + cetuximab in patients with BRAF V600E mutant mCRC following completion of a safety lead-in*

Key patient inclusion criteria

- BRAF V600E mutant mCRC
- Progressed after 1 or 2 previous regimens
- No prior treatment with RAF, MEK, EGFR inhibitors or irinotecan
- Eligible for cetuximab
- ECOG PS 0–1

(n=615)



Stratification

- BRAF V600E mutation status, ECOG PS, no. of prior regimens (1/2)

PRIMARY ENDPOINT

- ORR

SECONDARY ENDPOINTS

- OS, PFS, safety

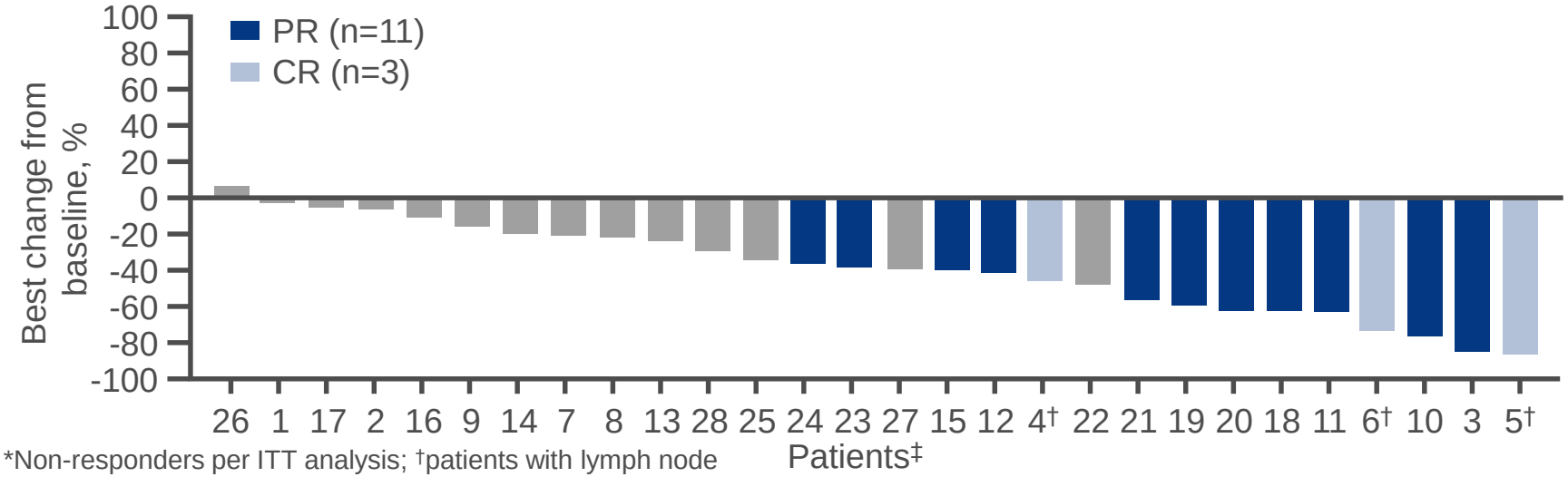
*Safety lead-in (n=30): binimetinib 45 mg bid; encorafenib 300 mg/day; cetuximab 400 mg/m^2 (initial) then 250 mg/m^2 qw

Van Cutsem E, et al. Ann Oncol 2018;29(suppl 5):abstr O-027

O-027: BEACON CRC study safety lead-in: Assessment of the BRAF inhibitor encorafenib + MEK inhibitor binimetinib + EGFR inhibitor cetuximab for *BRAF^{V600E}* mCRC – Van Cutsem E, et al

Key results

Confirmed best ORR (assessed per RECIST 1.1)	Patients with BRAF V600E mutations (n=29)
ORR (CR + PR), n (%) [95%CI]	14 (48) [29, 67]
CR, n (%)	3 (10)
PR, n (%)	11 (38)
SD, n (%)	13 (45)
PD, n (%)	0 (0)
Not evaluable for response*, n (%)	2 (7)

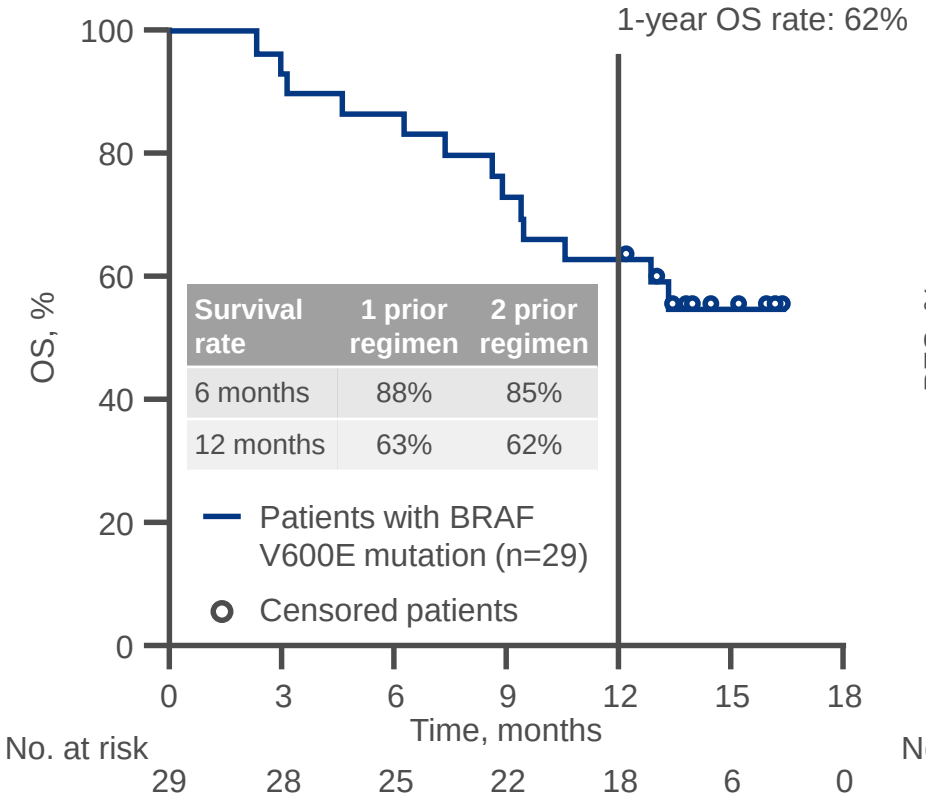


*Non-responders per ITT analysis; †patients with lymph node disease with decreases in short axis dimensions consistent with RECIST 1.1 defined CR; ‡one patient had no baseline sum of longest diameters and is not presented

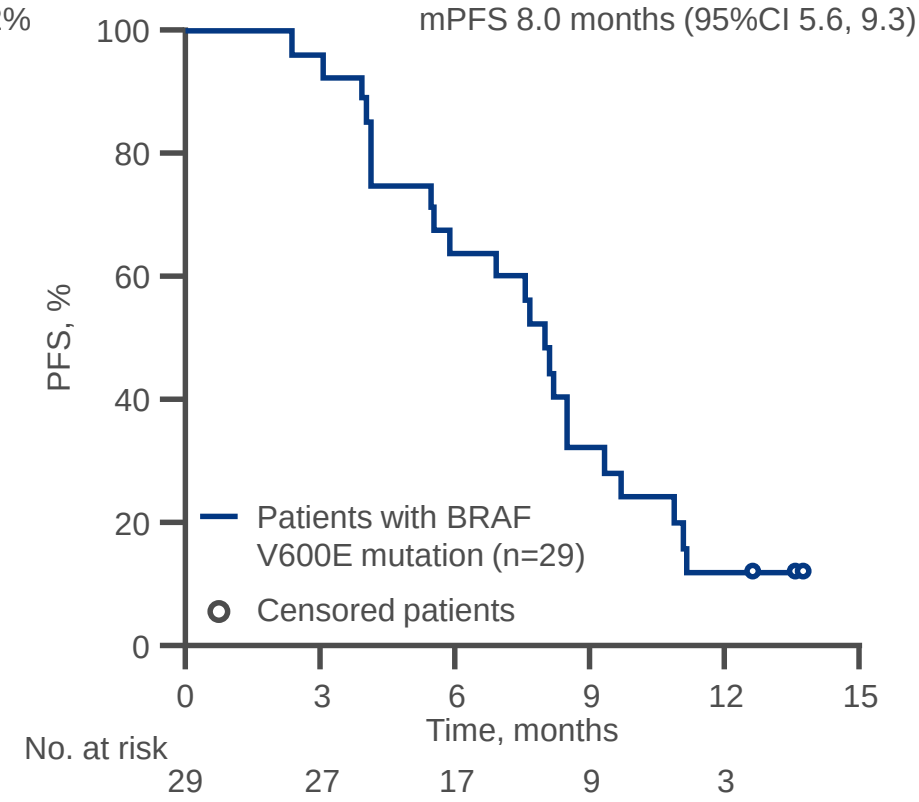
Van Cutsem E, et al. Ann Oncol 2018;29(suppl 5):abstr O-027

O-027: BEACON CRC study safety lead-in: Assessment of the BRAF inhibitor encorafenib + MEK inhibitor binimetinib + EGFR inhibitor cetuximab for *BRAF^{V600E}* mCRC – Van Cutsem E, et al

Key results (cont.)



Survival rate	1 prior regimen	2 prior regimen
6 months	88%	85%
12 months	63%	62%



- Median OS was not reached (data fully mature through 12.6 months)
- In patients with 1 and 2 prior regimens mPFS was 8.0 (95%CI 4.0, 9.3) and 8.1 (95%CI 4.1, 10.8) months, respectively

Van Cutsem E, et al. Ann Oncol 2018;29(suppl 5):abstr O-027

O-027: BEACON CRC study safety lead-in: Assessment of the BRAF inhibitor encorafenib + MEK inhibitor binimetinib + EGFR inhibitor cetuximab for *BRAF^{V600E}* mCRC – Van Cutsem E, et al

Key results (cont.)

AEs, n (%)	Patients (n=30)
Total AEs	30 (100)
Grade 3/4	21 (70)
Leading to discontinuation*†	6 (20)
Leading to dose interruption/change†	5 (17)
On-treatment deaths‡ (including those within 30 days of stopping study treatment)	5 (17)

Conclusions

- **In patients with BRAF V600E mutant mCRC, binimetinib, encorafenib plus cetuximab triplet therapy led to improvements in ORR, PFS and OS**
- **The triplet therapy had an acceptable safety profile with no unexpected toxicities**
- **Enrolment is ongoing for the BEACON CRC phase III trial**

*Includes increased blood bilirubin (n=1), drug hypersensitivity (n=1), dyspnoea (n=1), fatigue (n=1), hypersensitivity (n=1), malaise (n=1) and retinal detachment (n=1); †discontinuation or dose interruption/change of ≥1 study drug; ‡on-treatment deaths were due to disease progression

Van Cutsem E, et al. Ann Oncol 2018;29(suppl 5):abstr O-027