GI SLIDE DECK 2020

Selected abstracts from:

ESMO World Congress on Gastrointestinal Cancer
2020 Virtual Meeting

1–4 July 2020

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 summarize key findings in digestive cancers from the major congresses in 2020. This slide set specifically focuses on the **ESMO World Congress on Gastrointestinal Cancer 2020 Virtual Meeting** and is available in English, French, Chinese and Japanese.

The area of clinical research in oncology is a challenging and ever changing environment. Within this environment, we all value access to scientific data and research which helps to educate and inspire further advancements in our roles as scientists, clinicians and educators. 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 realization of this activity.

Yours sincerely,

Eric Van Cutsem
Thomas Seufferlein
Côme Lepage
Phillippe Rougier (hon.)

Thomas Gruenberger
Tamara Matysiak-Budnik
Jaroslaw Regula
Jean-Luc Van Laethem

(ESDO Governing Board)

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european society of digestive oncology

ESDO Medical Oncology Slide Deck
Editors 2020

COLORECTAL CANCERS



Prof Eric Van Cutsem	Digestive Oncology, University Hospitals, Leuven, Belgium
Prof Thomas Gruenberger	Department of Surgery, Kaiser-Franz-Josef Hospital, Vienna, Austria
Prof Jaroslaw Regula	Department of Gastroenterology and Hepatology, Institute of Oncology, Warsaw, Poland

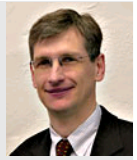
PANCREATIC CANCER AND HEPATOBILIARY TUMOURS


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

GASTRO-OESOPHAGEAL AND NEUROENDOCRINE TUMOURS


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

BIOMARKERS

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

esdo

Glossary

1L	first-line
2L	second-line
3L	third line
5FU	5-fluouracil
AE	adverse event
AFP	alpha-fetoprotein
ALBI	albumin-bilirubin
ALT	alanine aminotransferase
AJCC	American Joint Committee on Cancer
AST	aspartate aminotransferase
Atezo	atezolizumab
BD	budding grade
Bev	bevacizumab
(B)ICR	(blinded)-independent central review
bid	twice daily
BOR	best overall response
BSC	best supportive care
CAPIRI	capecitabine + irinotecan
CAPOX	capecitabine + oxaliplatin
CBR	clinical benefit rate
CCA	cholangiocarcinoma
CI	confidence interval
CPS	combined positive score
CR	complete response
CRC	colorectal cancer
CRT	chemoradiotherapy
CT	chemotherapy
D	day
DCR	disease control rate
DLTs	dose-limiting toxicities
dMMR	mismatch repair deficient
DoR	duration of response
ECOG	Eastern Cooperative Oncology Group
EGFR	epidermal growth factor receptor
EHS	extrahepatic spread
EORTC QLQ	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire
ESMO	European Society for Medical Oncology
FAS	full analysis set
FOLFIRI	folinic acid + 5-fluouracil + irinotecan
FOLFIRINOX	5-fluouracil + leucovorin + oxaliplatin + irinotecan
(m)FOLFOX	(modified) leucovorin + 5-fluorouracil + oxaliplatin
GEJ	gastroesophageal junction
GGT	gamma-glutamyl transferase
GI	gastrointestinal
GIST	gastrointestinal stromal tumour
Gy	Gray
HAIC	hepatic arterial infusion chemotherapy
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HIPEC	hyperthermic intraperitoneal chemotherapy
HR	hazard ratio
ICU	intensive care unit
IO	immunotherapy
IPI	ipilimumab
ia	intra-arterial
iv	intravenous
KPS	Karnofsky performance status
LV	leucovorin
mCRC	metastatic colorectal cancer
MMC	mitomycin C
mo	months
MSI	microsatellite instability
MSI-H	high microsatellite instability
MSS	microsatellite stable
MTB	multidisciplinary tumour board
MTD	maximum tolerated dose
MVI	microvascular invasion
NA	not available
NALIRIFOX	liposomal irinotecan + 5-fluouracil + leucovorin + oxaliplatin
NE	not evaluable/estimable
NIVO	nivolumab
NR	not reached
NS	non-significant
ORR	overall/objective response rate
(m)OS	(median) overall survival
PCI	Peritoneal Cancer Index
pCR	pathological complete response
PD	progressive disease
PDAC	pancreatic ductal adenocarcinoma
PD-(L)1	programmed death-(ligand) 1
PET	positron emission tomography
(m)PFS	(median) progression-free survival
PK	pharmacokinetics
pMMR	mismatch repair proficient
po	orally
PR	partial response
PRO	patient-reported outcome
PS	performance status
q(2/3/4/6)w	every (2/3/4/6) week(s)
QoL	quality of life
RAM	ramucirumab
R	randomized
R0	resection 0
R1	resection 1
RECIST	Response Evaluation Criteria In Solid Tumors
RFS	relapse-free survival
RR	response rate
SAE	serious adverse event
SD	stable disease
SOR	sorafenib
T-Dxd	trastuzumab deruxtecan
TEAE	treatment-emergent adverse event
TRAE	treatment-related adverse event
TRG	tumour regression grade
TSR	tumour-stroma ratio
TTD	time to deterioration
TTP	time to progression
TTR	time to response
UTI	urinary tract infection
WBC	white blood cell
WCGC	World Congress on Gastrointestinal Cancer
WT	wild type

Contents

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CANCERS OF THE OESOPHAGUS AND STOMACH

O-11: Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with HER2-positive advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma: A randomized, phase 2, multicenter, open-label study (DESTINY-Gastric01) – Yamaguchi K, et al

Study objective

- To evaluate the efficacy and safety of trastuzumab deruxtecan (T-Dxd) in patients with HER2-positive advanced gastric or GEJ adenocarcinoma

Key patient inclusion criteria

- Advanced gastric or GEJ adenocarcinoma
- HER2-positive (IHC3+ or IHC2+/ISH+)
- ≥2 prior regimens including a fluoropyrimidine and a platinum agent
- Progression on trastuzumab-containing regimen

(n=743)

R 2:1

- T-Dxd 6.4 mg/kg q3w (n=125)
- Irinotecan or paclitaxel (physician's choice) (n=62)

PRIMARY ENDPOINT

- ORR (ICR)

SECONDARY ENDPOINTS

- OS, PFS, safety

Yamaguchi K, et al. Ann Oncol 2020;31(suppl):abstr O-11

This talk was presented at the 22nd ESMO WCGC on 2 July 2020 at 14:56

O-11: Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with HER2-positive advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma: A randomized, phase 2, multicenter, open-label study (DESTINY-Gastric01) – Yamaguchi K, et al

Key results

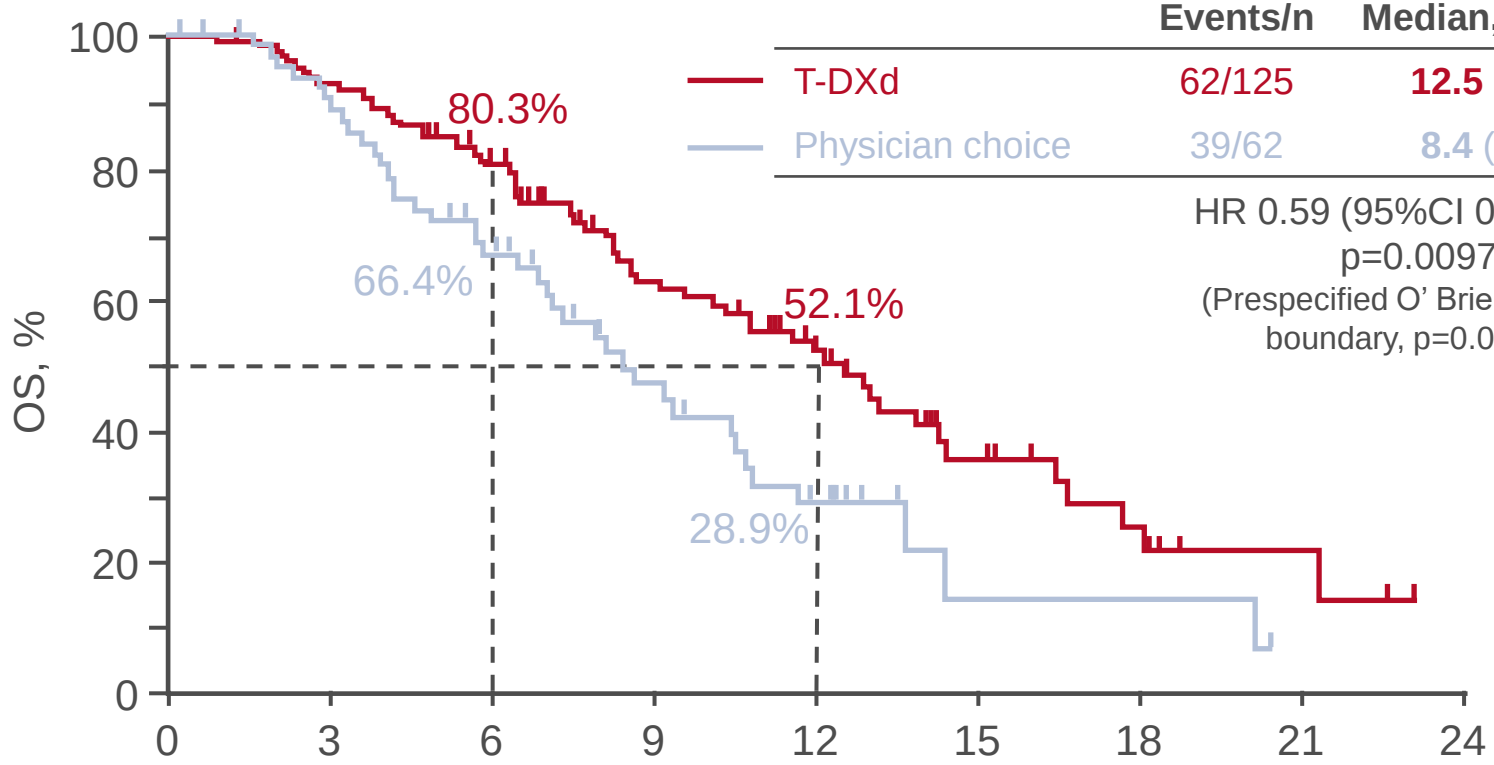
	T-Dxd (n=119)	Physician choice (n=56)
BOR, %		
CR	8.4	0
PR	34.5	12.5
SD	42.9	50.0
PD	11.8	30.4
NE	2.5	7.1
ORR by ICR, % (95%CI); p-value	51.3 (41.9, 60.5); <0.0001	14.3 (6.4, 26.3)
Confirmed ORR by ICR, % (95%CI)	42.9 (33.8, 52.3)	12.5 (5.2, 24.1)
Confirmed DCR, % (95%CI)	85.7 (78.1, 91.5)	62.5 (48.5, 75.1)
Confirmed median DoR, months (95%CI)	11.3 (5.6, NE)	3.9 (3.0, 4.9)

Yamaguchi K, et al. Ann Oncol 2020;31(suppl):abstr O-11

O-11: Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with HER2-positive advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma: A randomized, phase 2, multicenter, open-label study (DESTINY-Gastric01) – Yamaguchi K, et al

Key results (cont.)

Overall survival



	Events/n	Median, mo (95%CI)
T-DXd	62/125	**12.5** (9.6, 14.3)
Physician choice	39/62	**8.4** (6.9, 10.7)

HR 0.59 (95%CI 0.39 0.88)
p=0.0097
(Prespecified O' Brien-Fleming boundary, p=0.0202)*

No. at risk

T-DXd	125	115	88	54	33	14	7	3	0
Physician choice	62	54	37	19	10	2	2	0	0

Yamaguchi K, et al. Ann Oncol 2020;31(suppl):abstr O-11

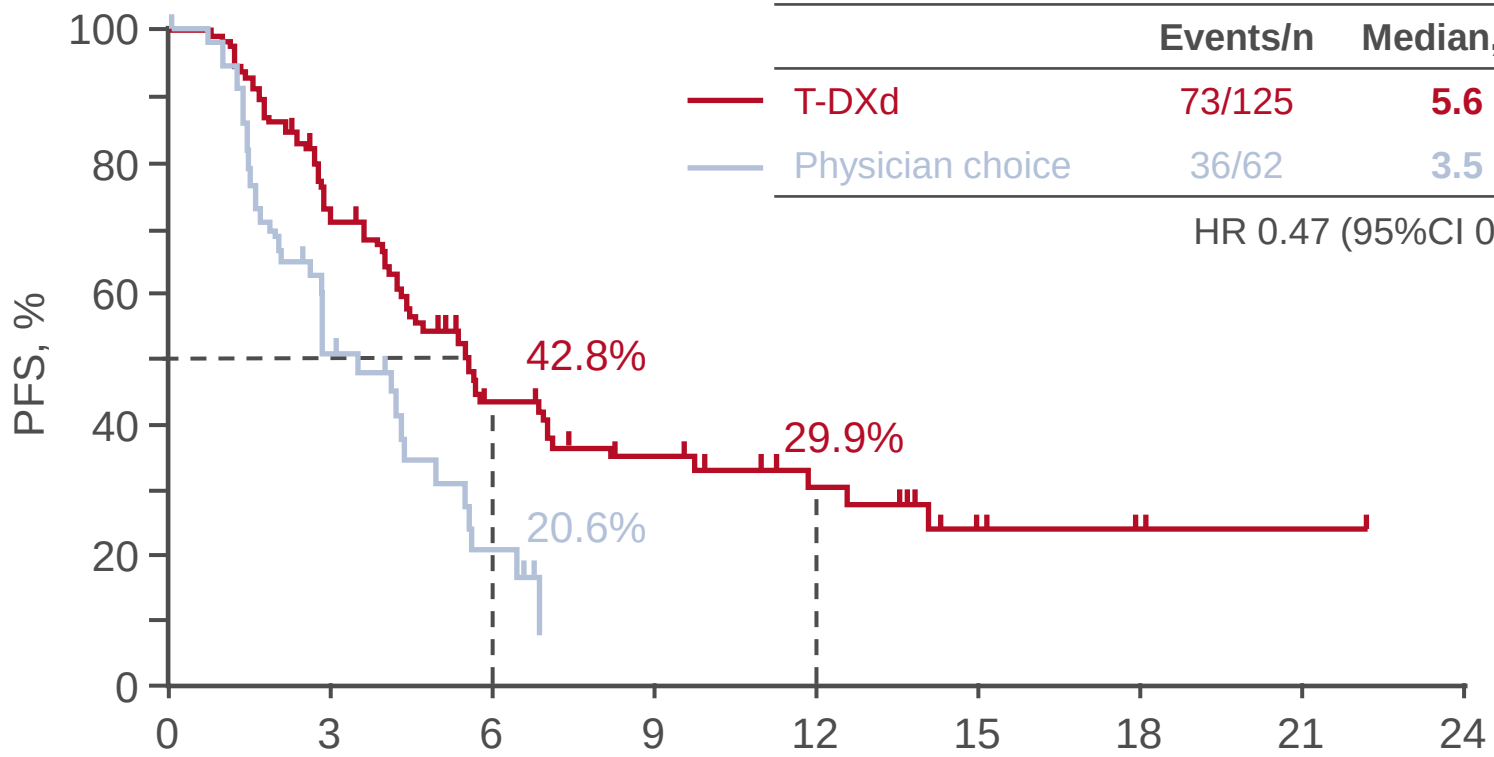
O-11: Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with HER2-positive advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma: A randomized, phase 2, multicenter, open-label study (DESTINY-Gastric01) – Yamaguchi K, et al

Key results (cont.)

Progression-free survival

	Events/n	Median, mo (95%CI)
T-DXd	73/125	**5.6** (4.3, 6.9)
Physician choice	36/62	**3.5** (2.0, 4.3)

HR 0.47 (95%CI 0.31, 0.71)



No. at risk

T-DXd	125	82	35	20	12	5	3	1	0
Physician choice	62	19	5	0	0	0	0	0	0

Yamaguchi K, et al. Ann Oncol 2020;31(suppl):abstr O-11

O-11: Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with HER2-positive advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma: A randomized, phase 2, multicenter, open-label study (DESTINY-Gastric01) – Yamaguchi K, et al

Key results (cont.)

TEAEs, n (%)	T-Dxd (n=125)	Physician choice (n=62)
Any	125 (100)	61 (98.4)
Grade ≥3	107 (85.6)	35 (56.5)
Serious	55 (44.0)	15 (24.2)
Leading to discontinuation	19 (15.2)	4 (6.5)
Leading to dose reduction	40 (32.0)	21 (33.9)
Leading to dose interruption	78 (62.4)	23 (37.1)
Leading to death	8 (6.4)	2 (3.2)

Conclusions

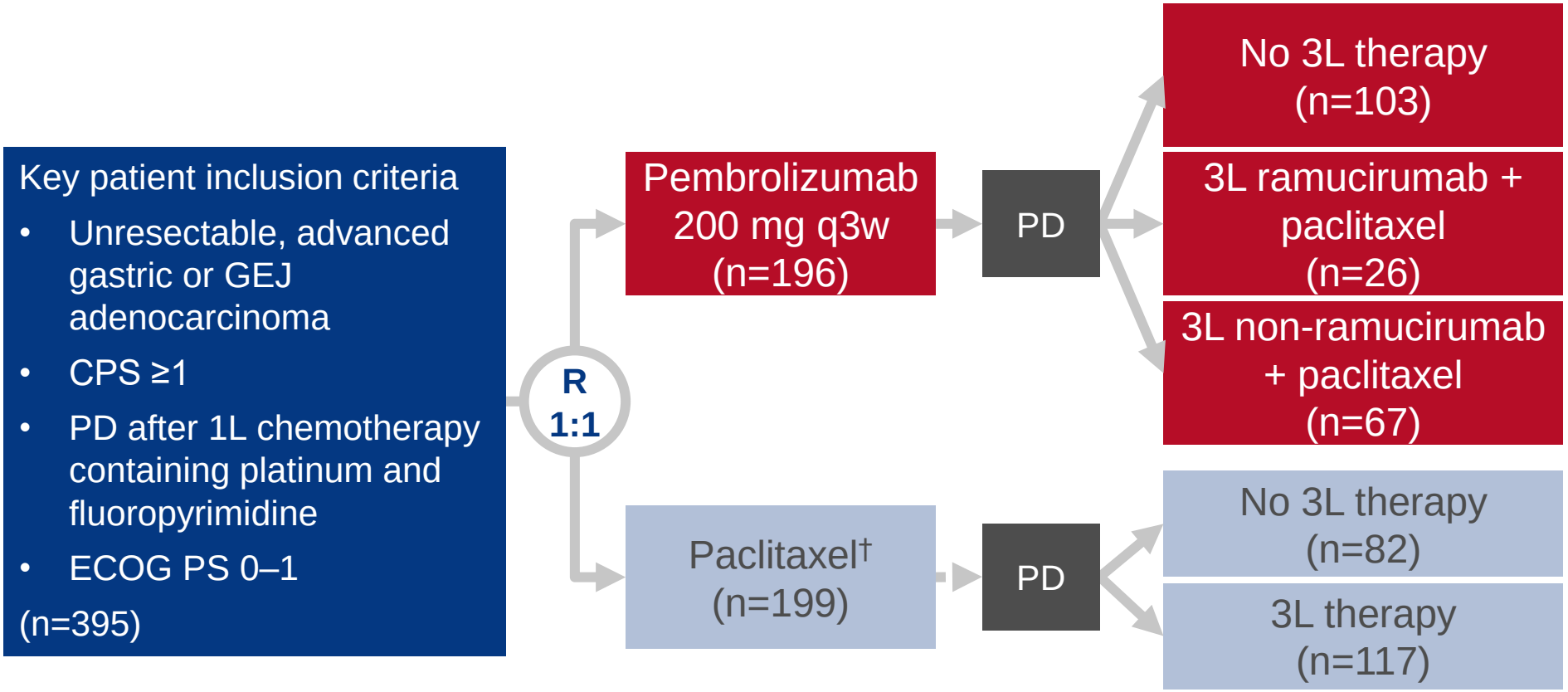
- **In patients with HER2-positive gastric or GEJ adenocarcinoma, T-Dxd demonstrated improvements in responses and survival compared with standard chemotherapy and was generally well-tolerated**

Yamaguchi K, et al. Ann Oncol 2020;31(suppl):abstr O-11

O-12: KEYNOTE-061: response to subsequent therapy following second-line pembrolizumab or paclitaxel in patients with advanced gastric or gastroesophageal junction adenocarcinoma – Yoon HH, et al

Study objective

- To evaluate responses to subsequent therapy in patients with advanced gastric or GEJ adenocarcinoma following 2L pembrolizumab or paclitaxel

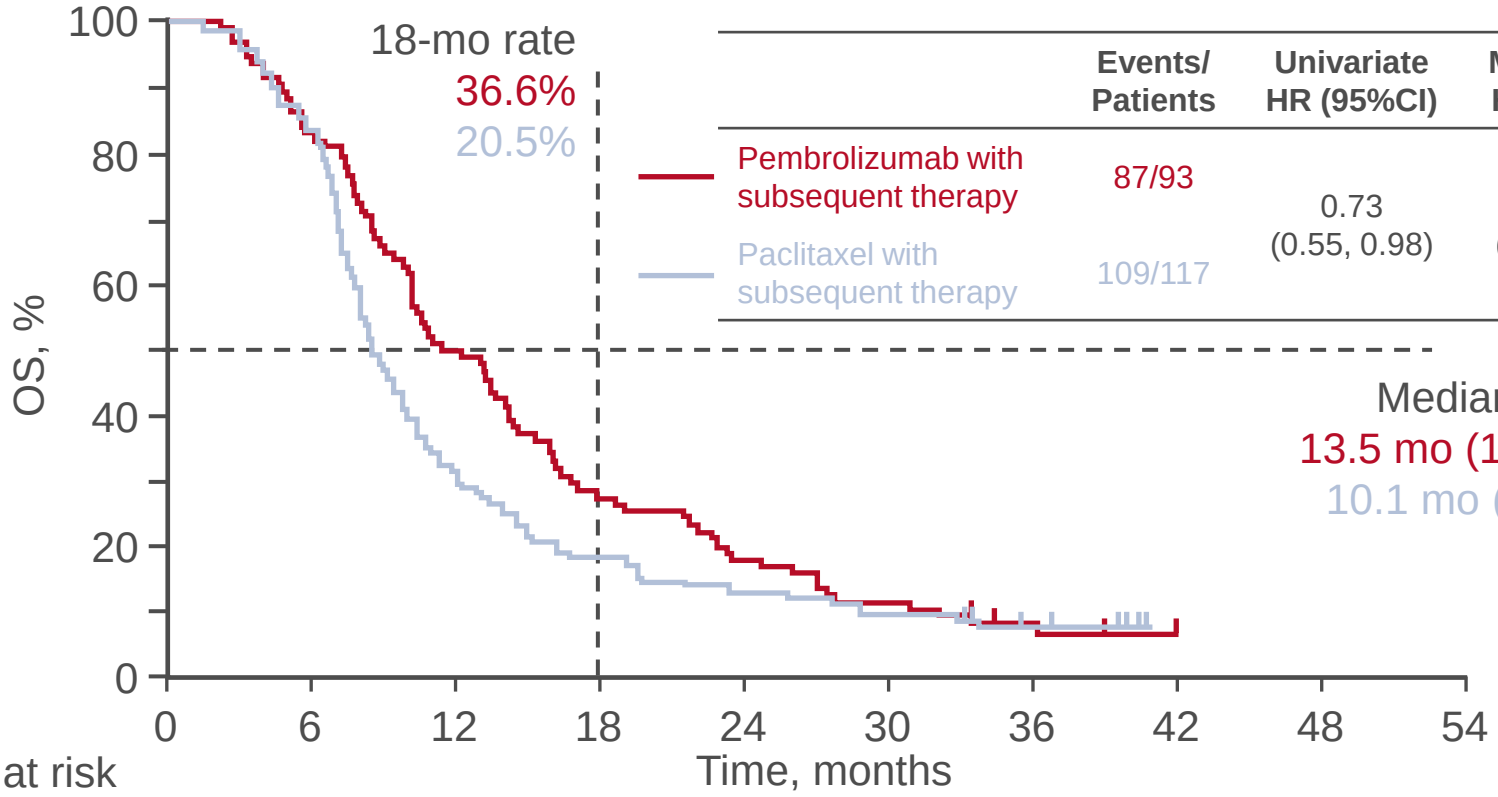


Yoon HH, et al. Ann Oncol 2020;31(suppl):abstr O-12

O-12: KEYNOTE-061: response to subsequent therapy following second-line pembrolizumab or paclitaxel in patients with advanced gastric or gastroesophageal junction adenocarcinoma – Yoon HH, et al

Key results

Overall survival from randomisation for pembrolizumab to any therapy vs. paclitaxel to any therapy



	Events/ Patients	Univariate HR (95%CI)	Multivariate HR (95%CI)
Pembrolizumab with subsequent therapy	87/93	0.73 (0.55, 0.98)	0.63 (0.46, 0.86)
Paclitaxel with subsequent therapy	109/117		

Median (95%CI)
13.5 mo (12.2, 17.0)
10.1 mo (9.2, 11.6)

No. at risk										
Pembrolizumab	93	81	57	34	23	15	10	5	2	0
Paclitaxel	117	102	45	24	16	14	10	6	2	0

Yoon HH, et al. Ann Oncol 2020;31(suppl):abstr O-12

O-12: KEYNOTE-061: response to subsequent therapy following second-line pembrolizumab or paclitaxel in patients with advanced gastric or gastroesophageal junction adenocarcinoma – Yoon HH, et al

Key results (cont.)

OS from randomisation	Events/n	Median, mo (95%CI)	HR (95%CI) Univariate	HR (95%CI) Multivariate
Pembrolizumab without subsequent therapy	89/103	3.2 (2.4, 4.8)	0.84 (0.61, 1.16)	-
Paclitaxel without subsequent therapy	81/82	4.2 (3.3, 5.2)		
Pembrolizumab with subsequent RAM + paclitaxel	25/26	13.1 (10.4, 17.0)	0.70 (0.44, 1.11)	0.61 (0.37, 1.00)
Paclitaxel with any subsequent therapy	109/117	10.1 (9.2, 11.6)		
Pembrolizumab with subsequent RAM + paclitaxel	25/26	13.1 (10.4, 17.0)	0.67 (0.39, 1.15)	0.46 (0.25, 0.85)
Paclitaxel with any multi-agent regimen	46/38	10.3 (8.9, 12.8)		
Pembrolizumab with subsequent RAM + paclitaxel	25/26	13.1 (10.4, 17.0)	0.89 (0.49, 1.59)	0.85 (0.46, 1.58)
Pembrolizumab with subsequent non-RAM + paclitaxel	62/67	14.7 (11.3, 19.0)		
OS from start of subsequent therapy				
Pembrolizumab with subsequent RAM + paclitaxel	25/26	9.0 (6.5, 12.5)	0.98 (0.54, 1.78)*	0.69 (0.36, 1.33)*
Pembrolizumab with subsequent non-RAM + paclitaxel	62/67	8.0 (4.3, 10.5)		
Paclitaxel with any subsequent therapy	109/117	6.0 (5.3, 6.7)	0.78 (0.49, 1.23)†	0.67 (0.41, 1.11)†

Conclusions

- **In patients with advanced gastric or GEJ adenocarcinoma, pembrolizumab appears to potentiate subsequent therapy and when combined with an anti-VEGF/VEGFR and a taxane there potentially may be a greater antitumor effect, although these data require confirmation in further studies**

Pembrolizumab with subsequent RAM + paclitaxel vs.
*pembrolizumab with subsequent non-RAM + paclitaxel or
†paclitaxel with any subsequent therapy

Yoon HH, et al. Ann Oncol 2020;31(suppl):abstr O-12

CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

Cancers of the pancreas, small bowel and hepatobiliary tract

PANCREATIC CANCER

LBA-1: First-line liposomal irinotecan + 5 fluorouracil/leucovorin + oxaliplatin in patients with pancreatic ductal adenocarcinoma: primary analysis from a phase 1/2 study – Wainberg ZA, et al

Study objective

- To evaluate the efficacy and safety of 1L liposomal irinotecan + 5FU/leucovorin + oxaliplatin (NALIRIFOX) in patients with PDAC

Key patient inclusion criteria

- Unresectable, locally advanced or metastatic PDAC
- Diagnosis ≤6 weeks prior to screening
- KPS ≥70*
- ECOG PS 0–1

(n=31)

- Cohort A (70/60): liposomal irinotecan 70 mg/m^2 + 5FU/LV† + oxaliplatin 60 mg/m^2 q2w (n=7)
- Cohort B (50/60): liposomal irinotecan 50 mg/m^2 + 5FU/LV† + oxaliplatin 60 mg/m^2 q2w (n=7)
- Cohort C (50/85): liposomal irinotecan 50 mg/m^2 + 5FU/LV† + oxaliplatin 85 mg/m^2 q2w (n=10)
- Cohort D (55/70): liposomal irinotecan 55 mg/m^2 + 5FU/LV† + oxaliplatin 70 mg/m^2 q2w (n=7)

Dose expansion
NALIRIFOX (50/60): liposomal irinotecan 50 mg/m^2 + 5FU/LV + oxaliplatin 60 mg/m^2 q2w (n=25)

PRIMARY ENDPOINTS

- Safety, DLTs

SECONDARY ENDPOINTS

- PFS, OS, ORR, DCR at 16 weeks, DoR, genomic profiling

*Dose expansion cohort only; †5FU 2400 mg/m^2 and LV 400 mg/m^2

Wainberg ZA, et al. Ann Oncol 2020;31(suppl):abstr LBA-1

This talk was presented at the 22nd ESMO WCGC on 1 July 2020 at 14:15

LBA-1: First-line liposomal irinotecan + 5 fluorouracil/leucovorin + oxaliplatin in patients with pancreatic ductal adenocarcinoma: primary analysis from a phase 1/2 study – Wainberg ZA, et al

Key results

AEs, n (%)	Dose exploration cohorts				Dose expansion (50/60) (n=25)	Pooled (50/60) (n=32)
	A (70/60) (n=7)	B (50/60) (n=7)	C (50/85) (n=10)	D (55/70) (n=7)		
TEAEs leading to						
Dose interruption	5 (71.4)	1 (14.3)	3 (30.0)	3 (42.9)	7 (28.0)	8 (25.0)
Dose adjustment	2 (28.6)	4 (57.1)	7 (70.0)	4 (57.1)	22 (88.0)	26 (81.3)
Death	0	1 (14.3)	1 (10.0)	1 (14.3)	2 (8.0)	3 (9.4)
Grade ≥3 TRAEs*	6 (85.7)	4 (57.1)	8 (80.0)	5 (71.4)	18 (72.0)	22 (68.8)
Neutropenia	1 (14.3)	2 (28.6)	3 (30.0)	1 (14.3)	8 (32.0)	10 (31.3)
Febrile neutropenia	0	1 (14.3)	0	0	3 (12.0)	4 (12.5)
Hypokalemia	1 (14.3)	2 (28.6)	2 (20.0)	2 (28.6)	2 (8.0)	4 (12.5)
Neutrophil count decreased	0	0	1 (10.0)	0	3 (12.0)	3 (9.4)
Diarrhoea	3 (42.9)	1 (14.3)	4 (40.0)	1 (14.3)	2 (8.0)	3 (9.4)
Nausea	0	0	2 (20.0)	0	3 (12.0)	3 (9.4)
Anaemia	0	1 (14.3)	0	0	1 (4.0)	2 (6.3)
Vomiting	1 (14.3)	0	3 (30.0)	0	2 (8.0)	2 (6.3)
Hyponatremia	0	0	0	0	2 (8.0)	2 (6.3)
ALT increased	0	0	0	0	2 (8.0)	2 (6.3)
GGT increased	0	0	0	0	2 (8.0)	2 (6.3)
Lymphocyte count decreased	0	0	0	0	2 (8.0)	2 (6.3)
WBC count decreased	0	0	0	0	2 (8.0)	2 (6.3)

*≥5% of patients in pooled 50/60 population

Wainberg ZA, et al. Ann Oncol 2020;31(suppl):abstr LBA-1

LBA-1: First-line liposomal irinotecan + 5 fluorouracil/leucovorin + oxaliplatin in patients with pancreatic ductal adenocarcinoma: primary analysis from a phase 1/2 study – Wainberg ZA, et al

Key results (cont.)

Response	Dose exploration cohorts				Dose expansion (50/60) (n=25)	Pooled (50/60) (n=32)
	A (70/60) (n=7)	B (50/60) (n=7)	C (50/85) (n=10)	D (55/70) (n=7)		
BOR, n (%)						
CR	0	0	0	0	1 (4.0)	1 (3.1)
PR	0	3 (42.9)	3 (30.0)	1 (14.3)	7 (28.0)	10 (31.3)
SD	2 (28.6)	3 (42.9)	1 (10.0)	3 (42.9)	12 (48.0)	15 (46.9)
PD	1 (14.3)	0	2 (20.0)	1 (14.3)	3 (12.0)	3 (9.4)
Non-PD/non-CR	1 (14.3)	0	0	0	0	0
NE	3 (42.9)	1 (14.3)	4 (40.0)	2 (28.6)	2 (8.0)	3 (9.4)
ORR, % (95%CI)	0 (0, 41.0)	42.9 (9.9, 81.6)	30.0 (6.7, 65.2)	14.3 (0.4, 57.9)	32.0 (14.9, 53.5)	34.4 (18.6, 53.2)
DCR at 16 week, % (95%CI)	42.9 (9.9, 81.6)	71.4 (29.0, 96.3)	40.0 (12.2, 73.8)	28.6 (3.7, 71.0)	72.0 (50.6, 87.9)	71.9 (53.3, 86.3)
DoR	(n=0)	(n=3)	(n=3)	(n=1)	(n=8)	(n=11)
Median, mo (95%CI)	NE (NE, NE)	28.4 (3.52, NE)	NE (NE, 16.39)	NE (NE, NE)	9.4 (2.2, NE)	9.4 (3.52, NE)
Rate at, % (95%CI)						
6 months	NE	66.7 (9.4, 99.2)	100 (29.2, 100)	0 (0, 97.5)	62.5 (24.5, 91.5)	63.6 (30.8, 89.1)
12 months	NE	33.3 (0.8, 90.6)	100 (29.2, 100)	0 (0, 97.5)	25.0 (3.2, 65.1)	27.3 (6.0, 61.0)
24 months	NE	33.3 (0.8, 90.6)	0 (0, 70.8)	0 (0, 97.5)	0 (0, 36.9)	9.1 (0.2, 41.3)

*≥5% of patients in pooled 50/60 population

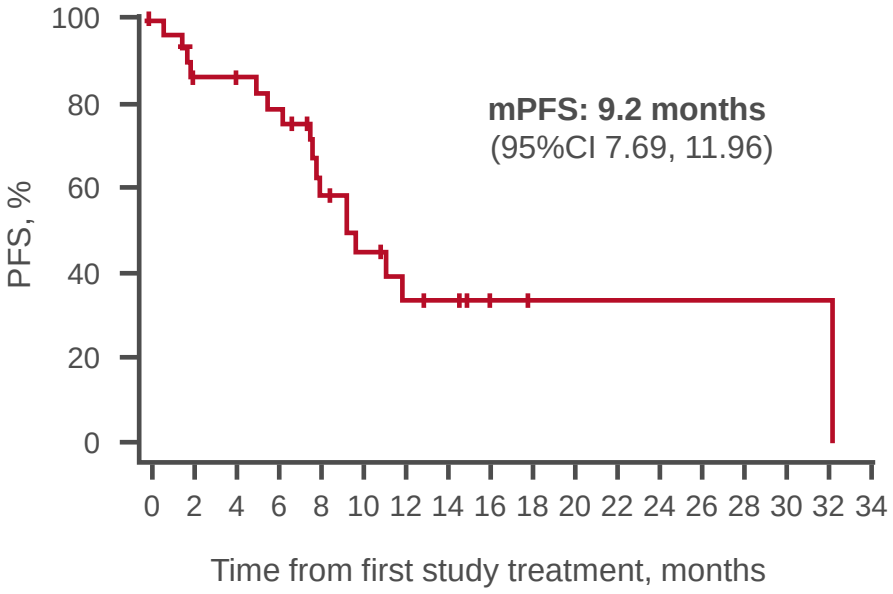
Wainberg ZA, et al. Ann Oncol 2020;31(suppl):abstr LBA-1

LBA-1: First-line liposomal irinotecan + 5 fluorouracil/leucovorin + oxaliplatin in patients with pancreatic ductal adenocarcinoma: primary analysis from a phase 1/2 study – Wainberg ZA, et al

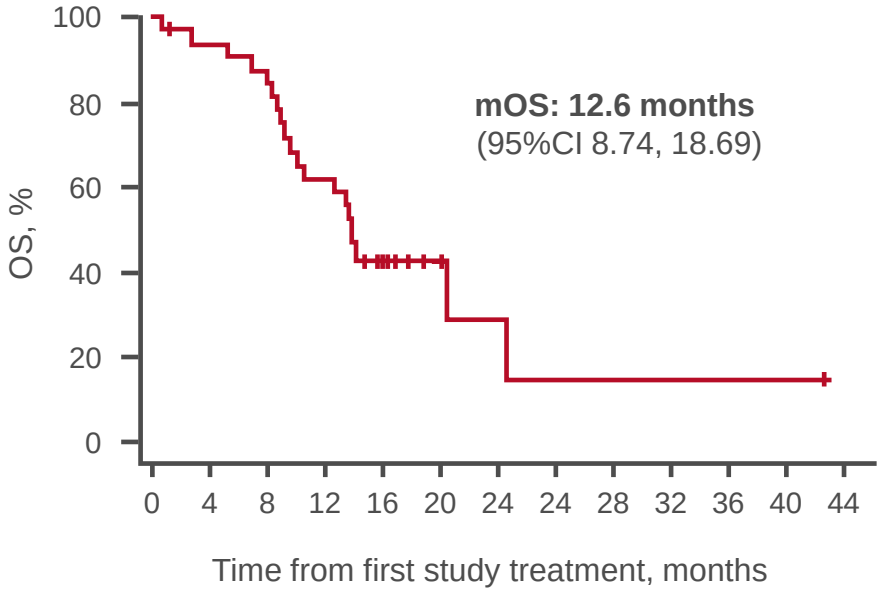
Key results (cont.)

Pooled 50/60 (n=32)

Progression-free survival



Overall survival



Conclusions

- **In patients with PDAC, 1L NALIRIFOX was generally well-tolerated and showed encouraging antitumor activity**

Wainberg ZA, et al. Ann Oncol 2020;31(suppl):abstr LBA-1

O-1: PanCO: Updated results of an open-label, single-arm pilot study of OncoSil phosphorus-32 microparticles in unresectable locally advanced pancreatic adenocarcinoma with gemcitabine + nab-paclitaxel or FOLFIRINOX chemotherapy – Ross P, et al

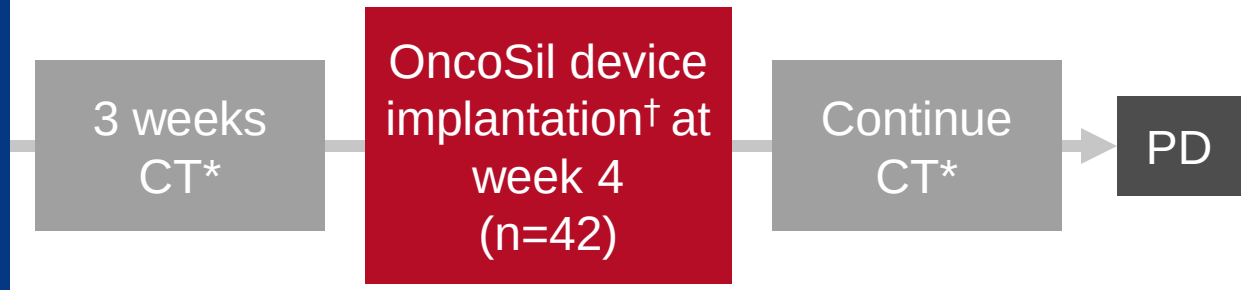
Study objective

- To evaluate the efficacy and safety of OncoSil phosphorus-32 microparticles with gemcitabine + nab-paclitaxel or FOLFIRINOX in patients with unresectable locally advanced PDAC

Key patient inclusion criteria

- Unresectable locally advanced pancreatic adenocarcinoma
- No prior radiotherapy or CT for PDAC
- Target tumour diameter 2–6 cm
- ECOG PS 0–1

(n=50)



PRIMARY ENDPOINT

- Safety

SECONDARY ENDPOINT

- Local DCR at 16 weeks

*FOLIRINOX 14-day cycles or gemcitabine + nab-paclitaxel 28-day cycles; †32P activity calculated from tumour volume to deliver 100 Gy

Ross P, et al. Ann Oncol 2020;31(suppl):abstr O-1

O-1: PanCO: Updated results of an open-label, single-arm pilot study of OncoSil phosphorus-32 microparticles in unresectable locally advanced pancreatic adenocarcinoma with gemcitabine + nab-paclitaxel or FOLFIRINOX chemotherapy – Ross P, et al

Key results

AEs occurring in ≥20% of patients, n (%)	AEs related to OncoSil		AEs related to chemotherapy	
	All grade	Grade ≥3	All grade	Grade ≥3
Any	16 (38.1)	3 (7.1)	42 (100)	28 (66.7)
Diarrhoea	-	-	22 (52.4)	1 (2.4)
Nausea	3 (7.1)	-	23 (54.8)	2 (4.8)
Abdominal pain	3(7.1)	1 (2.4)	5 (11.9)	1 (2.4)
Constipation	-	-	10 (23.8)	-
Vomiting	-	-	10 (23.8)	1 (2.4)
Fatigue	5 (11.9)	1 (2.4)	34 (81.0)	5 (11.9)
Pyrexia	-	-	10 (23.8)	2 (4.8)
Peripheral oedema	-	-	8 (19.0)	-
Neutropenia	2 (4.8)	1 (2.4)	21 (50.0)	16 (38.1)
Thrombocytopenia	1 (2.4)	1 (2.4)	12 (28.6)	3 (7.1)
Anaemia	1 (2.4)	-	12 (28.6)	5 (11.9)
Alopecia	-	-	16 (38.1)	-
Rash	-	-	13 (31.0)	-
Appetite decreased	-	-	16 (38.1)	-
Peripheral neuropathy	-	-	15 (35.7)	1 (2.4)
Weight decreased	1 (2.4)	0	10 (23.8)	1 (2.4)

- 33% of AEs occurred pre-OncoSil vs. 67% post-implant, with 6% vs. 94% attributed to the OncoSil device and/or implantation procedure vs. chemotherapy

Ross P, et al. Ann Oncol 2020;31(suppl):abstr O-1

O-1: PanCO: Updated results of an open-label, single-arm pilot study of OncoSil phosphorus-32 microparticles in unresectable locally advanced pancreatic adenocarcinoma with gemcitabine + nab-paclitaxel or FOLFIRINOX chemotherapy – Ross P, et al

Key results (cont.)

Response	OncoSil (n=42)
BOR, n (%)	
CR	0 (0)
PR	13 (31.0)
SD	29 (69.0)
PD	0
ORR, n (%)	13 (31.0)
mPFS, mo (95%CI)	9.3 (7.2, 12.2)
PFS at 12 mo, % (95%CI)	32.3 (20.4, 51.3)
mOS, mo (95%CI)	16.0 (11.1, NE)
OS at 12 mo, % (95%CI)	64.0 (47.5, 76.5)

	OncoSil implantation (n=42)
DCR, n (%) [95%CI]	42 (100) [91.6, 100]
Local DCR at 16 weeks, n (%) [95%CI]	38 (90.5) [77, 97]
p-value	<0.0001
Local DCR at 24 weeks, n (%) [95%CI]	30 (71.4) [55, 84]
Surgical resection, n (%)	10 (23.8)
R0 vs. R1	8 (80) vs. 2 (20)

Conclusions

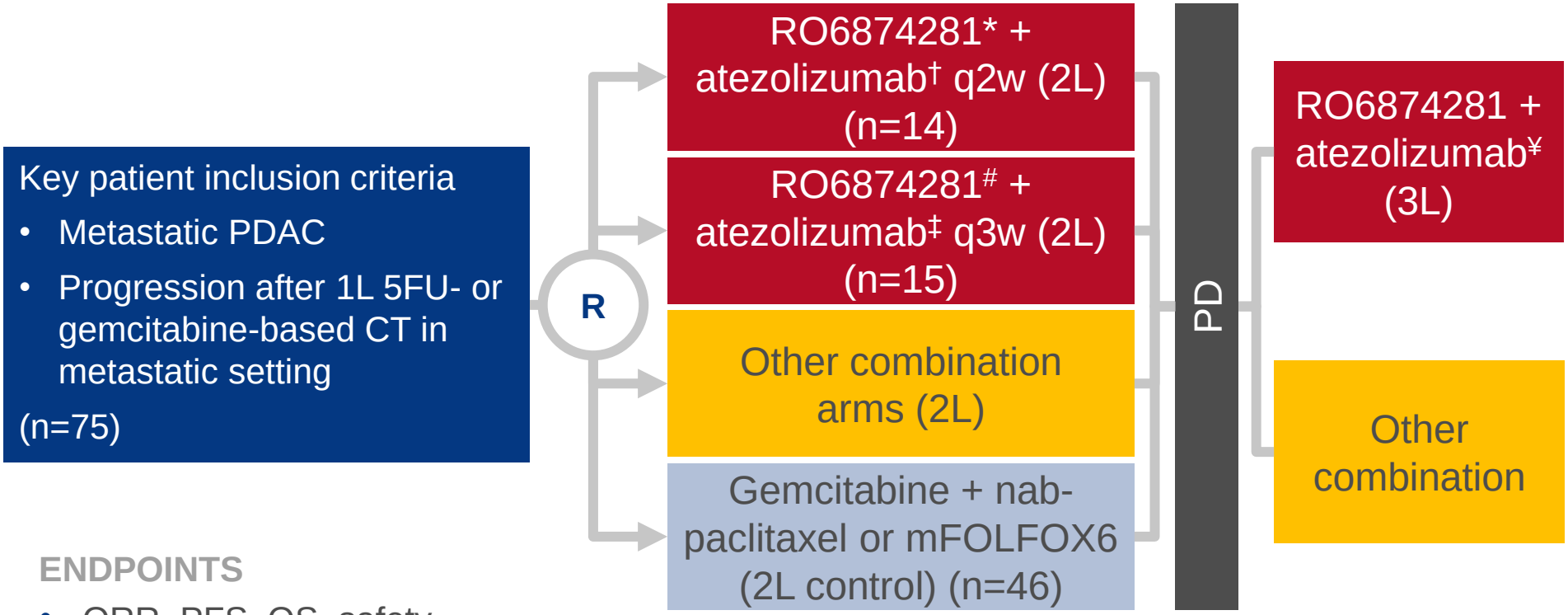
- **In patients with unresectable locally advanced PDAC, implantation with OncoSil device was feasible, well-tolerated and provided clinical benefit in combination with systemic chemotherapy**

Ross P, et al. Ann Oncol 2020;31(suppl):abstr O-1

SO-4: Phase Ib/II, open-label, randomised evaluation of atezolizumab plus RO6874281 vs control in MORPHEUS–pancreatic ductal adenocarcinoma (PDAC) – Chung V, et al

Study objective

- To evaluate the efficacy and safety of RO6874281 + atezolizumab in patients with metastatic PDAC



ENDPOINTS

- ORR, PFS, OS, safety

*10 mg iv D1, 15 mg iv D8, 15, 22 of cycle 1 then 15 mg D1, 15 each 28-day cycle; †840 mg iv in 28-day cycle; #10 mg iv in 21-day cycle; ‡1200 mg iv in 21-day cycle; ¥patients receiving 2L RO6874281 + atezolizumab not eligible to continue it in 3L

Chung V, et al. Ann Oncol 2020;31(suppl):abstr SO-4

SO-4: Phase Ib/II, open-label, randomised evaluation of atezolizumab plus RO6874281 vs control in MORPHEUS–pancreatic ductal adenocarcinoma (PDAC) – Chung V, et al

Key results

	RO6874281 + atezolizumab q2w (2L) (n=14)	RO6874281 + atezolizumab q3w (2L) (n=15)	Control (2L) (n=46)	RO6874281 + atezolizumab q3w* (3L) (n=6)
BOR, n (%) [95%CI]				
CR	0 (0) [0, 23.2]	0 (0) [0, 21.8]	0 (0) [0, 7.7]	0 (0) [0, 45.9]
PR	1 (7.1) [0.2, 33.9]	0 (0) [0, 21.8]	1 (2.2) [0.1, 11.5]	1 (16.7) [0.4, 64.1]
SD	2 (14.3) [1.8, 42.8]	2 (13.3) [1.7, 40.5]	19 (41.3) [27.0, 56.8]	1 (16.7) [0.4, 64.1]
PD	11 (78.6) [49.2, 95.3]	10 (66.7) [38.4, 88.2]	17 (37.0) [23.2, 52.5]	2 (33.3) [4.3, 77.7]
NE	0	3 (20.0)	9 (19.6)	2 (33.3)
Confirmed ORR, n (%) [95%CI]	1 (7.1) [0.2, 33.9]	0 (0) [0, 21.8]	1 (2.2) [0.1, 11.5]	1 (16.7) [0.4, 64.1]
DCR, n (%) [95%CI]	1 (7.1) [0.2, 33.9]	0 (0) [0, 21.8]	15 (32.6) [19.5, 48.0]	2 (33.3) [4.3, 77.7]
mPFS, mo (95%CI)	1.5 (1.3, 1.6)	1.4 (1.4, 2.7)	2.5 (1.6, 4.1)	1.7 (1.4, 4.7)
mOS, mo (95%CI)	7.3 (4.9, 9,7)	4.7 (3.8, 11.0)	7.0 (6.3, 9.6)	6.8 (1.9, NE)
Median duration of survival follow-up, mo (range)	6.6 (1.9–11.8)	4.4 (1.4–13.0)	6.6 (0.3–17.9)	4.4 (1.5–12.2)

*One patient received q2w regimen

Chung V, et al. Ann Oncol 2020;31(suppl):abstr SO-4

SO-4: Phase Ib/II, open-label, randomised evaluation of atezolizumab plus RO6874281 vs control in MORPHEUS–pancreatic ductal adenocarcinoma (PDAC) – Chung V, et al

Key results (cont.)

AEs, n (%)	RO6874281 + atezolizumab q2w (2L) (n=14)	RO6874281 + atezolizumab q3w (2L) (n=15)	Control (2L) (n=46)	RO6874281 + atezolizumab q3w* (3L) (n=6)
≥1 AE	14 (100)	15 (100)	45 (97.8)	6 (100)
TRAE	13 (92.9)	13 (86.7)	40 (87.0)	5 (83.3)
Grade 3/4 AEs	7 (50.0)	8 (53.3)	28 (60.9)	6 (100)
Grade 5 AEs	0	0	1 (2.2)	0
SAE	1 (7.1)	7 (46.7)	22 (47.8)	1 (16.7)
Treatment-related	0	5 (33.3)	7 (15.2)	0
Leading to dose modification/interruption	3 (21.4)	0	29 (63.0)	0
Leading to withdrawal from treatment	0	0	1 (2.2)	0

Conclusions

- **In patients with metastatic PDAC, RO6874281 + atezolizumab demonstrated limited responses compared with 2L chemotherapy, although was generally well-tolerated**

*One patient received q2w regimen

Chung V, et al. Ann Oncol 2020;31(suppl):abstr SO-4

Cancers of the pancreas, small bowel and hepatobiliary tract

HEPATOCELLULAR CARCINOMA

LBA-3: CheckMate 459: long-term efficacy outcomes with nivolumab versus sorafenib as first-line treatment in patients with advanced hepatocellular carcinoma – Sangro B, et al

Study objective

- To evaluate the long-term efficacy and safety of nivolumab as a 1L treatment for patients with advanced HCC

Key patient inclusion criteria

- Advanced HCC
- Ineligible for surgery and/or for loco-regional therapy or PD after surgery and/or loco-regional therapy
- Child-Pugh class A
- Systemic therapy naïve
- ECOG PS 0–1

(n=743)

R 1:1

Nivolumab 240 mg iv q2w (n=371) → PD/ toxicity

Sorafenib 400 mg po bid (n=372) → PD/ toxicity

Stratification

- Aetiology (HCV vs. non-HCV)
- Vascular invasion and/or extrahepatic spread (present vs. absent)
- Geography (Asia vs. non-Asia)

PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- ORR, PFS, efficacy by PD-L1 status, safety

Sangro B, et al. Ann Oncol 2020;31(suppl):abstr LBA-3

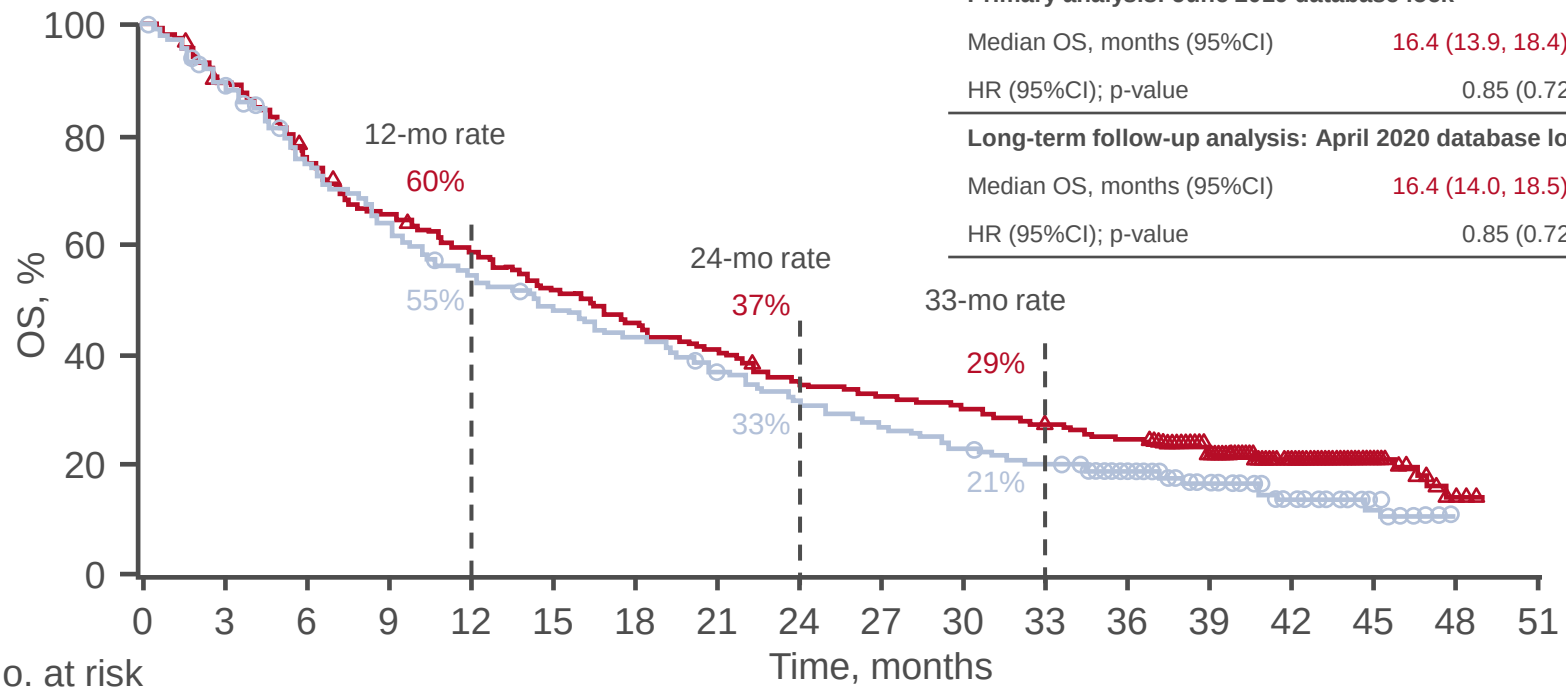
This talk was presented at the 22nd ESMO WCGC on 1 July 2020 at 18:20

LBA-3: CheckMate 459: long-term efficacy outcomes with nivolumab versus sorafenib as first-line treatment in patients with advanced hepatocellular carcinoma – Sangro B, et al

Key results

Overall survival

	Nivolumab (n=371)	Sorafenib (n=372)
Primary analysis: June 2019 database lock		
Median OS, months (95%CI)	16.4 (13.9, 18.4)	14.7 (11.9, 17.2)
HR (95%CI); p-value	0.85 (0.72, 1.02); 0.0752	
Long-term follow-up analysis: April 2020 database lock		
Median OS, months (95%CI)	16.4 (14.0, 18.5)	14.8 (12.1, 17.3)
HR (95%CI); p-value	0.85 (0.72, 1.00); 0.0522	



Sangro B, et al. Ann Oncol 2020;31(suppl):abstr LBA-3

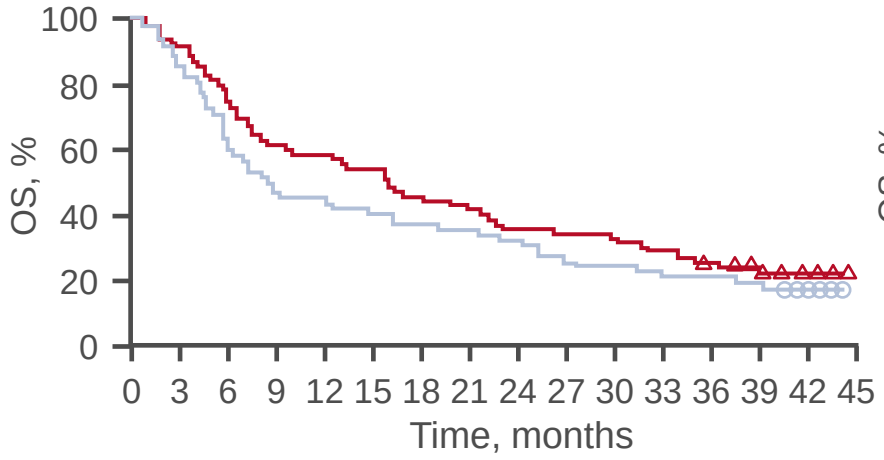
LBA-3: CheckMate 459: long-term efficacy outcomes with nivolumab versus sorafenib as first-line treatment in patients with advanced hepatocellular carcinoma – Sangro B, et al

Key results (cont.)

Overall survival by PD-L1 expression

Tumour-cell PD-L1 expression ≥1%

	Nivolumab (n=71)	Sorafenib (n=64)
Median OS, mo (95%CI)	16.1 (8.4, 22.3)	8.6 (5.7, 16.3)
HR (95%CI)	0.80 (0.54, 1.17)	

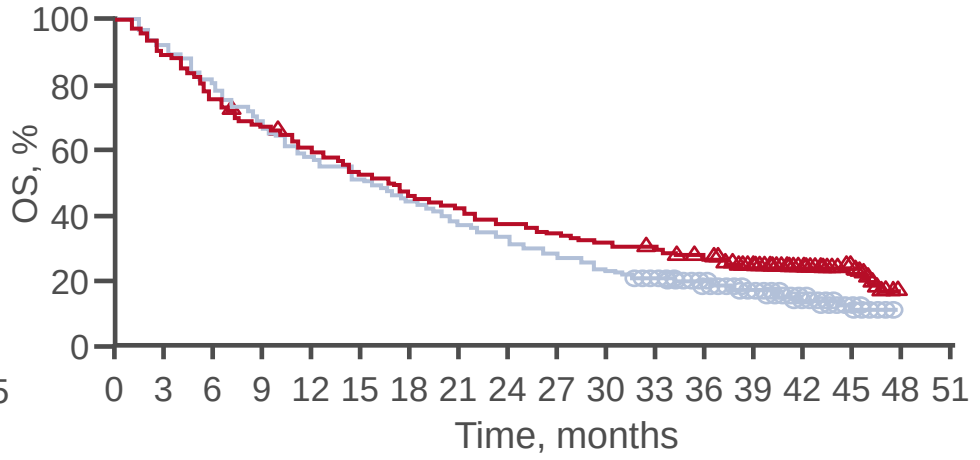


No. at risk

NIVO	71	64	53	43	41	38	32	29	25	24	23	20	16	12	8	0
SOR	64	53	37	29	28	25	23	22	20	17	15	14	13	12	7	0

Tumour-cell PD-L1 expression <1%

	Nivolumab (n=295)	Sorafenib (n=300)
Median OS, mo (95%CI)	16.7 (13.9, 19.4)	15.2 (12.7, 18.1)
HR (95%CI)	0.84 (0.70, 1.01)	



NIVO	295	257	216	190	169	148	133	117	104	95	88	81	69	50	34	23	2	0						
SOR	300	271	233	199	165	145	128	106	93	78	65	56	45	25	15	10	1	0						

Sangro B, et al. Ann Oncol 2020;31(suppl):abstr LBA-3

LBA-3: CheckMate 459: long-term efficacy outcomes with nivolumab versus sorafenib as first-line treatment in patients with advanced hepatocellular carcinoma – Sangro B, et al

Key results (cont.)

Overall survival by aetiology

HCV[a]

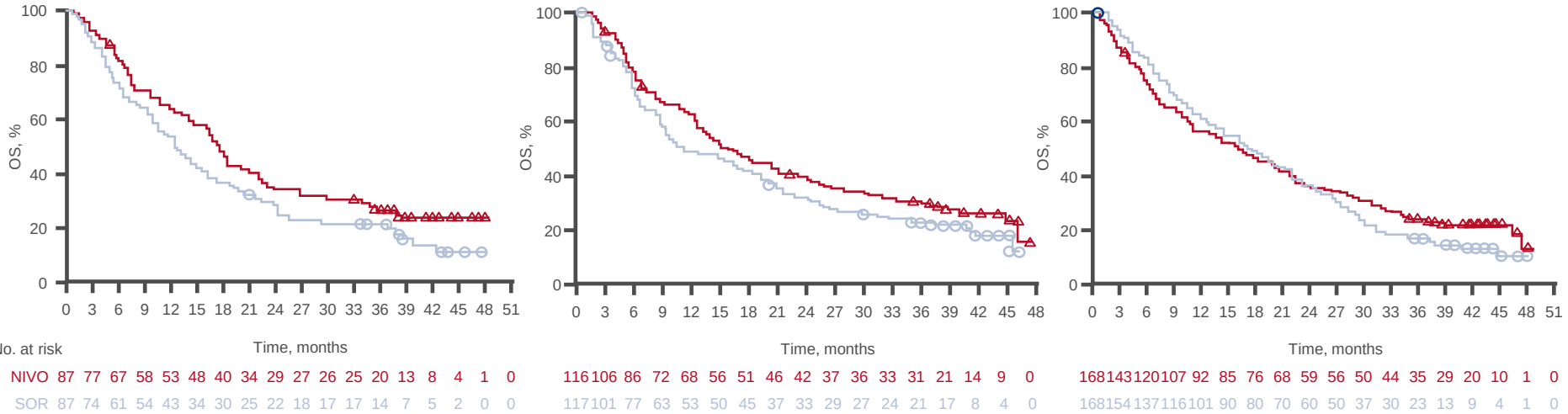
	Nivolumab (n=87)	Sorafenib (n=86)
Median OS, mo (95%CI)	17.5 (13.9, 21.9)	12.7 (9.9, 16.2)
HR (95%CI)	0.72 (0.51, 1.02)	

HBV[a]

	Nivolumab (n=116)	Sorafenib (n=117)
Median OS, mo (95%CI)	16.1 (12.5, 21.3)	10.4 (8.5, 17.3)
HR (95%CI)	0.79 (0.59, 1.07)	

Uninfected

	Nivolumab (n=168)	Sorafenib (n=168)
Median OS, mo (95%CI)	16.0 (10.8, 20.2)	17.4 (13.7, 21.3)
HR (95%CI)	0.91 (0.72, 1.16)	

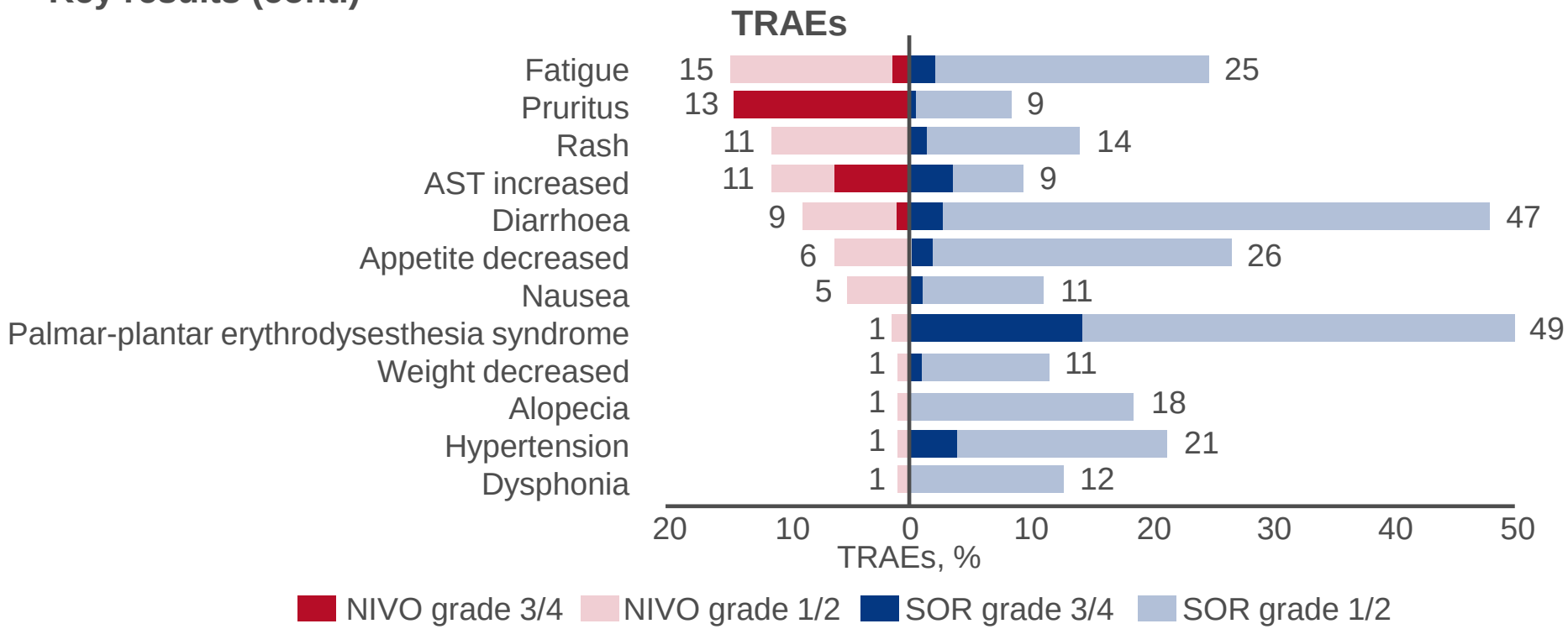


[a]Patients could have had active or resolved HBV or HCV infection as a risk factor for HCC

Sangro B, et al. Ann Oncol 2020;31(suppl):abstr LBA-3

LBA-3: CheckMate 459: long-term efficacy outcomes with nivolumab versus sorafenib as first-line treatment in patients with advanced hepatocellular carcinoma – Sangro B, et al

Key results (cont.)



Conclusions

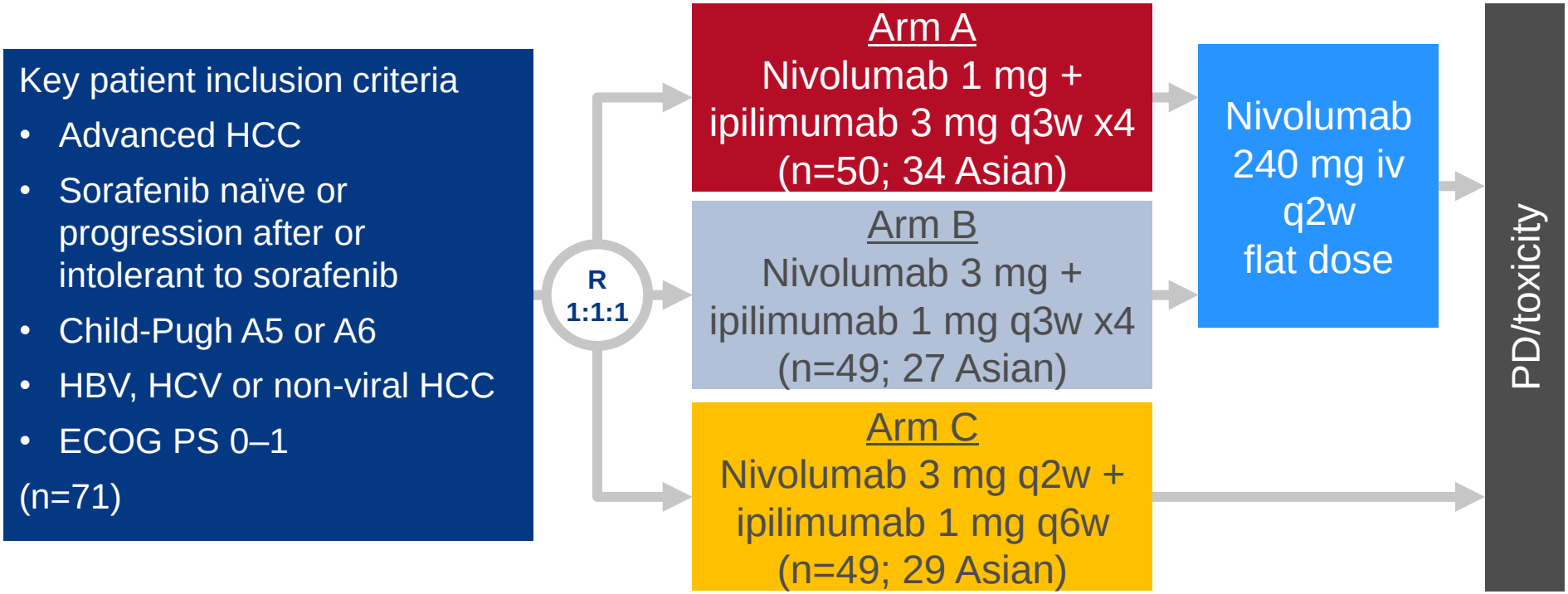
- **In patients with advanced HCC, 1L nivolumab continued to demonstrate improvements in OS regardless of PD-L1 status or viral aetiology and had a manageable safety profile**

Sangro B, et al. Ann Oncol 2020;31(suppl):abstr LBA-3

O-5: Efficacy and safety of nivolumab + ipilimumab in Asian patients with advanced hepatocellular carcinoma: subanalysis of the CheckMate 040 study – Yao T, et al

Study objective

- To evaluate the efficacy and safety of nivolumab + ipilimumab in Asian patients with advanced HCC



PRIMARY ENDPOINTS

- Safety, ORR (RECIST v1.1, investigator assessed), DoR

SECONDARY ENDPOINTS

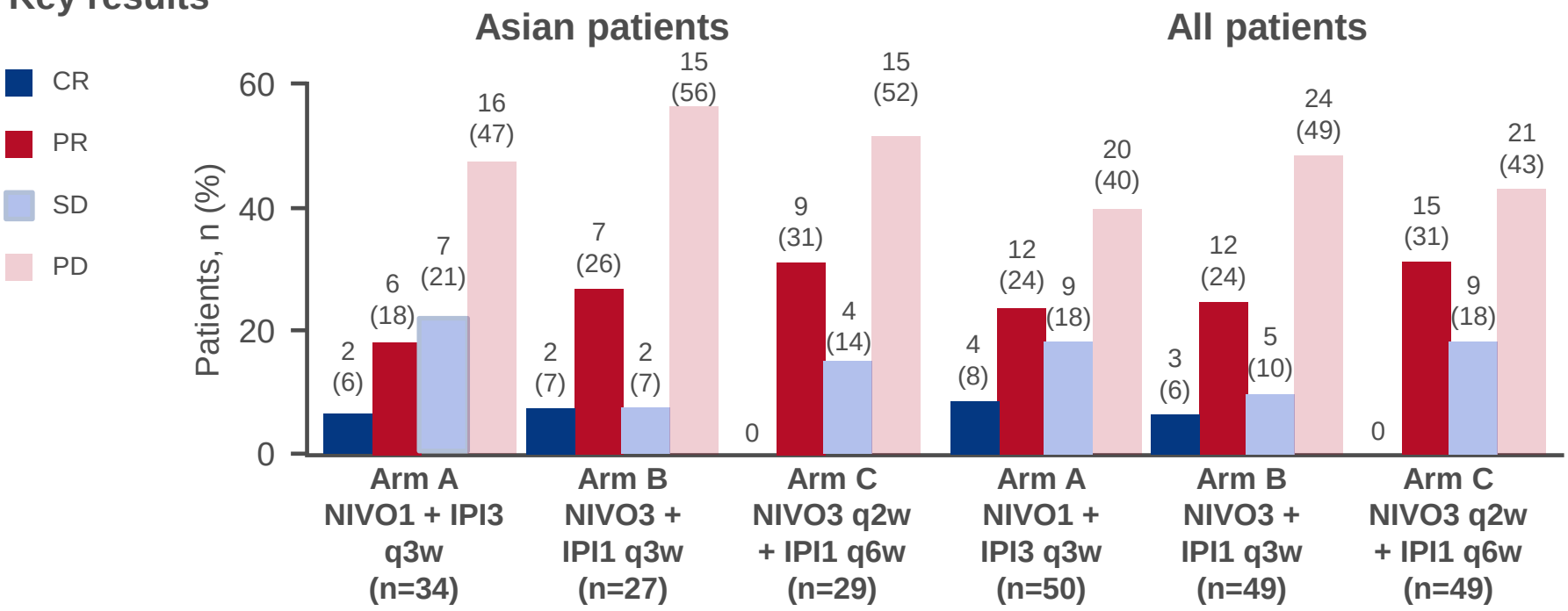
- DCR, TTR, TTP, PFS, OS

Yao T, et al. Ann Oncol 2020;31(suppl):abstr O-5

This talk was presented at the 22nd ESMO WCGC on 1 July 2020 at 18:29

O-5: Efficacy and safety of nivolumab + ipilimumab in Asian patients with advanced hepatocellular carcinoma: subanalysis of the CheckMate 040 study – Yao T, et al

Key results



	Arm A NIVO1 + IPI3 q3w (n=34)	Arm B NIVO3 + IPI1 q3w (n=27)	Arm C NIVO3 q2w + IPI1 q6w (n=29)	Arm A NIVO1 + IPI3 q3w (n=50)	Arm B NIVO3 + IPI1 q3w (n=49)	Arm C NIVO3 q2w + IPI1 q6w (n=49)
ORR, n (%)	8 (24)	9 (33)	9 (31)	16 (32)	15 (31)	15 (31)
DCR, n (%)	17 (50)	11 (41)	13 (45)	27 (54)	21 (43)	24 (49)
Median DoR, mo (95%CI)	9.8 (7.0, NR)	15.2 (4.2, NR)	11.1 (4.2, NR)	17.5 (8.3, NR)	22.2 (4.4, NR)	16.6 (4.3, NR)
Median OS, mo (95%CI)	16.4 (8.6, NR)	11.8 (6.1, 16.4)	11.2 (6.1, NR)	22.8 (9.4, NE)	12.5 (7.6, 16.4)	12.7 (7.4, 33.0)

Yao T, et al. Ann Oncol 2020;31(suppl):abstr O-5

O-5: Efficacy and safety of nivolumab + ipilimumab in Asian patients with advanced hepatocellular carcinoma: subanalysis of the CheckMate 040 study – Yao T, et al

Key results (cont.)

Grade 3/4 TRAEs, n (%)	Asian patients			All patients		
	Arm A NIVO1 + IPI3 q3w (n=33)	Arm B NIVO3 + IPI1 q3w (n=27)	Arm C NIVO3 q2w + IPI1 q6w (n=29)	Arm A NIVO1 + IPI3 q3w (n=49)	Arm B NIVO3 + IPI1 q3w (n=49)	Arm C NIVO3 q2w + IPI1 q6w (n=48)
Any	17 (52)	7 (26)	8 (28)	26 (53)	14 (29)	15 (31)
Pruritus	1 (3)	0	0	2 (4)	0	0
Rash	1 (3)	1 (4)	0	2 (4)	2 (4)	0
Diarrhoea	1 (3)	0	0	2 (4)	1 (2)	1 (2)
AST increased	5 (15)	3 (11)	2 (7)	8 (16)	4 (8)	2 (4)
Fatigue	0	0	0	1 (2)	0	0
ALT increased	3 (9)	2 (7)	0	4 (8)	3 (6)	0

Conclusions

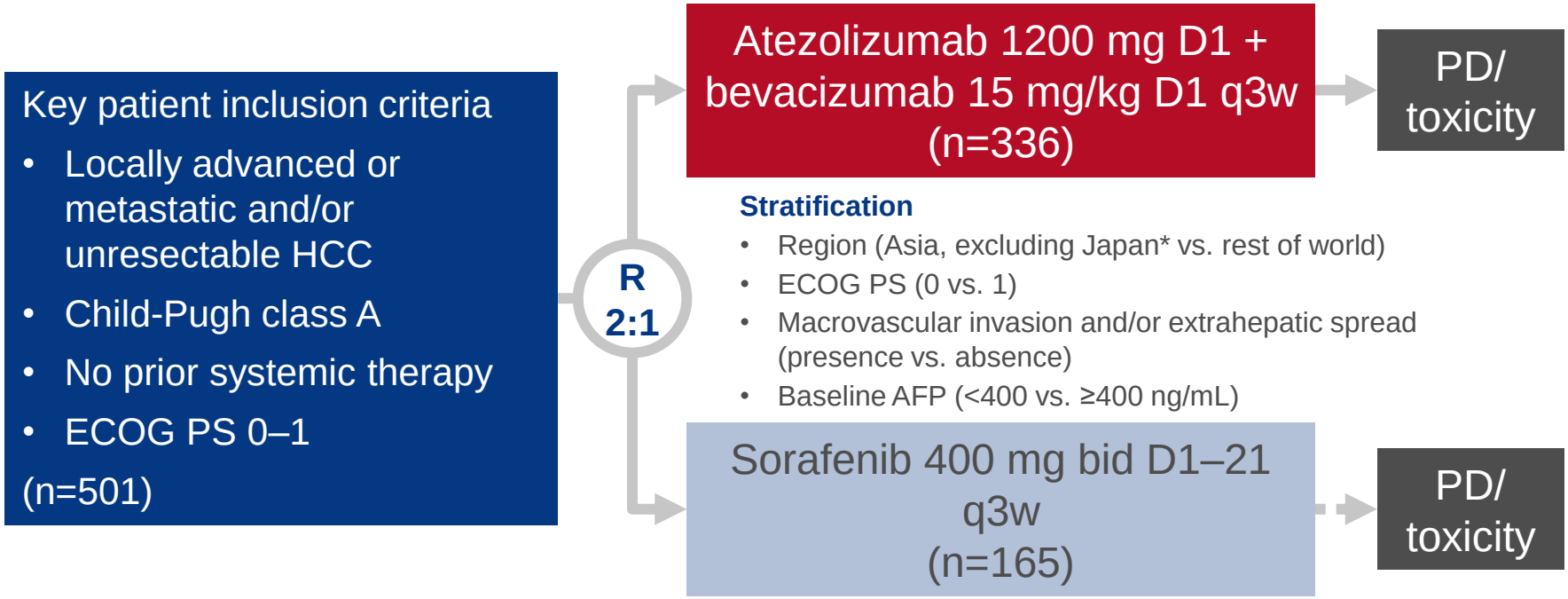
- **In Asian patients with advanced HCC, nivolumab + ipilimumab demonstrated clinically meaningful responses, particularly in the nivolumab 1 + ipilimumab 3 arm**
- **The safety profile was manageable with no new safety signals observed**

Yao T, et al. Ann Oncol 2020;31(suppl):abstr O-5

O-8: Atezolizumab + bevacizumab vs sorafenib for unresectable hepatocellular carcinoma (HCC): Results from older adults enrolled in IMbrave150 – Li D, et al

Study objective

- To evaluate the efficacy and safety of atezolizumab + bevacizumab in older patients with unresectable HCC



CO-PRIMARY ENDPOINTS†

- OS, PFS (RECIST v1.1)

SECONDARY ENDPOINTS

- PROs (TTD of QoL, physical and role functioning EORTC QLQ-C30 and EORTC QLQ-HCC18)

*Japan is included in rest of world;
†data previously presented at ESMO 2019

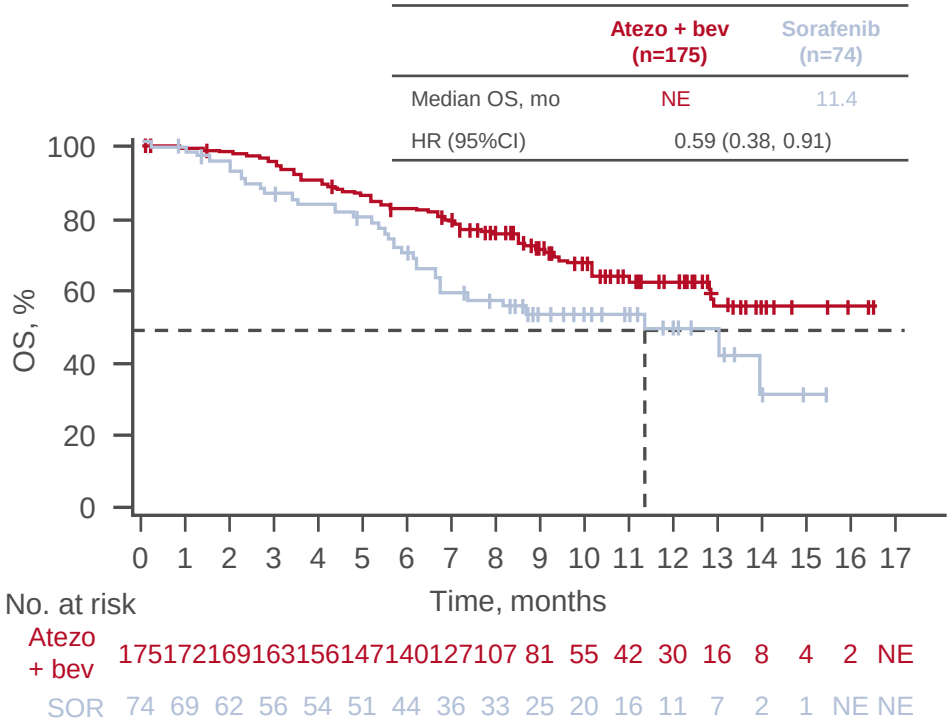
Li D, et al. Ann Oncol 2020;31(suppl):abstr O-8

O-8: Atezolizumab + bevacizumab vs sorafenib for unresectable hepatocellular carcinoma (HCC): Results from older adults enrolled in IMbrave150 – Li D, et al

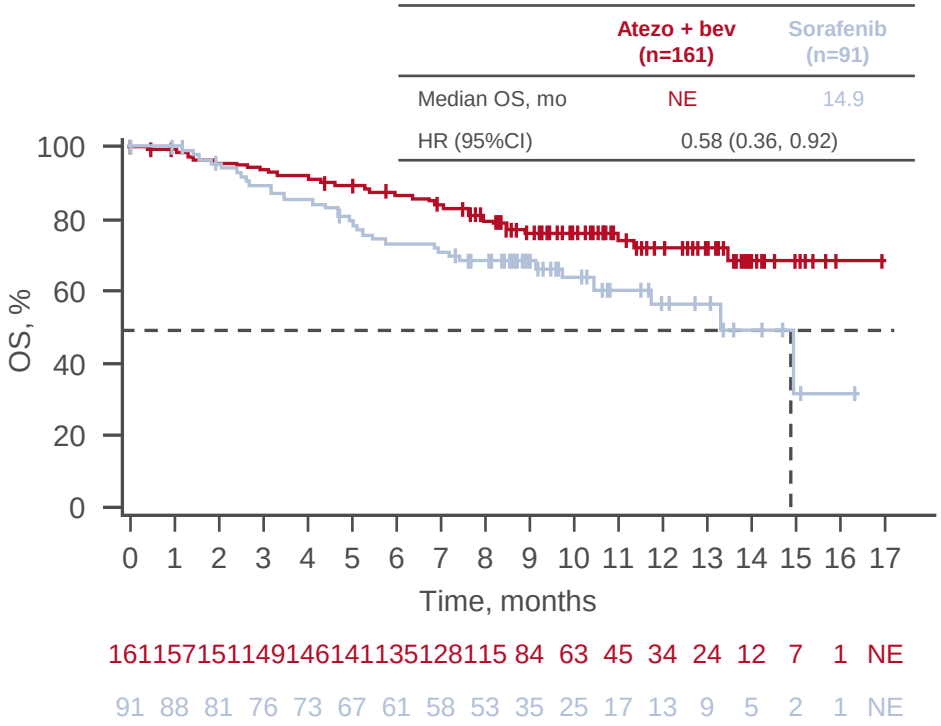
Key results

Overall survival

Age <65 years



Age ≥65 years



Li D, et al. Ann Oncol 2020;31(suppl):abstr O-8

O-8: Atezolizumab + bevacizumab vs sorafenib for unresectable hepatocellular carcinoma (HCC): Results from older adults enrolled in IMbrave150 – Li D, et al

Key results (cont.)

AEs occurring in ≥15% of patients treated with atezolizumab + bevacizumab, n (%)	<65 years (n=171)	≥65 years (n=158)
Hypertension	47 (27)	51 (32)
Fatigue	24 (14)	43 (27)
Diarrhoea	28 (16)	34 (22)
Appetite decreased	26 (15)	32 (20)
Pyrexia	29 (17)	30 (19)
Pruritus	35 (20)	29 (18)
Proteinuria	39 (23)	27 (17)
AST increased	39 (23)	25 (16)

Conclusions

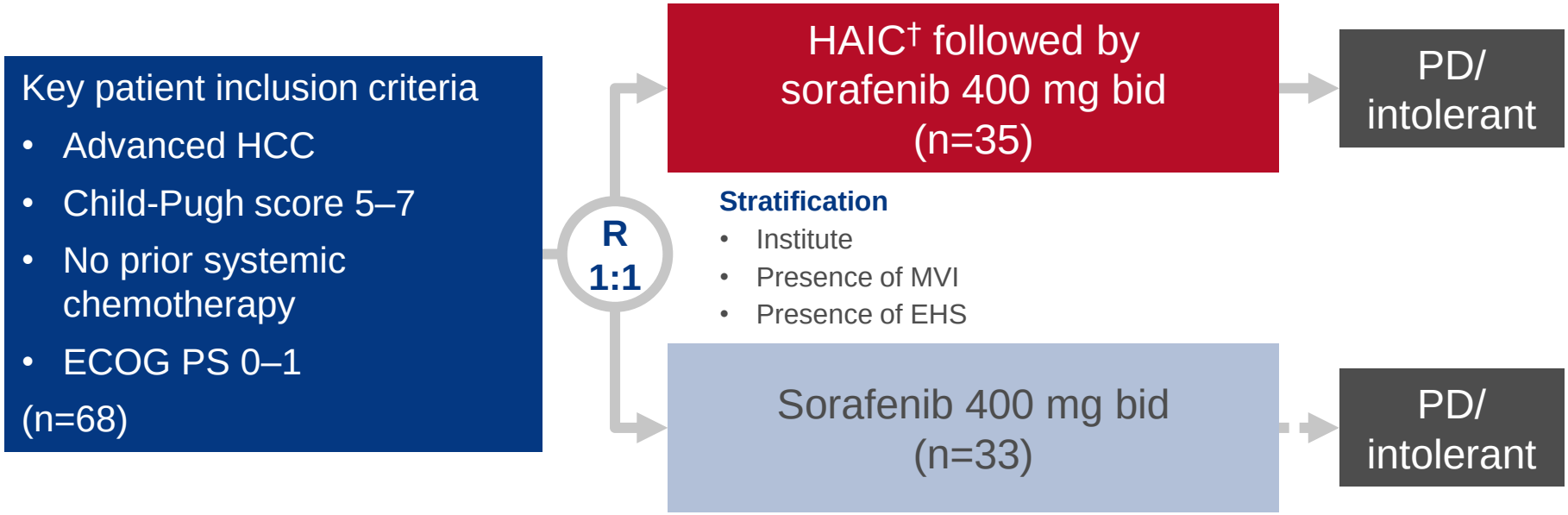
- **In older patients (≥65 years) with unresectable HCC, atezolizumab + bevacizumab demonstrated clinically meaningful benefits with no significant additional toxicities**

Li D, et al. Ann Oncol 2020;31(suppl):abstr O-8

SO-6: The influence of liver function on the outcomes of phase II trial of sorafenib vs. hepatic arterial infusion chemotherapy for advanced hepatocellular carcinoma – Kobayashi S, et al

Study objective

- To evaluate the efficacy and safety of hepatic arterial infusion chemotherapy (HAIC) + sorafenib according to liver function* in patients with advanced HCC



PRIMARY ENDPOINT

- 1-year survival

SECONDARY ENDPOINTS

- OS, 2-year survival, TTP, ORR, DCR, safety

*Defined using modified ALBI score, grade 1 ≤-2.60, grade 2a >-2.60 to ≤-2.27 and grade 2b >-2.27 to ≤-1.39; †cisplatin 65 mg/m^2 ia every 4–6 weeks

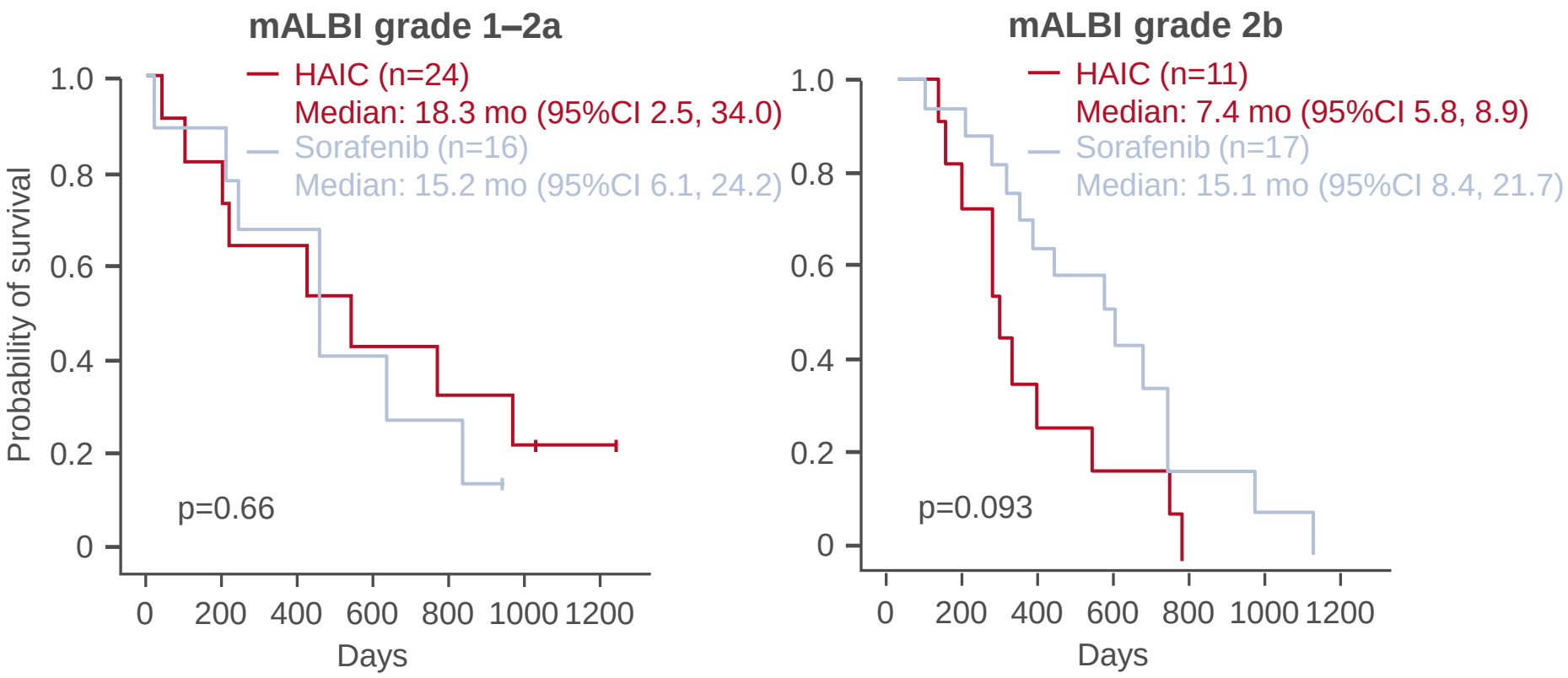
Kobayashi S, et al. Ann Oncol 2020;31(suppl):abstr SO-6

This talk was presented at the 22nd ESMO WCGC on 1 July 2020 at 19:12

SO-6: The influence of liver function on the outcomes of phase II trial of sorafenib vs. hepatic arterial infusion chemotherapy for advanced hepatocellular carcinoma – Kobayashi S, et al

Key results

Overall survival



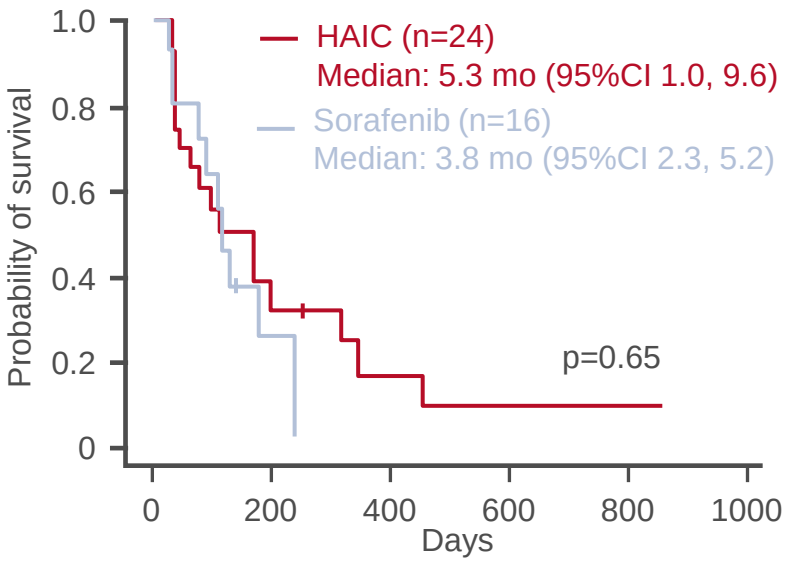
Kobayashi S, et al. Ann Oncol 2020;31(suppl):abstr SO-6

SO-6: The influence of liver function on the outcomes of phase II trial of sorafenib vs. hepatic arterial infusion chemotherapy for advanced hepatocellular carcinoma – Kobayashi S, et al

Key results (cont.)

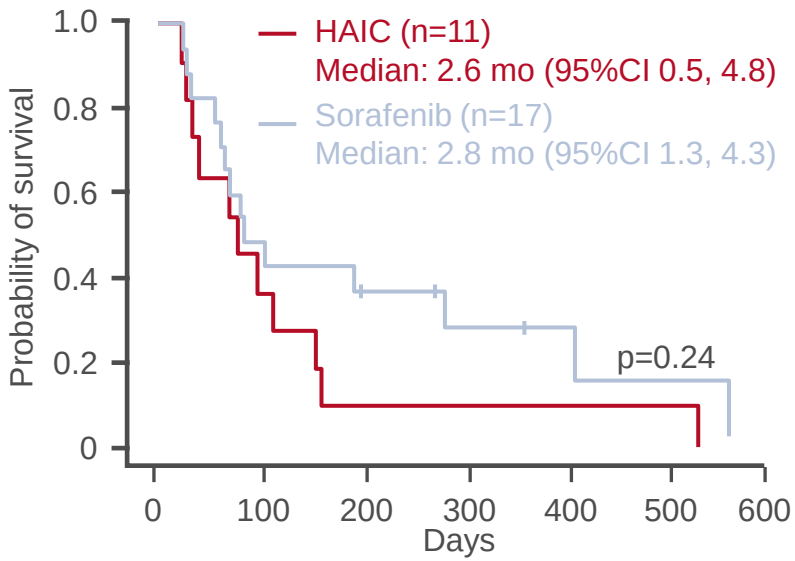
Time-to-progression and 2L treatment

mALBI grade 1–2a



2L treatment, n (%)	Sorafenib (n=16)	HAIC (n=24)
Sorafenib	0	17 (71)
HAIC	11 (69)	0
Others	2 (12)	4 (17)
BSC	3 (19)	3 (13)

mALBI grade 2b



2L treatment, n (%)	Sorafenib (n=17)	HAIC (n=11)
Sorafenib	0	7 (64)
HAIC	7 (41)	0
Others	6 (35)	1 (9)
BSC	4 (24)	3 (27)

Kobayashi S, et al. Ann Oncol 2020;31(suppl):abstr SO-6

SO-6: The influence of liver function on the outcomes of phase II trial of sorafenib vs. hepatic arterial infusion chemotherapy for advanced hepatocellular carcinoma – Kobayashi S, et al

Conclusions

- **In patients with advanced HCC and mALBI grade 2b, sorafenib demonstrated better OS than HAIC followed by sorafenib, however, OS was comparable between the two treatment arms in those with mALBI grade 1–2a**

Kobayashi S, et al. Ann Oncol 2020;31(suppl):abstr SO-6

SO-9: Outcomes for patients with advanced hepatocellular carcinoma (HCC) and Child-Pugh B liver function in the phase 3 CELESTIAL study of cabozantinib vs placebo – El-Khoueiry A, et al

Study objective

- To evaluate the efficacy and safety of cabozantinib in the subgroup of patients with advanced HCC whose liver function had deteriorated to Child-Pugh B by Week 8

Key patient inclusion criteria

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

(n=707)

R 2:1

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

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

Stratification

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

PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR, safety

El-Khoueiry A, et al. Ann Oncol 2020;31(suppl):abstr SO-9

This talk was presented at the 22nd ESMO WCGC on 1 July 2020 at 19:32

SO-9: Outcomes for patients with advanced hepatocellular carcinoma (HCC) and Child-Pugh B liver function in the phase 3 CELESTIAL study of cabozantinib vs placebo – El-Khoueiry A, et al

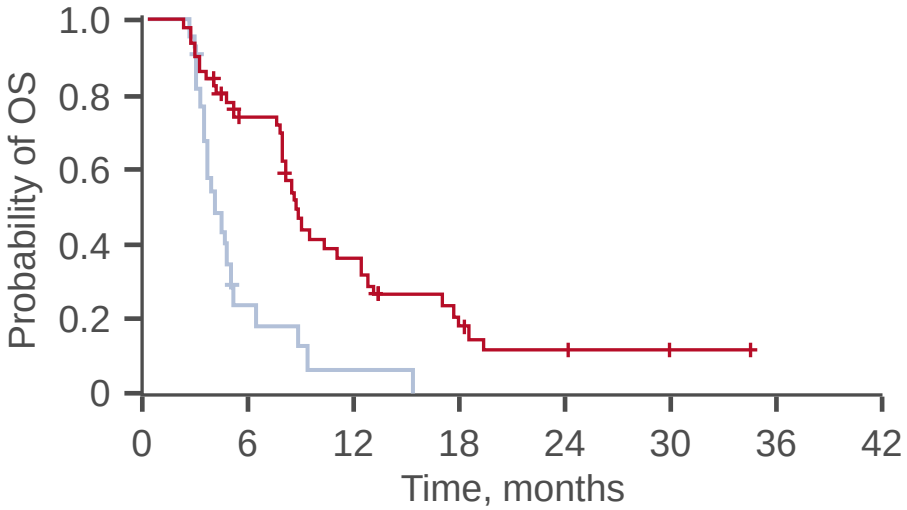
Key results

Overall survival

Child-Pugh B subgroup

	Median OS, mo (95%CI)	No. of deaths
Cabozantinib (n=51)	8.5 (7.7, 12.2)	37
Placebo (n=22)	3.8 (3.3, 4.8)	20

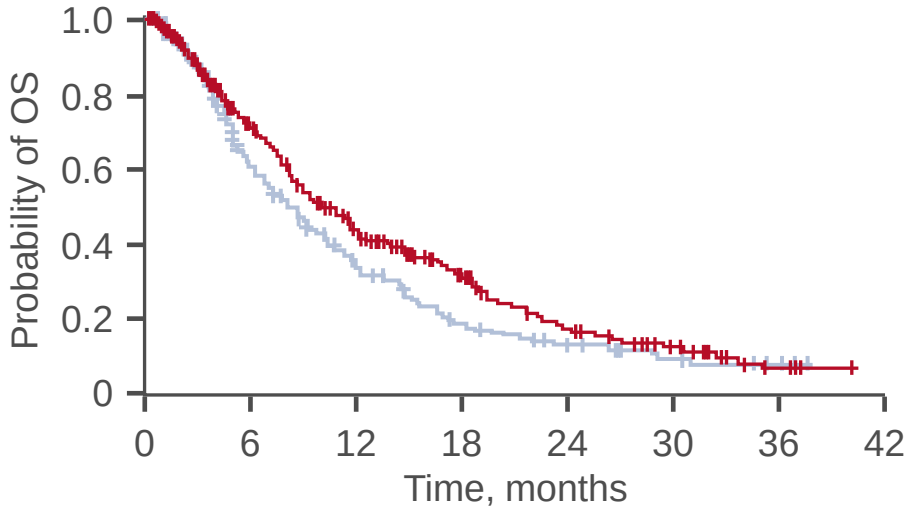
HR 0.32 (95%CI 0.18, 0.58)



Overall

	Median OS, mo (95%CI)	No. of deaths
Cabozantinib (n=470)	10.2 (9.1, 12.0)	317
Placebo (n=237)	8.0 (6.8, 9.4)	167

HR 0.76 (95%CI 0.63, 0.92); p=0.005



El-Khoueiry A, et al. Ann Oncol 2020;31(suppl):abstr SO-9

SO-9: Outcomes for patients with advanced hepatocellular carcinoma (HCC) and Child-Pugh B liver function in the phase 3 CELESTIAL study of cabozantinib vs placebo – El-Khoueiry A, et al

Key results (cont.)

Grade 3/4 AEs, %	Child-Pugh B subgroup (n=51)	Overall population (n=467)
Any	71	68
Fatigue	20	10
Ascites	14	4
AST increased	14	12
Thrombocytopenia	12	3
Palmar-plantar erythrodysesthesia	8	17
Hypertension	8	16

Conclusions

- **In patients with advanced HCC and Child-Pugh B liver function by Week 8, cabozantinib demonstrated similar outcomes to those of the overall population and had a manageable safety profile**

El-Khoueiry A, et al. Ann Oncol 2020;31(suppl):abstr SO-9

Cancers of the pancreas, small bowel and hepatobiliary tract

GALL BLADDER

LBA-2: Two arm randomized prospective superiority phase II multicentric clinical trial to evaluate the efficacy of capecitabine-irinotecan (CAPIRI) versus irinotecan in advanced gall bladder cancer progressing on first line chemotherapy – Ramaswamy A, et al

Study objective

- To evaluate the efficacy and safety of capecitabine-irinotecan (CAPIRI) in patients with gall bladder cancer who had progressed on 1L chemotherapy

Key patient inclusion criteria
- Stage IV or recurrent gall bladder cancer
- Previous 1L treatment with gemcitabine-based regimen

(n=98)

R
1:1

CAPIRI: Capecitabine 1700 mg/m^2/day d1–14 + irinotecan 200 mg/m^2 q3w (n=49)

Irinotecan 240 mg/m^2 q3w (n=49)

PRIMARY ENDPOINT

- OS at 6 months

SECONDARY ENDPOINTS

- PFS at 6 months, RR, QoL, safety

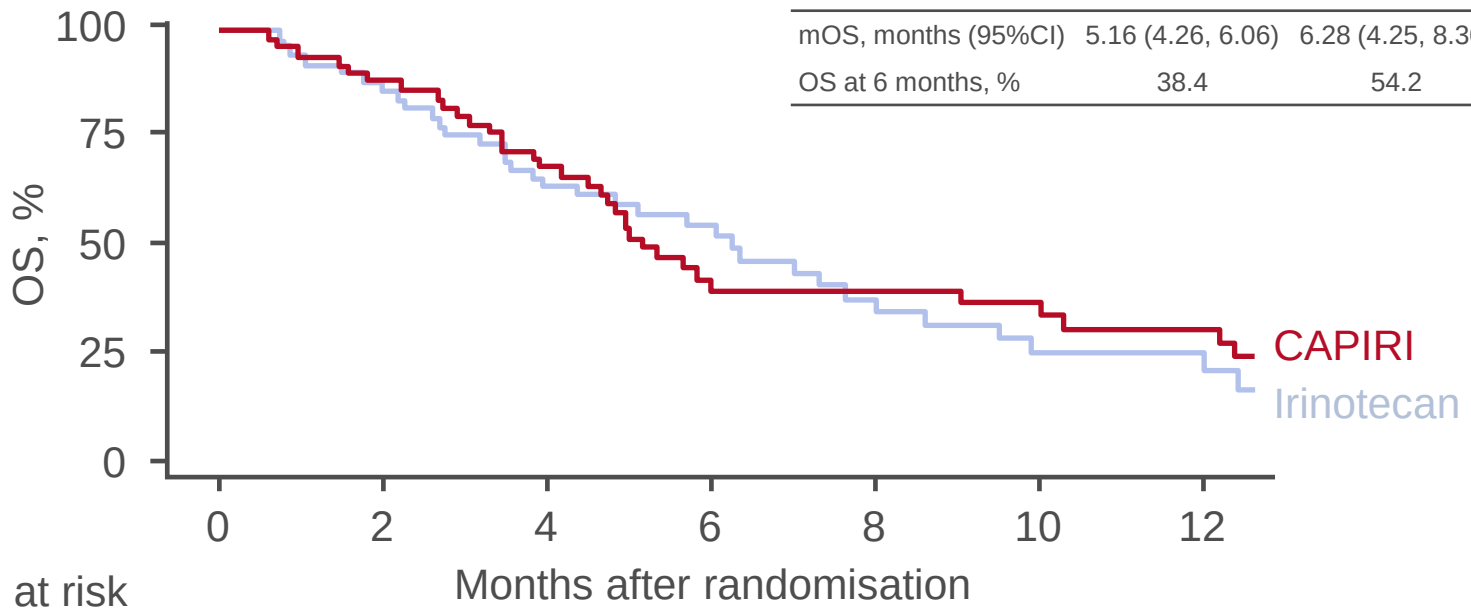
Ramaswamy A, et al. Ann Oncol 2020;31(suppl):abstr LBA-2

LBA-2: Two arm randomized prospective superiority phase II multicentric clinical trial to evaluate the efficacy of capecitabine-irinotecan (CAPIRI) versus irinotecan in advanced gall bladder cancer progressing on first line chemotherapy – Ramaswamy A, et al

Key results

OS

	CAPIRI	Irinotecan	p-value
mOS, months (95%CI)	5.16 (4.26, 6.06)	6.28 (4.25, 8.30)	
OS at 6 months, %	38.4	54.2	0.93



No. at risk

CAPIRI	49	43	33	15	14	12	9
Irinotecan	49	43	31	20	12	8	5

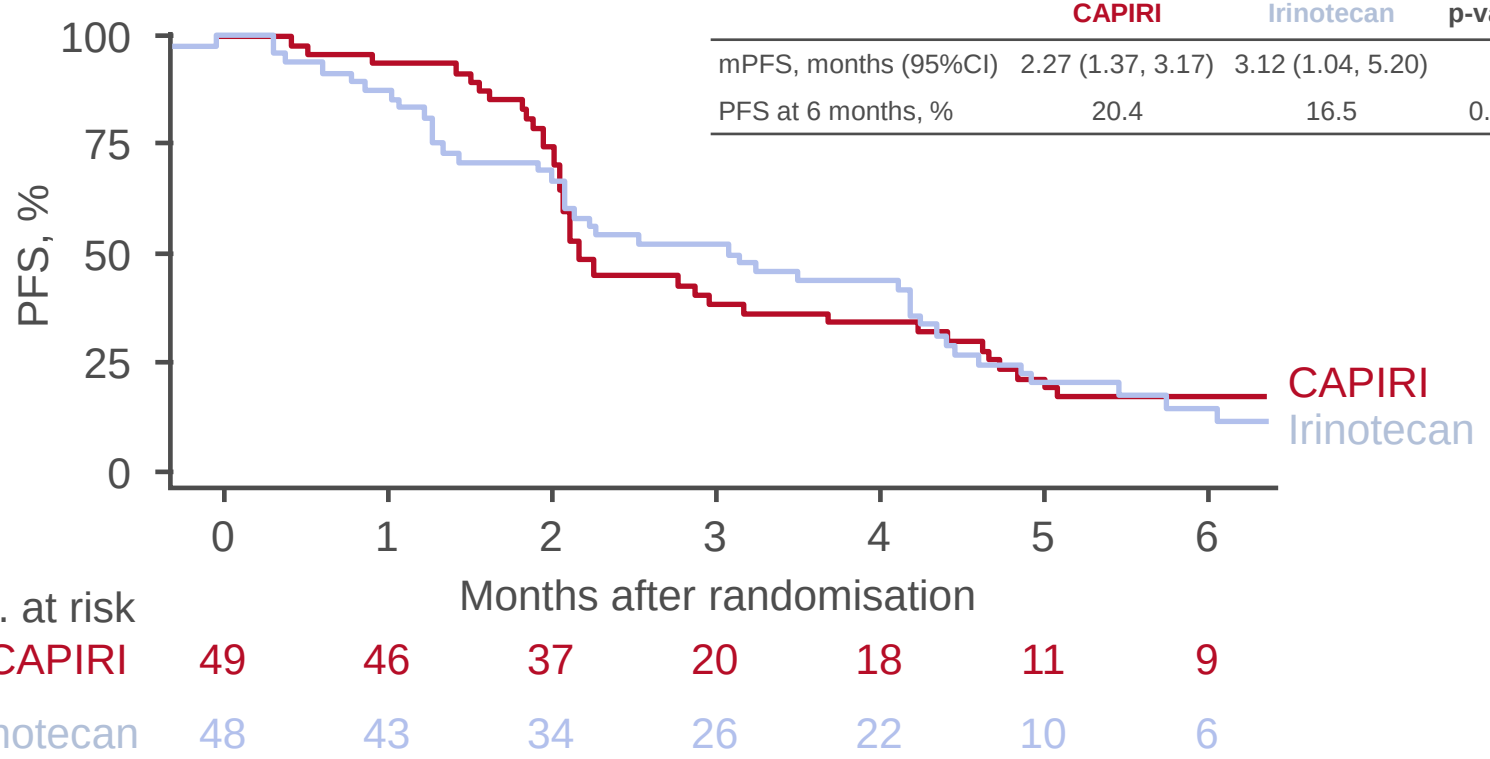
Ramaswamy A, et al. Ann Oncol 2020;31(suppl):abstr LBA-2

LBA-2: Two arm randomized prospective superiority phase II multicentric clinical trial to evaluate the efficacy of capecitabine-irinotecan (CAPIRI) versus irinotecan in advanced gall bladder cancer progressing on first line chemotherapy – Ramaswamy A, et al

Key results (cont.)

PFS

	CAPIRI	Irinotecan	p-value
mPFS, months (95%CI)	2.27 (1.37, 3.17)	3.12 (1.04, 5.20)	
PFS at 6 months, %	20.4	16.5	0.56



Ramaswamy A, et al. Ann Oncol 2020;31(suppl):abstr LBA-2

LBA-2: Two arm randomized prospective superiority phase II multicentric clinical trial to evaluate the efficacy of capecitabine-irinotecan (CAPIRI) versus irinotecan in advanced gall bladder cancer progressing on first line chemotherapy – Ramaswamy A, et al

Key results (cont.)

	CAPIRI (n=49)	Irinotecan (n=49)
BOR, n (%)		
CR	2 (4)	0
PR	1 (2)	0
SD	17 (35)	23 (47)
RR, n (%)	3 (6)	0
CBR, n (%)	20 (41)	23 (47)
Number of cycles, mean	3	4
Continued on treatment, n (%)	6 (12)	6 (12)

- QoL: no difference in delta HEP scores – F(1, 21) = 0.805; p=0.38
- Higher rate of dose modifications with CAPIRI (27%) vs. irinotecan (9%); p=0.03

Ramaswamy A, et al. Ann Oncol 2020;31(suppl):abstr LBA-2

LBA-2: Two arm randomized prospective superiority phase II multicentric clinical trial to evaluate the efficacy of capecitabine-irinotecan (CAPIRI) versus irinotecan in advanced gall bladder cancer progressing on first line chemotherapy – Ramaswamy A, et al

Key results (cont.)

Grade 3/4 AEs, n (%)	CAPIRI (n=49)	Irinotecan (n=49)
Fatigue	10 (20)	7 (14)
Diarrhoea	8 (16)	5 (10)
Constipation	4 (8)	2 (4)
Nausea/vomiting	2 (4)	4 (8)
Hyponatremia	2 (4)	3 (6)
Hematological		
Anaemia	2 (4)	2 (4)
Febrile neutropenia	2 (4)	0
Thrombocytopenia	2 (4)	2 (4)
Neutropenia	1 (2)	4 (8)

Conclusions

- **In patients with advanced gall bladder cancer with progression on 1L chemotherapy, clinical benefit was similar between CAPIRI and irinotecan monotherapy; however, there was an increase in dose modifications and AEs with the combination therapy**

Ramaswamy A, et al. Ann Oncol 2020;31(suppl):abstr LBA-2

CANCERS OF THE COLON, RECTUM AND ANUS

LBA-5: ANCHOR CRC: a single-arm, phase 2 study of encorafenib, binimetinib plus cetuximab in previously untreated BRAF V600E–mutant metastatic colorectal cancer – Grothey A, et al

Study objective

- To evaluate the efficacy and safety of encorafenib + binimetinib + cetuximab as a 1L treatment for patients with BRAF V600E-mutant mCRC

Key patient inclusion criteria
- mCRC with BRAF V600E mutation
- Untreated in metastatic setting
- No prior RAF, MEK or EGFR inhibitors
- ECOG PS 0–1

(n=95)

→ Encorafenib + binimetinib + cetuximab (stage 1 n=41; stage 2* n=54)

→ PD/ toxicity/ withdrawal

PRIMARY ENDPOINT

- ORR (investigator assessed)

SECONDARY ENDPOINTS

- PFS, OS, PK, QoL, safety

*Enrolment after ≥12 responses occurred in stage 1

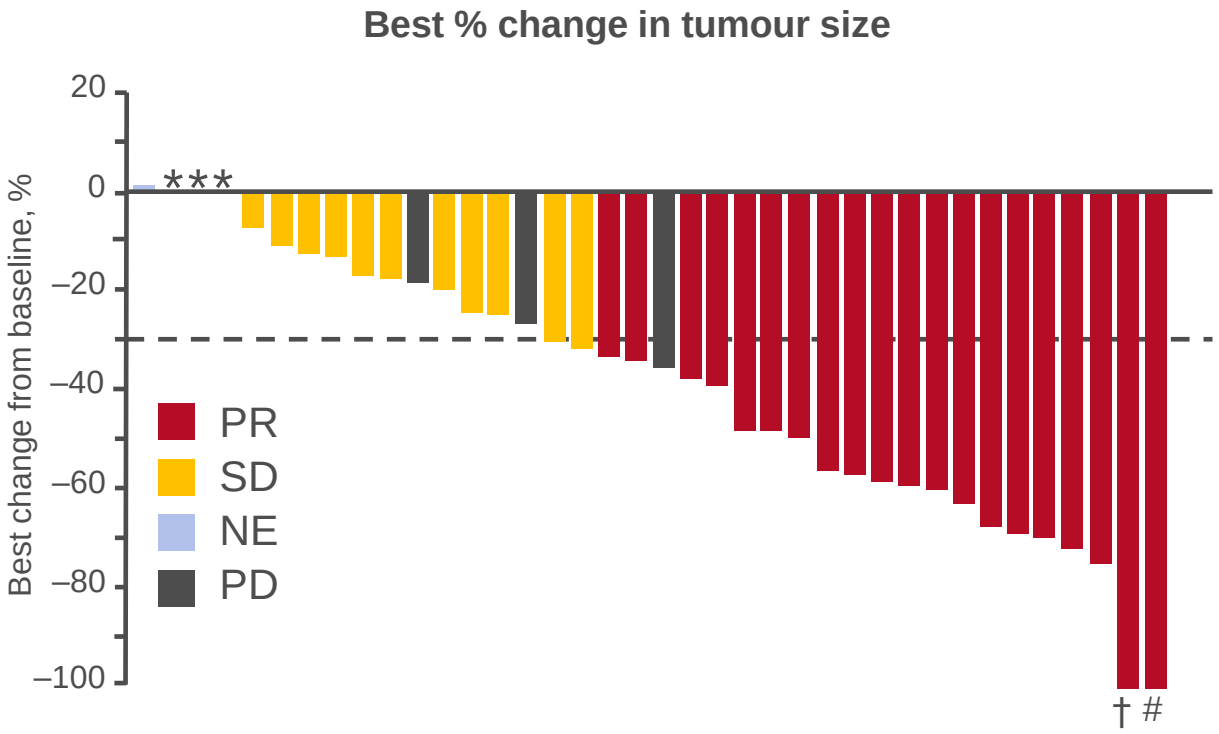
Grothey A, et al. Ann Oncol 2020;31(suppl):abstr LBA-5

This talk was presented at the 22nd ESMO WCGC on 3 July 2020 at 15:06

LBA-5: ANCHOR CRC: a single-arm, phase 2 study of encorafenib, binimetinib plus cetuximab in previously untreated BRAF V600E–mutant metastatic colorectal cancer – Grothey A, et al

Key results

	Stage 1 (n=40)
BOR, n (%)	
CR	0
PR	20 (50)
SD	14 (35)
PD	4 (10)
NE	2 (5)
ORR, n (%) [95%CI]	20 (50) [34, 66]
DCR, n (%)	34 (85)



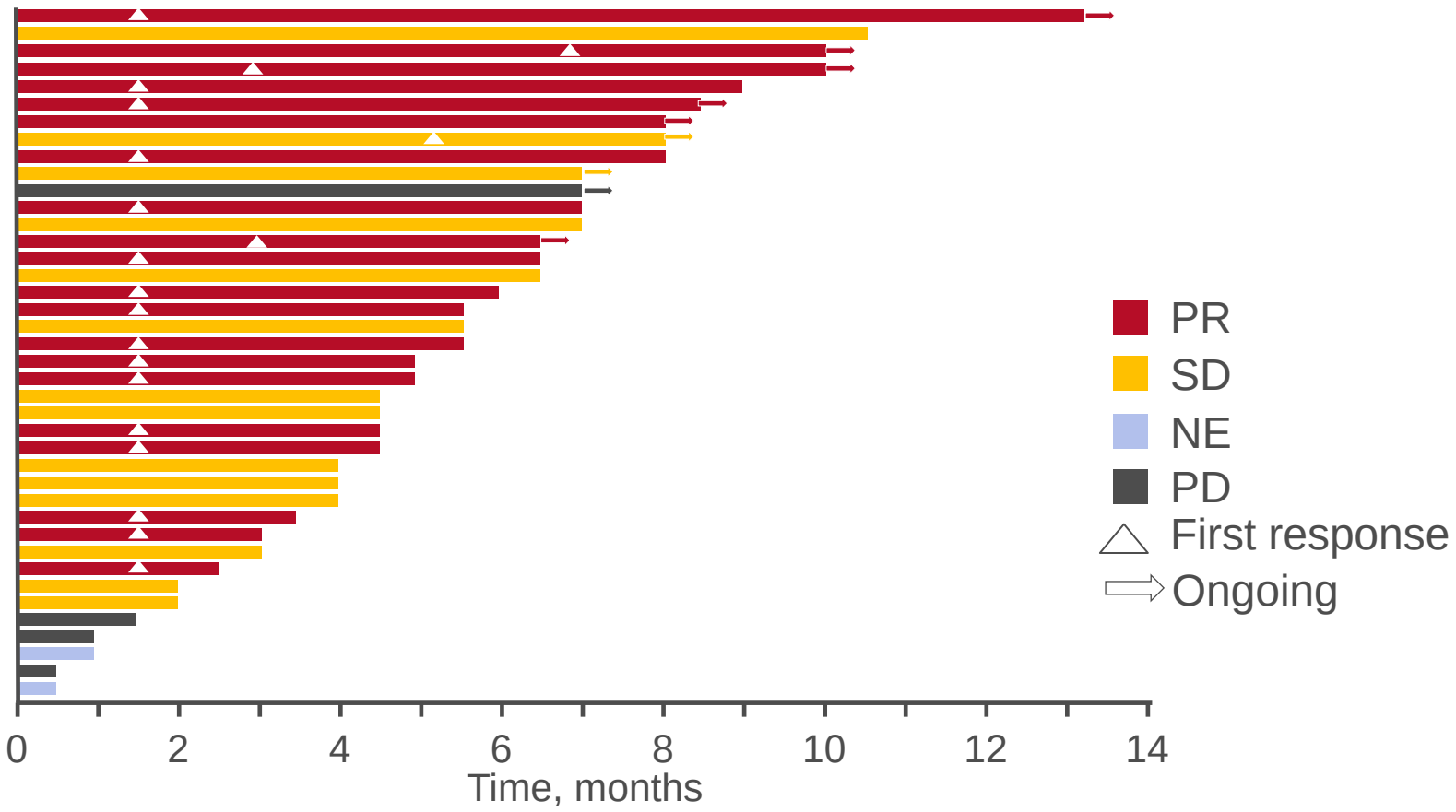
Median time on treatment: 4.9 months; *confirmed SD; †CR on target lesion but non-target still present; #CR not confirmed

Grothey A, et al. Ann Oncol 2020;31(suppl):abstr LBA-5

LBA-5: ANCHOR CRC: a single-arm, phase 2 study of encorafenib, binimetinib plus cetuximab in previously untreated BRAF V600E–mutant metastatic colorectal cancer – Grothey A, et al

Key results (cont.)

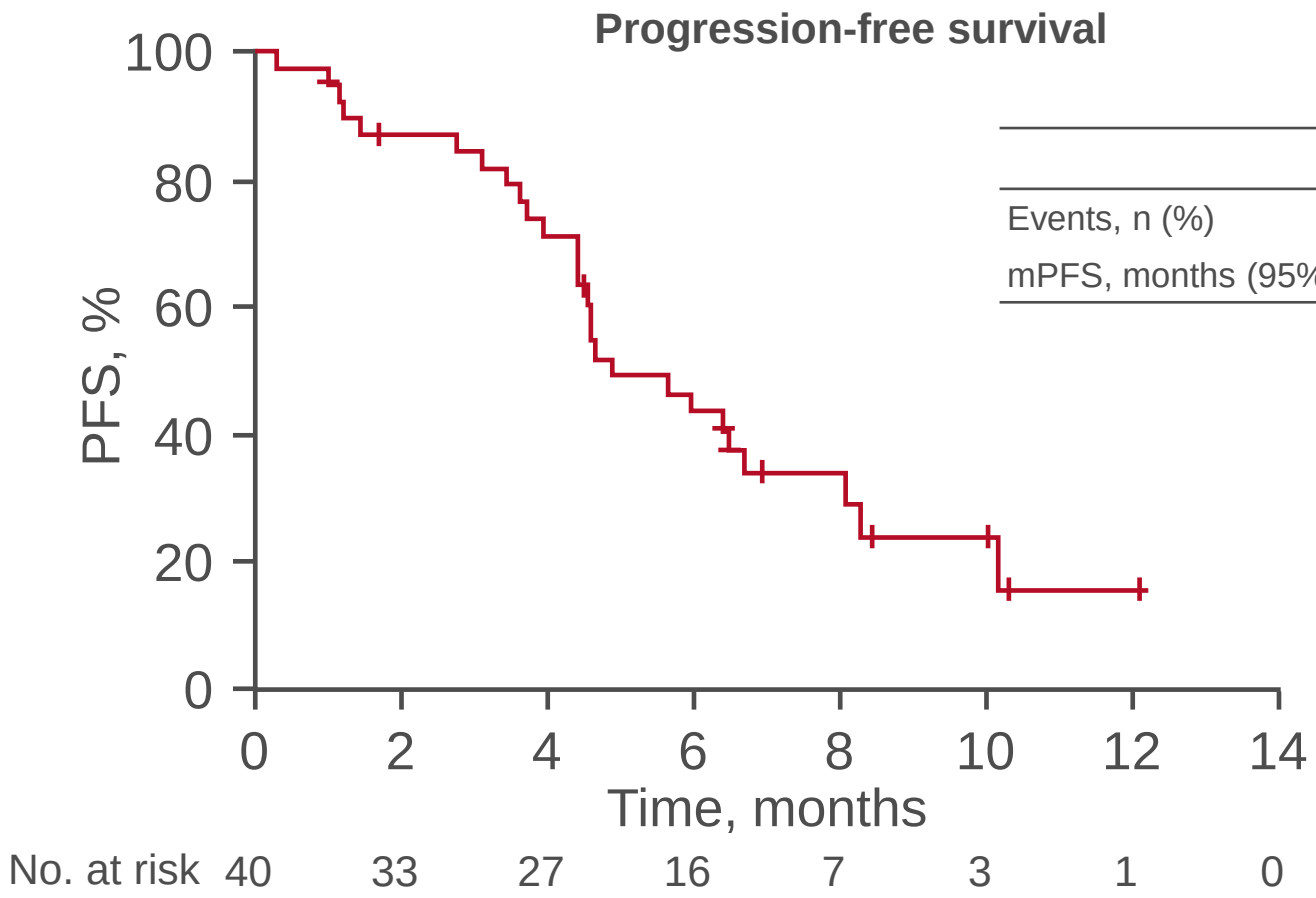
Duration of treatment and BOR



Grothey A, et al. Ann Oncol 2020;31(suppl):abstr LBA-5

LBA-5: ANCHOR CRC: a single-arm, phase 2 study of encorafenib, binimetinib plus cetuximab in previously untreated BRAF V600E–mutant metastatic colorectal cancer – Grothey A, et al

Key results (cont.)



	Stage 1 (n=40)
Events, n (%)	27 (68)
mPFS, months (95%CI)	4.9 (4.4, 8.1)

Grothey A, et al. Ann Oncol 2020;31(suppl):abstr LBA-5

LBA-5: ANCHOR CRC: a single-arm, phase 2 study of encorafenib, binimetinib plus cetuximab in previously untreated BRAF V600E–mutant metastatic colorectal cancer – Grothey A, et al

Key results (cont.)

AEs, n (%)	Stage 1 (n=41)	
	Any grade	Grade ≥3
Any	41 (100)	28 (68)
SAEs	23 (56)	20 (49)
Leading to dose modification	28 (68)	18 (44)
Leading to discontinuation	8 (20)	7 (17)
Leading to death	3 (7)	3 (7)

Grade ≥3 AEs, n (%)	Stage 1 (n=41)
Diarrhoea	6 (15)
Anaemia	5 (12)
Acute kidney injury	5 (12)
Nausea	3 (7)
Abdominal pain	2 (5)
Asthenia	1 (2)
Vomiting	1 (2)
Acneiform dermatitis	1 (2)
Appetite decreased	1 (2)

Conclusions

- **In patients with BRAF V600E-mutant mCRC, 1L treatment with encorafenib + binimetinib + cetuximab demonstrated clinical activity and was well-tolerated**

Grothey A, et al. Ann Oncol 2020;31(suppl):abstr LBA-5

LBA-6: Safety, feasibility, tolerability, and preliminary efficacy of perioperative systemic therapy for resectable colorectal peritoneal metastases: pilot phase of a randomised trial (CAIRO6) – Rovers K, et al

Study objective

- To evaluate the efficacy and safety of perioperative systemic therapy in patients with resectable colorectal peritoneal metastases

Key patient inclusion criteria

- Resectable non-appendiceal colorectal adenocarcinoma
- Peritoneal metastases
- No extra-peritoneal metastases
- No systemic therapy in prior 6 months
- No previous cytoreductive surgery with HIPEC

(n=79)

R 1:1

Perioperative systemic therapy (investigator choice)* (n=37)

Cytoreductive surgery with HIPEC (n=42)

ENDPOINTS

- No. of patients with complete cytoreductive surgery with HIPEC, no. of patients with Clavien-Dindo grade 3–5 postoperative morbidity, feasibility of trial accrual, safety

*4 neoadjuvant + adjuvant cycles of CAPOX (1st 3 neoadjuvant with bevacizumab); 6 neoadjuvant + adjuvant cycles of FOLFOX (1st 4 neoadjuvant with bevacizumab); or 6 neoadjuvant cycles of FOLFIRI + 4 or 6 adjuvant cycles of capecitabine or 5FU-leucovorin (1st 4 neoadjuvant cycles with bevacizumab)

Rovers K, et al. Ann Oncol 2020;31(suppl):abstr LBA-6

This talk was presented at the 22nd ESMO WCGC on 3 July 2020 at 18:23

LBA-6: Safety, feasibility, tolerability, and preliminary efficacy of perioperative systemic therapy for resectable colorectal peritoneal metastases: pilot phase of a randomised trial (CAIRO6) – Rovers K, et al

Key results

Main outcome, n (%)	Perioperative systemic therapy (n=37)	Cytoreductive surgery with HIPEC (n=42)	p-value
No. of patients undergoing complete cytoreductive surgery with HIPEC	33 (89)	36 (86)	0.74
No. of patients with major postoperative morbidity	8 (22)	14 (33)	0.25
Surgery-related deaths	0	0	

Other outcomes, %	
Grade 3–5 systemic toxicity	35
Objective radiological response RECIST PCI	 16 (non-evaluable 59) 28 (non-evaluable 0)
Major pathological regression TRG1–2 TRG1 (no residual cancer cells)	 39 24

Rovers K, et al. Ann Oncol 2020;31(suppl):abstr LBA-6

LBA-6: Safety, feasibility, tolerability, and preliminary efficacy of perioperative systemic therapy for resectable colorectal peritoneal metastases: pilot phase of a randomised trial (CAIRO6) – Rovers K, et al

Conclusions

- **In patients with resectable colorectal peritoneal metastases, perioperative systemic therapy seems to be feasible, safe and tolerated providing radiological and pathological tumour responses**

Rovers K, et al. Ann Oncol 2020;31(suppl):abstr LBA-6

SO-16: The tumour-stroma ratio as additional parameter to the TNM classification; the UNITED study – Mesker W, et al

Study objective

- To evaluate the use of the tumour-stroma ratio (TSR) in addition to TNM classification

Methods

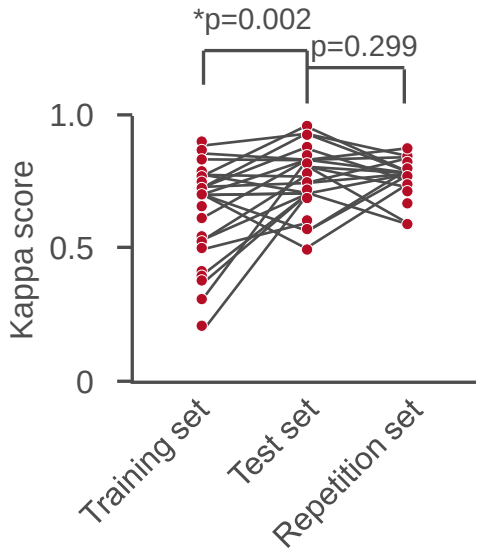
- The UNITED study was designed to prepare for the implementation of TSR in diagnostic pathology. The study assessed:
  - An e-learning module on TSR with quality assessment program (n=40)
    - TSR scored x2 on two occasions; repetition test after 1 year
  - Reliability and reproducibility of stained tumour tissues
  - Automation of scoring method
  - Validation in a prospective cohort of stage II-III colon cancer patients (recruiting and active; aim for 1500 patients)

Mesker W, et al. Ann Oncol 2020;31(suppl):abstr SO-16

SO-16: The tumour-stroma ratio as additional parameter to the TNM classification; the UNITED study – Mesker W, et al

Key results

- The e-learning module was passed by ~70% through auto-instruction and by ~90% through training
- Significant improvement from training to test set (p=0.002)
- No change from test to repetition set (p=0.299)



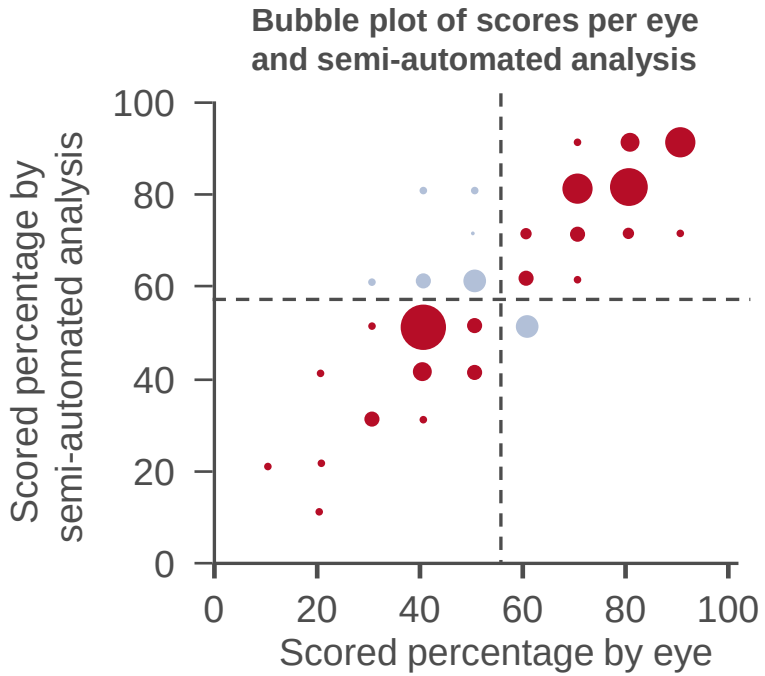
- E-learning can be used to instruct pathologists for scoring TSR

Mesker W, et al. Ann Oncol 2020;31(suppl):abstr SO-16

SO-16: The tumour-stroma ratio as additional parameter to the TNM classification; the UNITED study – Mesker W, et al

Key results (cont.)

- Inter-correlation coefficient = 0.832
  - 95%CI 0.71, 0.90
- Semi-automated analysis could be helpful for pathologists when scoring TSR, for quantifying the exact stroma-percentage



Conclusions

- **The TSR scoring method is reproducible and easily learned through auto-instruction and short training**
- **Semi-automated analysis can be useful for quantifying exact stroma-percentage**

Mesker W, et al. Ann Oncol 2020;31(suppl):abstr SO-16

SO-17: Association between tumor budding grade to T stage as prognostic value for recurrence with high-risk stage II colon cancer; a retrospective study – Kodama H, et al

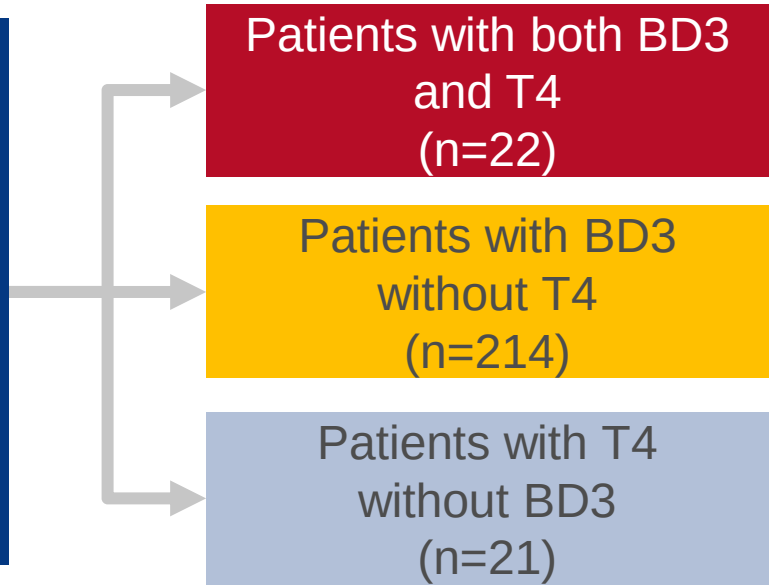
Study objective

- To evaluate the prognostic and predictive value of the association between tumour budding grade (BD) and T stage for determining recurrence in patients with high-risk pathological stage II CRC

Key patient inclusion criteria

- Pathological stage II CRC
- 1 of following high-risk factors: <12 lymph node, lymphatic or venous invasion, T4, BD3, undifferentiated tumour type
- Retrospective review of patients treated between 2013 and 2018*

(n=448)



*Initial analysis aimed to confirm the risk factors for recurrence in high-risk patients

Kodama H, et al. Ann Oncol 2020;31(suppl):abstr SO-17

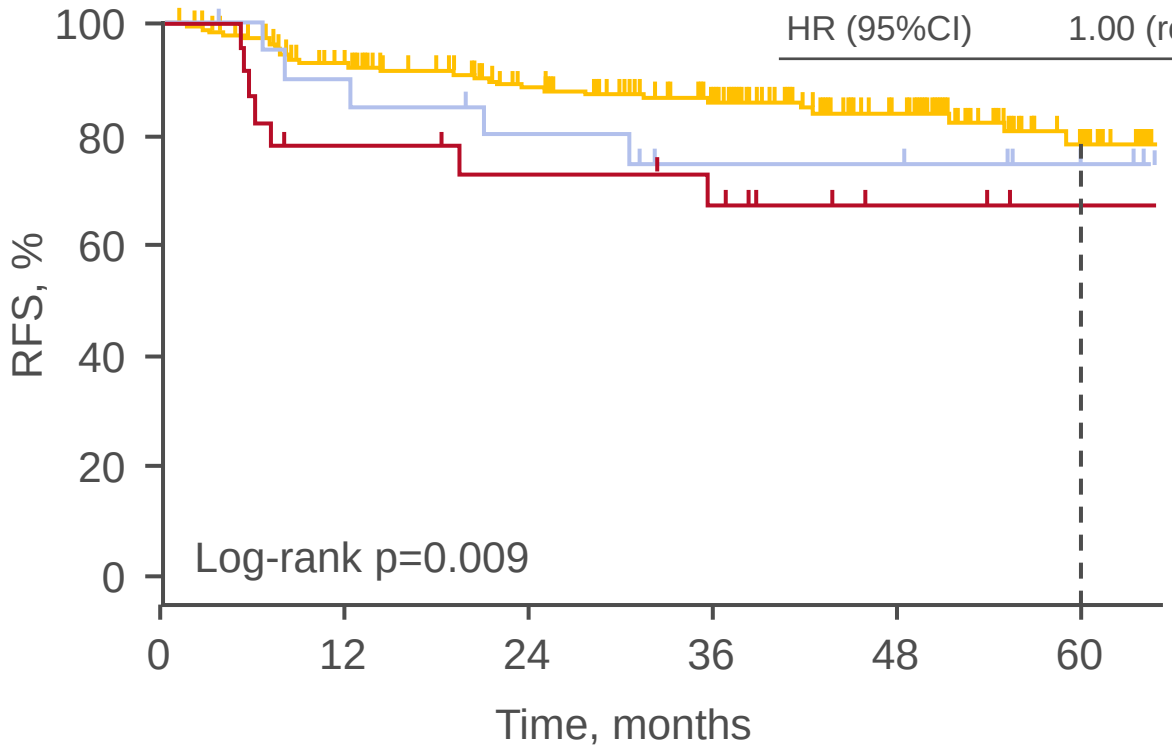
This talk was presented at the 22nd ESMO WCGC on 3 July 2020 at 13:33

SO-17: Association between tumor budding grade to T stage as prognostic value for recurrence with high-risk stage II colon cancer; a retrospective study – Kodama H, et al

Key results

Association between T4 and BD3 for RFS

	BD3 (n=214)	T4 (n=21)	BD3 + T4 (n=22)
5-year RFS, %	78.5	74.4	66.6
HR (95%CI)	1.00 (ref)	1.41 (0.54, 3.64)	3.03 (1.44, 6.37)



Kodama H, et al. Ann Oncol 2020;31(suppl):abstr SO-17

SO-17: Association between tumor budding grade to T stage as prognostic value for recurrence with high-risk stage II colon cancer; a retrospective study – Kodama H, et al

Key results (cont.)

		Univariate analysis, HR (95%CI)	p-value	Multivariate analysis, HR (95%CI)	p-value
Number of lymph nodes	≥12 <12	1 1.63 (0.90, 2.98)	0.1054	1 2.00 (1.08, 3.72)	0.0272
Lymphatic or venous invasion	Negative Positive	1 1.36 (0.62, 2.98)	0.4417	1 1.67 (0.66, 4.24)	0.2778
T stage	T3 T4	1 2.41 (1.33, 4.35)	0.0036	1 2.87 (1.50, 5.50)	0.0014
Tumour BD	BD1 BD2 BD3	1 1.21 (0.52, 2.85) 1.64 (0.87, 3.06)	0.6522 0.1229	1 1.36 (0.55, 3.40) 2.06 (1.05, 4.02)	0.5033 0.0342
Adjuvant chemotherapy	Yes No	1 1.36 (0.71, 2.60)	0.351	1 1.07 (0.48, 2.38)	0.7643
Histology	Differentiated Undifferentiated	1 0.83 (0.30, 2.30)	0.7273	1 0.45 (0.12, 1.64)	0.2279

Conclusions

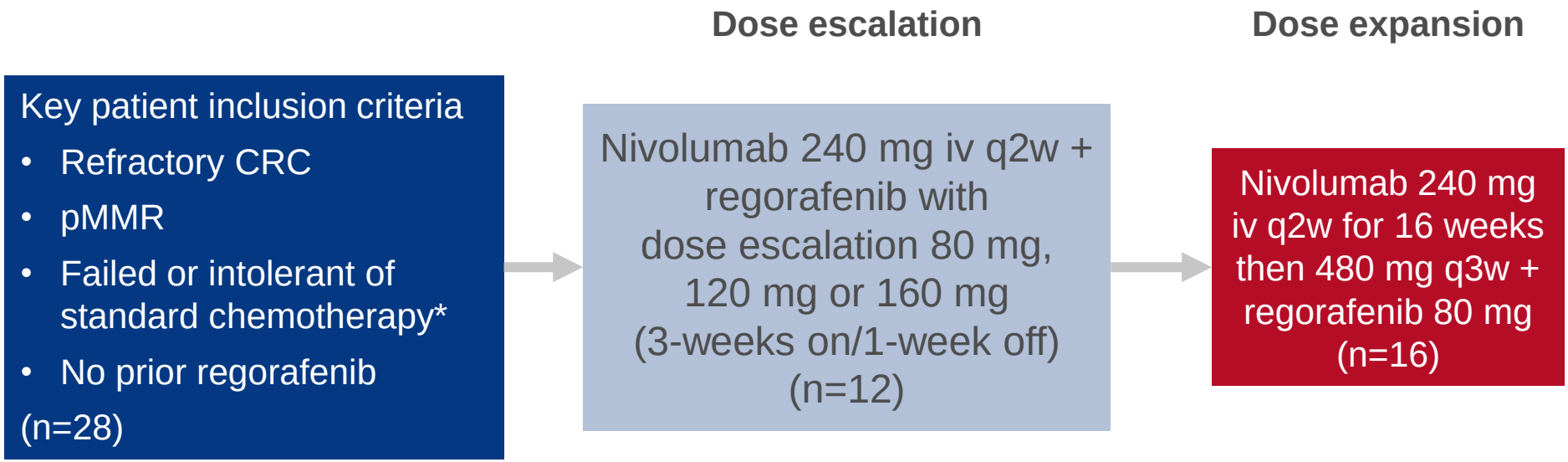
- **In patients with stage II CRC, BD3, T4 and <12 lymph nodes were identified as independent risk factors that impacted RFS**
- **Presence of both BD3 and T4 indicated poor prognosis**

Kodama H, et al. Ann Oncol 2020;31(suppl):abstr SO-17

O-20: Phase I/IB study of regorafenib and nivolumab in mismatch repair (MMR) proficient advanced refractory colorectal cancer – Kim R, et al

Study objective

- To evaluate the efficacy and safety of regorafenib + nivolumab in patients with pMMR advanced refractory CRC



PRIMARY ENDPOINT

- MTD

SECONDARY ENDPOINTS

- RR, PFS, OS, safety

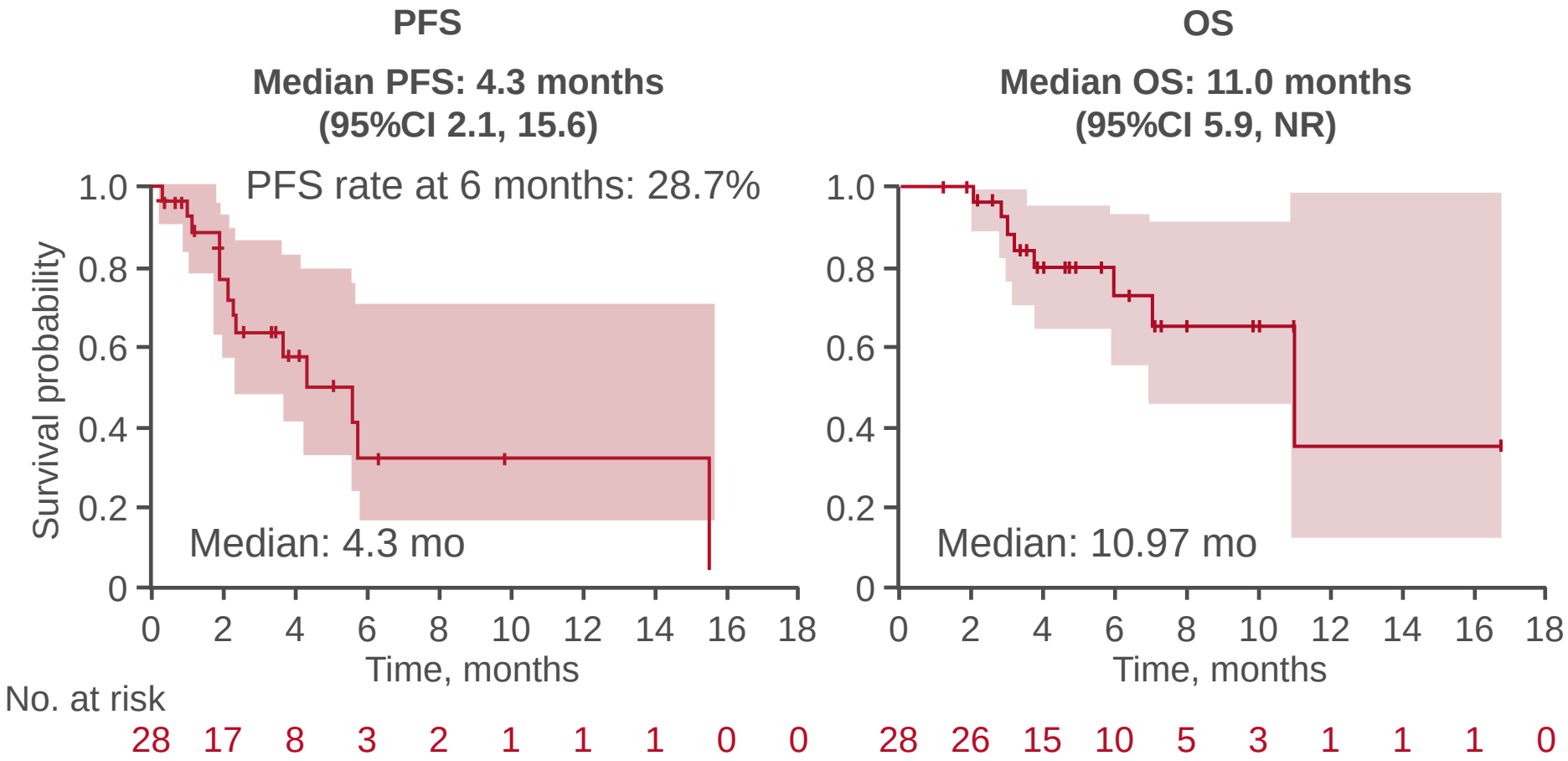
*Fluoropyrimidine, irinotecan, oxaliplatin or bevacizumab or if KRAS WT cetuximab or panitumumab containing regimens

Kim R, et al. Ann Oncol 2020;31(suppl):abstr O-20

This talk was presented at the 22nd ESMO WCGC on 3 July 2020 at 14:28

O-20: Phase I/IB study of regorafenib and nivolumab in mismatch repair (MMR) proficient advanced refractory colorectal cancer – Kim R, et al

Key results



Kim R, et al. Ann Oncol 2020;31(suppl):abstr O-20

O-20: Phase I/IB study of regorafenib and nivolumab in mismatch repair (MMR) proficient advanced refractory colorectal cancer – Kim R, et al

Key results (cont.)

BOR, n (%)	n=21
PR (unconfirmed)	1 (4.8)
SD	14 (66.7)
DCR	15 (71.4)
PD	6 (28.6)

Grade ≥3 TRAEs, n (%)	All (n=28)
Rash	4 (14.3)
Fatigue	1 (3.6)
Palmar-plantar erythrodysesthesia	1 (3.6)
Hypertension	4 (14.3)
Hypophosphatemia	1 (3.6)
Lymphopenia	1 (3.6)
Anaemia	2 (7.1)

Conclusions

- **In patients with pMMR advanced refractory CRC, nivolumab + regorafenib demonstrated some clinical activity and was generally well-tolerated**

Kim R, et al. Ann Oncol 2020;31(suppl):abstr O-20

SO-21: Management of adverse events associated with encorafenib plus cetuximab in patients with BRAF V600E-mutant metastatic colorectal cancer (the BEACON CRC study) – Tabernero J, et al

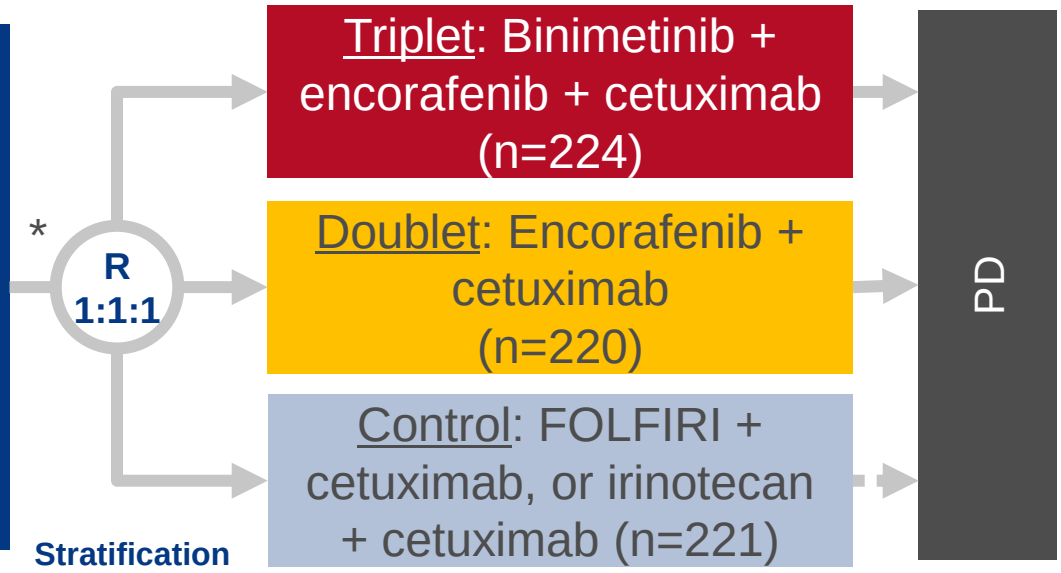
Study objective

- To evaluate the management of AEs associated with encorafenib + cetuximab in patients with BRAF V600E-mutant mCRC

Key patient inclusion criteria

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

(n=665)



Stratification

- ECOG PS (0 vs. 1), prior irinotecan, cetuximab (US- vs. EU-approved)

CO-PRIMARY ENDPOINTS

- OS, ORR (BICR)†

SECONDARY ENDPOINTS

- OS and ORR (for doublet vs control and doublet vs triplet), PFS, QoL 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; †data previously presented at ESMO WCGC 2019

Tabernero J, et al. Ann Oncol 2020;31(suppl):abstr SO-21

This talk was presented at the 22nd ESMO WCGC on 3 July 2020 at 14:59

SO-21: Management of adverse events associated with encorafenib plus cetuximab in patients with BRAF V600E-mutant metastatic colorectal cancer (the BEACON CRC study) – Tabernero J, et al

Key results

AEs of interest, %	Encorafenib + cetuximab (n=216)		Control (n=193)		Management of AEs of interest
	Any grade	Grade ≥3	Any grade	Grade ≥3	
GI AEs					Diarrhoea: dietary modification (eat frequent small meals); reduce fibre consumption; increase fluid intake; replace lost salt; consider treatment with loperamide Nausea/vomiting: avoid fried and spicy foods; eat small and frequent meals; eat lukewarm or cold foods; remain sitting up or standing within 1h after eating; prevent dehydration; anti-emetics Encorafenib modification guidance • For recurrent grade 2 or first occurrence of any grade 3 or 4 AEs, permanently discontinue encorafenib (grade 4) or withhold encorafenib for up to 4 weeks
Diarrhoea	38	3	49	10	
Nausea	38	<1	44	2	
Vomiting	27	1	32	3	
Dose reductions due to GI AEs					
Encorafenib	3	2	NA	NA	
Cetuximab	0	0	2	1	
Discontinuation due to GI AEs	4	3	5	3	
Skins AEs					Avoid sun exposure; consider referral to dermatologist and/or skin biopsy; mild rash: use topical corticosteroids (e.g., mometasone cream) and/or topical antibiotic (e.g., erythromycin); moderate rash: use topical erythromycin or clindamycin + topical mometasone or topical pimecrolimus + oral antibiotics; severe rash: consider oral prednisolone or oral isotretinoin Encorafenib modification guidance (other than hand-foot skin reaction) • For grade 2, if no improvement within 2 weeks, withhold encorafenib until grade 0–1, resume at same dose • For grade 3, withhold encorafenib until grade 0–1, resume at same dose if first occurrence or reduce dose if recurrent; • For grade 4, permanently discontinue encorafenib
Dermatitis acneiform	30	<1	40	3	
Melanocytic nevus	16	0	0	0	
Rash	15	0	15	2	
Dry skin	13	0	8	1	
Pruritus	11	0	5	0	
Dose reductions due to skin AEs					
Encorafenib	1	0	NA	NA	
Cetuximab	0	0	2	1	
Discontinuation due to skin AEs	0	0	2	1	

Tabernero J, et al. Ann Oncol 2020;31(suppl):abstr SO-21

SO-21: Management of adverse events associated with encorafenib plus cetuximab in patients with BRAF V600E-mutant metastatic colorectal cancer (the BEACON CRC study) – Tabernero J, et al

Key results (cont.)

AEs of interest, %	Encorafenib + cetuximab (n=216)		Control (n=193)		Management of AEs of interest
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	
Arthralgia	23	1	2	0	
Myalgia	15	<1	2	0	• Advise patients to rest area with pain • Recommend use of pain relievers • Consider stretching
Dose reductions					
Encorafenib					
Arthralgia	1	<1	NA	NA	Encorafenib modification guidance • For recurrent grade 2 or first occurrence of any grade 3 or 4 AE, permanently discontinue encorafenib (grade 4) or withhold encorafenib for up to 4 weeks
Myalgia	<1	0	NA	NA	
Cetuximab	0	0	0	0	
Discontinuations	0	0	0	0	
Renal AEs					Maintain adequate fluid intake during treatment; advise patients to avoid all nephrotoxic medications and maintain adequate hydration; ensure any concurrent urinary tract infections are promptly treated; evaluate patients for other causes of renal dysfunction and treat accordingly; seek nephrologist consultation as required
UTI	8	2	3	1	
Abnormal lab values					
Creatinine	54	3	38	1	
Albumin	18	<1	24	0	Encorafenib modification guidance • For recurrent grade 2 or first occurrence of any grade 3 or 4 AE, permanently discontinue encorafenib (grade 4) or withhold encorafenib for up to 4 weeks
Dose reductions due to renal AEs	0	0	0	0	
Discontinuation due to renal AEs	1	1	0	0	

Tabernero J, et al. Ann Oncol 2020;31(suppl):abstr SO-21

SO-21: Management of adverse events associated with encorafenib plus cetuximab in patients with BRAF V600E-mutant metastatic colorectal cancer (the BEACON CRC study) – Tabernero J, et al

Key results (cont.)

AEs of interest, %	Encorafenib + cetuximab (n=216)		Control (n=193)		Management of AEs of interest
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	
Other AEs					
Fatigue	33	4	28	5	
Asthenia	24	4	27	5	
Headache	20	0	3	0	• Advise patients to drink plenty of fluids, eat a healthy diet, exercise regularly if possible, and rest when needed • Recommend use of pain relievers to manage symptoms as appropriate
Pyrexia	19	1	15	1	
Dose reductions					
Encorafenib					
Fatigue	1	0	NA	NA	Encorafenib modification guidance • For recurrent grade 2 or first occurrence of any grade 3 or 4 AE, permanently discontinue encorafenib (grade 4) or withhold encorafenib for up to 4 weeks
Asthenia	1	<1	NA	NA	
Cetuximab	0	0	0	0	
Discontinuations,					
Fatigue	<1	<1	<1	0	
Asthenia	0	0	1	0	

Conclusions

- **In patients with BRAF V600E-mutant mCRC, AEs reported with encorafenib + cetuximab were generally manageable through supportive care and practical approaches**

Tabernero J, et al. Ann Oncol 2020;31(suppl):abstr SO-21

SO-23: Prognostic impact of microsatellite instability/mismatch repair deficiency on patients with stage III colon cancer and stage IV colorectal cancers (CRC): analysis of 42,984 Patients in the National Cancer Database (NCDB) – Salem M, et al

Study objective

- To evaluate the prognostic impact of MSI/dMMR on OS in patients with stage III colon cancer or stage IV CRC

Methods

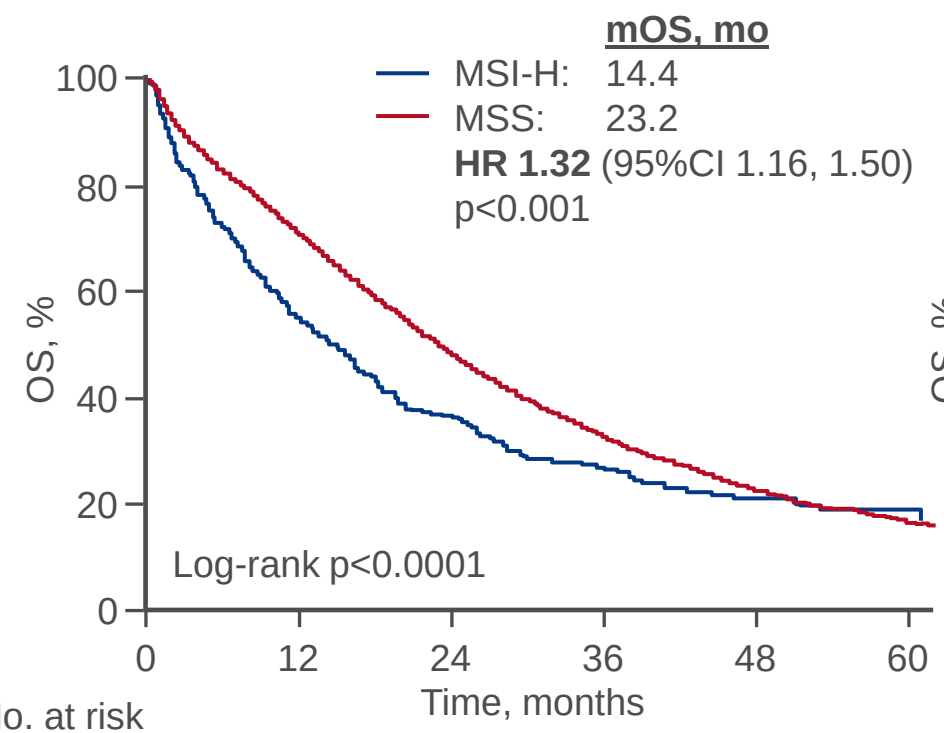
- Retrospective review of patients in the National Cancer Database diagnosed between 2004 and 2016
- 22,132 patients with stage III colon cancer included
  - 1704 with MSI-H
  - 20,428 with MSS
- 11,848 patients with stage IV CRC
  - 470 with MSI-H
  - 11,378 with MSS

Salem M, et al. Ann Oncol 2020;31(suppl):abstr SO-23

SO-23: Prognostic impact of microsatellite instability/mismatch repair deficiency on patients with stage III colon cancer and stage IV colorectal cancers (CRC): analysis of 42,984 Patients in the National Cancer Database (NCDB) – Salem M, et al

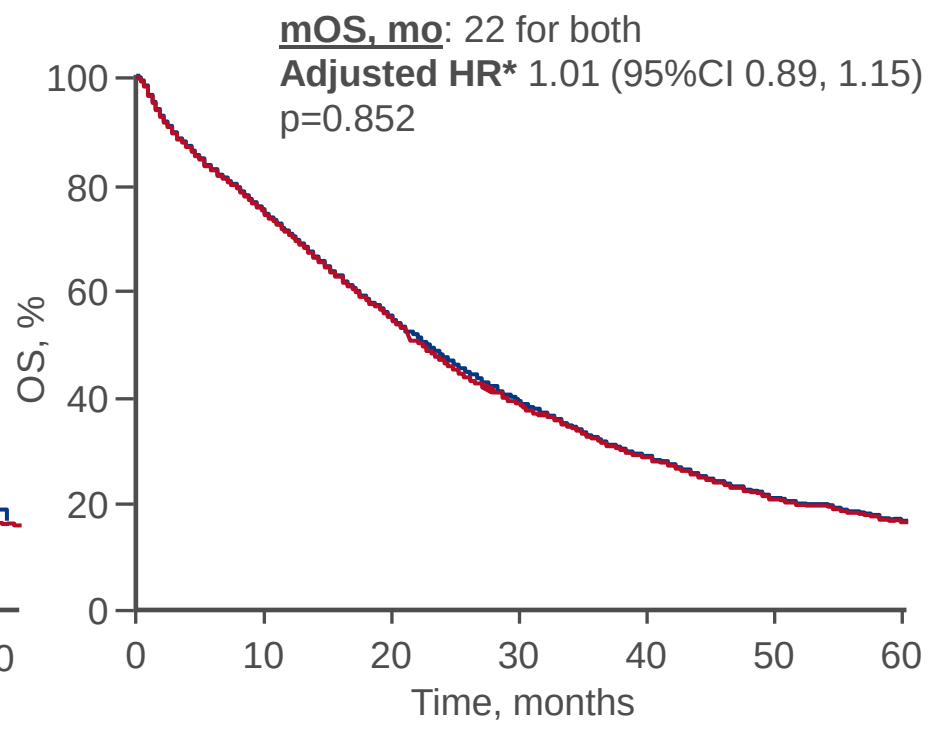
Key results

Overall survival – stage IV



No. at risk

MSI-H	357	181	99	56	27	12
MSS	8240	5475	3266	1743	838	377



*Adjusted for tumour location, gender, race, treatment, tumour differentiation and insurance status

Salem M, et al. Ann Oncol 2020;31(suppl):abstr SO-23

SO-23: Prognostic impact of microsatellite instability/mismatch repair deficiency on patients with stage III colon cancer and stage IV colorectal cancers (CRC): analysis of 42,984 Patients in the National Cancer Database (NCDB) – Salem M, et al

Key results (cont.)

Multivariable analysis of OS – stage IV

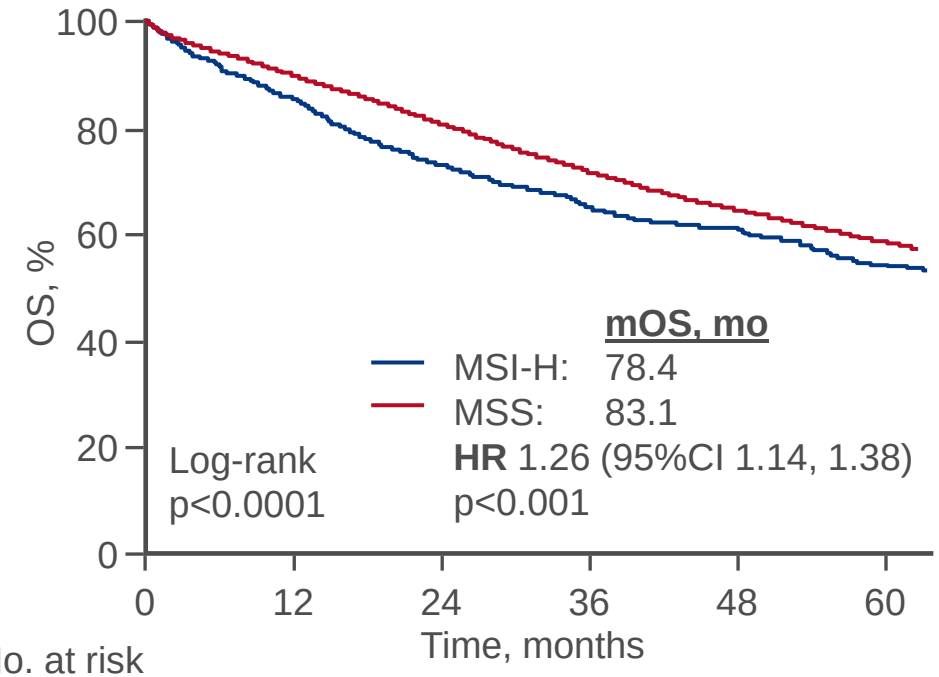
	Adjusted HR (95%CI)	p-value
Age at diagnosis	1.02 (1.01, 1.02)	<0.001
MSI-H status	1.01 (0.89, 1.15)	0.852
Poorly differentiated tumour grade	1.60 (1.50, 1.70)	<0.001
Right-sided tumour location	1.44 (1.36, 1.53)	<0.001
Insurance status		
None	1.38 (1.08, 1.75)	<0.001
Gov	1.23 (1.16, 1.31)	

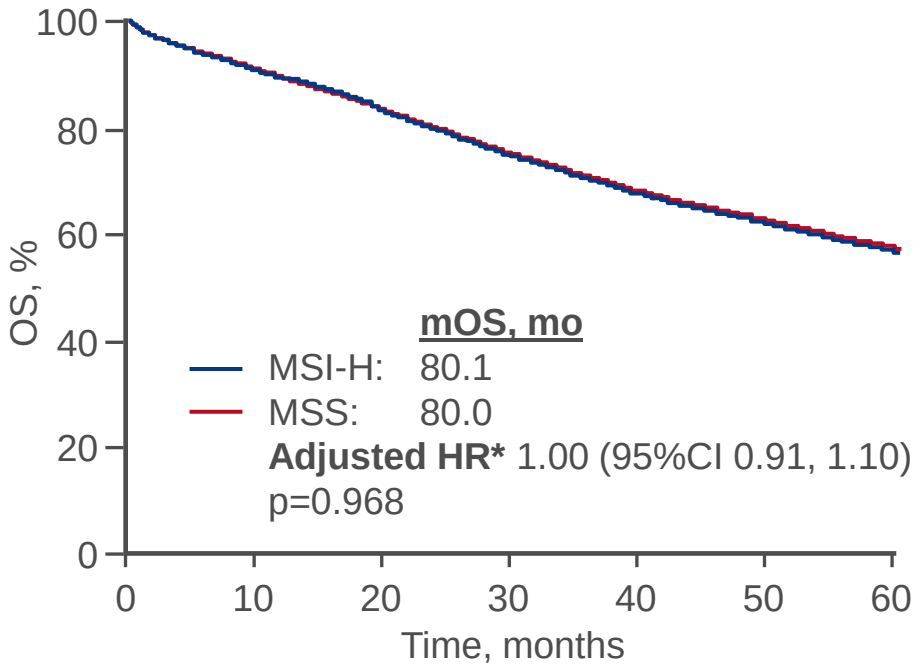
Salem M, et al. Ann Oncol 2020;31(suppl):abstr SO-23

SO-23: Prognostic impact of microsatellite instability/mismatch repair deficiency on patients with stage III colon cancer and stage IV colorectal cancers (CRC): analysis of 42,984 Patients in the National Cancer Database (NCDB) – Salem M, et al

Key results (cont.)

Overall survival – stage III





No. at risk

MSI-H	1384	1054	775	531	347	181
MSS	16,075	12,917	9858	6579	4181	2301

*Adjusted for tumour location, gender, race, treatment, tumour differentiation and insurance status

Salem M, et al. Ann Oncol 2020;31(suppl):abstr SO-23

SO-23: Prognostic impact of microsatellite instability/mismatch repair deficiency on patients with stage III colon cancer and stage IV colorectal cancers (CRC): analysis of 42,984 Patients in the National Cancer Database (NCDB) – Salem M, et al

Key results (cont.)

Multivariable analysis of OS – stage III

	Adjusted HR (95%CI)	p-value
Age at diagnosis	1.04 (1.03, 1.04)	<0.001
MSI-H status	1.00 (0.91, 1.10)	0.968
Poorly differentiated tumour grade	1.46 (1.37, 1.55)	<0.001
Right-sided tumour location	1.17 (1.10, 1.25)	<0.001
Insurance status		
None	1.15 (0.86, 1.53)	<0.001
Gov	1.31 (1.22, 1.41)	

Conclusions

- **In patients with either stage III colon cancer or stage IV CRC, after adjusting for tumour location, gender, race, treatment, tumour differentiation and insurance status, MSI-H/dMMR status had no prognostic impact on OS**

Salem M, et al. Ann Oncol 2020;31(suppl):abstr SO-23

SO-26: Clinical efficacy of combined BRAF, MEK, and PD-1 inhibition in BRAF V600E colorectal cancer patients – Corcoran R, et al

Study objective

- To evaluate the efficacy and safety of combining BRAF (dabrafenib), MEK (trametinib) and PD-1 (spartalizumab) inhibitors in patients with BRAF V600E-mutant CRC

Key patient inclusion criteria
- BRAF V600E-mutant mCRC
- MSI or MSS

(n=25)

→ Spartalizumab 400 mg iv q4w + dabrafenib 150 mg po bid + trametinib 2 mg/day po

ENDPOINTS

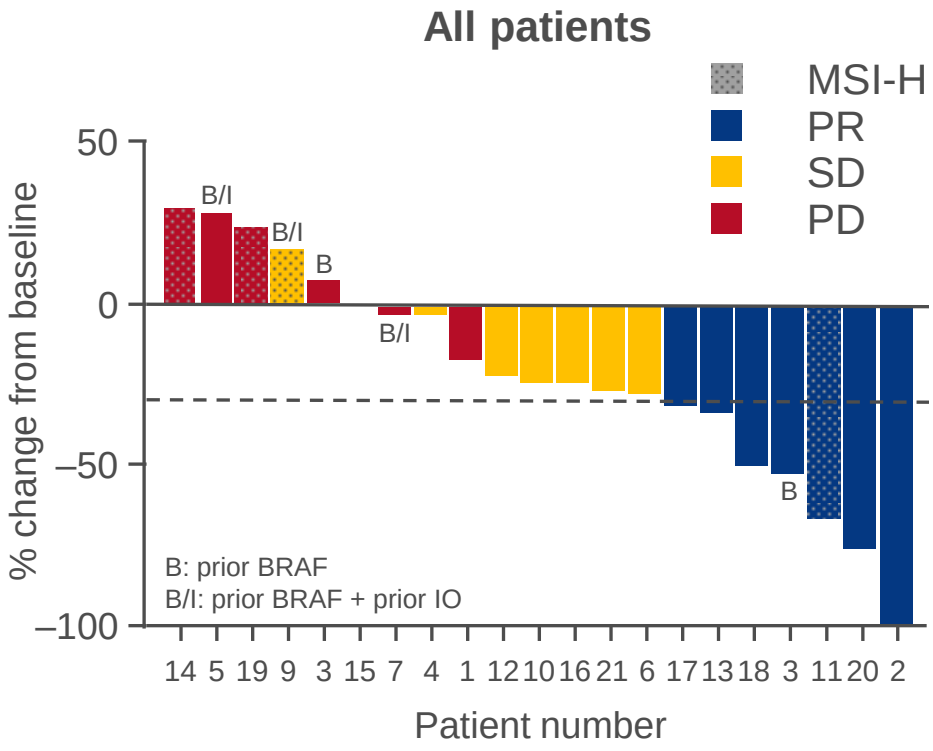
- RR, DoR, safety

Trial amended after first 9 patients to exclude prior BRAF or MEK inhibitor or IO

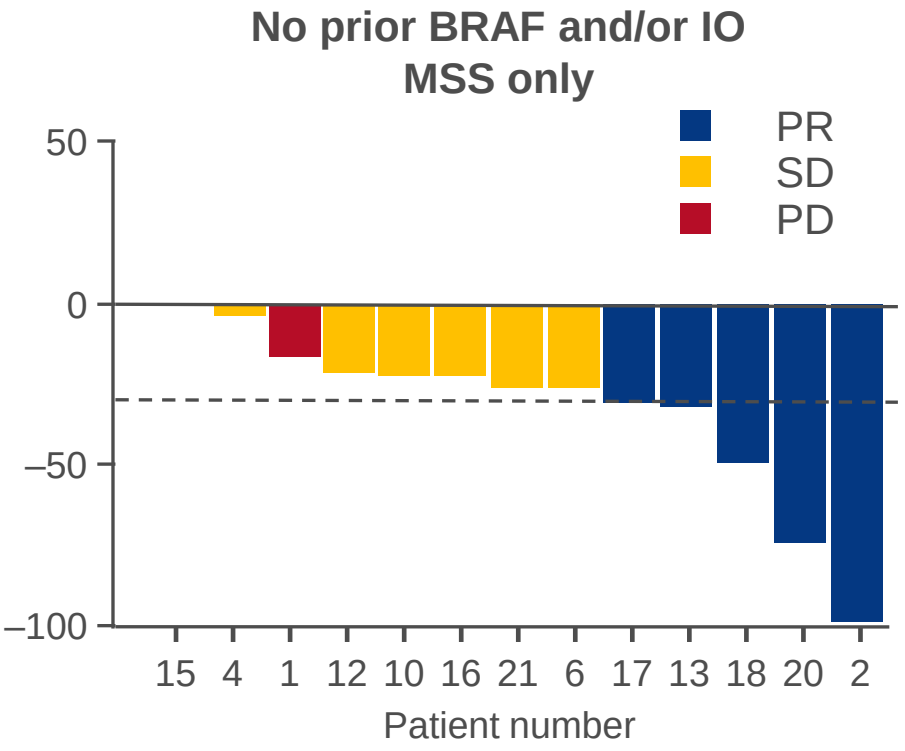
Corcoran R, et al. Ann Oncol 2020;31(suppl):abstr SO-26

SO-26: Clinical efficacy of combined BRAF, MEK, and PD-1 inhibition in BRAF V600E colorectal cancer patients – Corcoran R, et al

Key results



RR 33%, DCR 76%



RR 38%, DCR 92%

Corcoran R, et al. Ann Oncol 2020;31(suppl):abstr SO-26

SO-26: Clinical efficacy of combined BRAF, MEK, and PD-1 inhibition in BRAF V600E colorectal cancer patients – Corcoran R, et al

Key results (cont.)

Grade ≥3 AEs, n (%)	
Lipase increased	3 (14.2)
Fever	2 (9.5)
Serum amylase increased	2 (9.5)
Fatigue	1 (4.7)
Hyponatremia	1 (4.7)
Anaemia	1 (4.7)
Maculopapular rash	1 (4.7)
Hypertension	1 (4.7)
Colitis	1 (4.7)
Hypokalemia	1 (4.7)

Conclusions

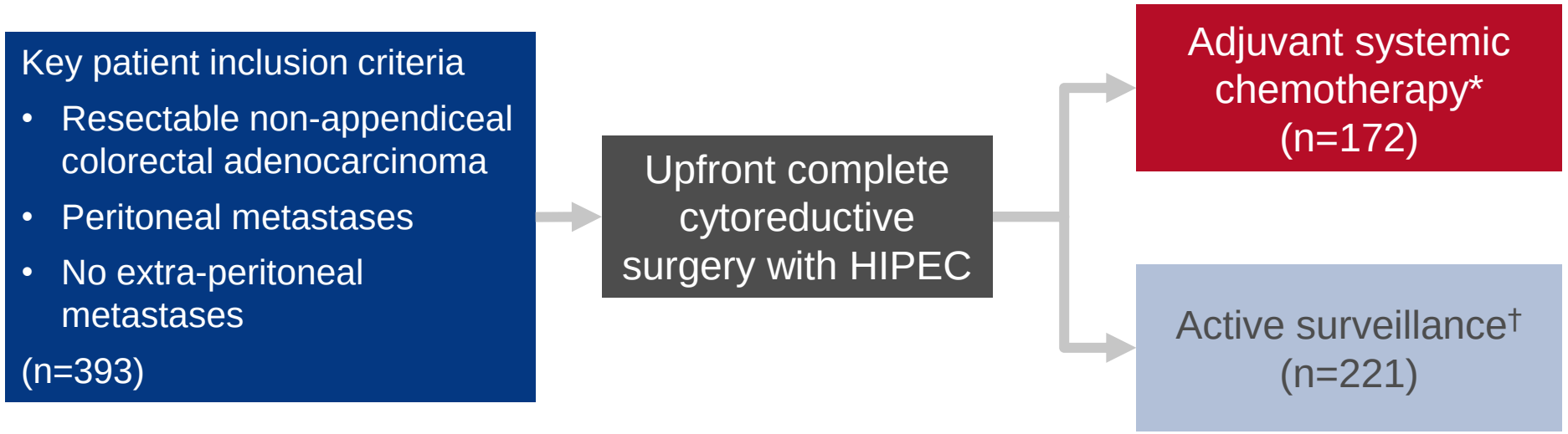
- **In patients with BRAF V600E-mutant CRC, a triplet combination of spartalizumab, dabrafenib and trametinib demonstrated encouraging activity and was generally well-tolerated**

Corcoran R, et al. Ann Oncol 2020;31(suppl):abstr SO-26

SO-30: Adjuvant systemic chemotherapy versus active surveillance following upfront resection of isolated synchronous colorectal peritoneal metastases: propensity score-matched analysis of a nationwide registry – Rovers K, et al

Study objective

- To evaluate the efficacy and safety of adjuvant systemic chemotherapy following upfront resection in patients with isolated synchronous colorectal peritoneal metastases



PRIMARY ENDPOINT

- OS in matched group (propensity score-matching included sex, age, location, TNM, histology – differentiation and hospital stay)

*Started systemic chemotherapy without targeted therapy within 3 months postoperatively; †started systemic chemotherapy later than 3 months postoperatively or targeted therapy within 3 months postoperatively

Rovers K, et al. Ann Oncol 2020;31(suppl):abstr SO-30

This talk was presented at the 22nd ESMO WCGC on 3 July 2020 at 18:43

SO-30: Adjuvant systemic chemotherapy versus active surveillance following upfront resection of isolated synchronous colorectal peritoneal metastases: propensity score-matched analysis of a nationwide registry – Rovers K, et al

Key results

- Median OS: 38 months in adjuvant systemic chemotherapy group and 24 months in active surveillance group (HR 0.64, 95%CI 0.48, 0.86; p=0.003)

Adjustment	HR (95%CI); p-value
Patients who deceased between 3 and 6 months postoperatively	0.68 (0.50, 0.93); 0.02
Patients who received targeted therapy within 3 months postoperatively	0.68 (0.50, 0.93); 0.01
Patients who started systemic chemotherapy between 3 and 4 months postoperatively	0.65 (0.48, 0.87); 0.004
All of the above	0.70 (0.50, 0.97); 0.03

Conclusions

- **In patients with isolated synchronous colorectal peritoneal metastases, adjuvant systemic chemotherapy after upfront resection was associated with improved OS**

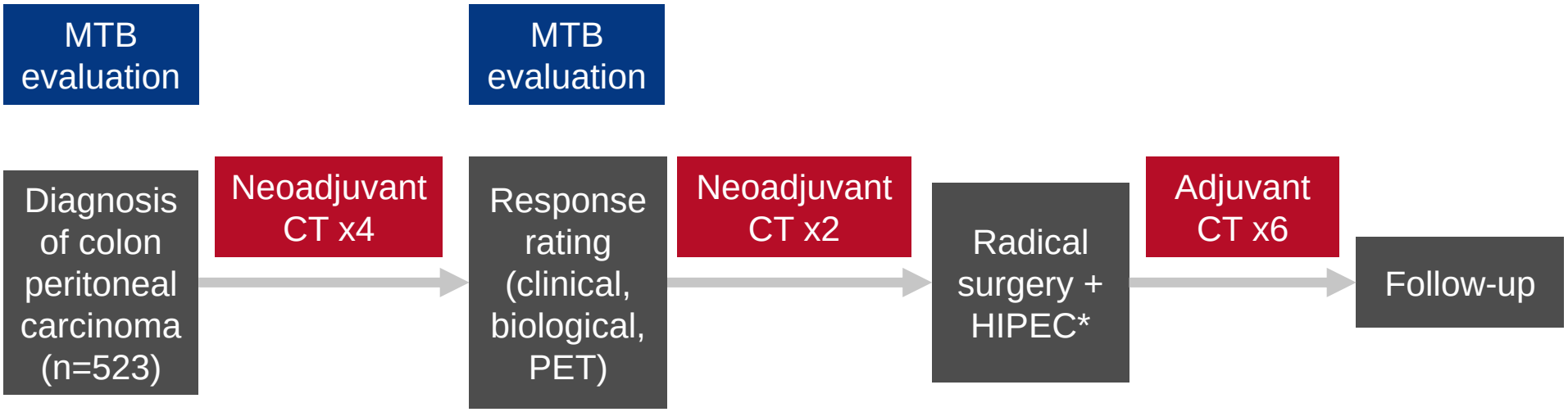
Rovers K, et al. Ann Oncol 2020;31(suppl):abstr SO-30

SO-31: Centralization of care leads to optimal selection and outcomes for patients with peritoneal metastases of colorectal cancer - the Catalonian regional program experience – Ramos M, et al

Study objective

- To evaluate the centralisation of care on optimal selection and outcomes in patients with colorectal peritoneal metastases

Treatment plan



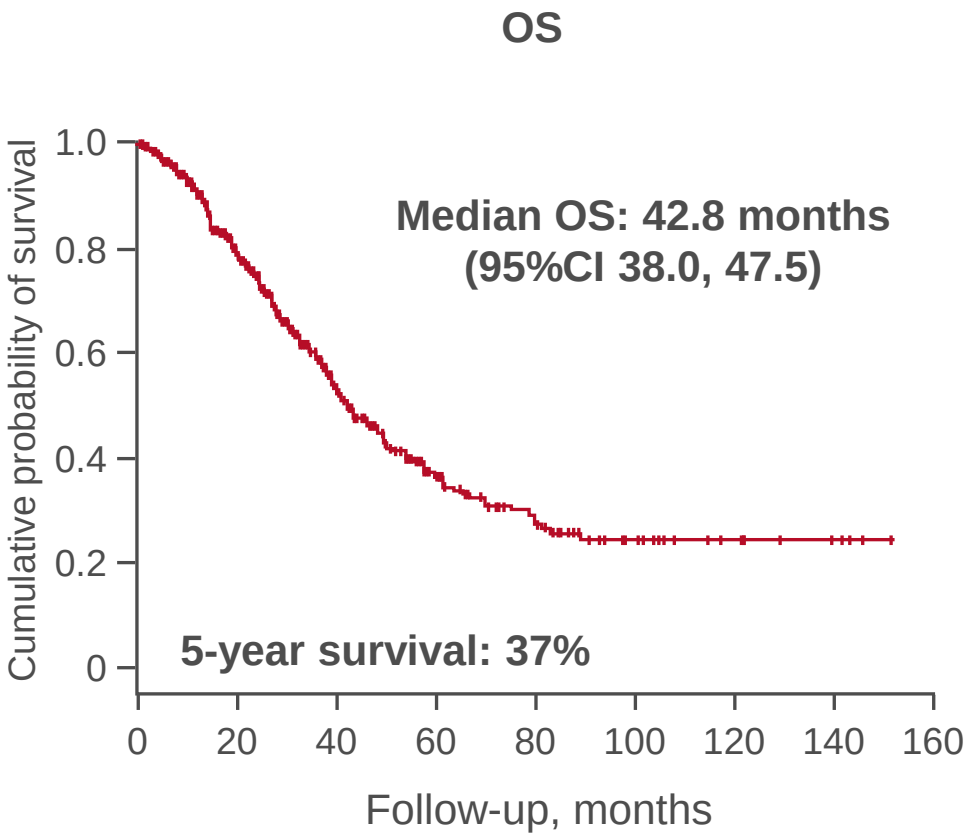
*Oxaliplatin 460 mg/m^2 for 30 min at 43°C; irinotecan 400 mg/m^2 for 30 min at 43°C; MMC 30 mg/m^2 for 60 min at 42°C

Ramos M, et al. Ann Oncol 2020;31(suppl):abstr SO-31

SO-31: Centralization of care leads to optimal selection and outcomes for patients with peritoneal metastases of colorectal cancer - the Catalonian regional program experience – Ramos M, et al

Key results

Postoperative complications, %	
Grade 3/4	21.0
Urgent reoperation	6.3
30-day readmission	4.5
ICU readmission	3.5
Mortality	0.4



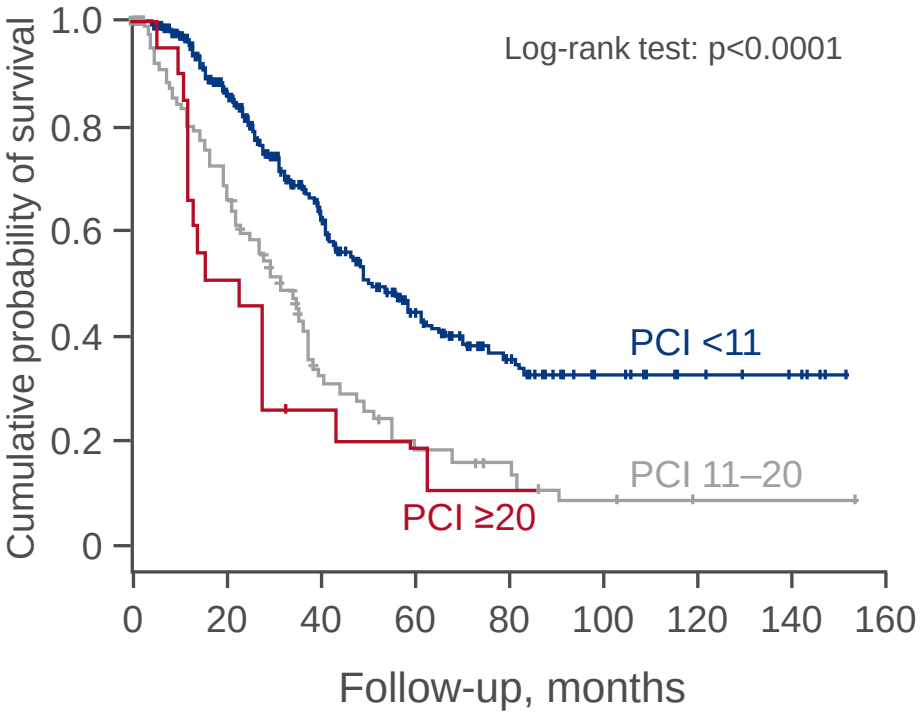
Ramos M, et al. Ann Oncol 2020;31(suppl):abstr SO-31

SO-31: Centralization of care leads to optimal selection and outcomes for patients with peritoneal metastases of colorectal cancer - the Catalonian regional program experience – Ramos M, et al

Key results (cont.)

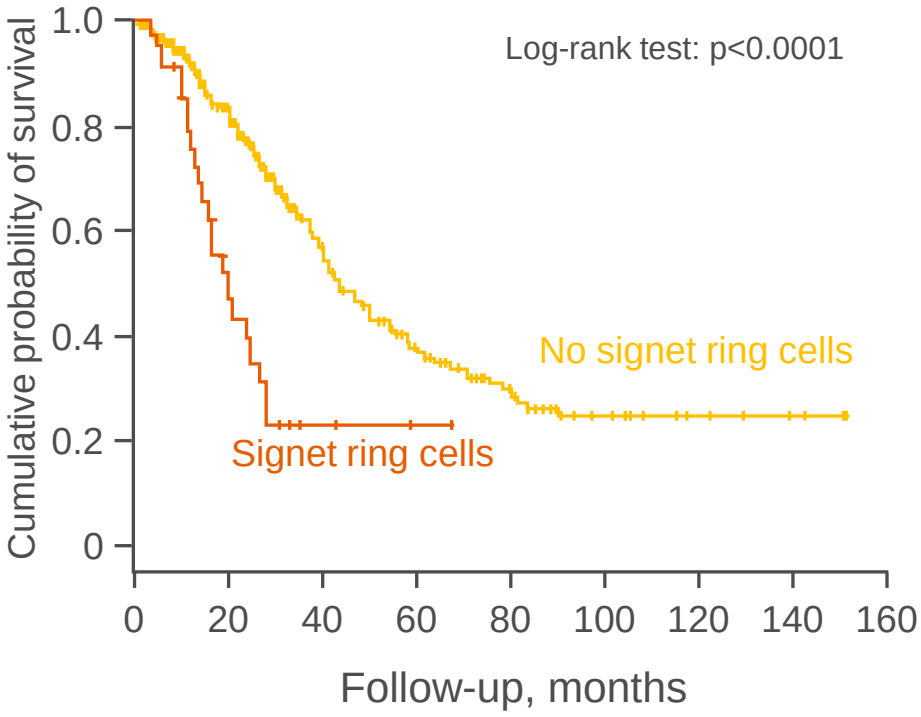
PCI

OS 49 (<11) vs.30 (11–20) months



Signet ring histology

OS 44 vs.19 months



Ramos M, et al. Ann Oncol 2020;31(suppl):abstr SO-31

SO-31: Centralization of care leads to optimal selection and outcomes for patients with peritoneal metastases of colorectal cancer - the Catalonian regional program experience – Ramos M, et al

Key results (cont.)

Clinical variable associated with survival	Univariate analysis p-value	Multivariate analysis p-value
Signet ring cell histology	<0.001	<0.001
AJCC staging at diagnosis		
T	0.038	NS
N	0.001	0.024
M	0.01	NS
Presence of visceral involvement	<0.001	0.003
Presence of small bowel involvement	<0.001	<0.001
Synchronous vs. metachronous peritoneal metastases	0.015	NS
Use of preoperative chemotherapy	0.04	NS
Completion of cytoreductive score	<0.001	NS
Peritoneal cancer index	<0.001	NS
Sidedness of primary colonic tumour	NS	-
KRAS status	NS	-
Age	NS	-
Gender	NS	-

Ramos M, et al. Ann Oncol 2020;31(suppl):abstr SO-31

SO-31: Centralization of care leads to optimal selection and outcomes for patients with peritoneal metastases of colorectal cancer - the Catalonian regional program experience – Ramos M, et al

Key results (cont.)

Grade 3–5 AEs occurring in ≥2%, n (%)	
Hemoperitoneum	30 (5.7)
Ileum	27 (5.1)
Chemotherapy toxicity	25 (4.7)
UTI/urinary sepsis	22 (4.2)
Central line infection	17 (3.2)

Conclusions

- **In optimally selected patients with colorectal peritoneal metastases, radical surgery + HIPEC with systemic chemotherapy greatly improved survival outcomes and was associated with low postoperative morbidity and mortality**
- **Better survival was demonstrated in patients with N0 stage, absence of signet ring histology and absence of any visceral or small bowel involvement**

Ramos M, et al. Ann Oncol 2020;31(suppl):abstr SO-31

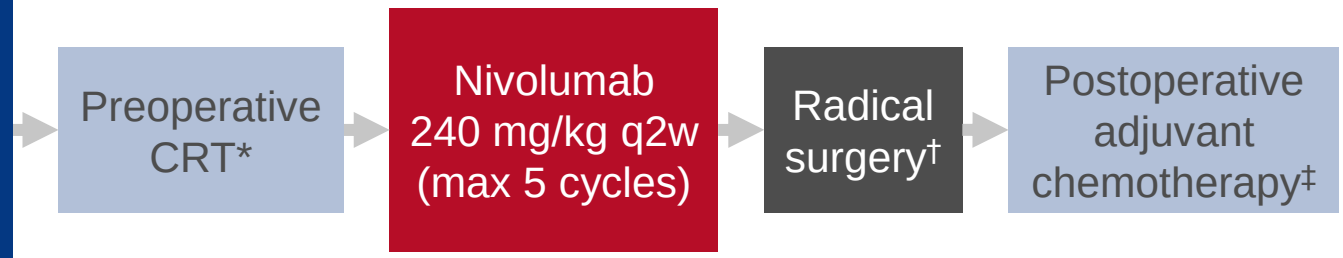
SO-37: Short-term results of VOLTAGE-A: nivolumab monotherapy and subsequent radical surgery following preoperative chemoradiotherapy in patients with microsatellite stable and microsatellite instability-high locally advanced rectal cancer (EPOC 1504) – Yuki S, et al

Study objective

- To evaluate the efficacy and safety of nivolumab followed by radical surgery after preoperative chemoradiotherapy in patients with MSS or MSI-H locally advanced rectal cancer

Key patient inclusion criteria

- Locally advanced resectable rectal cancer
- cT3–4, N any, M0
- Inferior margin ≤12 cm from anal verge
- Cohort A1: MSS (n=37)
- Cohort A2: MSI-H (n=5)



PRIMARY ENDPOINT

- Pathological response

SECONDARY ENDPOINT

- Safety

*Capecitabine 1650 mg/m^2 + 50.4 Gy; †total mesorectal excision or tumour specific mesorectal excision + bilateral lateral lymph node dissection if required; ‡FOLFOX or CAPOX

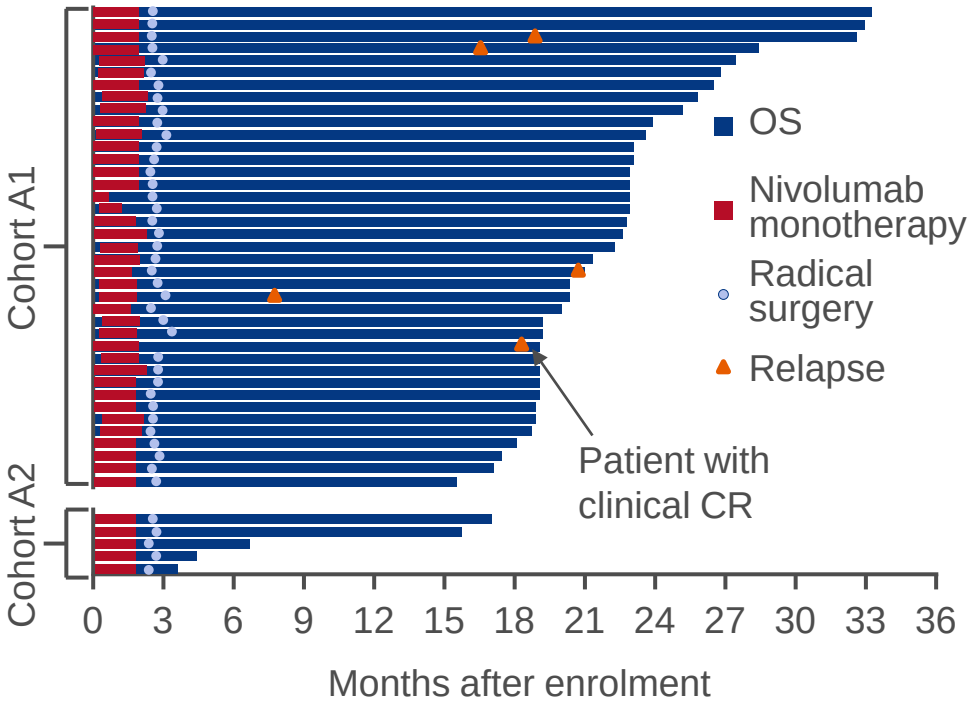
Yuki S, et al. Ann Oncol 2020;31(suppl):abstr SO-37

This talk was presented at the 22nd ESMO WCGC on 4 July 2020 at 13:47

SO-37: Short-term results of VOLTAGE-A: nivolumab monotherapy and subsequent radical surgery following preoperative chemoradiotherapy in patients with microsatellite stable and microsatellite instability-high locally advanced rectal cancer (EPOC 1504) – Yuki S, et al

Key results

AJCC grade, n (%)	Cohort A1 (MSS, n=37)	Cohort A2 (MSI-H, n=5)
0 (pCR)	11 (30)	3 (60)
1	3 (8)	0
2	15 (41)	2 (40)
3	7 (19)	0
NE	1 (3)	0
Neoadjuvant rectal score	8.4 (0, 50.4)	0.9 (0.9, 20.4)



Yuki S, et al. Ann Oncol 2020;31(suppl):abstr SO-37

SO-37: Short-term results of VOLTAGE-A: nivolumab monotherapy and subsequent radical surgery following preoperative chemoradiotherapy in patients with microsatellite stable and microsatellite instability-high locally advanced rectal cancer (EPOC 1504) – Yuki S, et al

Key results (cont.)

Grade 3/4 AEs, n (%)	Cohort A1 (MSS, n=39)	Cohort A2 (MSI-H, n=5)
All nivolumab-related	4 (10.3)	0
AST elevation	2 (5.1)	0
All surgery-related	4 (10.5)	3 (60)
Pelvic abscess	4 (10.5)	1 (20)

Conclusions

- **In patients with locally advanced MSS or MSI-H rectal cancer, nivolumab followed by radical surgery after preoperative chemoradiotherapy demonstrated encouraging pathological complete response rates and was generally well-tolerated**

Yuki S, et al. Ann Oncol 2020;31(suppl):abstr SO-37

GASTROINTESTINAL CANCERS

O-3: Efficacy and safety of entrectinib in NTRK fusion-positive gastrointestinal cancers: updated integrated analysis of three clinical trials (STARTRK-2, STARTRK-1 and ALKA-372-001) – Patel M, et al

Study objective

- To evaluate the efficacy and safety entrectinib in patients with NTRK fusion-positive gastrointestinal 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

(Efficacy n=74; GI tumours n=12)

(Safety n=504; GI tumours n=16)

→ Entrectinib dose escalation (n=3, GI tumours, n=1) or entrectinib 600 mg/day q4w (n=71; GI tumours, n=11)

PRIMARY ENDPOINTS

- ORR, DoR

SECONDARY ENDPOINTS

- PFS, OS, intracranial ORR and DoR, safety

Patel M, et al. Ann Oncol 2020;31(suppl):abstr O-3

This talk was presented at the 22nd ESMO WCGC on 1 July 2020 at 15:44

O-3: Efficacy and safety of entrectinib in NTRK fusion-positive gastrointestinal cancers: updated integrated analysis of three clinical trials (STARTRK-2, STARTRK-1 and ALKA-372-001) – Patel M, et al

Key results

Efficacy	GI tumours				All GI cohort (n=12)
	CCA (n=1)	CRC (n=7)	Other GI (n=1)	Pancreatic (n=3)	
BOR, n (%)					
CR	0	0	0	0	0
PR	1 (100)	2 (29)	1 (100)	2 (67)	6 (50)
SD	0	0	0	1 (33)	1 (8)
PD	0	3 (43)	0	0	3 (25)
NE	0	2 (29)	0	0	2 (17)
ORR, %	1 (100)	2 (29)	1 (100)	2 (67)	6 (50)
Median DoR, mo (95%CI)	9.3 (NE)	15.1 (NE)	NE (NE)	10.0 (7.1, 12.9)	12.9 (7.1, 15.1)
DoR at 12 mo, %	NE	100	NE	50	53
mPFS, mo (95%CI)	12.0 (NE)	2.4 (1.0, 16.0)	NE (NE)	8.0 (6.2, 17.5)	7.1 (2.4, 16.0)
PFS at 12 mo, %	NE	29	NE	33	27
mOS, mo (95%CI)	NE (NE)	16.0 (2.4, NE)	NE (NE)	13.4 (11.2, NE)	16.0 (11.2, NE)

Patel M, et al. Ann Oncol 2020;31(suppl):abstr O-3

O-3: Efficacy and safety of entrectinib in NTRK fusion-positive gastrointestinal cancers: updated integrated analysis of three clinical trials (STARTRK-2, STARTRK-1 and ALKA-372-001) – Patel M, et al

Key results (cont.)

TRAEs in ≥10% patients, n (%)	Overall GI safety population (n=16)		
	Grade 1	Grade 2	Grade 3
Dysgeusia	5 (31.3)	1 (6.3)	0
Diarrhoea	2 (12.5)	3 (18.8)	0
Vomiting	4 (25.0)	0	0
Weight increased	1 (6.3)	0	2 (12.5)
Fatigue	2 (12.5)	0	1 (6.3)
Nausea	2 (12.5)	1 (6.3)	0
Dizziness	2 (12.5)	1 (6.3)	0
Myalgia	2 (12.5)	1 (6.3)	0
AST increased	0	2 (12.5)	0
ALT increased	0	2 (12.5)	0
Constipation	2 (12.5)	0	0
Dry mouth	2 (12.5)	0	0
Oral paresthesia	2 (12.5)	0	0
Hyperesthesia	2 (12.5)	0	0
Paraesthesia	2 (12.5)	0	0
Oedema peripheral	2 (12.5)	0	0
Oedema peripheral	2 (12.5)	0	0

Conclusions

- **In patients with a range of NTRK fusion-positive GI carcinomas, treatment with entrectinib provided clinically meaningful responses and was generally well-tolerated**

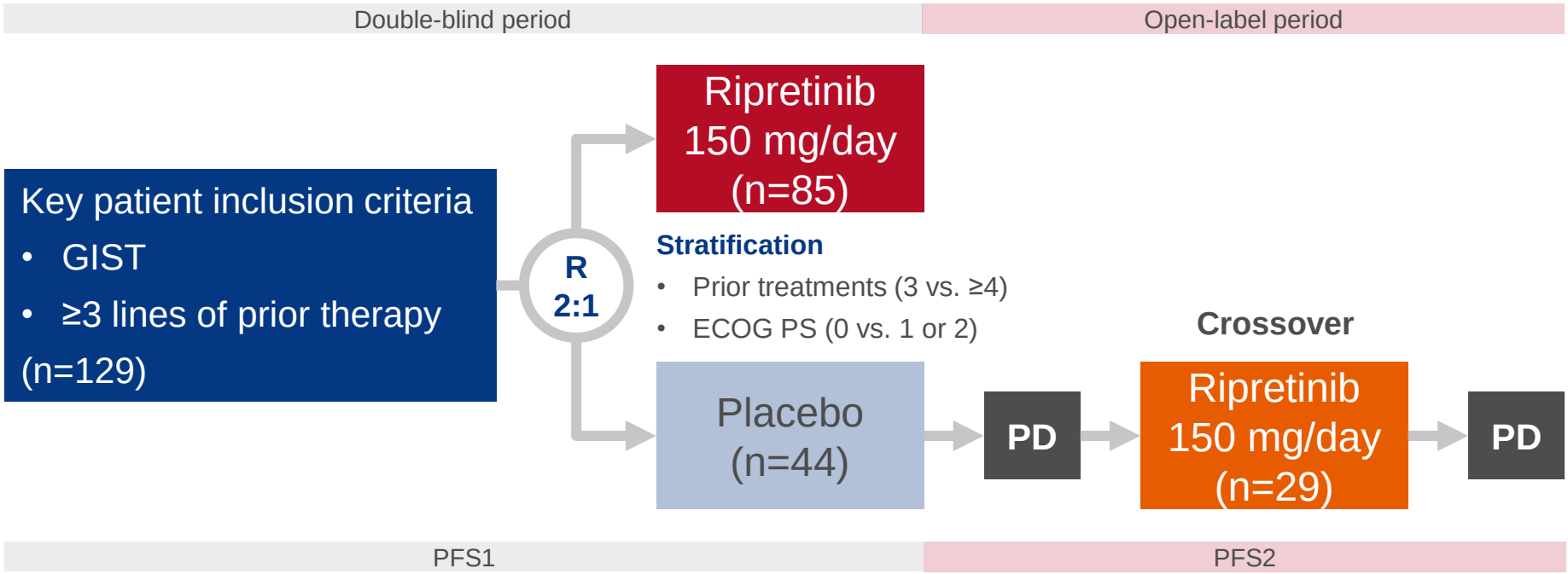
Patel M, et al. Ann Oncol 2020;31(suppl):abstr O-3

GIST

O-13: Efficacy and safety of ripretinib as ≥4th-line therapy for patients with gastrointestinal stromal tumor (GIST) following crossover from placebo: Analyses from INVICTUS – Serrano C, et al

Study objective

- To evaluate the efficacy and safety ripretinib, a tyrosine kinase switch control inhibitor, in heavily pre-treated patients with GIST



PRIMARY ENDPOINT

- PFS (RECIST v1.1, BICR)

SECONDARY ENDPOINTS

- ORR, OS, safety

Serrano C, et al. Ann Oncol 2020;31(suppl):abstr O-13

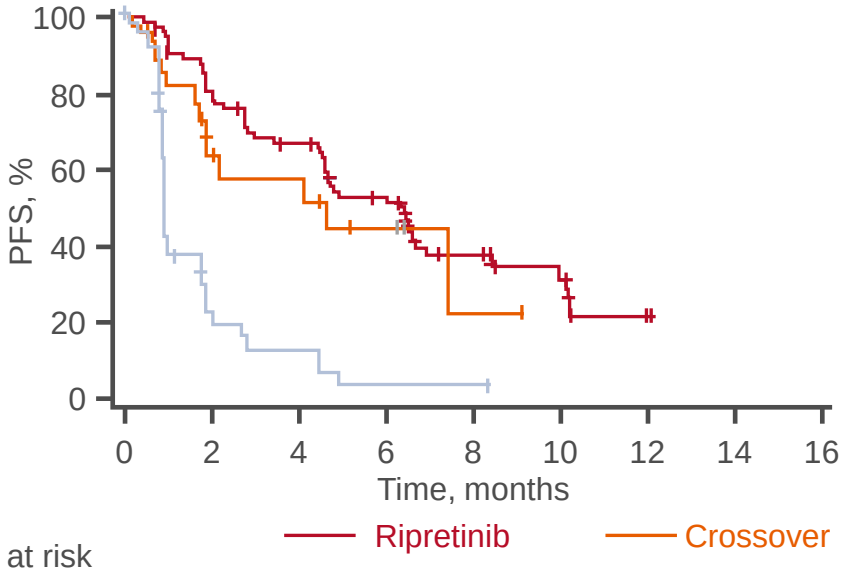
This talk was presented at the 22nd ESMO WCGC on 2 July 2020 at 18:00

O-13: Efficacy and safety of ripretinib as ≥4th-line therapy for patients with gastrointestinal stromal tumor (GIST) following crossover from placebo: Analyses from INVICTUS – Serrano C, et al

Key results

Progression-free survival

	Median PFS, mo (95%CI)
Ripretinib PFS1	6.3 (4.6, 6.9)
Crossover to ripretinib PFS2	4.6 (1.8, NE)
Placebo PFS1	1.0 (0.9, 1.7)

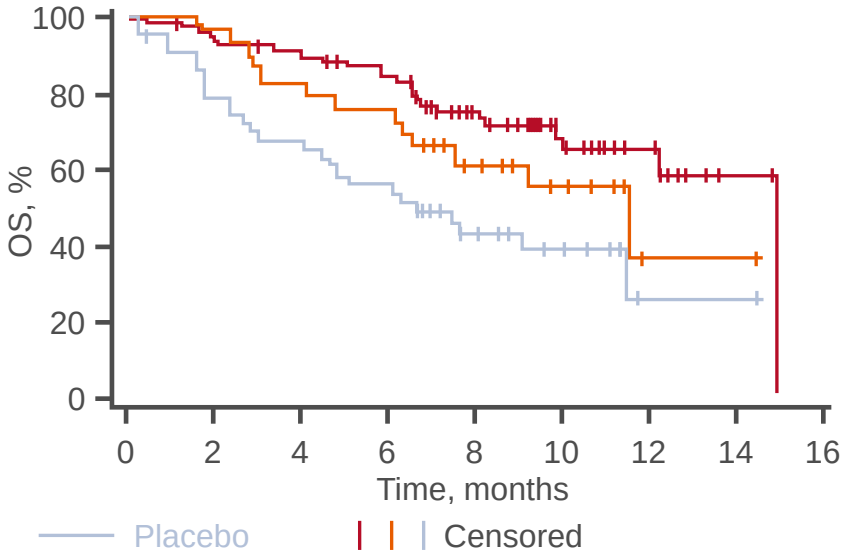


No. at risk

Ripretinib PFS1	85	65	52	37	18	8	1	0
Crossover PFS2	29	11	10	5	1	0		
Placebo PFS1	44	7	4	1	1	0		

Overall survival

	Median OS, mo (95%CI)
Ripretinib	15.1 (12.3, 15.1)
Crossover to ripretinib	11.6 (6.3, NE)
Placebo	6.6 (4.1, 11.6)



Ripretinib	85	81	76	67	42	24	10	2	0
Crossover	29	28	24	22	13	8	1	1	0
Placebo	44	34	29	24	14	8	1	1	0

Serrano C, et al. Ann Oncol 2020;31(suppl):abstr O-13

O-13: Efficacy and safety of ripretinib as ≥4th-line therapy for patients with gastrointestinal stromal tumor (GIST) following crossover from placebo: Analyses from INVICTUS – Serrano C, et al

Key results (cont.)

Grade 3/4 TEAEs, n (%)	Open-label period	Double-blind period	
	Crossover to ripretinib (n=29)	Ripretinib (n=85)	Placebo (n=43)
Anaemia	6 (21.0)	8 (9.4)	6 (14.0)
Fatigue	3 (10.0)	3 (3.5)	1 (2.3)
Myalgia	0	1 (1.2)	0
Constipation	1 (3.4)	1 (1.2)	0
Abdominal pain	2 (6.9)	6 (7.1)	2 (4.7)
Appetite decreased	0	1 (1.2)	1 (2.3)

Conclusions

- **In heavily pre-treated patients with GIST who crossed over from placebo, ripretinib demonstrated clinically meaningful benefit and was generally well-tolerated**

Serrano C, et al. Ann Oncol 2020;31(suppl):abstr O-13