GI SLIDE DECK 2022
Selected abstracts from:

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 2022. This slide set specifically focuses on the **2022 ESMO World Congress on Gastrointestinal Cancer** and **ESMO Congress 2022** and is available in English and Japanese.

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

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

Yours sincerely,

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ESDO Medical Oncology Slide Deck
Editors 2022

COLORECTAL CANCERS



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esdo

Glossary

1L	first-line
2L	second-line
3L	third-line
5FU	5-fluouracil
AE	adverse event
AFP	alpha-fetoprotein
ALT	alanine aminotransferase
AST	aspartate aminotransferase
AUC	area under the curve
Bev	bevacizumab
BICR	blinded independent committee review
BID	twice daily
BCLC	Barcelona Clinic Liver Cancer
BOR	best overall response
BRAF	B-Ref proto-oncogene
BRCA	breast cancer gene
BSC	best supportive care
C	cycle
Camrel	camrelizumab
Cape	capecitabine
CAPOX	capecitabine + oxaliplatin
CEA	carcinoembryonic antigen
CES2	carboxylesterase 2
Chemo	chemotherapy
CI	confidence interval
Cis	cisplatin
CPS	combined positive score
CR	complete response
CRC	colorectal cancer
CT	computed tomography
ctDNA	circulating tumour DNA
CTLA4	cytotoxic T-lymphocyte associated protein 4
D	day
DCR	disease control rate
DFS	disease-free survival
dMMR	mismatch repair deficient
(m)DoR	(median) duration of response
Durv	durvalumab
ECOG	Eastern Cooperative Oncology Group
EGA	esophagogastric adenocarcinoma
EGFR	epidermal growth factor receptor
EHS	extrahepatic spread
EOT	end of therapy
ESCC	esophageal squamous cell carcinoma
FGF(R)	fibroblast growth factor (receptor)
FOLFIRI	irinotecan +oxaliplatin + 5-fluouracil + folinic acid
FOLFIRINOX	irinotecan + 5-fluouracil + folinic acid
(m)FOLFOX	(modified) leucovorin + 5-fluorouracil + oxaliplatin
FOLFOXIRI	oxaliplatin + irinotecan + 5-fluouracil + folinic acid
FP	fluoropyrimidine
FTD/TPI	trifluridine/tipiracil
FUFA	5-fluouracil + folinic acid
GEJ	gastro-esophageal junction
Gem	gemcitabine
GI	gastrointestinal
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HDAC	histone deacetylase
HER	human epidermal growth factor receptor
HIPEC	hyperthermic intraperitoneal chemotherapy
HR	hazard ratio
HRQoL	health-related quality of life
ICI	immune checkpoint inhibitor
ID	identification
Ig	immunoglobulin
IHC	immunohistochemistry
IQR	interquartile range
IO	immunotherapy
irAE	immune-related adverse event
ISH	in-situ hybridization
(m)ITT	modified intent-to-treat
IV	intravenous
KRAS	Ki-ras2 Kirsten rat sarcoma viral oncogene homolog
LDH	lactate dehydrogenase
Len	lenvatinib
LV	leucovorin
mAb	monoclonal antibody
MAPK	mitogen-activated protein kinase
mCRC	metastatic colorectal cancer
mo	months
mPP	modified per protocol
Mpr	major pathologic response
MRI	magnetic resonance imaging
MSI	microsatellite instability
MSS	microsatellite stable
MVI	macroscopic vascular invasion
NA	not available
NAT	normal adjacent tissue
Nal-IRI	nal-irinotecan
ND	not determined
NE	not evaluable/estimable
neg	negative
NGS	next generation sequencing
NLR	neutrophil to lymphocyte ratio
NR	not reached
NSCLC	non-small cell lung cancer
opt	optimal
OR	odds ratio
ORR	overall/objective response rate
(m)OS	(median) overall survival
Pan	panitumumab
PARP(i)	poly(ADP-ribose)polymerase (inhibitor)
PBO	placebo
pCR	pathologic complete response
PCR	polymerase chain reaction
PD	progressive disease
PD-(L)1	programmed death (-ligand) 1
Pem	pembrolizumab
PET	positron emission tomography
(m)PFS	(median) progression-free survival
pMMR	mismatch repair proficient
PO	orally
pos	positive
PR	partial response
PS	performance status
q(2/3/4/6)w	every (2/3/4) week(s)
QoL	quality of life
R	randomized
R0/1	resection 0/1
RAS	rat sarcoma virus
RDI	relative dose intensity
RECIST	Response Evaluation Criteria In Solid Tumors
RIFLE	Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease
Rivo	rivoceranib
RoW	rest of world
RR	response rate
RVT	residual viable tumour
SAE	serious adverse event
SD	stable disease
SoC	standard of care
T-DXd	trastuzumab deruxtecan
TEAE	treatment-emergent adverse event
Tis	tislelizumab
TKI	tyrosine kinase inhibitor
TRAE	treatment-related adverse event
Trem	tremelimumab
TTF	time to treatment failure
(m)TTP	(median) time to progression
(m)TTR	(median) time to response
UK	United Kingdom
US	Unitedd States
VEGF(R)	vascular endothelial growth factor (receptor)
WBC	white blood cell
WHO	World Health Organization
WT	wild-type

Mechanism of action for new molecules

Molecule		Mechanism of action
Balstilimab	Human IgG4 monoclonal antibody	Binds to the programmed cell death receptor, PD-1, which blocks the PD-1/PD-L1 pathway and reactivates T-cells to kill cancer cells
Botensilimab	Fc-engineered IgG1 anti-CTLA4 human monoclonal antibody	Binds to CTLA-4 expressed on T cells, and potently blocks engagement of CD80 and CD86, leading to enhanced T cell priming and responsiveness with depletion of regulatory T cells population
Camrelizumab	Human IgG4 monoclonal antibody	Binds to the programmed cell death receptor, PD-1, which blocks the PD-1/PD-L1 pathway and reactivates T-cells to kill cancer cells
Domatinostat	Class I HDAC inhibitor	Binds to and inhibits class I HDACs leading to an accumulation of highly acetylated histones, which may led to induction of chromatin remodelling, selective transcription of tumour suppressor genes, and tumour suppressor protein-mediated inhibition of tumour cell division and eventually induction of tumour cell apoptosis
Fruquintinib	Small molecule kinase inhibitor of VEGFR1, 2 and 3	Binds to and inhibits VEGR-induced phosphorylation of VEGFR1, 2 and 3, which may lead to inhibition of migration, proliferation and survival of endothelial cells, microvessel formation, inhibition of tumour cell proliferation and tumour cell death
Pemigatinib	Small molecule kinase inhibitor of FGFR1, 2 and 3	Binds to and inhibits FGFR1/2/3, which may lead to inhibition of FGFR1/2/3-related signal transduction pathways and proliferation in FGFR1/2/3-overexpressing tumour cells
Rivoceranib	Small molecule tyrosine kinase inhibitor of VEGFR2	Binds to and inhibits VEGFR2), which inhibits VEGF-stimulated endothelial cell migration and proliferation, leading to a decrease in tumour microvessel density
Tislelizumab	Human IgG4 monoclonal antibody	Binds to the programmed cell death receptor, PD-1, which blocks the PD-1/PD-L1 pathway and reactivates T-cells to kill cancer cells
Tucatinib	Tyrosine kinase inhibitor	Inhibits phosphorylation of HER2 and HER3, resulting in inhibition of downstream MAPK and AKT signaling and cell proliferation

Contents

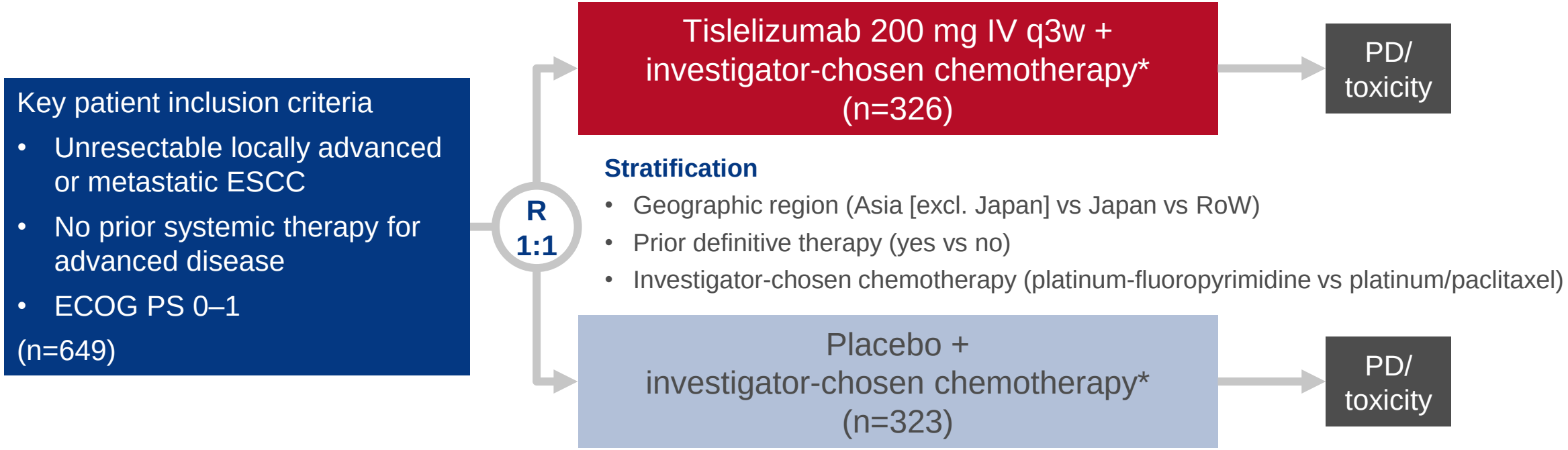
Note: To jump to a section, right click on the number and ‘Open Hyperlink’

CANCERS OF THE OESOPHAGUS AND STOMACH

LBA-1: RATIONALE-306: Randomized, global, Phase 3 study of tislelizumab plus chemotherapy versus chemotherapy as first-line treatment for locally advanced unresectable or metastatic esophageal squamous cell carcinoma (ESCC) – Yoon H, et al

Study objective

- To evaluate the efficacy and safety of 1L tislelizumab + chemotherapy in patients with locally advanced or metastatic ESCC in the RATIONALE-306 study



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR, DoR, HRQoL, safety

*Option A: platinum (cisplatin or oxaliplatin) + fluoropyrimidine; option B: platinum (cisplatin or oxaliplatin) + paclitaxel

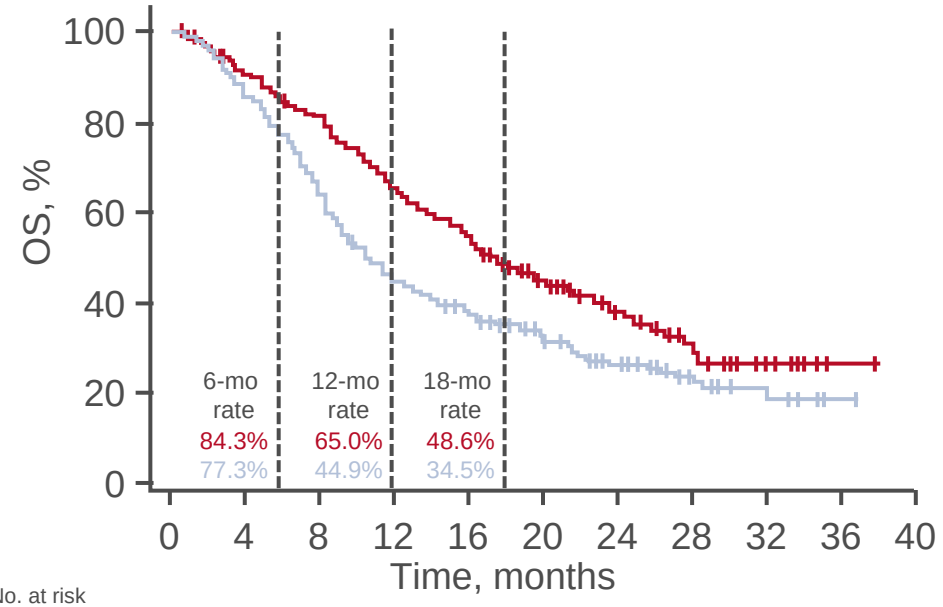
Presented at ESMO WCGC 2022
Yoon H, et al. Ann Oncol 2022;33(suppl):abstr LBA-1

LBA-1: RATIONALE-306: Randomized, global, Phase 3 study of tislelizumab plus chemotherapy versus chemotherapy as first-line treatment for locally advanced unresectable or metastatic esophageal squamous cell carcinoma (ESCC) – Yoon H, et al

Key results

Overall survival

	Tislelizumab + chemotherapy (n=326)	Placebo + chemotherapy (n=323)
Events, n (%)	196 (60.1)	226 (70.0)
mOS, mo (95%CI)	17.2 (15.8, 20.1)	10.6 (9.3, 12.1)
HR (95%CI); p-value	0.66 (0.54, 0.80); <0.0001	

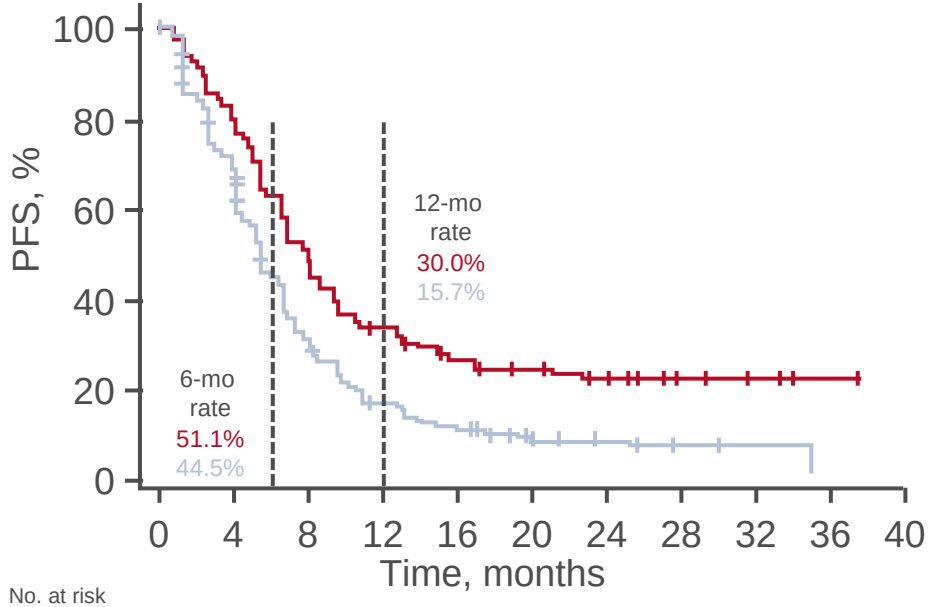


No. at risk

Tis + chemo	325	311	287	264	253	227	201	183	167	136	101	79	58	41	28	14	8	4	1	1
PBO + chemo	323	304	268	239	195	158	135	122	112	91	71	54	40	32	22	11	8	6	1	0

Progression-free survival

	Tislelizumab + chemotherapy (n=326)	Placebo + chemotherapy (n=323)
Events, n (%)	220 (67.5)	254 (78.6)
mPFS, mo (95%CI)	7.3 (6.9, 8.3)	5.8 (4.9, 6.0)
HR (95%CI)	0.62 (0.52, 0.75); <0.0001	



No. at risk

Tis + chemo	326	283	236	168	125	84	73	62	50	38	32	27	18	12	8	5	4	2	1	0
PBO + chemo	323	248	196	119	80	49	36	27	24	17	12	9	7	4	3	1	1	1	0	0

Yoon H, et al. Ann Oncol 2022;33(suppl):abstr LBA-1

LBA-1: RATIONALE-306: Randomized, global, Phase 3 study of tislelizumab plus chemotherapy versus chemotherapy as first-line treatment for locally advanced unresectable or metastatic esophageal squamous cell carcinoma (ESCC) – Yoon H, et al

Key results

Outcomes for patients receiving 3L therapy	Tislelizumab + chemotherapy (n=326)	Placebo + chemotherapy (n=323)
ORR, n (%) [95%CI]	207 (63.5) [58.0, 68.7]	137 (42.4) [37.0, 48.0]
OR (95%CI); p-value	2.38 (1.73, 3.27); <0.0001	
BOR, n (%)		
CR	15 (4.6)	8 (2.5)
PR	192 (58.9)	129 (39.9)
SD	83 (25.5)	122 (37.8)
PD	13 (4.0)	42 (13.0)
ND	23 (7.1)	22 (6.8)
mDoR, mo (95%CI)	7.1 (6.1, 8.1)	5.7 (4.4, 7.1)

AEs, n (%)	Tislelizumab + chemotherapy (n=324)	Placebo + chemotherapy (n=321)
TRAE		
Any	313 (96.6)	309 (96.3)
Grade ≥3	216 (66.7)	207 (64.5)
Serious	93 (28.7)	62 (19.3)
Led to death	6 (1.9)	4 (1.2)
TEAE led to discontinuation	103 (31.8)	72 (22.4)
irAE	70 (21.6)	19 (5.9)
Grade ≥3	28 (8.6)	5 (1.6)

Conclusions

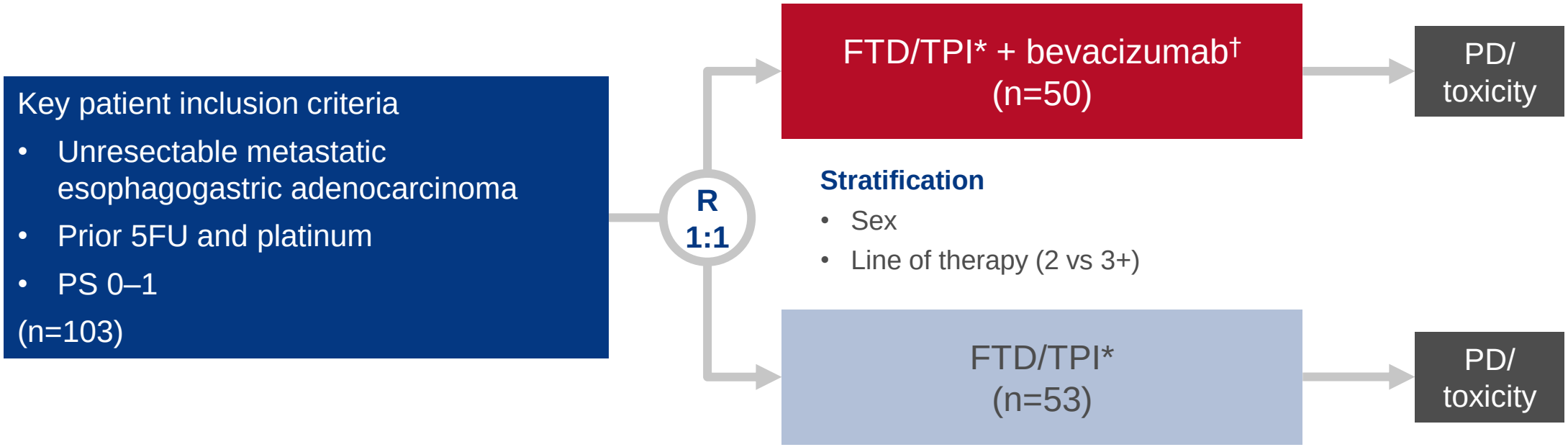
- **In patients with locally advanced or metastatic ESCC, 1L tislelizumab + chemotherapy demonstrated significant improvements in survival and durable tumour response compared with chemotherapy alone and had a manageable safety profile**

Yoon H, et al. Ann Oncol 2022;33(suppl):abstr LBA-1

O-4: Trifluridine/tipiracil (TAS-102) with or without bevacizumab in patients with pretreated metastatic esophagogastric adenocarcinoma (mEGA): A Danish randomized trial (LonGas) – Pfeiffer P, et al

Study objective

- To evaluate the efficacy and safety of trifluridine/tipiracil (FTD/TPI) ± bevacizumab in previously treated patients with metastatic esophagogastric adenocarcinoma in Danish centers in the LonGas study



PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

- OS, safety

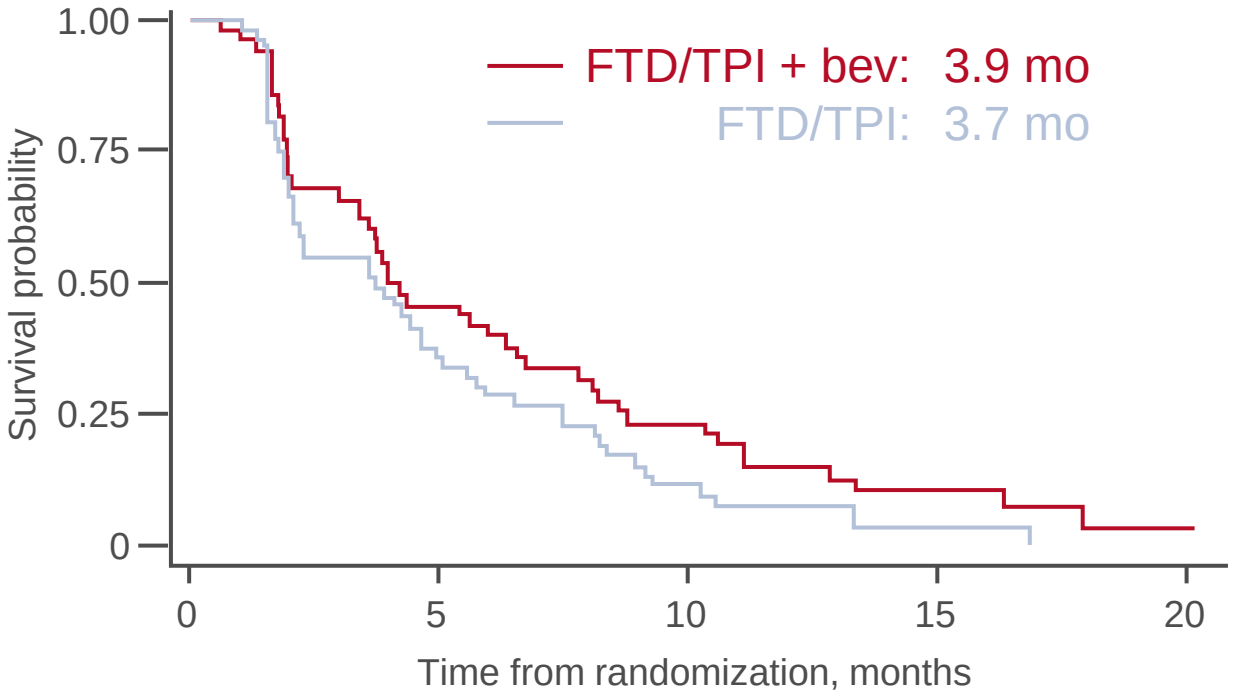
*35 mg/m^2 BID PO D1–5, 8–12 q4w; †5 mg/kg IV q2w

Presented at ESMO WCGC 2022
Pfeiffer P, et al. Ann Oncol 2022;33(suppl):abstr O-4

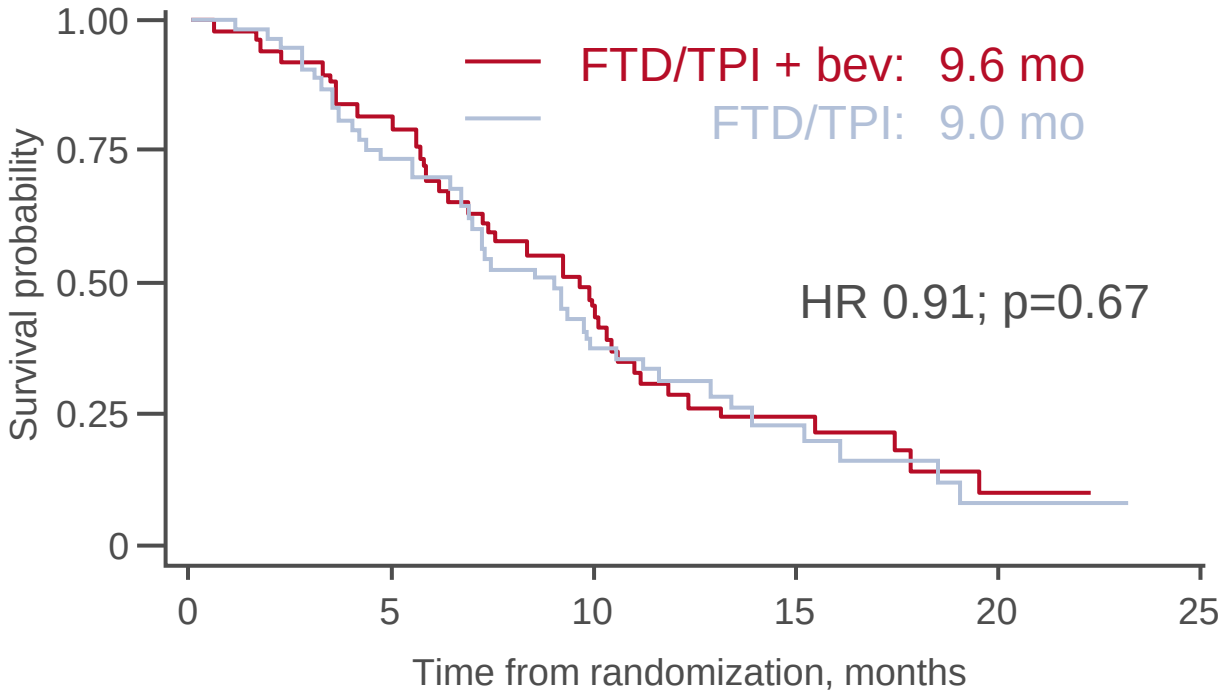
O-4: Trifluridine/tipiracil (TAS-102) with or without bevacizumab in patients with pretreated metastatic esophagogastric adenocarcinoma (mEGA): A Danish randomized trial (LonGas) – Pfeiffer P, et al

Key results

Progression-free survival



Overall survival



Pfeiffer P, et al. Ann Oncol 2022;33(suppl):abstr O-4

O-4: Trifluridine/tipiracil (TAS-102) with or without bevacizumab in patients with pretreated metastatic esophagogastric adenocarcinoma (mEGA): A Danish randomized trial (LonGas) – Pfeiffer P, et al

Key results

Outcomes	FTD/TPI + bevacizumab (n=50)	FTD/TPI (n=53)
Response rate, n (%)	4 (8)	1 (2)
DCR, n (%)	33 (66)	26 (49)

Outcomes for patients receiving 3L therapy	FTD/TPI + bevacizumab (n=23)	FTD/TPI (n=25)
PFS, mo	3.8	2.1
HR; p-value	0.46; 0.015	
OS, mo	7.6	7.1
HR, p-value	0.77; 0.41	

Grade 3–4 AEs, n (%)	FTD/TPI + bevacizumab	FTD/TPI
Hematologic		
Neutropenia	23 (46)	26 (49)
Anemia	5 (10)	5 (9)
Thrombocytopenia	1 (2)	1 (2)
Non-hematologic		
Nausea	3 (6)	3 (6)
Diarrhea	2 (4)	0
Vomiting	4 (8)	1 (2)
Fatigue	5 (10)	2 (4)
Febrile neutropenia	5 (10)	4 (8)

Conclusions

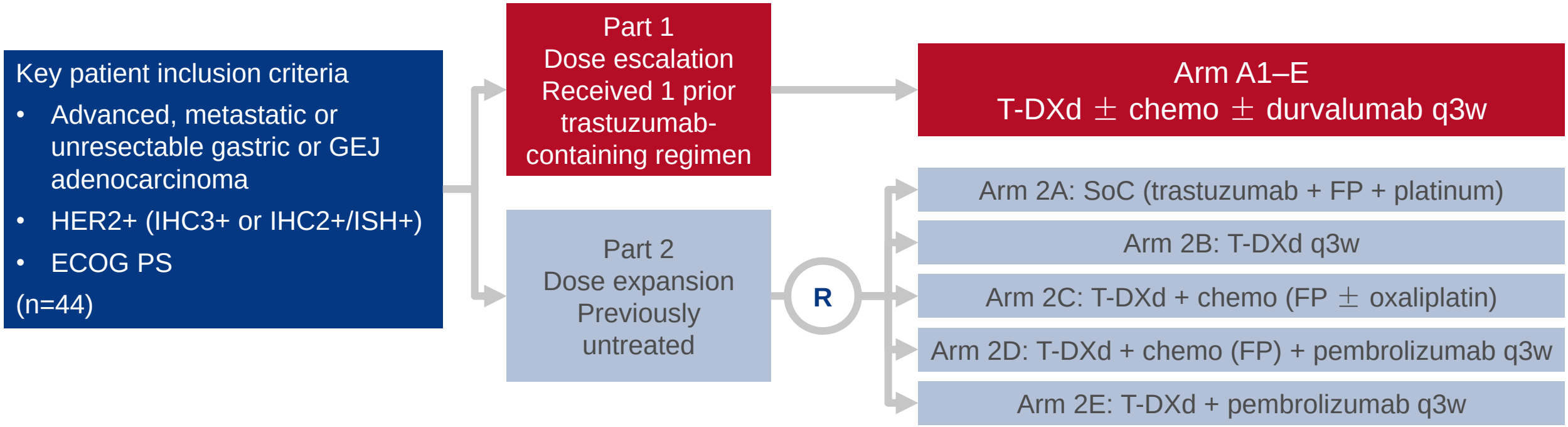
- **In previously treated patients with metastatic esophagogastric adenocarcinoma, adding bevacizumab to trifluridine/tipiracil did not provide any additional survival benefit**

Pfeiffer P, et al. Ann Oncol 2022;33(suppl):abstr O-4

SO-7: Co-occurring HER2 and PD-L1 expression in patients with HER2-positive trastuzumab-refractory gastric cancer (GC)/gastroesophageal junction adenocarcinoma (GEJA): biomarker analysis from the trastuzumab deruxtecan (T-DXd) DESTINY-Gastric03 trial – Janjigian Y, et al

Study objective

- To evaluate the association between PD-L1 and HER2 expression in a subset of patients with HER2+ trastuzumab-refractory gastric or GEJ adenocarcinoma in the DESTINY-Gastric03 study



ENDPOINTS

- Central assessment of HER2 status and PD-L1 expression*

*PD-L1 positivity defined as CPS ≥1

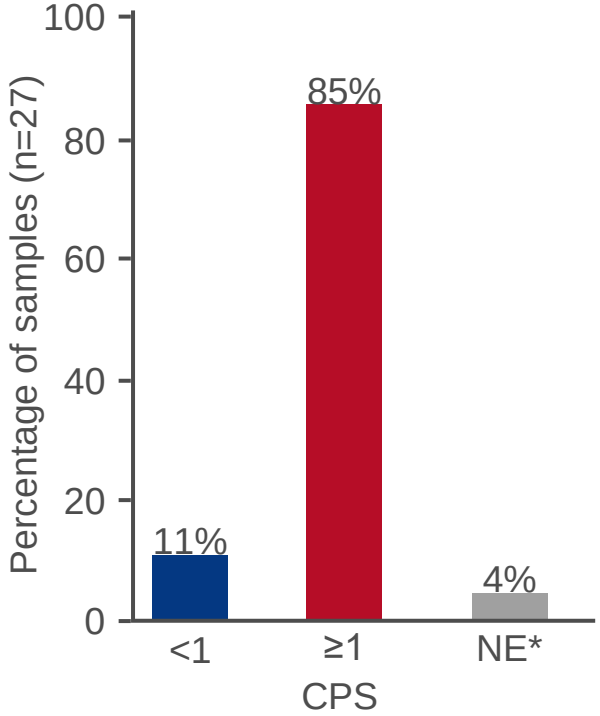
Presented at ESMO WCGC 2022
Janjigian Y, et al. Ann Oncol 2022;33(suppl):abstr SO-7

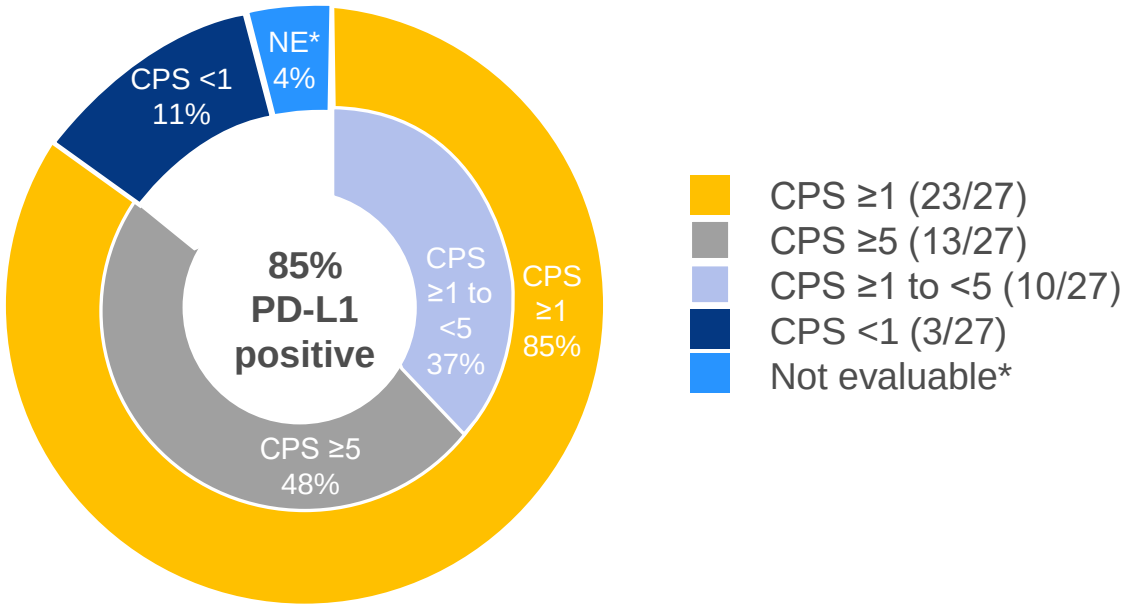
SO-7: Co-occurring HER2 and PD-L1 expression in patients with HER2-positive trastuzumab-refractory gastric cancer (GC)/gastroesophageal junction adenocarcinoma (GEJA): biomarker analysis from the trastuzumab deruxtecan (T-DXd) DESTINY-Gastric03 trial – Janjigian Y, et al

Key results

- There was 80% concordance between local and central testing for HER2 status

PD-L1 expression by central assessment





Conclusions

- **In patients with HER2+ trastuzumab-refractory gastric or GEJ adenocarcinoma, there was a substantial overlap between HER2 and PD-L1 positivity, which supports the use of dual therapy with an anti-HER2 and anti-PD-L1 agents**

*Not evaluable, there was insufficient number of viable tumour cells (<100) present for PD-L1 testing

Janjigian Y, et al. Ann Oncol 2022;33(suppl):abstr SO-7

PD-2: EMERGE: A multi-centre, non-randomised, single-arm phase II study investigating domatinostat plus avelumab in patients with previously treated advanced mismatch repair-proficient oesophagogastric and colorectal adenocarcinoma – Slater S, et al

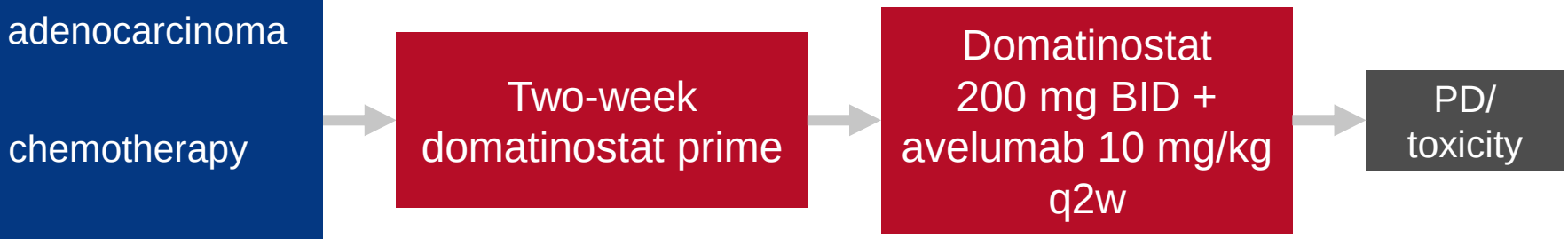
Study objective

- To evaluate the efficacy and safety of domatinostat, a class I HDAC inhibitor, + avelumab in previously treated patients with advanced pMMR esophagogastric or colorectal adenocarcinoma in UK centers in the phase 2 EMERGE study

Key patient inclusion criteria

- Advanced, unresectable or metastatic esophagogastric or colorectal adenocarcinoma
- pMMR
- Progressed on or after 1 prior chemotherapy (no immunotherapy)
- ECOG PS 0–1

(n=19; n=9 esophagogastric, n=10 CRC)



PRIMARY ENDPOINT

- ORR (RECIST v1.1)

SECONDARY ENDPOINTS

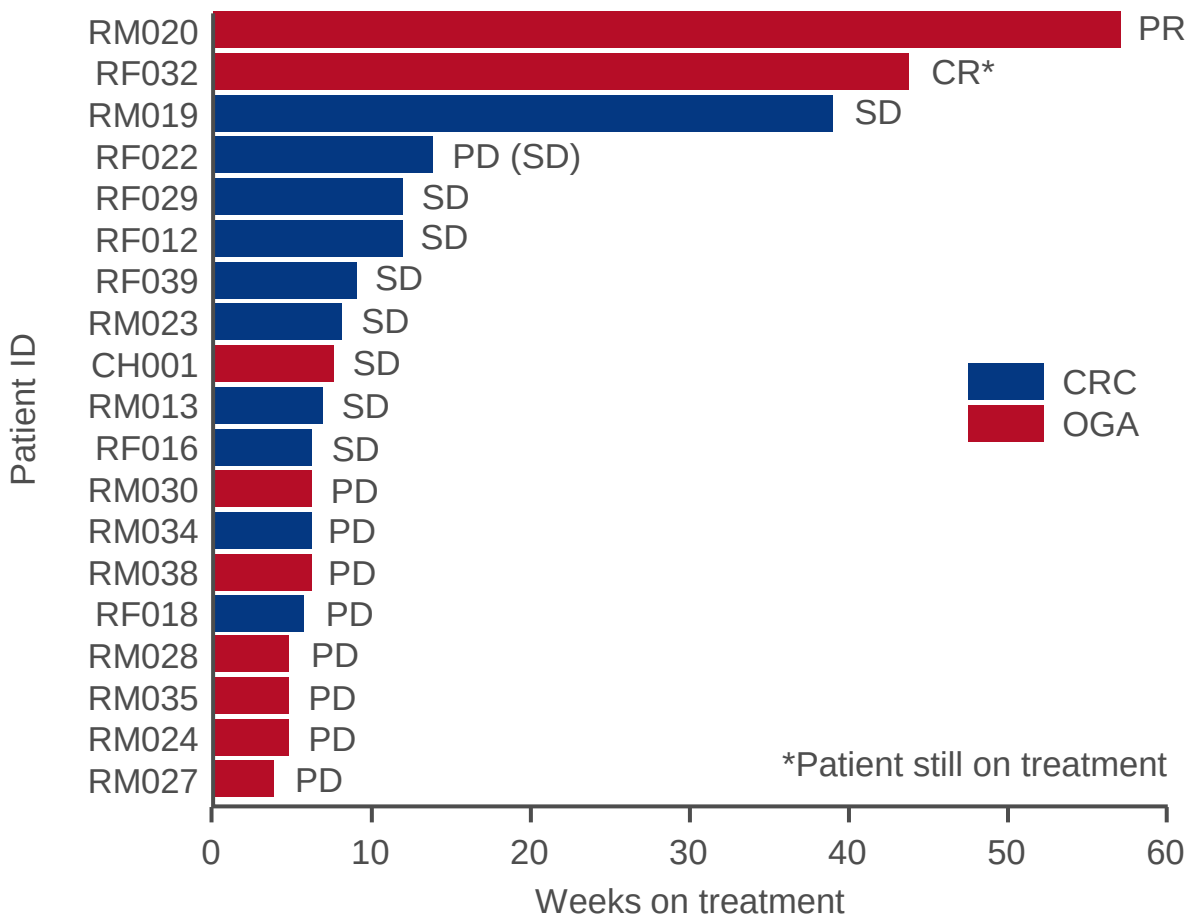
- DoR, PFS, DCR, safety

Presented at ESMO WCGC 2022
Slater S, et al. Ann Oncol 2022;33(suppl):abstr PD-2

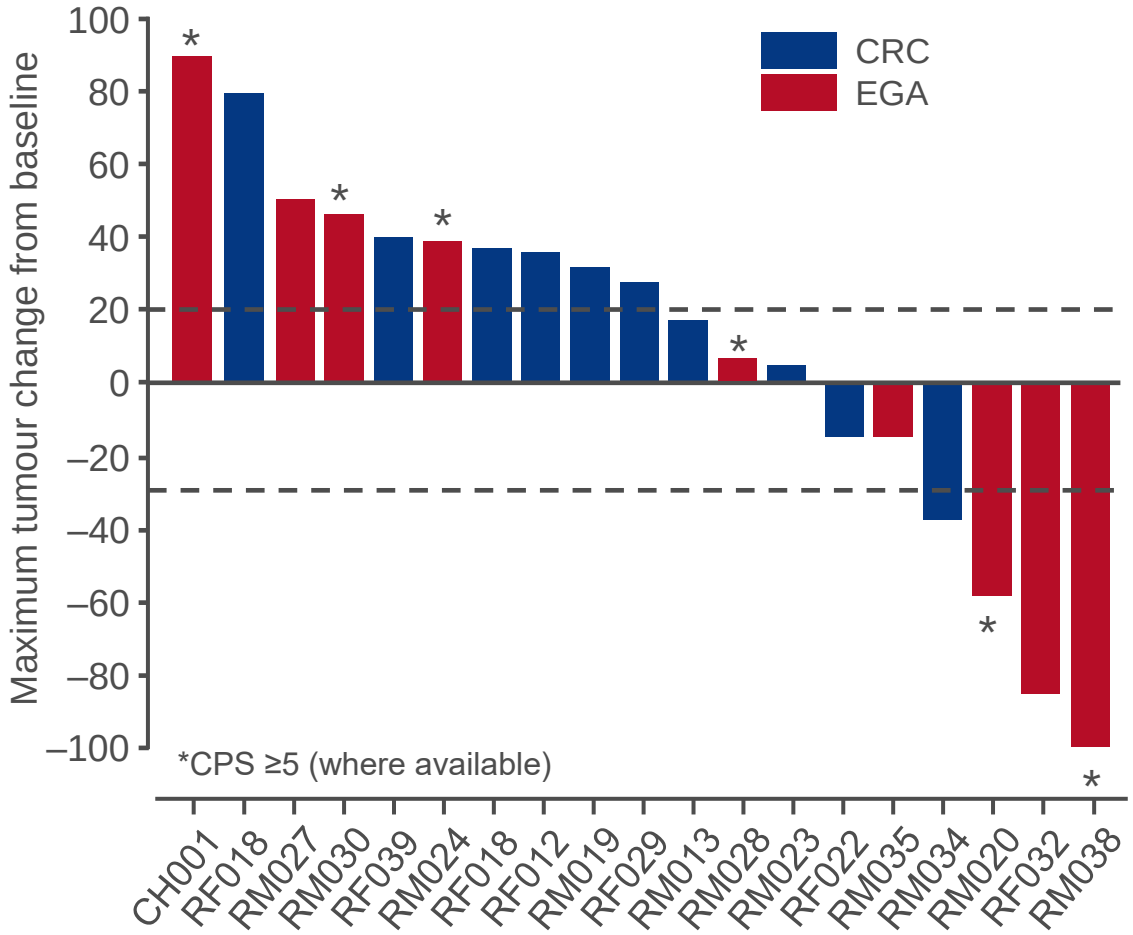
PD-2: EMERGE: A multi-centre, non-randomised, single-arm phase II study investigating domatinostat plus avelumab in patients with previously treated advanced mismatch repair-proficient oesophagogastric and colorectal adenocarcinoma – Slater S, et al

Key results

Duration of treatment and best response by RECIST v1.1 (n=19)



Maximum tumour change from baseline (n=19)



Slater S, et al. Ann Oncol 2022;33(suppl):abstr PD-2

PD-2: EMERGE: A multi-centre, non-randomised, single-arm phase II study investigating domatinostat plus avelumab in patients with previously treated advanced mismatch repair-proficient oesophagogastric and colorectal adenocarcinoma – Slater S, et al

Key results

Outcome	Esophagogastric (n=9)	CRC (n=10)
ORR, % (95%CI)	22.2 (2.8, 60.0)	-
BOR, n CR PR	 1 1	 0 0
Median duration of treatment, mo (IQR)	1.4 (1.1–1.8)	2.0 (1.4–2.8)
Longest duration of treatment, mo	13	9
DCR, % (95%CI)	-	30.0 (6.7, 65.2)

TRAEs, n (%)	All patients (n=19)
Fatigue	12 (63)
Anemia	6 (32)
Anorexia	6 (32)
Nausea	6 (32)
Diarrhea	5 (26)
Fever	5 (26)
Maculo-papular rash	4 (21)
Vomiting	4 (21)
Infusion-related reaction	3 (16)
Insomnia	3 (16)
Constipation	2 (11)
Cough	2 (11)
Dyspnea	2 (11)
Oral mucositis	2 (11)
Pain	2 (11)
Serum amylase increased	2 (11)

Conclusions

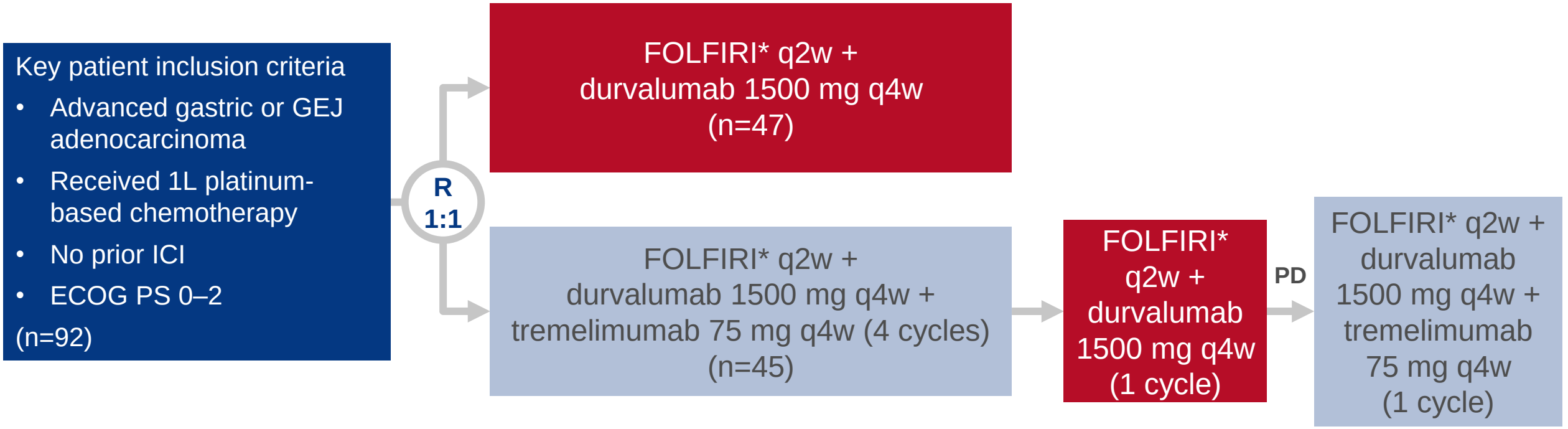
- **In patients with esophagogastric adenocarcinoma, domatinostat + avelumab showed some antitumor activity with a manageable safety profile, but there were no responses in those with CRC. Development of domatinostat has since been discontinued**

Slater S, et al. Ann Oncol 2022;33(suppl):abstr PD-2

1204MO: PRODIGE 59 - DURIGAST trial: A randomised phase II study evaluating FOLFIRI plus durvalumab and FOLFIRI plus durvalumab plus tremelimumab in second-line treatment of patients with advanced gastric or gastro-oesophageal junction adenocarcinoma – Tougeron D, et al

Study objective

- To evaluate the efficacy and safety of 2L FOLFIRI + durvalumab ± tremelimumab in patients with advanced gastric or GEJ adenocarcinoma in French centres in the phase 2 PRODIGE 59 - DURIGAST study



PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

- DCR, DoR, OS, safety

*Including irinotecan 180 mg/m^2

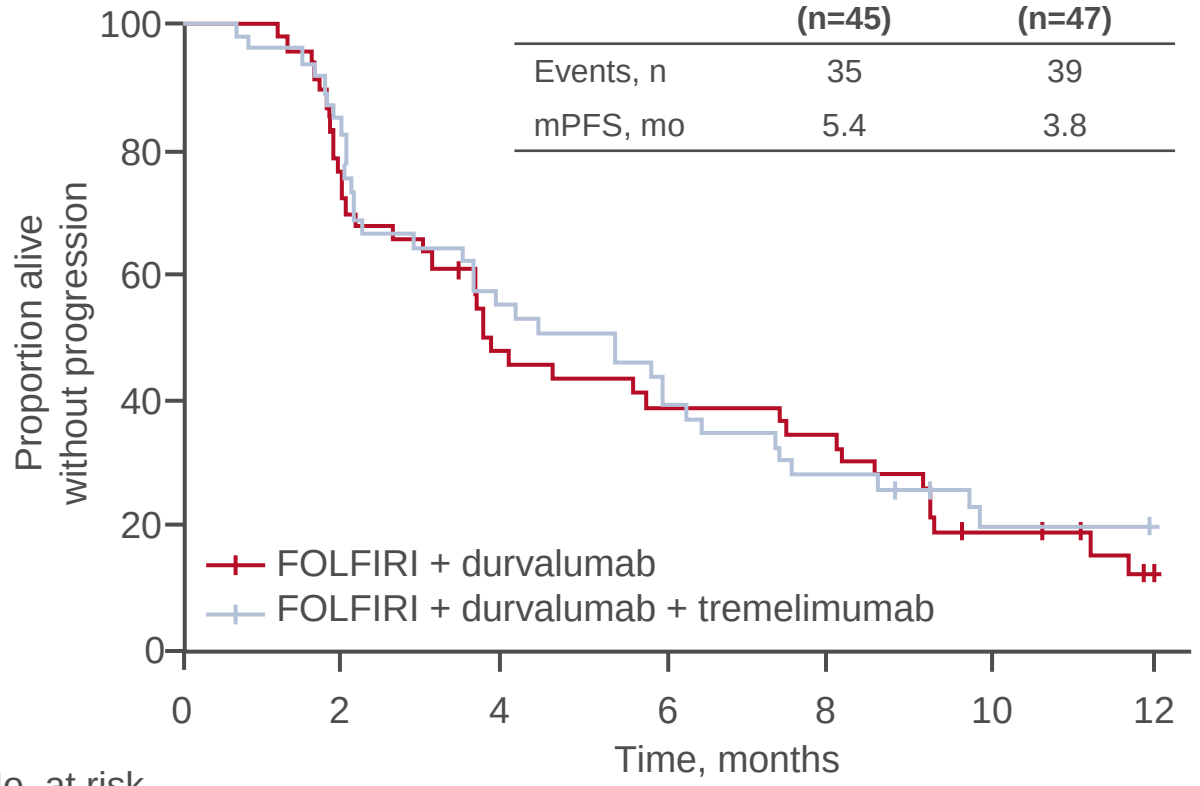
Presented at ESMO Congress 2022
Tougeron D, et al. Ann Oncol 2022;33(suppl):abstr 1204MO

1204MO: PRODIGE 59 - DURIGAST trial: A randomised phase II study evaluating FOLFIRI plus durvalumab and FOLFIRI plus durvalumab plus tremelimumab in second-line treatment of patients with advanced gastric or gastro-oesophageal junction adenocarcinoma – Tougeron D, et al

Key results

Progression-free survival

	F + D + T (n=45)	F + D (n=47)
Events, n	35	39
mPFS, mo	5.4	3.8

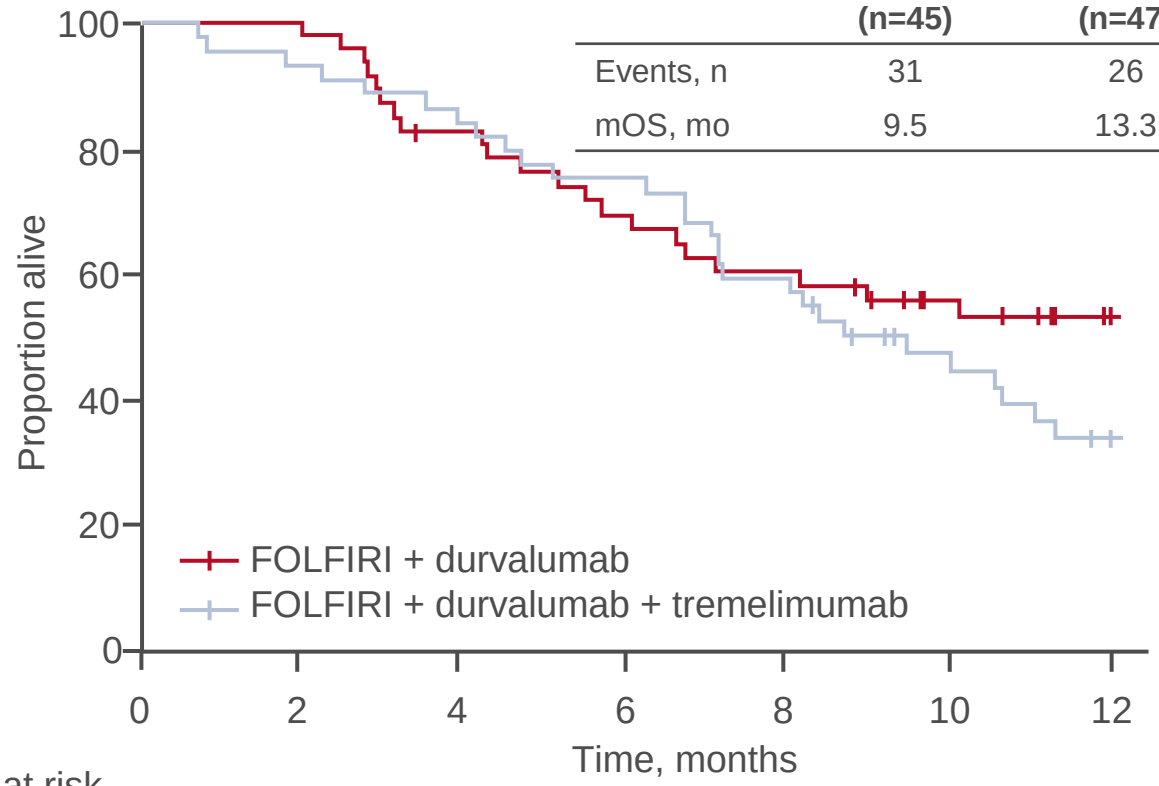


No. at risk

F + D	47	33	22	18	16	8	3
F + D + T	45	35	25	18	13	7	7

Overall survival

	F + D + T (n=45)	F + D (n=47)
Events, n	31	26
mOS, mo	9.5	13.3



No. at risk

F + D	47	46	38	32	28	20	13
F + D + T	45	42	38	34	27	18	12

Tougeron D, et al. Ann Oncol 2022;33(suppl):abstr 1204MO

1204MO: PRODIGE 59 - DURIGAST trial: A randomised phase II study evaluating FOLFIRI plus durvalumab and FOLFIRI plus durvalumab plus tremelimumab in second-line treatment of patients with advanced gastric or gastro-oesophageal junction adenocarcinoma – Tougeron D, et al

Key results

	FOLFIRI + durvalumab (n=46)	FOLFIRI + durvalumab + tremelimumab (n=46)
4-mo PFS, % (90%CI)	44.7 (32.2, 57.7)	55.6 (42.3, 68.3)
DCR, %	67.4	68.9
mDoR, mo	5.1	4.3

Grade 3–5 TRAEs, n (%)	FOLFIRI + durvalumab (n=46)	FOLFIRI + durvalumab + tremelimumab (n=46)
Any	22 (47.8)	22 (47.8)
Diarrhea	1 (2.2)	5 (10.9)
Colitis	2 (4.3)	-
Vomiting	3 (6.5)	1 (2.2)
Neutrophil decreased	7 (15.2)	11 (23.9)
Lymphocyte decreased	1 (2.2)	2 (4.3)

Conclusions

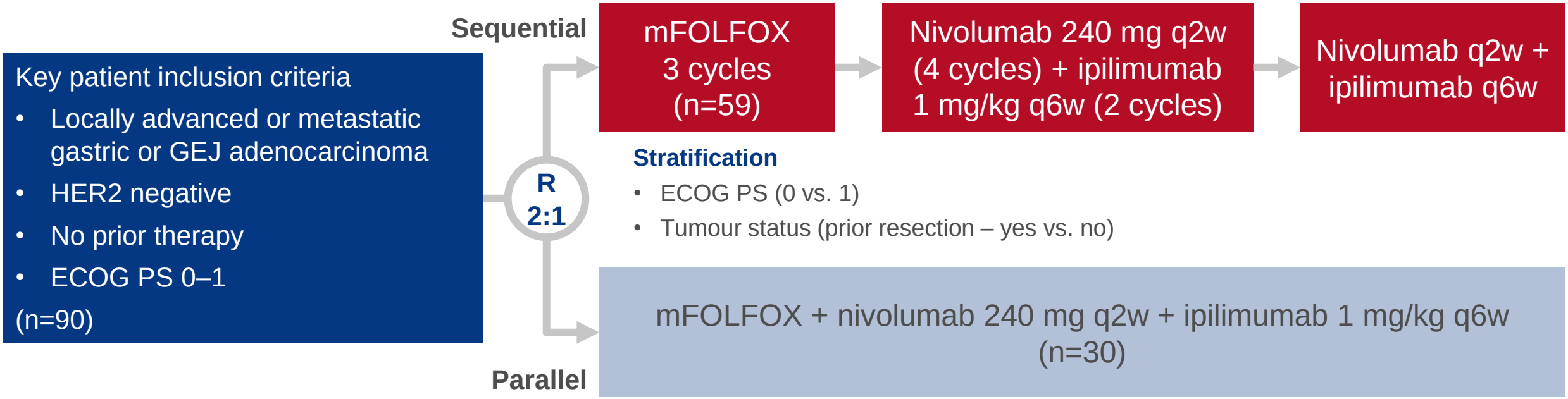
- **In patients with advanced gastric or GEJ adenocarcinoma, 2L FOLFIRI + durvalumab ± tremelimumab failed to meet the primary PFS endpoint and had an acceptable safety profile**

Tougeron D, et al. Ann Oncol 2022;33(suppl):abstr 1204MO

1203O: FOLFOX plus nivolumab and ipilimumab versus FOLFOX induction followed by nivolumab and ipilimumab in patients with previously untreated advanced or metastatic adenocarcinoma of the stomach or gastroesophageal junction – results from the randomized phase 2 Moonlight trial of the AIO – Lorenzen S, et al

Study objective

- To evaluate the efficacy and safety of mFOLFOX induction therapy followed by nivolumab + ipilimumab in previously untreated patients with advanced or metastatic gastric or GEJ adenocarcinoma in the Moonlight study



PRIMARY ENDPOINT

- 6-mo PFS rate

SECONDARY ENDPOINTS

- OS, ORR, safety

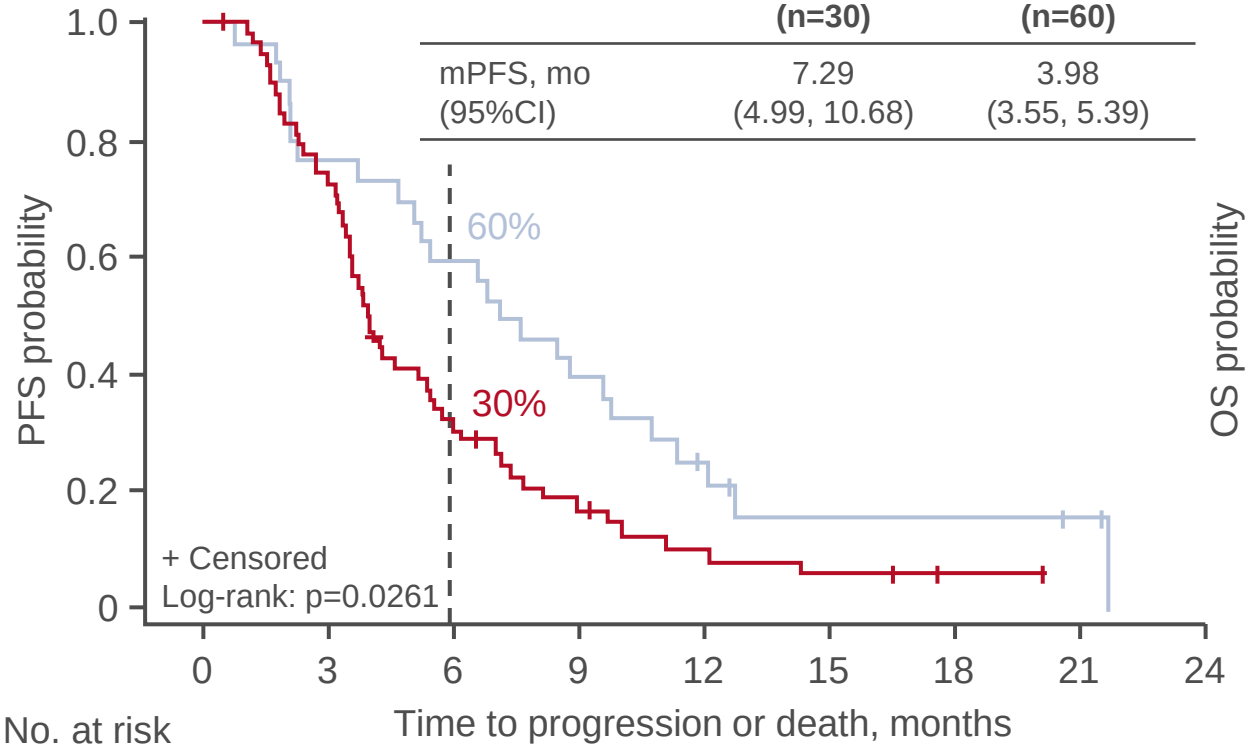
Presented at ESMO Congress 2022
Lorenzen S, et al. Ann Oncol 2022;33(suppl):abstr 1203O

1203O: FOLFOX plus nivolumab and ipilimumab versus FOLFOX induction followed by nivolumab and ipilimumab in patients with previously untreated advanced or metastatic adenocarcinoma of the stomach or gastroesophageal junction – results from the randomized phase 2 Moonlight trial of the AIO – Lorenzen S, et al

Key results

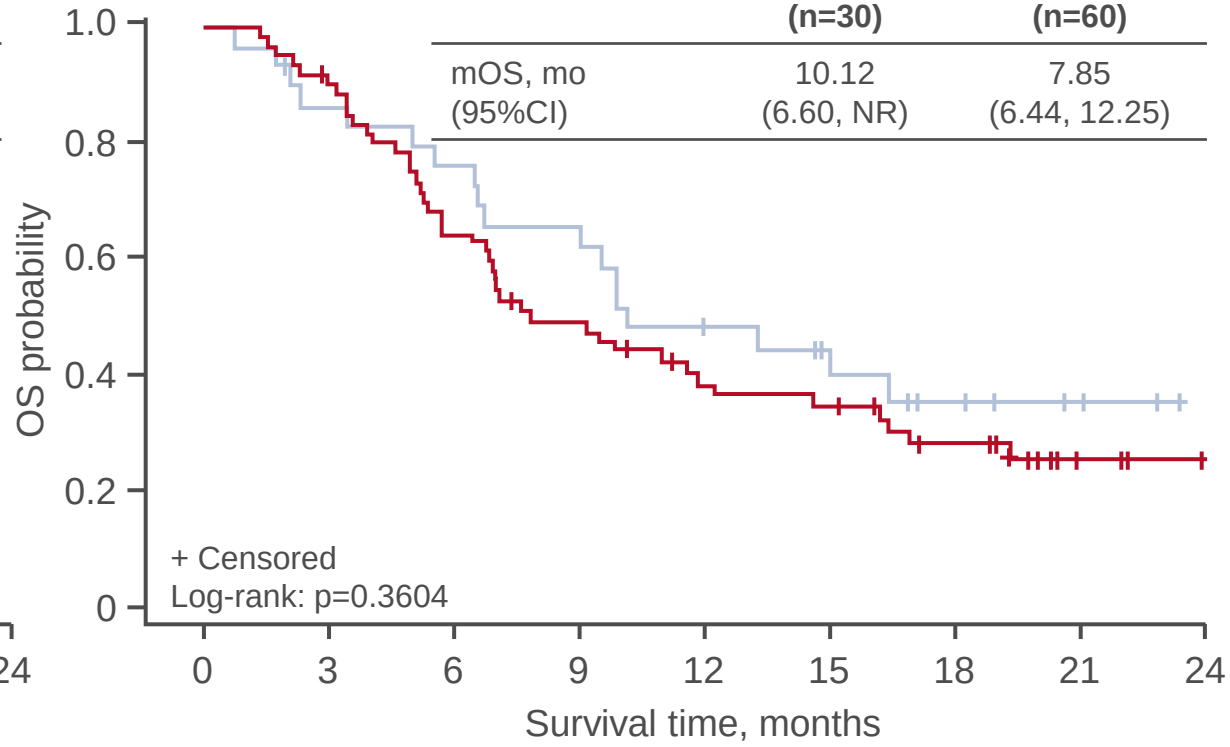
Progression-free survival

	Parallel (n=30)	Sequential (n=60)
mPFS, mo (95%CI)	7.29 (4.99, 10.68)	3.98 (3.55, 5.39)



Overall survival

	Parallel (n=30)	Sequential (n=60)
mOS, mo (95%CI)	10.12 (6.60, NR)	7.85 (6.44, 12.25)



No. at risk

Parallel 30	23	18	12	5	3	3	2	0	
Sequential 60	43	18	10	5	3	1	0		

Parallel 30	30	25	22	19	13	10	7	4	0
Sequential 60	60	54	38	28	20	18	12	3	0

Lorenzen S, et al. Ann Oncol 2022;33(suppl):abstr 1203O

1203O: FOLFOX plus nivolumab and ipilimumab versus FOLFOX induction followed by nivolumab and ipilimumab in patients with previously untreated advanced or metastatic adenocarcinoma of the stomach or gastroesophageal junction – results from the randomized phase 2 Moonlight trial of the AIO – Lorenzen S, et al

Key results

	Parallel (n=30)	Sequential (n=60)
ORR, % (95%CI)	46.7 (28, 66)	30.0 (19, 43)
BOR, %		
CR	10.0	6.7
PR	36.7	23.3
SD	33.3	43.3
PD	10.0	15.0
mDoR, mo (95%CI)	8.36 (2.99, 18.76)	4.30 (1.91, 8.74)
PD-L1 CPS ≥1, n	13	24
mOS, mo (95%CI)	16.46 (2.07, NR)	6.87 (5.13, 7.59)
mPFS, mo (95%CI)	5.22 (2.07, NR)	3.75 (3.06, 5.55)
PD-L1 CPS <1, n	14	17
mPFS, mo (95%CI)	6.87 (2.07, 9.53)	3.98 (2.23, 6.21)

Grade ≥3 TRAEs, n (%)	Parallel (n=30)	Sequential (n=60)
Any	21 (70.0)	26 (43.3)
Serious	10 (33.3)	10 (16.7)
Led to death	1 (3.3)	1 (1.7)

Conclusions

- **In patients with advanced or metastatic gastric or GEJ adenocarcinoma, 1L FOLFOX + nivolumab + ipilimumab given in parallel demonstrated greater benefits than sequential treatment, although this should be interpreted with caution as the patient numbers were small and PD-L1 expression was low**

Lorenzen S, et al. Ann Oncol 2022;33(suppl):abstr 1203O

CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

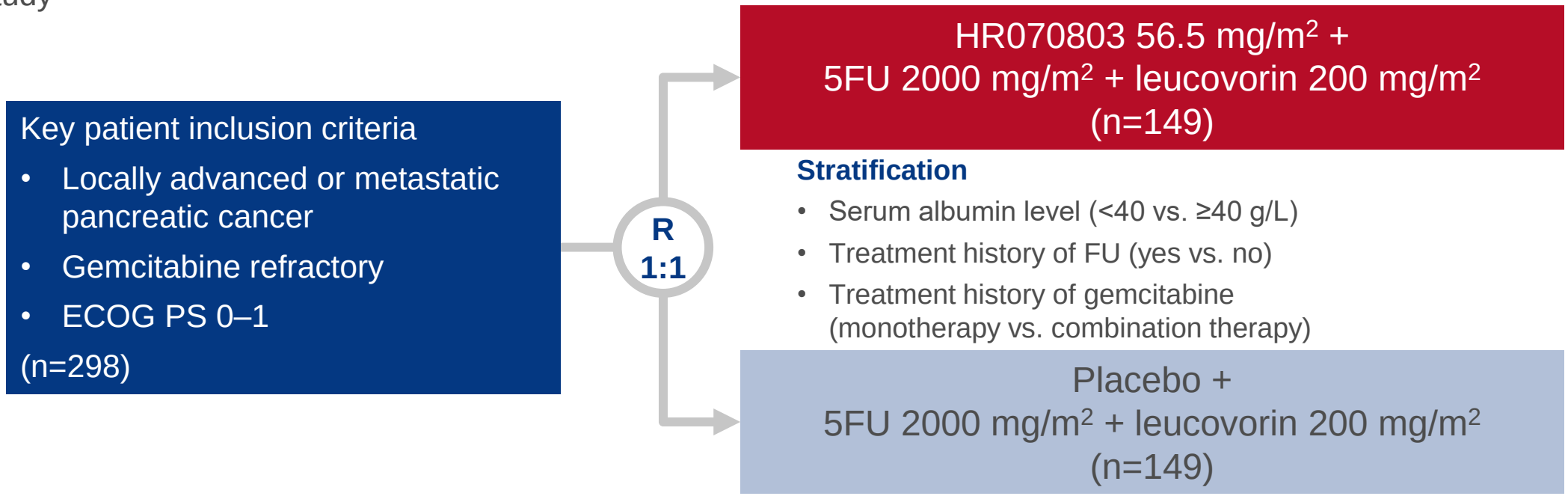
Cancers of the pancreas, small bowel and hepatobiliary tract

PANCREATIC CANCER

LBA61: HR070803 plus 5-FU/LV versus placebo plus 5-FU/LV in second-line therapy for gemcitabine-refractory locally advanced or metastatic pancreatic cancer: a multicentered, randomized, double-blind, parallel-controlled phase III trial (HR-IRI-APC) – Wang L, et al

Study objective

- To evaluate the efficacy and safety of 2L HR070803 (a liposome formulation of irinotecan) + 5FU/LV in patients with gemcitabine-refractory locally advanced or metastatic pancreatic cancer in Chinese centres in the phase 3 HR-IRI-APC study



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR, TTF, safety

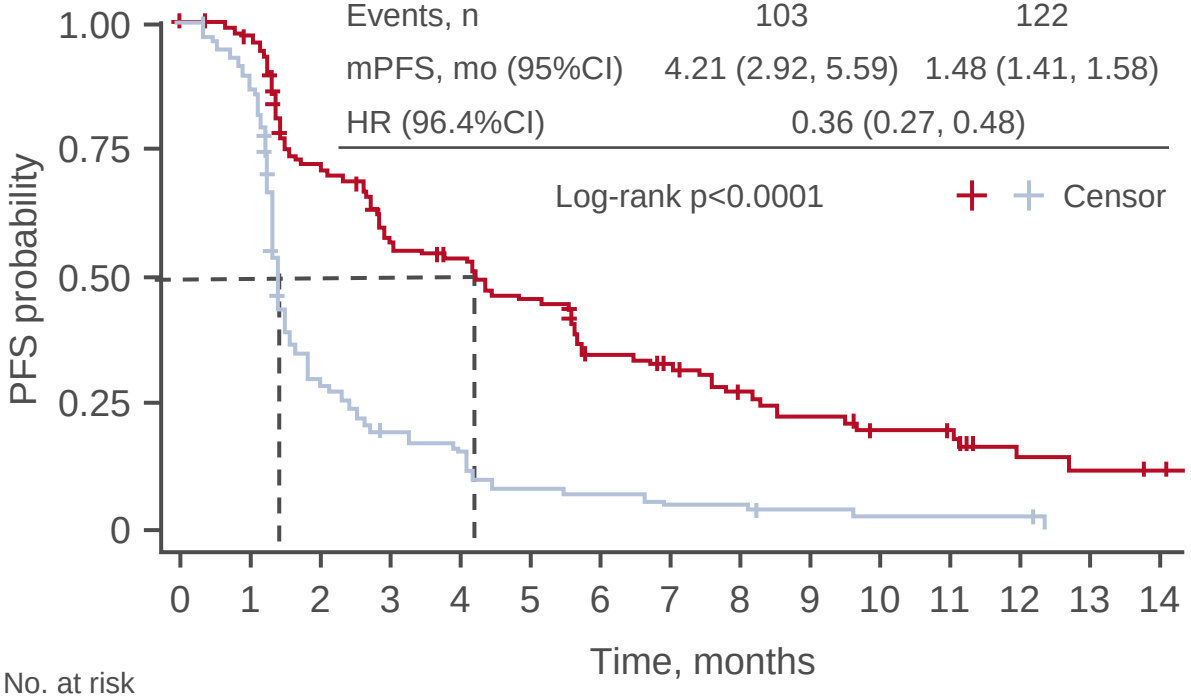
Presented at ESMO Congress 2022
Wang L, et al. Ann Oncol 2022;33(suppl):abstr LBA61

LBA61: HR070803 plus 5-FU/LV versus placebo plus 5-FU/LV in second-line therapy for gemcitabine-refractory locally advanced or metastatic pancreatic cancer: a multicentered, randomized, double-blind, parallel-controlled phase III trial (HR-IRI-APC) – Wang L, et al

Key results

Progression-free survival

	HR070803 (n=149)	Placebo (n=149)
Events, n	103	122
mPFS, mo (95%CI)	4.21 (2.92, 5.59)	1.48 (1.41, 1.58)
HR (96.4%CI)	0.36 (0.27, 0.48)	

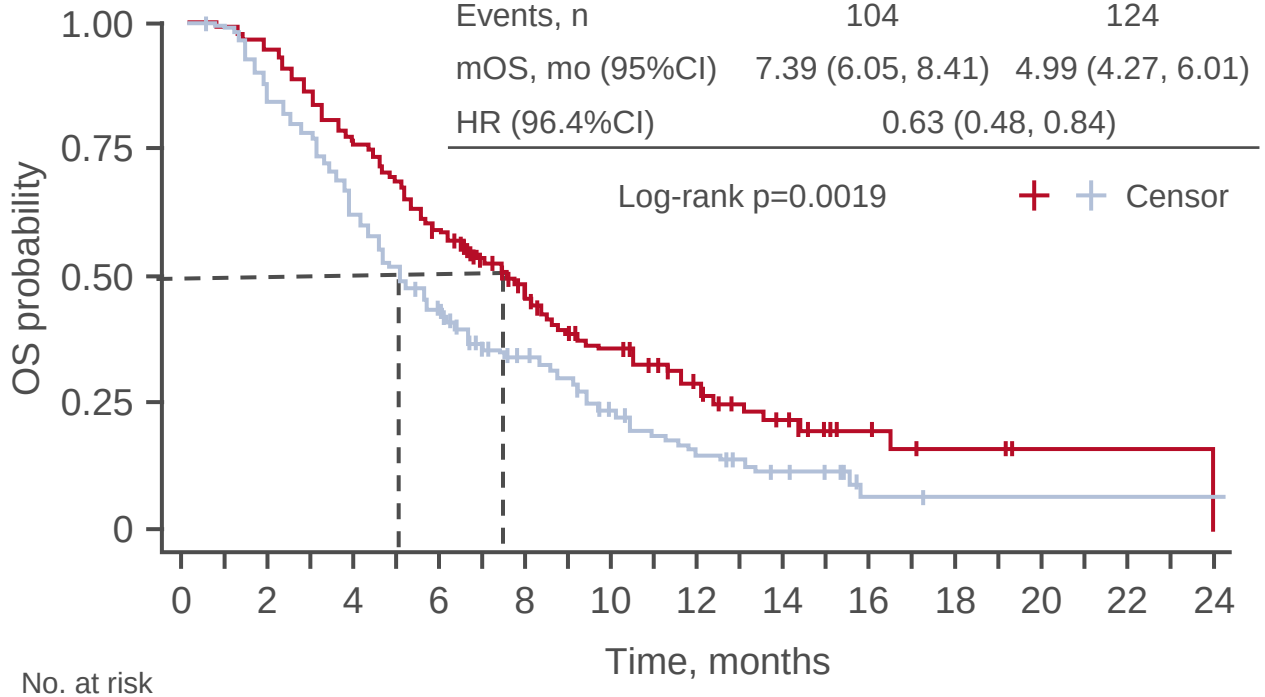


No. at risk

HR070803	149	137	95	73	66	54	35	30	22	18	13	13	6	5	4
Placebo	149	122	36	20	17	9	7	6	5	3	2	2	2	0	

Overall survival

	HR070803 (n=149)	Placebo (n=149)
Events, n	104	124
mOS, mo (95%CI)	7.39 (6.05, 8.41)	4.99 (4.27, 6.01)
HR (96.4%CI)	0.63 (0.48, 0.84)	



No. at risk

HR070803	149	148	141	125	113	100	86	74	51	42	36	30	21	15	13	7	6	4	3	3	1	1	1	1	0
Placebo	149	147	127	114	92	74	63	47	40	33	22	18	14	11	8	7	2	2	1	1	1	1	1	1	1

Wang L, et al. Ann Oncol 2022;33(suppl):abstr LBA61

LBA61: HR070803 plus 5-FU/LV versus placebo plus 5-FU/LV in second-line therapy for gemcitabine-refractory locally advanced or metastatic pancreatic cancer: a multicentered, randomized, double-blind, parallel-controlled phase III trial (HR-IRI-APC) – Wang L, et al

Key results

AEs, %	HR070803 + 5FU/LV (n=147)	Placebo + 5FU/LV (n=149)
Any	99.3	97.3
Grade ≥3	53.1	46.3
Serious	24.5	17.5
Led to dose adjustment	4.1	9.4
Led to discontinuation	21.1	5.4

Grade ≥3 TEAEs, %	HR070803 + 5FU/LV (n=147)	Placebo + 5FU/LV (n=149)
Nausea	1.4	0
Vomiting	4.8	2.0
Fatigue	4.1	2.0
Diarrhea	4.1	2.7
Anorexia	2.7	1.3
Neutropenia	12.9	0
ALT increased	4.1	2.0

Conclusions

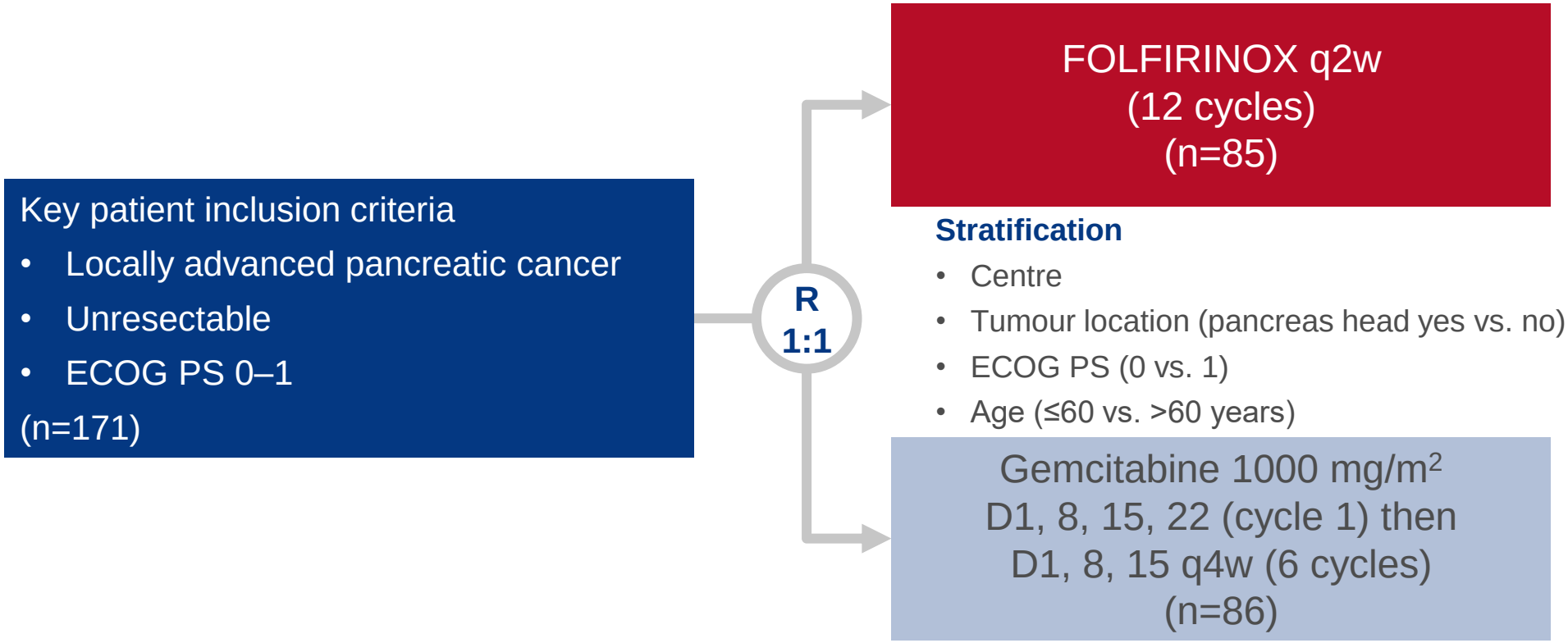
- **In patients with gemcitabine-refractory, locally advanced or metastatic pancreatic cancer, HR070803 + 5FU/LV demonstrated significant improvements in survival compared with 5FU/LV and was generally well-tolerated with no new safety signals observed**

Wang L, et al. Ann Oncol 2022;33(suppl):abstr LBA61

1296MO: PRODIGE 29-UCGI 26(NEOPAN): A phase III randomised trial comparing chemotherapy with FOLFIRINOX or gemcitabine in locally advanced pancreatic carcinoma (LAPC) – Ducreux MP, et al

Study objective

- To evaluate the efficacy and safety of FOLFIRINOX compared with gemcitabine in patients with locally advanced pancreatic carcinoma in French centres in the phase 3 NEOPAN study



PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

- OS, ORR, DCR, safety

Presented at ESMO Congress 2022
Ducreux MP, et al. Ann Oncol 2022;33(suppl):abstr 1296MO

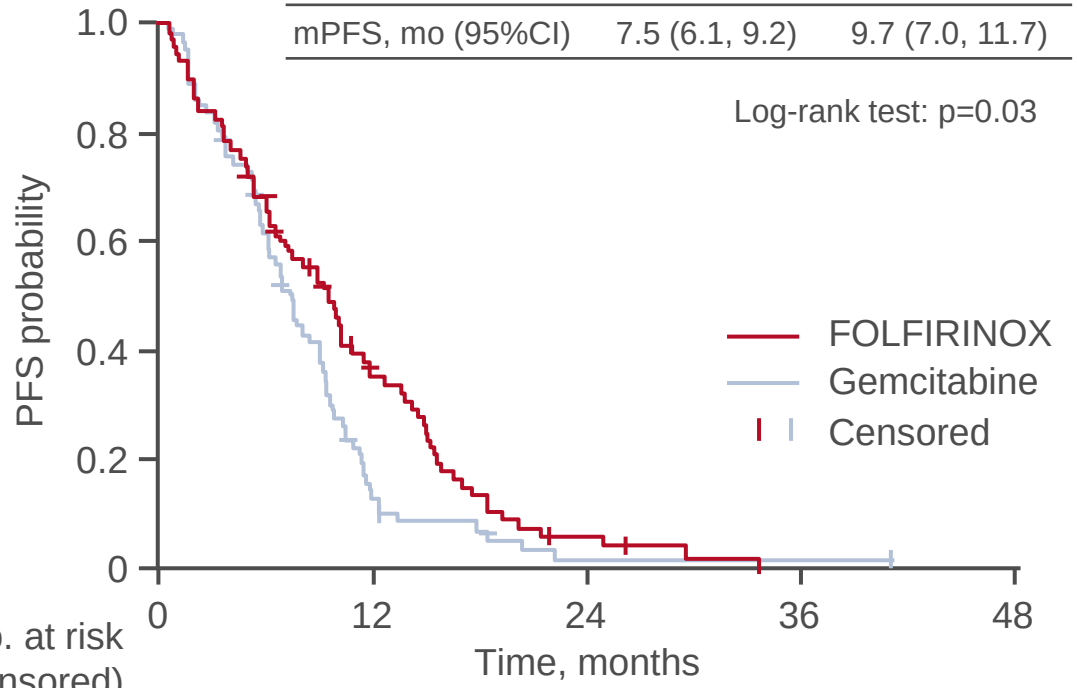
1296MO: PRODIGE 29-UCGI 26(NEOPAN): A Phase III randomised trial comparing chemotherapy with FOLFIRINOX or gemcitabine in locally advanced pancreatic carcinoma (LAPC) – Ducreux MP, et al

Key results

Progression-free survival

	Gemcitabine	FOLFIRINOX
mPFS, mo (95%CI)	7.5 (6.1, 9.2)	9.7 (7.0, 11.7)

Log-rank test: p=0.03

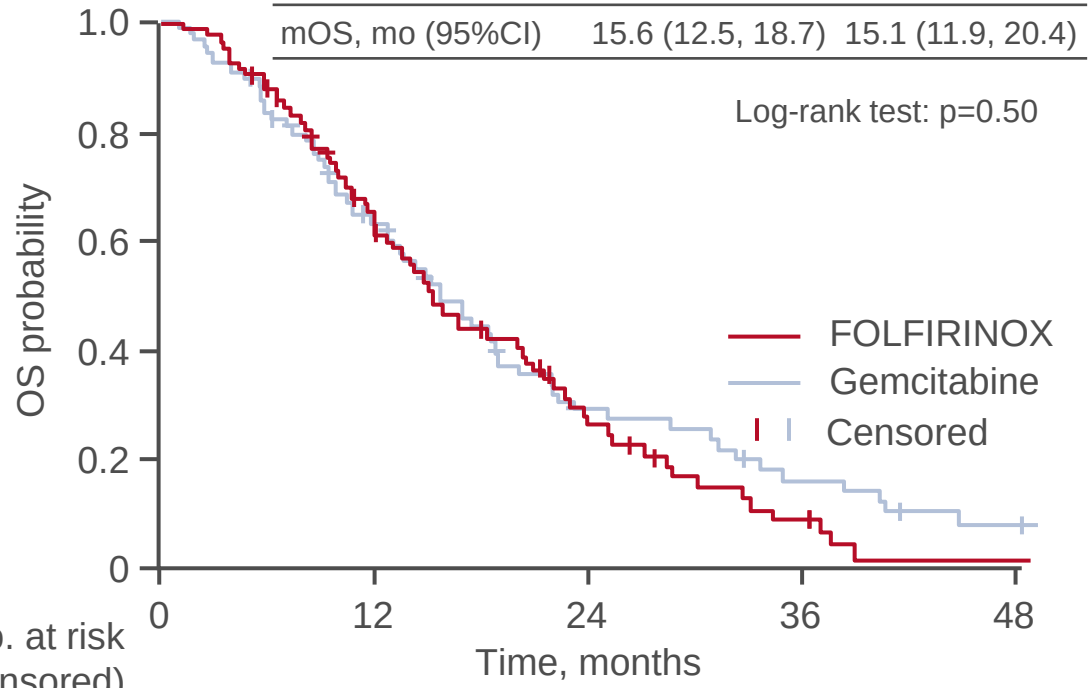


No. at risk (censored)					
FOLFIRINOX	85 (0)	25 (8)	4 (9)	0 (10)	
Gemcitabine	86 (0)	11 (6)	1 (8)	1 (8)	0 (9)

Overall survival

	Gemcitabine	FOLFIRINOX
mOS, mo (95%CI)	15.6 (12.5, 18.7)	15.1 (11.9, 20.4)

Log-rank test: p=0.50



No. at risk (censored)					
FOLFIRINOX	85 (0)	45 (9)	16 (15)	5 (17)	1 (18)
Gemcitabine	86 (0)	46 (10)	16 (17)	8 (18)	3 (19)

Ducreux MP, et al. Ann Oncol 2022;33(suppl):abstr 1296MO

1296MO: PRODIGE 29-UCGI 26(NEOPAN): A Phase III randomised trial comparing chemotherapy with FOLFIRINOX or gemcitabine in locally advanced pancreatic carcinoma (LAPC) – Ducreux MP, et al

Key results

AEs, %	FOLFIRINOX		Gemcitabine	
	Grade 3	Grade 4	Grade 3	Grade 4
Nausea	12	-	5	-
Vomiting	10	1	5	-
Anemia	5	-	5	-
Neutropenia	12	1	22	11
Febrile neutropenia	2	-	1	-
Thrombocytopenia	5	1	5	-
Fatigue	18	-	5	-
Fever	2	-	1	-

Conclusions

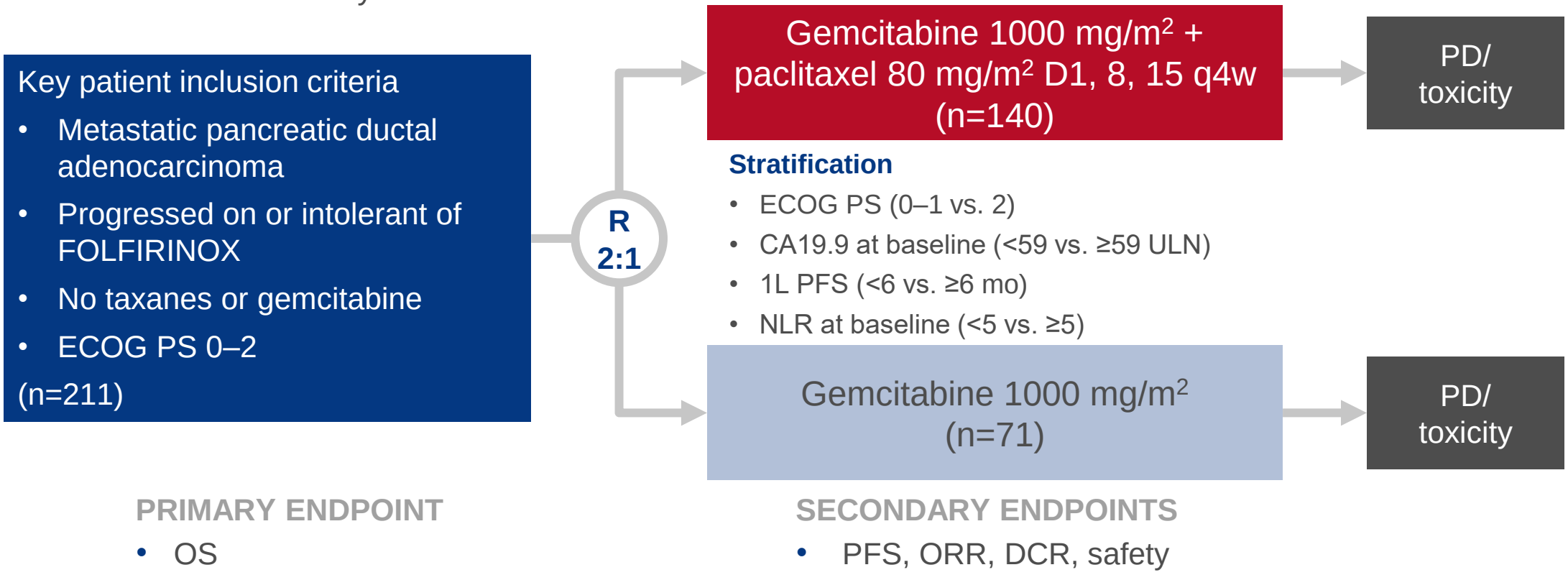
- **In patients with locally advanced pancreatic carcinoma, FOLFIRINOX demonstrated a significant improvement in PFS, but not OS, compared with gemcitabine and was generally well-tolerated**

Ducreux MP, et al. Ann Oncol 2022;33(suppl):abstr 1296MO

LBA60: Evaluation of gemcitabine and paclitaxel versus gemcitabine alone after FOLFIRINOX failure or intolerance in metastatic Pancreatic Ductal Adenocarcinoma: Results of the randomized phase III PRODIGE 65 – UCGI 36 – GEMPAX UNICANCER study – De la Fouchardiere C, et al

Study objective

- To evaluate the efficacy and safety of gemcitabine + paclitaxel vs. gemcitabine alone in patients with metastatic pancreatic ductal adenocarcinoma who have progressed on or were intolerant of FOLFIRINOX in French centres in the phase 3 GEMPAX UNICANCER study



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

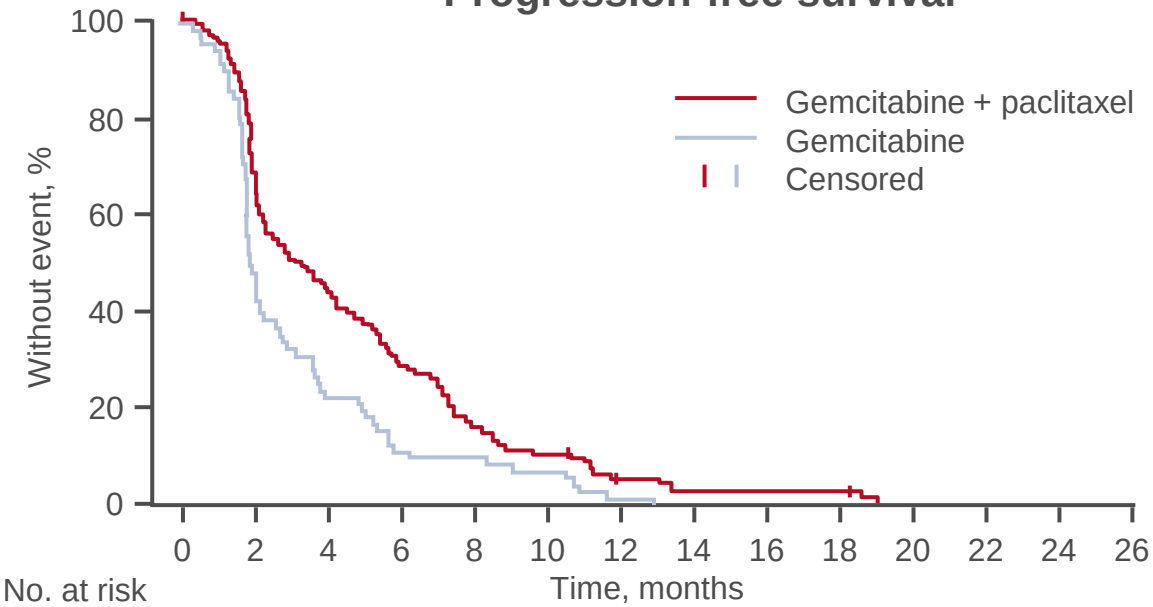
- PFS, ORR, DCR, safety

Presented at ESMO Congress 2022
De la Fouchardiere C, et al. Ann Oncol 2022;33(suppl):abstr LBA60

LBA60: Evaluation of gemcitabine and paclitaxel versus gemcitabine alone after FOLFIRINOX failure or intolerance in metastatic Pancreatic Ductal Adenocarcinoma: Results of the randomized phase III PRODIGE 65 – UCGI 36 – GEMPAX UNICANCER study – De la Fouchardiere C, et al

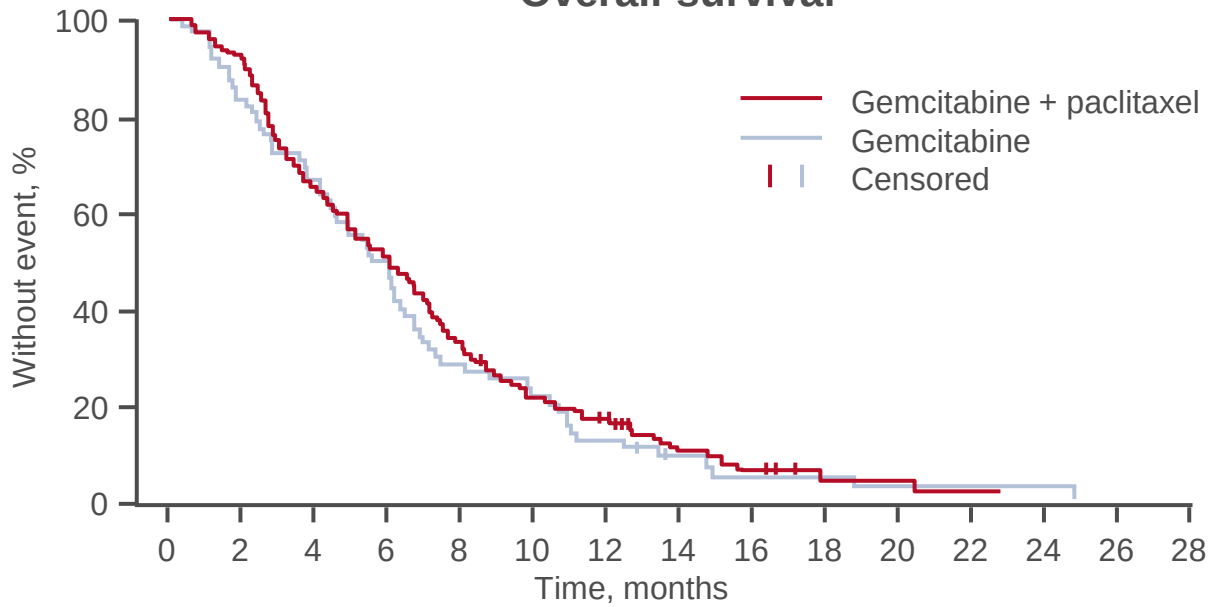
Key results

Progression-free survival



	Events, n	mPFS, mo (95%CI)	PFS rate, % (95%CI)
Gemcitabine + paclitaxel (n=140)	137	3.1 (2.2, 4.3)	4 mo: 43.9 (35.5, 51.9) 6 mo: 28.8 (21.5, 36.4)
Gemcitabine (n=71)	71	2.0 (1.9, 2.3)	4 mo: 22.5 (13.7, 32.8) 6 mo: 11.3 (5.3, 19.8)

Overall survival



	Events, n	mOS, mo (95%CI)	OS rate, % (95%CI)
Gemcitabine + paclitaxel (n=140)	131/140	6.4 (5.2, 7.4)	6 mo: 51.8 (43.2, 59.7) 12 mo: 18.0 (12.1, 24.8)
Gemcitabine (n=71)	68/71	5.9 (4.6, 6.9)	6 mo: 49.3 (37.3, 60.2) 12 mo: 12.2 (5.8, 21.1)

De la Fouchardiere C, et al. Ann Oncol 2022;33(suppl):abstr LBA60

LBA60: Evaluation of gemcitabine and paclitaxel versus gemcitabine alone after FOLFIRINOX failure or intolerance in metastatic Pancreatic Ductal Adenocarcinoma: Results of the randomized phase III PRODIGE 65 – UCGI 36 – GEMPAX UNICANCER study – De la Fouchardiere C, et al

Key results

Response	Gemcitabine + paclitaxel (n=125)	Gemcitabine (n=63)
ORR, % (95%CI)	19.2 (12.7, 27.2)	4.8 (1.0, 13.3)

Grade 3–4 TRAEs, %	Gemcitabine + paclitaxel (n=138)	Gemcitabine (n=70)
Any	58	27
Anemia	15	4
Neutropenia	16	16
Thrombocytopenia	20	4
Asthenia	10	3
Neuropathy	12	0

Conclusions

- **In patients with metastatic pancreatic ductal adenocarcinoma, gemcitabine + paclitaxel did not significantly improve OS compared with gemcitabine alone, although PFS and ORR were significantly improved with the combination**

De la Fouchardiere C, et al. Ann Oncol 2022;33(suppl):abstr LBA60

Cancers of the pancreas, small bowel and hepatobiliary tract

HEPATOCELLULAR CARCINOMA

PD-7: Cabozantinib plus atezolizumab in previously untreated advanced hepatocellular carcinoma (aHCC) and previously treated gastric cancer (GC) and gastroesophageal junction adenocarcinoma (GEJ): Results of the COSMIC-021 study – Li D, et al

Study objective

- To evaluate the efficacy and safety of cabozantinib + atezolizumab in treatment-naïve patients with advanced HCC or previously treated patients with gastric or GEJ adenocarcinoma in the COSMIC-021 study

Key patient inclusion criteria

Advanced HCC

- Child-Pugh A
- No prior systemic therapy
- ECOG PS 0–1

(n=30)

Gastric or GEJ adenocarcinoma

- Progression on or after platinum- or fluoropyrimidine-based chemotherapy
- ≤2 prior lines of therapy
- ECOG PS 0–1

(n=30)

Cabozantinib 40 mg/day PO + atezolizumab 1200 mg IV q3w

PRIMARY ENDPOINT

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

SECONDARY ENDPOINTS

- DoR, PFS, safety

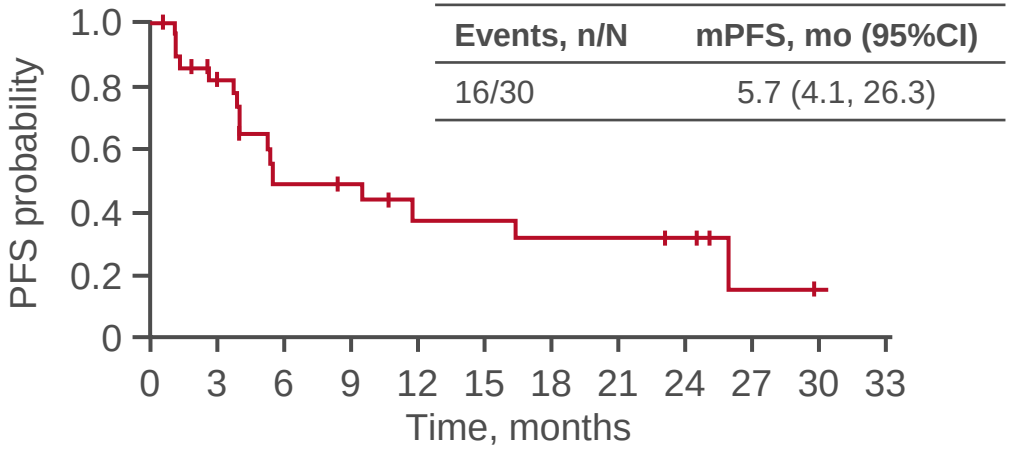
Presented at ESMO WCGC 2022
Li D, et al. Ann Oncol 2022;33(suppl):abstr PD-7

PD-7: Cabozantinib plus atezolizumab in previously untreated advanced hepatocellular carcinoma (aHCC) and previously treated gastric cancer (GC) and gastroesophageal junction adenocarcinoma (GEJ): Results of the COSMIC-021 study – Li D, et al

Key results

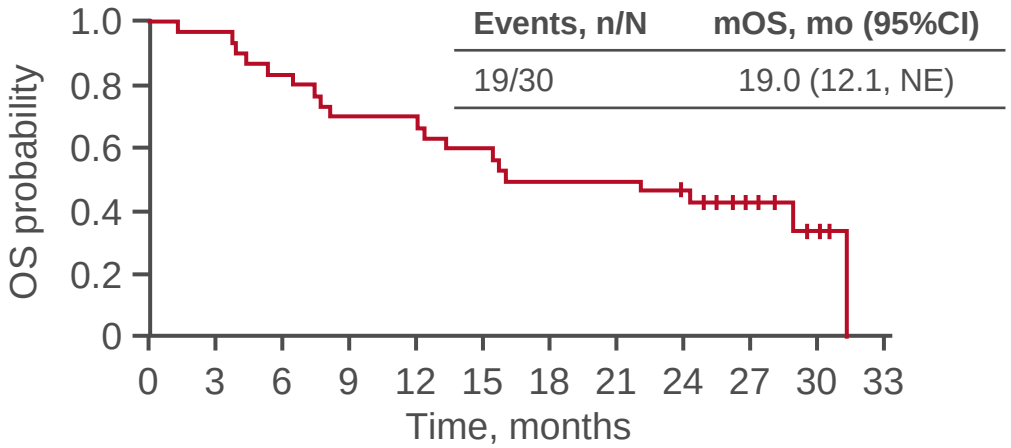
Advanced HCC

PFS



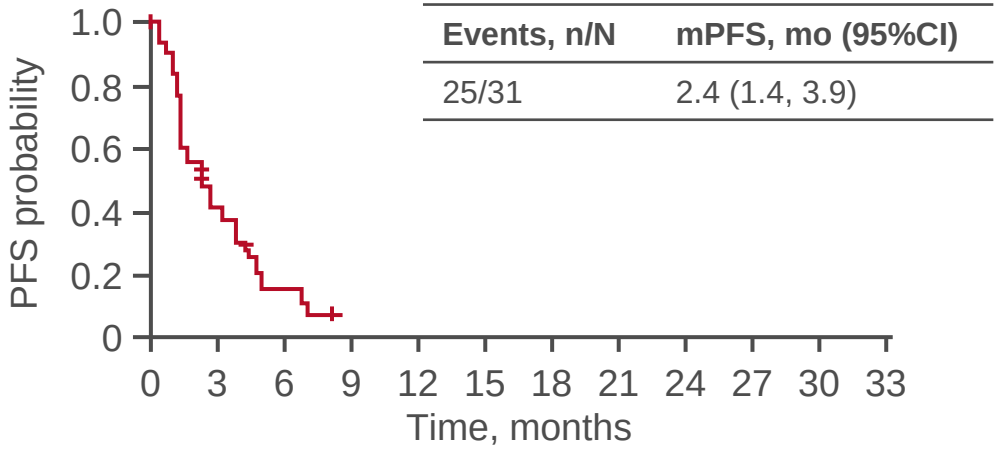
Events, n/N	mPFS, mo (95%CI)
16/30	5.7 (4.1, 26.3)

OS

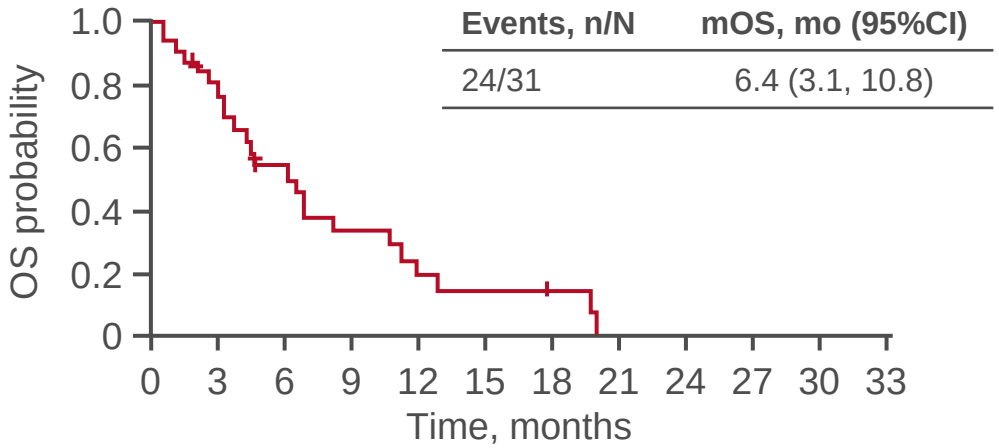


Events, n/N	mOS, mo (95%CI)
19/30	19.0 (12.1, NE)

Gastric or GEJ adenocarcinoma



Events, n/N	mPFS, mo (95%CI)
25/31	2.4 (1.4, 3.9)



Events, n/N	mOS, mo (95%CI)
24/31	6.4 (3.1, 10.8)

Li D, et al. Ann Oncol 2022;33(suppl):abstr PD-7

PD-7: Cabozantinib plus atezolizumab in previously untreated advanced hepatocellular carcinoma (aHCC) and previously treated gastric cancer (GC) and gastroesophageal junction adenocarcinoma (GEJ): Results of the COSMIC-021 study – Li D, et al

Key results

Outcomes	HCC (n=30)	Gastric/GEJ (n=31)
ORR, % (80%CI)	13 (6, 25)	0 (0, 7)
BOR, n (%)		
CR	0	0
PR	4 (13)	0
SD	21 (70)	15 (48)
PD	3 (10)	10 (32)
NA	2 (7)	6 (19)
DCR, % (80%CI)	83 (7, 92)	48 (36, 61)
mDoR, mo (range)	22 (7–NE)	NA
mTTP, mo (range)	11 (4–23)	NA

Grade 3–4 TRAEs, n (%)	HCC (n=30)	Gastric/GEJ (n=31)
Any	12 (40)	11 (35)
Palmar-plantar erythrodysesthesia	2 (7)	0
Diarrhea	3 (10)	2 (6)
AST increased	4 (13)	1 (3)
ALT increased	1 (3)	0
Hypertension	1 (3)	1 (3)
Rash	0	1 (3)
Thrombocytopenia	0	2 (6)
WBC count decreased	0	1 (3)

Conclusions

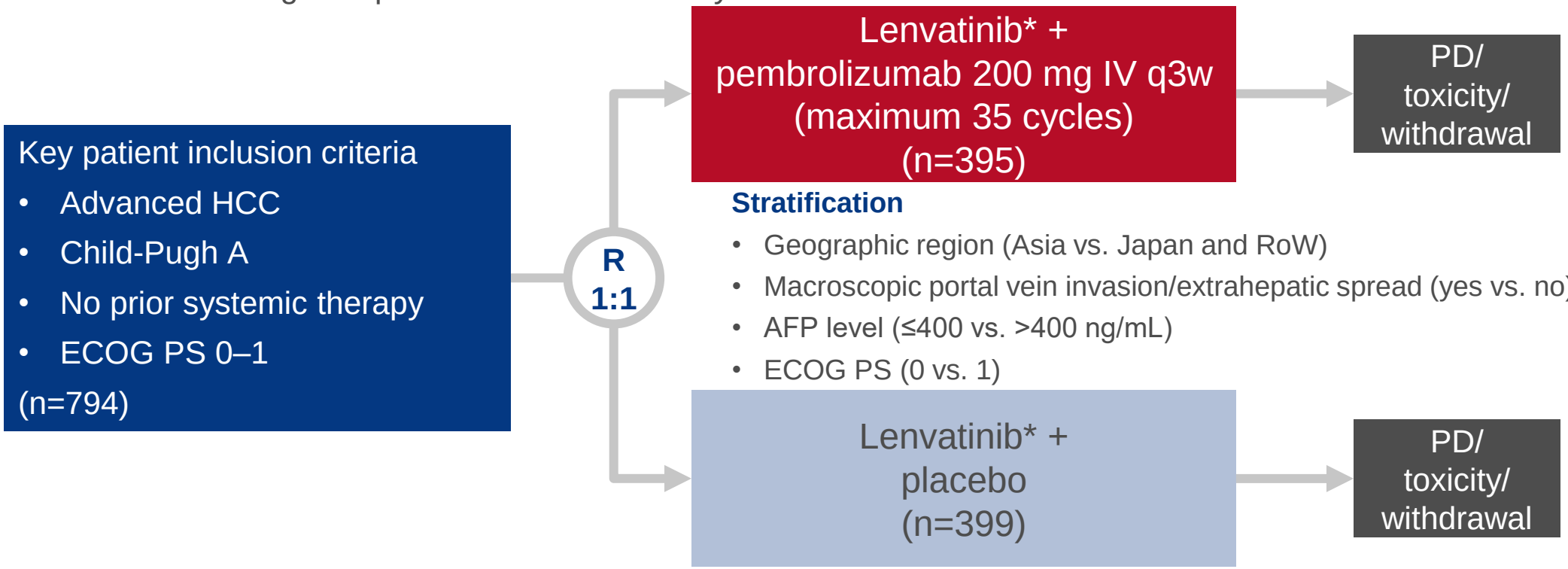
- **In patients with previously untreated advanced HCC, cabozantinib + atezolizumab demonstrated clinical activity with a manageable safety profile, while in previously treated patients with gastric or GEJ adenocarcinoma there was minimal clinical activity with cabozantinib + atezolizumab**

Li D, et al. Ann Oncol 2022;33(suppl):abstr PD-7

LBA34: Primary results from the phase 3 LEAP-002 study: lenvatinib plus pembrolizumab versus lenvatinib as first-line (1L) therapy for advanced hepatocellular carcinoma (aHCC) – Finn RS, et al

Study objective

- To evaluate the efficacy and safety of 1L lenvatinib + pembrolizumab compared with lenvatinib alone in patients with advanced HCC in the global phase 3 LEAP-002 study



PRIMARY ENDPOINTS

- OS, PFS

SECONDARY ENDPOINTS

- ORR, DoR, safety

*8 mg/day if body weight <60 kg or 12 mg/day if body weight ≥60 kg

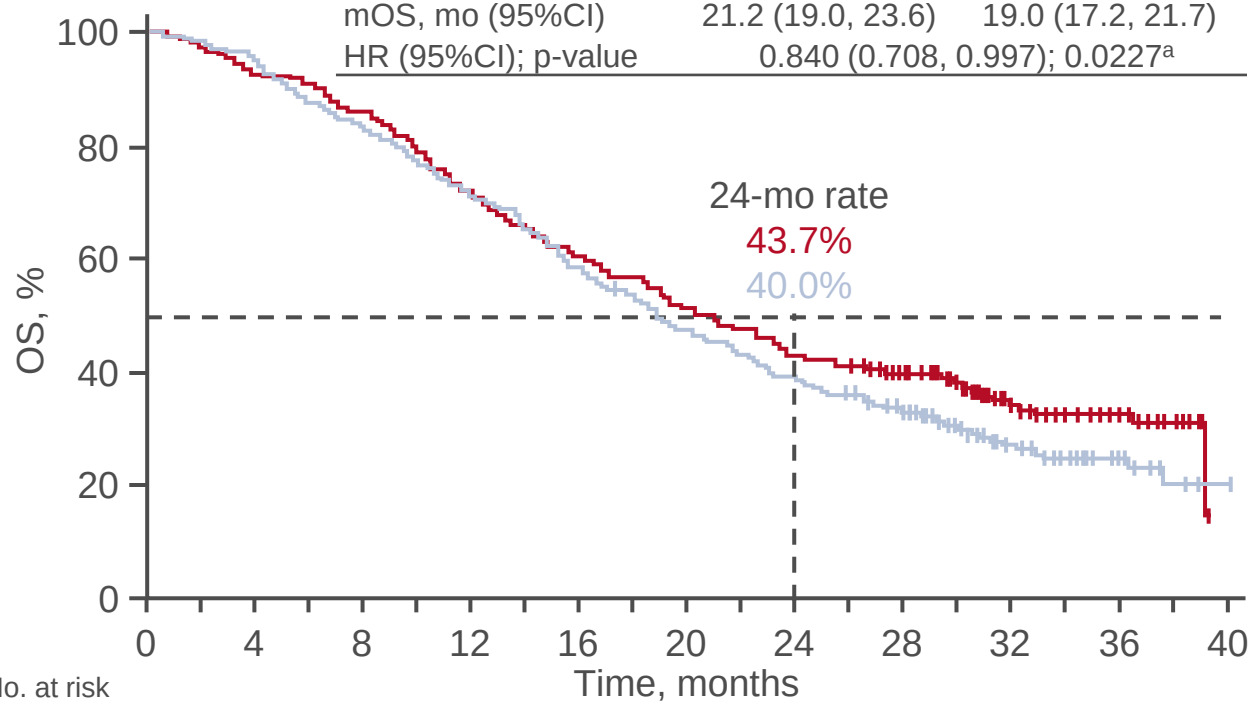
Presented at ESMO Congress 2022
Finn RS, et al. Ann Oncol 2022;33(suppl):abstr LBA34

LBA34: Primary results from the phase 3 LEAP-002 study: lenvatinib plus pembrolizumab versus lenvatinib as first-line (1L) therapy for advanced hepatocellular carcinoma (aHCC) – Finn RS, et al

Key results

Overall survival

	Lenvatinib + pembrolizumab	Lenvatinib + placebo
Events, n	252	282
mOS, mo (95%CI)	21.2 (19.0, 23.6)	19.0 (17.2, 21.7)
HR (95%CI); p-value	0.840 (0.708, 0.997); 0.0227[a]	



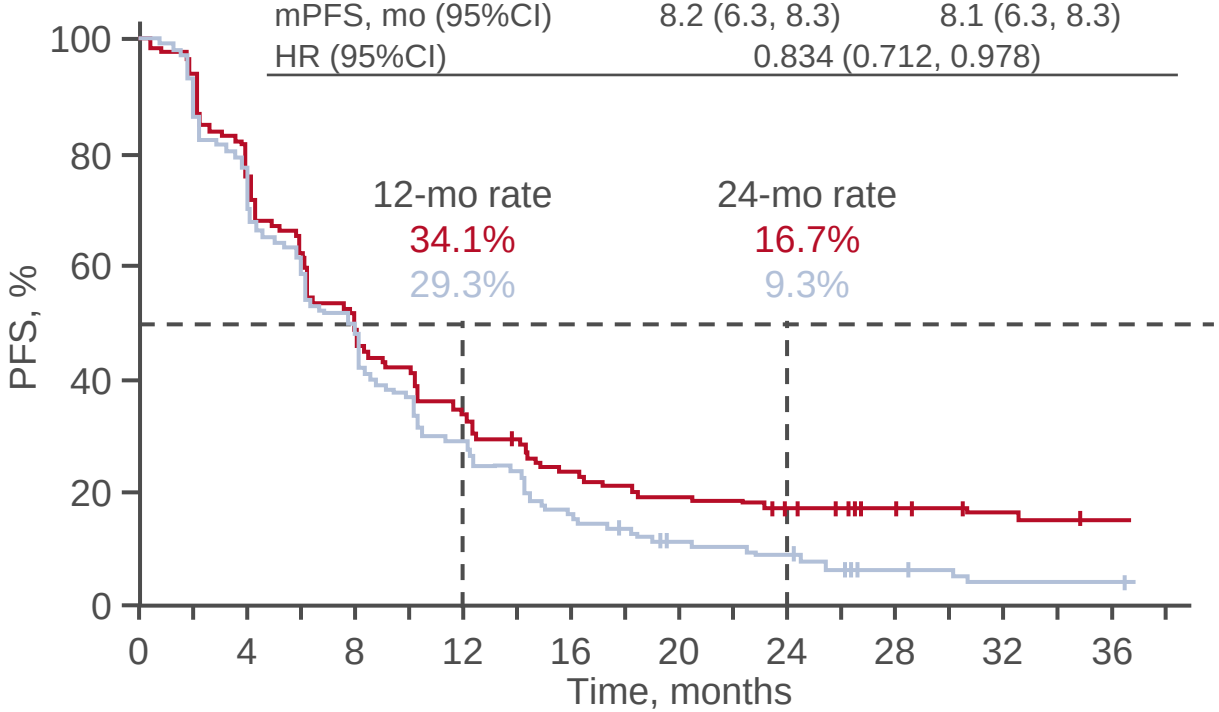
No. at risk

Len + pem	395	382	365	357	337	313	284	257	238	225	204	190	171	165	142	108	74	51	29	10	0
Len + PBO	399	389	378	349	330	308	282	261	234	215	191	173	158	142	119	82	53	35	17	6	1

[a]Did not reach superiority threshold of one-sided α=0.0185

Progression-free survival (final analysis)

	Lenvatinib + pembrolizumab	Lenvatinib + placebo
Events, n	293	336
mPFS, mo (95%CI)	8.2 (6.3, 8.3)	8.1 (6.3, 8.3)
HR (95%CI)	0.834 (0.712, 0.978)	



Len + pem	395	358	290	228	179	137	112	91	72	64	56	53	48	44	37	26	15	7	1	0	
Len + PBO	399	363	294	233	184	132	101	83	57	45	33	31	25	17	13	7	2	2	2	0	

Finn RS, et al. Ann Oncol 2022;33(suppl):abstr LBA34

LBA34: Primary results from the phase 3 LEAP-002 study: lenvatinib plus pembrolizumab versus lenvatinib as first-line (1L) therapy for advanced hepatocellular carcinoma (aHCC) – Finn RS, et al

Key results

	Lenvatinib + pembrolizumab	Lenvatinib + placebo
ORR, %	26.1	17.5
BOR, %		
CR	1.5	1.5
SD	55.2	60.9
PD	12.2	15.0
DCR, %	81.3	78.4
mDoR, mo (range)	16.6 (2.0+ to 33.6+)	10.4 (1.9 to 35.1+)

TRAEs, n (%)	Lenvatinib + pembrolizumab (n=395)	Lenvatinib + placebo (n=395)
Any	381 (96.5)	378 (95.7)
Grade 3–4	243 (61.5)	224 (56.7)
Grade 5	4 (1.0)	3 (0.8)
Led to discontinuation of any treatment	71 (18.0)	42 (10.6)
Led to discontinuation of both treatments	22 (5.6)	18 (4.6)

Conclusions

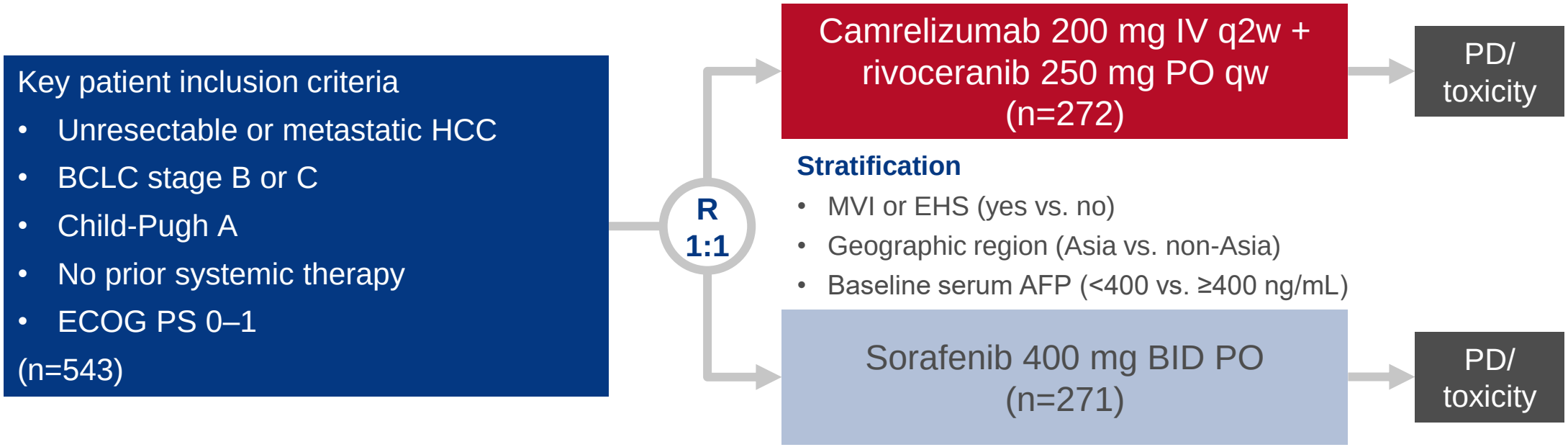
- **In patients with advanced HCC, 1L lenvatinib + pembrolizumab did not provide a significant improvement in OS over lenvatinib alone, although was generally well-tolerated with no new safety signals**

Finn RS, et al. Ann Oncol 2022;33(suppl):abstr LBA34

LBA35: Camrelizumab (C) plus rivoceranib (R) vs. sorafenib (S) as first-line therapy for unresectable hepatocellular carcinoma (uHCC): a randomized, phase III trial – Qin S, et al

Study objective

- To evaluate the efficacy and safety of 1L camrelizumab (an anti-PD-1) + rivoceranib (an anti-VEGFR2-targeted TKI) in patients with unresectable HCC in a global phase 3 study



PRIMARY ENDPOINTS

- PFS, OS

SECONDARY ENDPOINTS

- ORR, safety

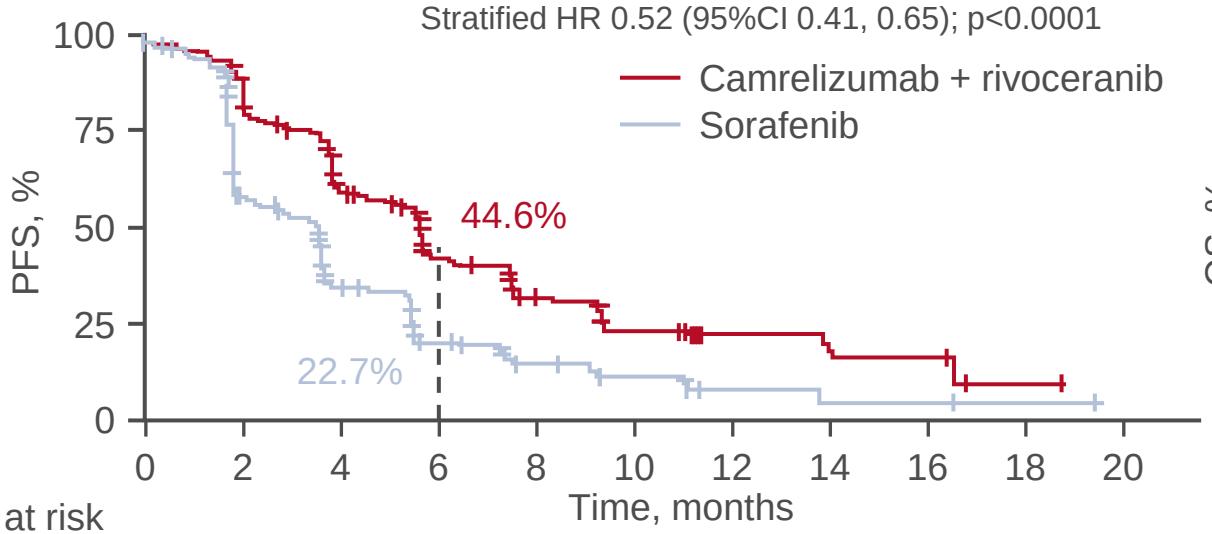
Presented at ESMO Congress 2022
Qin S, et al. Ann Oncol 2022;33(suppl):abstr LBA35

LBA35: Camrelizumab (C) plus rivoceranib (R) vs. sorafenib (S) as first-line therapy for unresectable hepatocellular carcinoma (uHCC): a randomized, phase III trial – Qin S, et al

Key results

Progression-free survival

	Camrelizumab + rivoceranib	Sorafenib
Events, n (%)	158 (58.1)	181 (66.8)
mPFS, mo (95%CI)	5.6 (5.5, 6.3)	3.7 (2.8, 3.7)

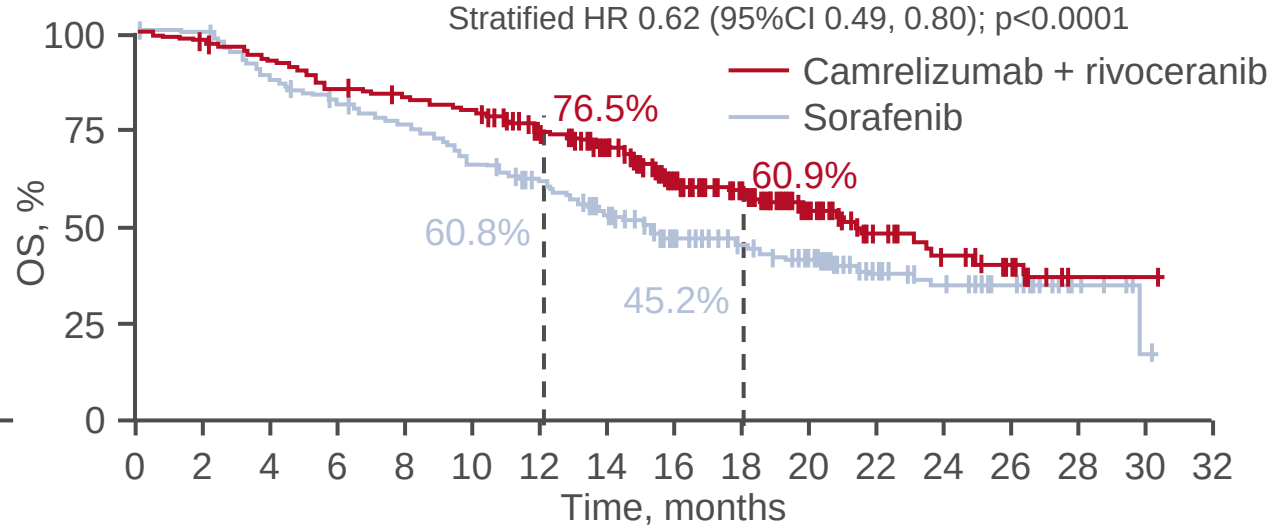


No. at risk

Camrel + rivo	272	197	131	79	50	27	12	9	9	1	0
Sorafenib	271	138	71	34	18	10	3	2	2	1	0

Overall survival

	Camrelizumab + rivoceranib	Sorafenib
Events, n (%)	111 (40.8)	151 (55.7)
mOS, mo (95%CI)	22.1 (19.1, 27.2)	15.2 (13.0, 18.5)



No. at risk

Camrel + rivo	272	265	250	231	224	215	190	165	118	80	57	34	25	18	5	1	0
Sorafenib	271	268	232	214	198	171	149	124	91	70	53	31	22	17	5	1	0

Qin S, et al. Ann Oncol 2022;33(suppl):abstr LBA35

LBA35: Camrelizumab (C) plus rivoceranib (R) vs. sorafenib (S) as first-line therapy for unresectable hepatocellular carcinoma (uHCC): a randomized, phase III trial – Qin S, et al

Key results

	Camrelizumab + rivoceranib (n=272)	Sorafenib (n=271)
ORR, % (95%CI)	25.4 (20.3, 31.0)	5.9 (3.4, 9.4)
p-value	<0.001	
BOR, n (%)		
CR	3 (1.1)	1 (0.4)
PR	66 (24.3)	15 (5.5)
SD	144 (52.9)	130 (48.0)
PD	44 (16.2)	99 (36.5)
NE	15 (5.5)	26 (9.6)
mDoR, mo (95%Ci)	14.8 (8.4, NR)	9.2 (5.3, NR)
mTTR, mo (range)	1.9 (1.7, 13.9)	3.7 (1.8, 11.1)
DCR, % (95%CI)	78.3 (72.9, 83.1)	53.9 (47.7, 59.9)
mTTP, mo (95%CI)	7.2 (5.6, 8.2)	3.7 (3.6, 3.7)

TRAEs, n (%)	Camrelizumab + rivoceranib (n=272)	Sorafenib (n=269)
Any	265 (97.4)	249 (92.6)
Grade 3–4	219 (80.5)	140 (52.0)
Grade 5	1 (0.4)	1 (0.4)
Serious	66 (24.3)	16 (5.9)
Led to dose modification or interruption	219 (80.5)	135 (50.2)
Led to discontinuation of any component	66 (24.3)	12 (4.5)
Led to discontinuation of all components	10 (3.7)	12 (4.5)

Conclusions

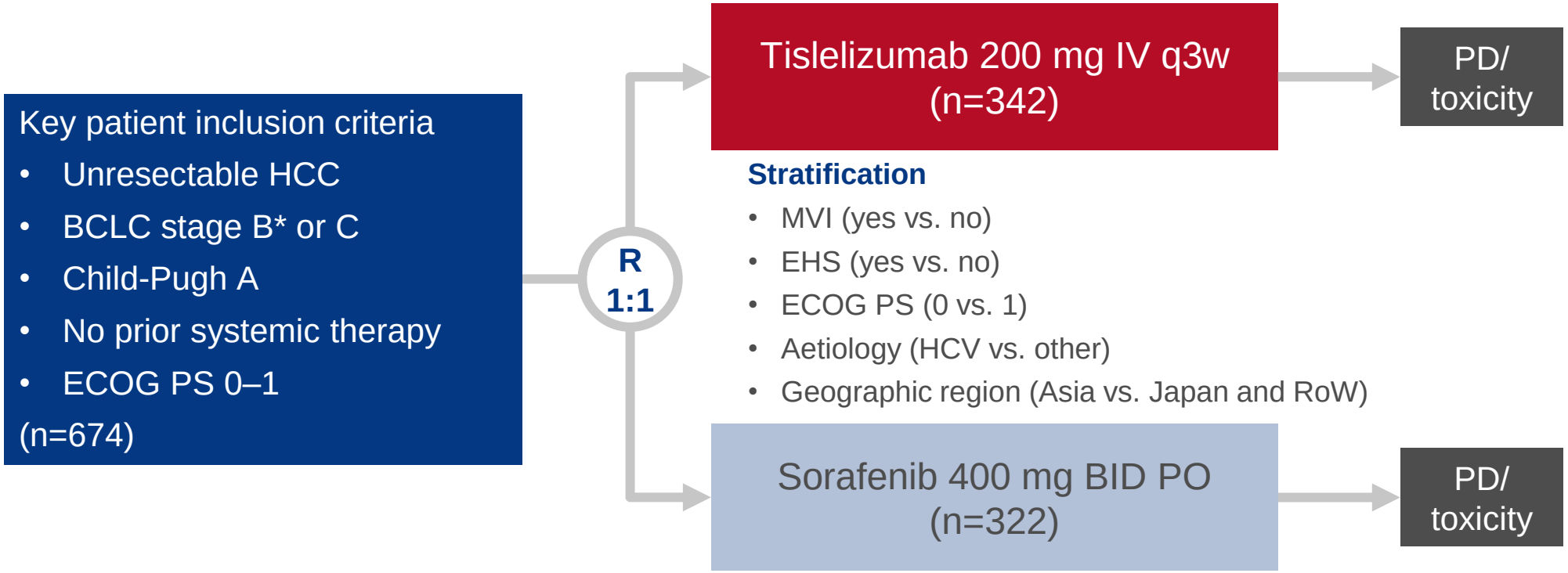
- **In patients with unresectable HCC, camrelizumab + rivoceranib demonstrated significant improvement in survival and responses over sorafenib and was generally well-tolerated**

Qin S, et al. Ann Oncol 2022;33(suppl):abstr LBA35

LBA36: Final analysis of RATIONALE-301: Randomized, phase 3 study of tislelizumab versus sorafenib as first-line treatment for unresectable hepatocellular carcinoma – Kudo M, et al

Study objective

- To evaluate the final efficacy and safety of 1L tislelizumab in patients with unresectable HCC in the global phase 3 RATIONALE-301 study



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- ORR, OFS, DoR, safety

*Not amenable to or progressed after locoregional therapy

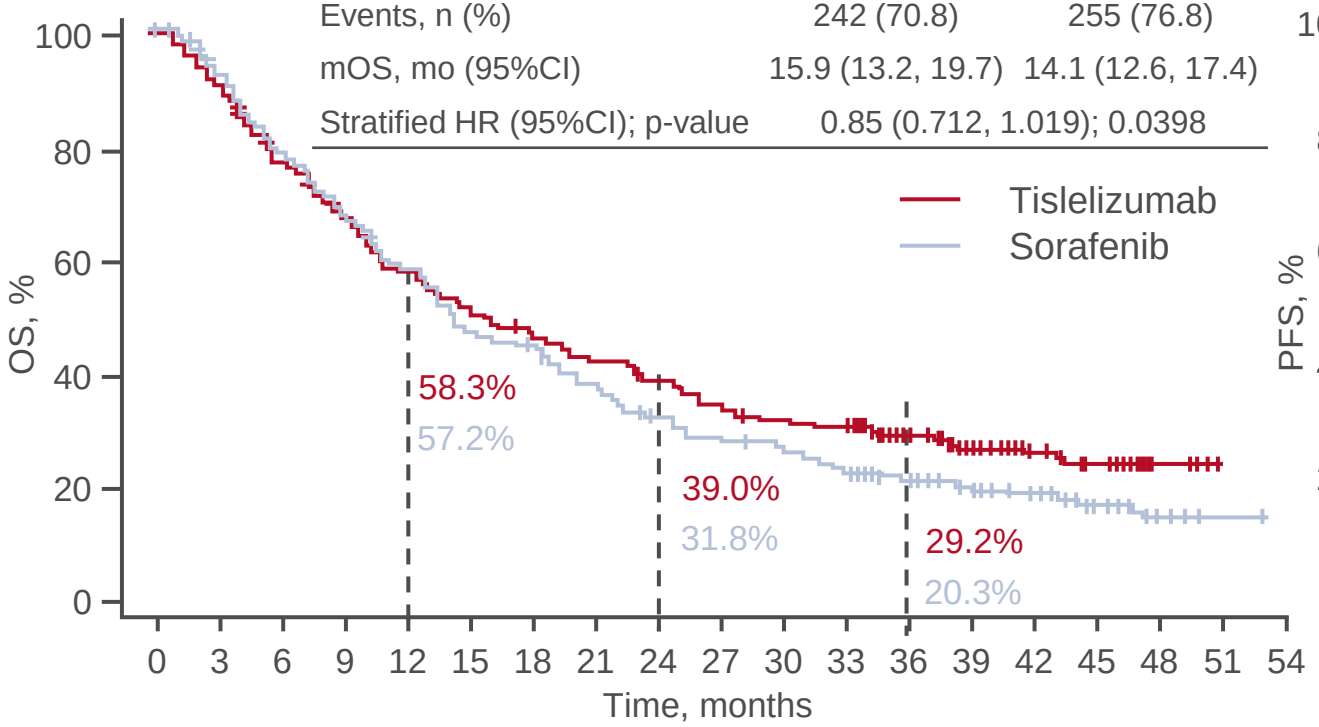
Presented at ESMO Congress 2022
Kudo M, et al. Ann Oncol 2022;33(suppl):abstr LBA36

LBA36: Final analysis of RATIONALE-301: Randomized, phase 3 study of tislelizumab versus sorafenib as first-line treatment for unresectable hepatocellular carcinoma – Kudo M, et al

Key results

Overall survival

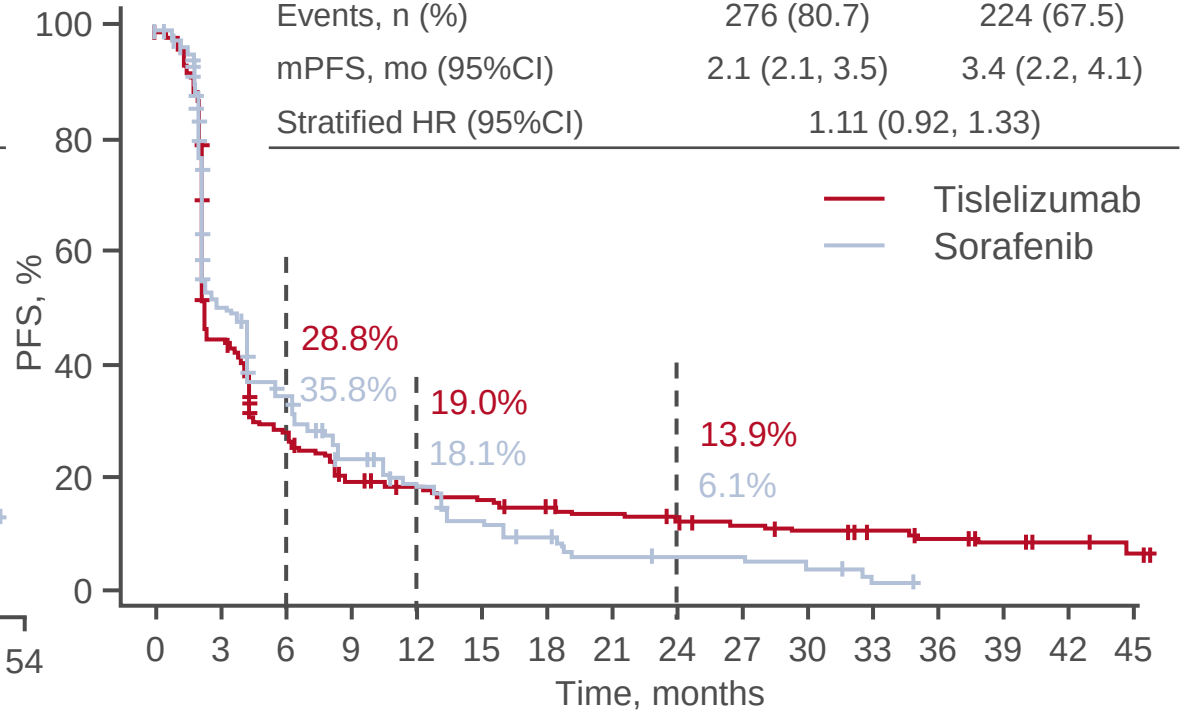
	Tislelizumab (n=342)	Sorafenib (n=332)
Events, n (%)	242 (70.8)	255 (76.8)
mOS, mo (95%CI)	15.9 (13.2, 19.7)	14.1 (12.6, 17.4)
Stratified HR (95%CI); p-value	0.85 (0.712, 1.019); 0.0398	



Tislelizumab	342	307	259	228	191	170	155	137	126	111	101	98	77	53	33	18	4	0	0
Sorafenib	332	291	247	208	179	147	136	113	96	84	77	66	52	39	29	13	4	1	0

Progression-free survival

	Tislelizumab (n=342)	Sorafenib (n=332)
Events, n (%)	276 (80.7)	224 (67.5)
mPFS, mo (95%CI)	2.1 (2.1, 3.5)	3.4 (2.2, 4.1)
Stratified HR (95%CI)	1.11 (0.92, 1.33)	



Tislelizumab	342	145	79	54	47	41	38	32	30	25	22	19	16	11	7	4				
Sorafenib	332	125	80	38	26	17	12	7	6	5	4	1	0	0	0	0				

Kudo M, et al. Ann Oncol 2022;33(suppl):abstr LBA36

LBA36: Final analysis of RATIONALE-301: Randomized, phase 3 study of tislelizumab versus sorafenib as first-line treatment for unresectable hepatocellular carcinoma – Kudo M, et al

Key results

	Tislelizumab (n=342)	Sorafenib (n=332)
ORR, n (%) [95%CI]	49 (14.3) [10.8, 18.5]	18 (5.4) [3.2, 8.4]
BOR, n (%)		
CR	10 (2.9)	1 (0.3)
PR	39 (11.4)	17 (5.1)
SD	94 (27.5)	139 (41.9)
PD	169 (49.4)	121 (36.4)
NE	22 (6.4)	44 (13.3)
Non-CR/non-PD	8 (2.3)	10 (3.0)
Responders, n	49	18
mDoR, mo (95%CI)	36.1 (16.8, NE)	11.0 (6.2, 14.7)
Ongoing response, n/N (%)	20/28 (71.4)	2/5 (40.0)

TRAEs, n (%)	Tislelizumab (n=338)	Sorafenib (n=324)
Any	259 (76.6)	311 (96.0)
Grade ≥3	75 (22.2)	173 (53.4)
Serious	40 (11.8)	33 (10.2)
Led to modification	68 (20.1)	187 (57.7)
Led to discontinuation	21 (6.2)	33 (10.2)
Led to death	3 (0.9)	2 (0.6)
ir-AEs	58 (17.2)	10 (3.1)
ir-AEs treated with systemic corticosteroids	43 (12.7)	10 (3.1)
ir-AEs occurring in ≥5%		
Hepatitis	18 (5.3)	1 (0.3)
Hypothyroidism	18 (5.3)	0

Conclusions

- **In patients with unresectable HCC, 1L tislelizumab demonstrated non-inferiority in OS to sorafenib with higher response rates and more durable responses as well as an acceptable safety profile**

Kudo M, et al. Ann Oncol 2022;33(suppl):abstr LBA36

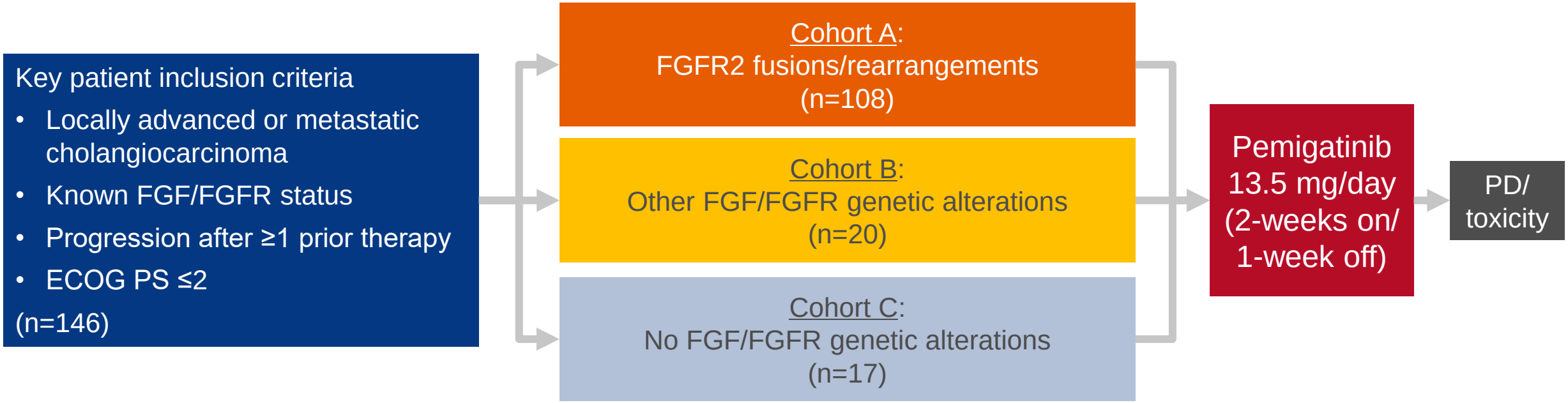
Cancers of the pancreas, small bowel and hepatobiliary tract

GALLBLADDER CANCER

O-2: Pemigatinib for previously treated locally advanced or metastatic cholangiocarcinoma: final results from FIGHT-202 – Vogel A, et al

Study objective

- To evaluate the updated efficacy and safety of pemigatinib, an FGFR1, 2 and 3 inhibitor, in previously treated patients with locally advanced or metastatic cholangiocarcinoma and FGFR2 fusions or rearrangements in the phase 2 FIGHT-202 study



PRIMARY ENDPOINT

- ORR

SECONDARY ENDPOINTS

- DoR, DCR, PFS, OS, safety

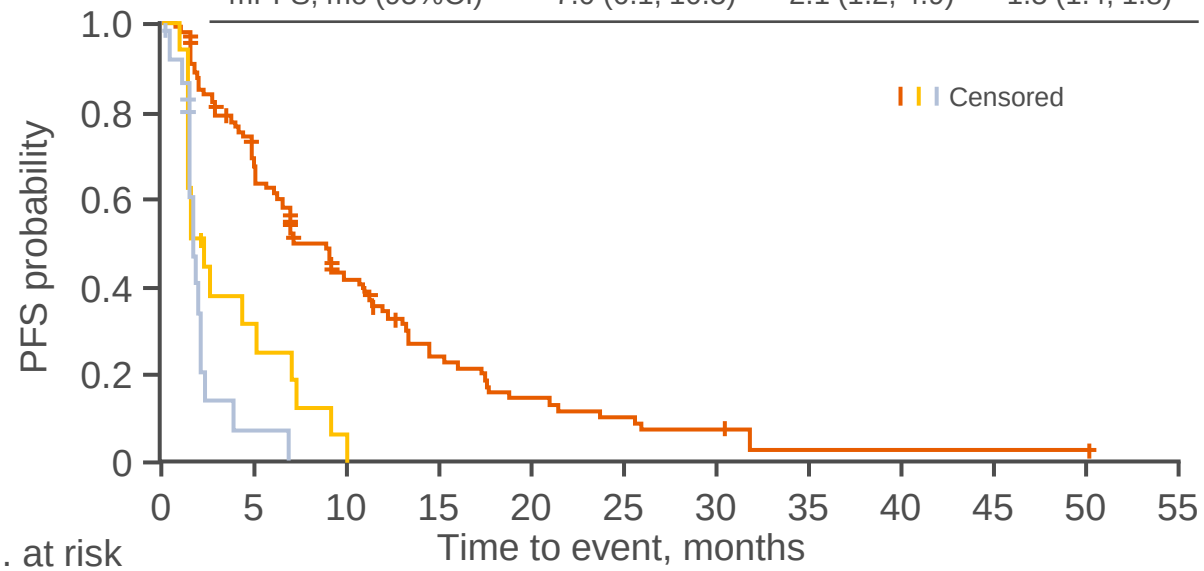
Presented at ESMO WCGC 2022
Vogel R, et al. Ann Oncol 2022;33(suppl):abstr O-2

O-2: Pemigatinib for previously treated locally advanced or metastatic cholangiocarcinoma: final results from FIGHT-202 – Vogel A, et al

Key results

Progression-free survival

	Cohort A	Cohort B	Cohort C
Evaluable patients, n	108	20	17
Events, n (%)	85 (78.7)	17 (85.0)	15 (88.2)
Censored, n (%)	23 (21.3)	3 (15.0)	2 (11.8)
mPFS, mo (95%CI)	7.0 (6.1, 10.5)	2.1 (1.2, 4.9)	1.5 (1.4, 1.8)

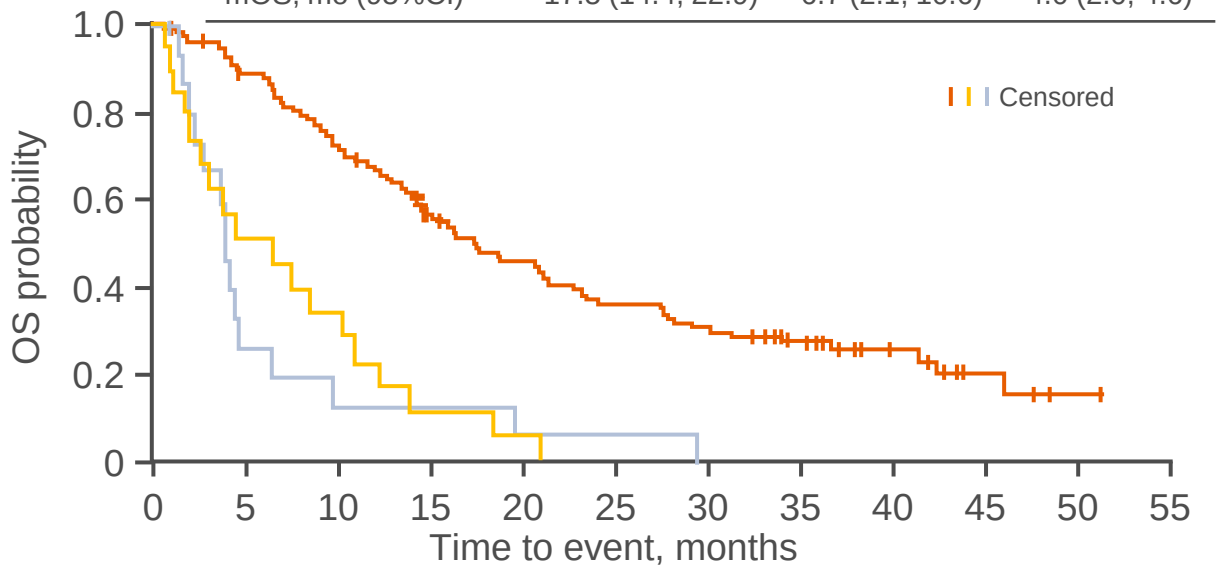


No. at risk

Cohort A	108	63	34	17	10	7	5	1	1	1	1	0
Cohort B	20	4	0									
Cohort C	17	1	0									

Overall survival

	Cohort A	Cohort B	Cohort C
Evaluable patients, n	108	20	17
Events, n (%)	76 (70.4)	18 (90.0)	15 (88.2)
Censored, n (%)	32 (29.6)	2 (10.0)	2 (11.8)
mOS, mo (95%CI)	17.5 (14.4, 22.9)	6.7 (2.1, 10.6)	4.0 (2.0, 4.6)



Cohort A	108	93	75	55	43	34	29	20	12	4	1	0
Cohort B	20	9	6	2	1	0						
Cohort C	17	4	2	2	1	1	0					

Vogel R, et al. Ann Oncol 2022;33(suppl):abstr O-2

O-2: Pemigatinib for previously treated locally advanced or metastatic cholangiocarcinoma: final results from FIGHT-202 – Vogel A, et al

Key results

Outcomes	Cohort A (n=108)	Cohort B (n=20)	Cohort C (n=17)
ORR, % (95%CI)	37 (28, 47)	0 (0 ,17)	0 (0, 20)
BOR, %			
CR	3	0	0
PR	34	0	0
SD	45	40	18
PD	15	35	65
NE	3	25	18
DCR, % (95%CI)	82 (74, 89)	40 (19, 64)	18 (4, 43)
mDoR, mo (95%CI)	9.1 (6.0, 14.5)	-	-

Grade ≥3 TEAEs, %	Cohort A (n=108)	Cohort B (n=20)	Cohort C (n=17)
Any	67	75	76
Diarrhea	4	0	6
Fatigue	5	0	18
Nausea	3	0	0
Stomatitis	9	0	0
Constipation	1	0	0
Appetite decreased	1	5	6
Arthralgia	6	10	0
Vomiting	2	0	0
Dry eye	0	0	0

Conclusions

- **In previously treated patients with locally advanced or metastatic cholangiocarcinoma and FGFR2 fusions or rearrangements, pemigatinib continued to show durable responses and improved survival with a manageable safety profile**

Vogel R, et al. Ann Oncol 2022;33(suppl):abstr O-2

SO-3: Gene mutational profile of BRCAness and clinical implication in predicting response to platinum-based chemotherapy in patients with intrahepatic-cholangiocarcinoma – Rimini M, et al

Study objective

- To evaluate the use of a gene mutational profile for predicting response to platinum-based chemotherapy in patients with intrahepatic cholangiocarcinoma and BRCAness*

Methods

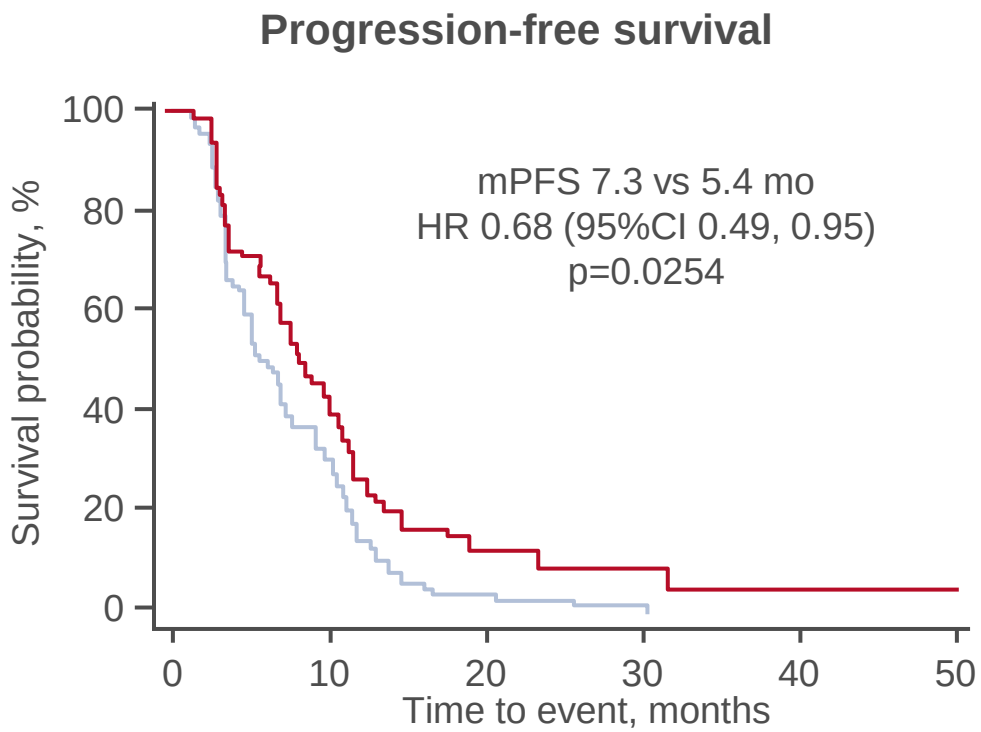
- Data for patients with unresectable locally advanced or metastatic biliary tract cancer (n=150) who were receiving platinum-based chemotherapy at 6 institutions in Italy and Spain were assessed to determine the association between BRCAness and survival outcomes as well as undergoing a comparative genomic analysis

*At least one alteration in: ATM, BAP1, BARD1, BLM, BRCA1, BRCA2, BRIP1, CHEK2, FAM175A, FANGA, FANCC, NBN, PALB2, RAD50, RAD51, RAD51C, RETL1, ARID1A, ATR, ATRX, CHEK1, RAD51L1, RAD51L3

Presented at ESMO WCGC 2022
Rimini M, et al. Ann Oncol 2022;33(suppl):abstr SO-3

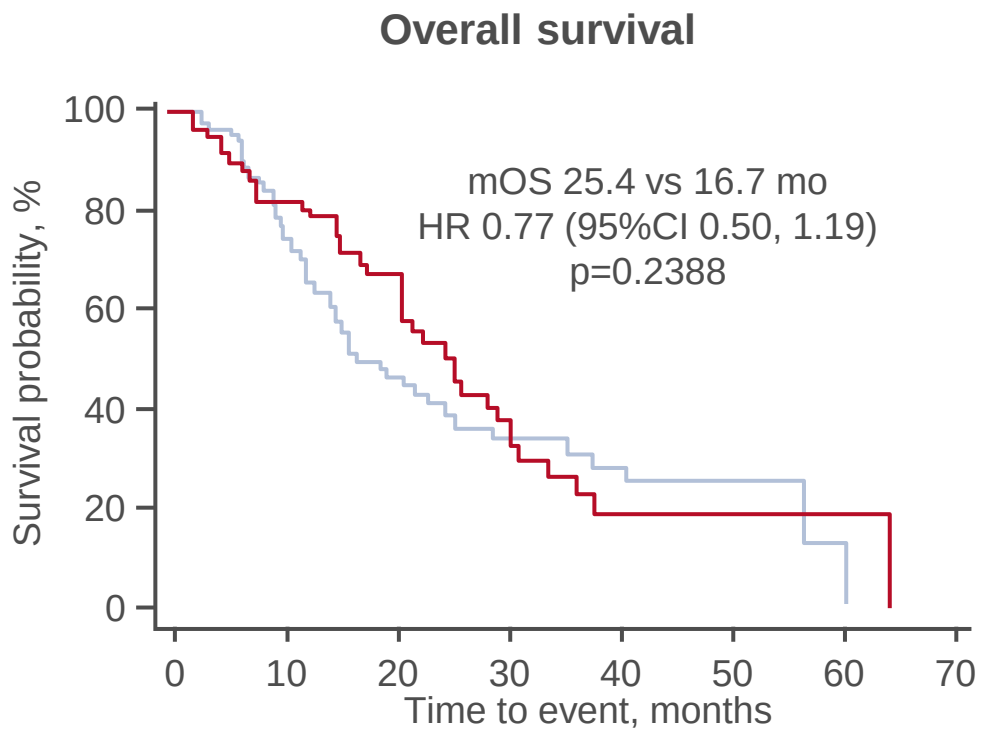
SO-3: Gene mutational profile of BRCAness and clinical implication in predicting response to platinum-based chemotherapy in patients with intrahepatic-cholangiocarcinoma – Rimini M, et al

Key results



No. at risk

WT	92	23	3	0	0	0
Mutated	80	25	4	3	1	0



No. at risk

WT	92	61	28	13	10	5	2	0
Mutated	80	60	30	14	4	1	1	0

Rimini M, et al. Ann Oncol 2022;33(suppl):abstr SO-3

SO-3: Gene mutational profile of BRCAness and clinical implication in predicting response to platinum-based chemotherapy in patients with intrahepatic-cholangiocarcinoma – Rimini M, et al

Key results

Clinical outcomes in patients with BRCAness who received PARP inhibitors							
Stage at diagnosis	Gene mutated	Still alive	OS from diagnosis, mo	OS from olaparib, mo	PFS, mo	Ongoing PARPi	Response to platin
II	BRCA2	No	44.8	2.4	0.5	No	Yes
III	ATM	No	55.3	11.4	10.3	No	Yes
IV	PALB2	No	28.1	4.0	3.2	No	Yes

Conclusions

- **In patients with intrahepatic cholangiocarcinoma treated with platinum-based chemotherapy, those with BRCAness appeared to have better PFS and a trend to better OS than those with BRCAness WT**

Rimini M, et al. Ann Oncol 2022;33(suppl):abstr SO-3

52MO: A randomized phase II trial of durvalumab and tremelIMUmab with gemcitabine or gemcitabine and cisplatin compared to gemcitabine and cisplatin in treatment-naïve patients with CHolangio- and gallbladdEr Carcinoma (IMMUCHEC) – Vogel A, et al

Study objective

- To evaluate the efficacy and safety of 1L durvalumab + tremelimumab + gemcitabine ± cisplatin in patients with cholangiocarcinoma or gallbladder carcinoma in German centres in the phase 2 IMMUCHEC study

Key patient inclusion criteria

- Advanced, unresectable and/or metastatic cholangio- or gallbladder carcinoma
- No prior therapy
- ECOG PS 0–1

(n=138)

Part A

R 1:1:1

- **Arm A**: Durvalumab 1.5 g q3w + 4x tremelimumab 75 mg q3w + gemcitabine 1000 mg/m^2 (n=22)
- **Arm B**: Durvalumab 1.5 g q3w + 4x tremelimumab 75 mg q3w + gemcitabine 1000 mg/m^2 + cisplatin 25 mg/m^2 (n=22)
- **Arm C**: Gemcitabine 1000 mg/m^2 + cisplatin 25 mg/m^2 (n=21)

Part B

R 1:2:2

- **Arm C**: Gemcitabine 1000 mg/m^2 + cisplatin 25 mg/m^2 (n=13)
- **Arm D**: Durvalumab 1.5 g q3w 1x bolus + tremelimumab 300 mg + gemcitabine 1000 mg/m^2 + cisplatin 25 mg/m^2 (n=30)
- **Arm E**: Durvalumab 1.5 g q3w + gemcitabine 1000 mg/m^2 + cisplatin 25 mg/m^2 (n=28)

PRIMARY ENDPOINT

- ORR (RECIST v1.1)

SECONDARY ENDPOINTS

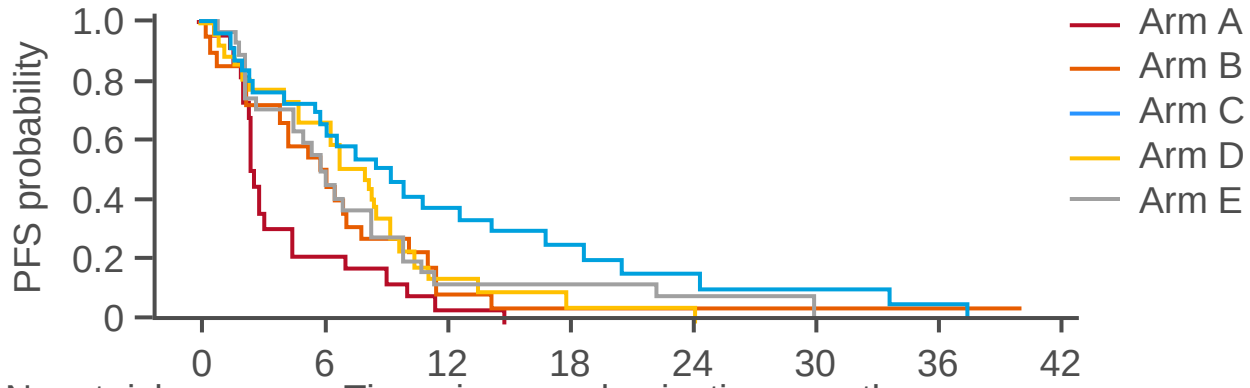
- OS, PFS, DoR, safety

Presented at ESMO Congress 2022
Vogel A, et al. Ann Oncol 2022;33(suppl):abstr 52MO

52MO: A randomized phase II trial of durvalumab and tremelIMUmab with gemcitabine or gemcitabine and cisplatin compared to gemcitabine and cisplatin in treatment-naïve patients with CHolangio- and gallbladdEr Carcinoma (IMMUCHEC) – Vogel A, et al

Key results

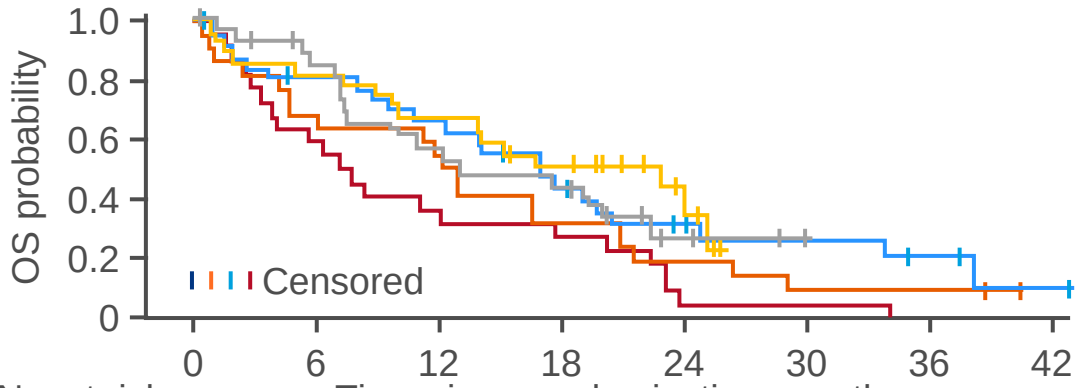
Progression-free survival



No. at risk

Arm A	22	5	1	0				
Arm B	22	11	2	1	1	1	1	0
Arm C	30	18	9	6	3	2	1	0
Arm D	27	18	3	1	1	0		
Arm E	27	12	3	3	1	0		

Overall survival



No. at risk

Arm A	22	13	7	6	1	1	0	
Arm B	22	14	12	7	4	2	2	0
Arm C	35	23	19	11	6	5	3	1
Arm D	30	22	18	13	6	0		
Arm E	29	22	12	10	3	0		

ITT	Arm A: Tremx4/Durv/Gem (n=22)	Arm B: Tremx4/Durv/Cis/Gem (n=22)	Arm C: Cis/Gem (n=35)	Arm D: Tremx1/Durv/Cis/Gem (n=30)	Arm E: Durv/Cis/Gem (n=29)
mPFS, mo (95%CI)	2.75 (2.23, 4.50)	5.98 (2.63, 7.93)	8.70 (5.73, 14.33)	8.13 (4.60, 9.33)	5.97 (2.80, 8.43)
mOS, mo (95%CI)	7.38 (3.20, 17.57)	12.32 (4.53, 20.83)	16.93 (9.37, 20.70)	22.73 (9.53, 25.10)	12.87 (7.20, 22.13)

Vogel A, et al. Ann Oncol 2022;33(suppl):abstr 52MO

52MO: A randomized phase II trial of durvalumab and tremelIMUmab with gemcitabine or gemcitabine and cisplatin compared to gemcitabine and cisplatin in treatment-naïve patients with CHolangio- and gallbladdEr Carcinoma (IMMUCHEC) – Vogel A, et al

Key results

Outcomes	Arm A (n=22)	Arm B (n=22)	Arm C (n=35)	Arm D (n=30)	Arm E (n=29)
ORR, % (95%CI)	4.6 (0, 0.28)	18.2 (0.05, 0.04)	28.6 (0.15, 0.46)	26.7 (0.12, 0.46)	20.7 (0.08, 0.40)
BOR, n (%)					
CR	0	1 (4.5)	1 (2.9)	0	0
PR	1 (4.5)	3 (13.6)	9 (25.7)	8 (26.7)	6 (20.7)
SD	7 (31.8)	11 (50.0)	13 (37.1)	13 (43.3)	13 (44.8)
PD	9 (40.9)	3 (13.6)	2 (5.7)	3 (10.0)	6 (20.7)
NE	5 (22.7)	4 (18.2)	10 (28.6)	6 (20.0)	4 (13.8)
mDoR, mo	2.20	7.18	6.07	6.78	NR

AEs	Arm A (n=23)	Arm B (n=20)	Arm C (n=30)	Arm D (n=29)	Arm E (n=27)
Any, n	236	239	310	273	228
TRAEs, n	108	121	146	153	124
Grade ≥3 TRAEs, n	20	24	35	34	30
Patients with grade ≥3 TRAEs, n (%)	12 (52.5)	14 (70.0)	15 (50.0)	16 (55.2)	12 (44.4)
Patients with TRAE led to death, n (%)	2 (8.7)	1 (5.0)	1 (3.3)	1 (3.4)	1 (3.7)

Conclusions

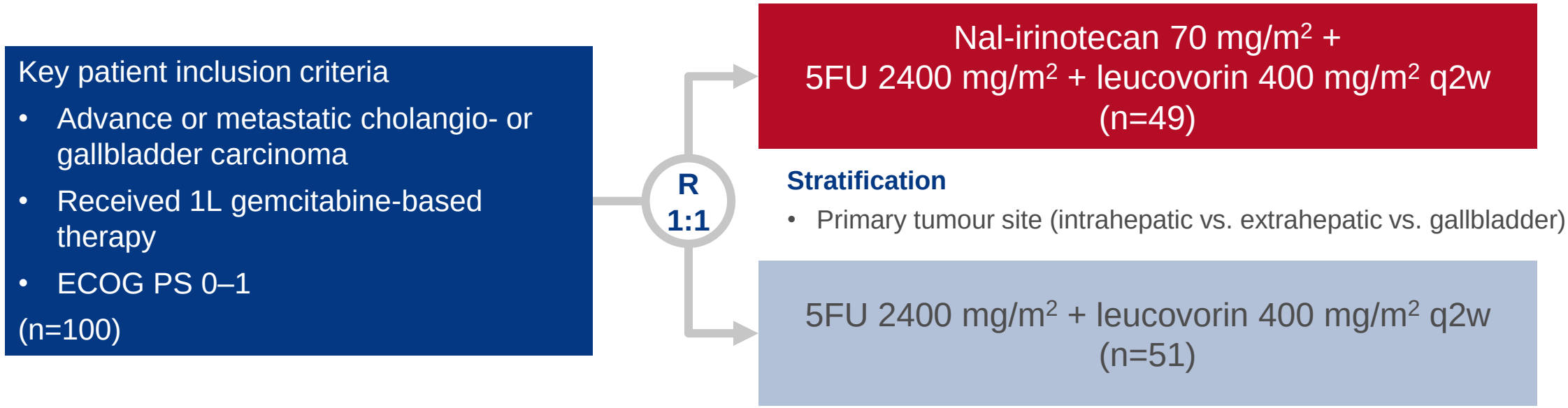
- **In patients with cholangiocarcinoma or gallbladder carcinoma, 1L durvalumab ± tremelimumab + gemcitabine ± cisplatin did not demonstrate a significant improvement in ORR compared with chemotherapy alone, although OS was numerically longer with durvalumab + tremelimumab + gemcitabine + cisplatin**

Vogel A, et al. Ann Oncol 2022;33(suppl):abstr 52MO

53MO: Nal-IRI and 5-FU/LV compared to 5-FU/LV in patients with cholangio- and gallbladder carcinoma previously treated with gemcitabine-based therapies (NALIRICC – AIO-HEP-0116) – Vogel A, et al

Study objective

- To evaluate the efficacy and safety of nal-irinotecan + 5FU/LV in previously treated patients with cholangiocarcinoma or gallbladder carcinoma in German centres in the phase 2 NALIRICC study



Stratification

- Primary tumour site (intrahepatic vs. extrahepatic vs. gallbladder)

PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

- OS, ORR, QoL, safety

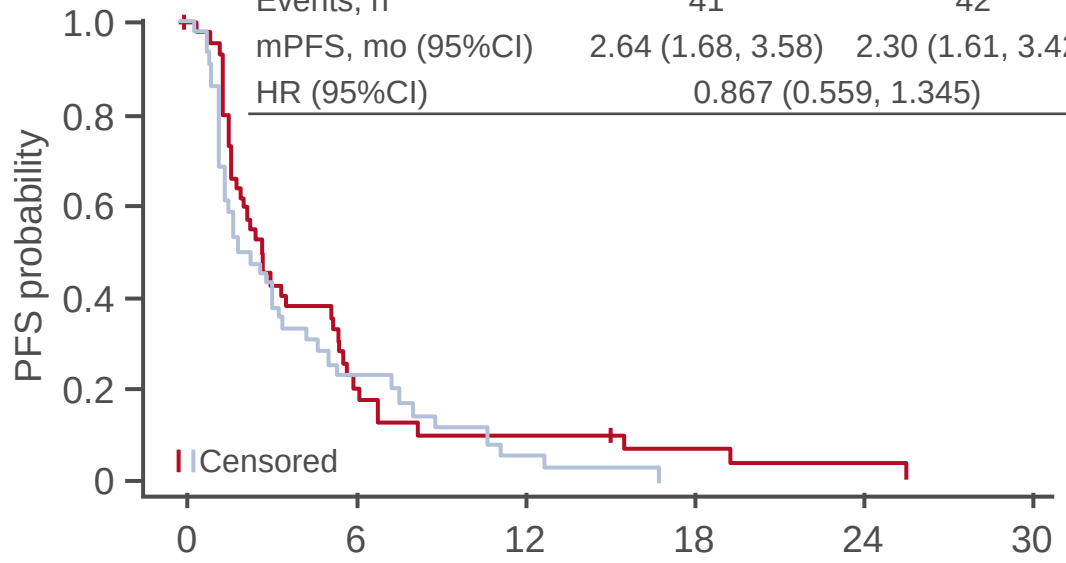
Presented at ESMO Congress 2022
Vogel A, et al. Ann Oncol 2022;33(suppl):abstr 53MO

53MO: Nal-IRI and 5-FU/LV compared to 5-FU/LV in patients with cholangio- and gallbladder carcinoma previously treated with gemcitabine-based therapies (NALIRICC – AIO-HEP-0116) – Vogel A, et al

Key results

Progression-free survival

	Nal-IRI + 5FU/LV	5FU/LV
Events, n	41	42
mPFS, mo (95%CI)	2.64 (1.68, 3.58)	2.30 (1.61, 3.42)
HR (95%CI)	0.867 (0.559, 1.345)	

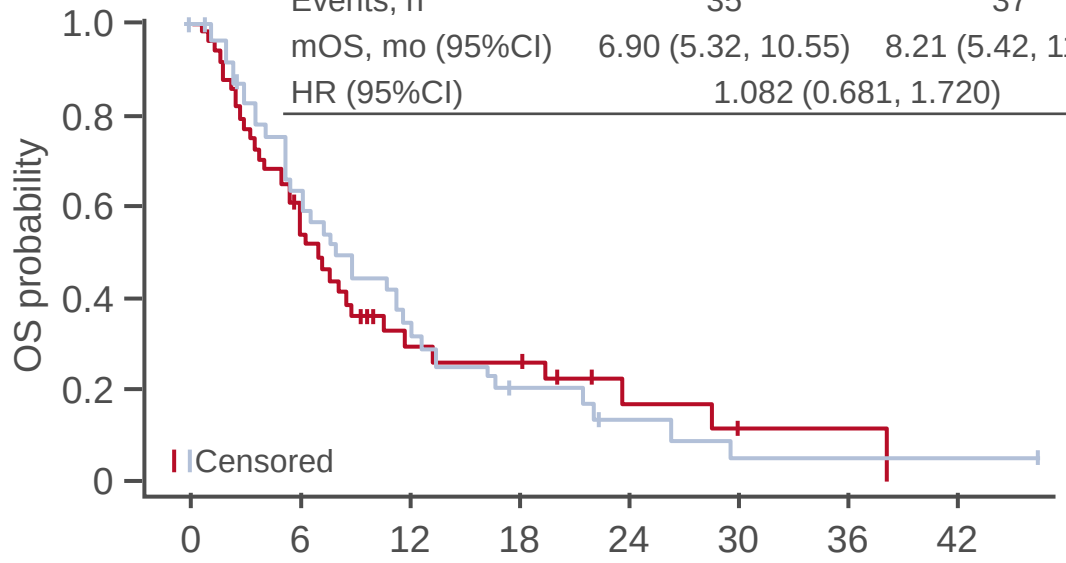


No. at risk

Nal-IRI + 5FU/LV	49	9	4	2	1	0
5FU/LV	51	8	2	0		

Overall survival

	Nal-IRI + 5FU/LV	5FU/LV
Events, n	35	37
mOS, mo (95%CI)	6.90 (5.32, 10.55)	8.21 (5.42, 11.89)
HR (95%CI)	1.082 (0.681, 1.720)	



Nal-IRI + 5FU/LV	49	22	9	7	3	2	1	0
5FU/LV	51	26	13	6	3	1	1	1

Outcomes, n (%)	CR	PR	SD	PD	NA	ORR	DCR
Nal-IRI + 5FU/LV (n=49)	1 (2.0)	6 (12.2)	18 (36.7)	12 (24.5)	12 (24.5)	7 (14.3)	25 (51.0)
5FU/LV (n=51)	1 (2.0)	1 (2.0)	21 (41.2)	20 (39.2)	8 (15.7)	2 (3.9)	23 (45.1)

Vogel A, et al. Ann Oncol 2022;33(suppl):abstr 53MO

53MO: Nal-IRI and 5-FU/LV compared to 5-FU/LV in patients with cholangio- and gallbladder carcinoma previously treated with gemcitabine-based therapies (NALIRICC – AIO-HEP-0116) – Vogel A, et al

Key results

	Nal-irinotecan + 5FU/LV	5FU/LV
mPFS, mo (95%CI)		
CES2 <37.29	3.45 (1.58, 5.82)	2.53 (0.85, 7.72)
CES2 ≥37.19	1.70 (1.41, 5.49)	1.61 (1.18, 11.34)
mOS, mo (95%CI)		
CES2 <37.29	4.42 (2.53, 13.37)	5.78 (2.17, 16.59)
CES2 ≥37.19	5.95 (1.68, 8.87)	21.82 (4.3, NR)

TRAEs, n (%)	Nal-irinotecan + 5FU/LV (n=48)	5FU/LV (n=48)
Any	293 (53.9)	127 (34.0)
Grade ≥3	24 (50.0)	3 (6.3)

Conclusions

- **In previously treated patients with cholangiocarcinoma or gallbladder carcinoma, nal-irinotecan + 5FU/LV did not significantly improve survival compared with 5FU/LV alone and had higher rates of toxicity**

Vogel A, et al. Ann Oncol 2022;33(suppl):abstr 53MO

Cancers of the pancreas, small bowel and hepatobiliary tract

NEUROENDOCRINE TUMOURS

496MO: Final overall survival results from the NICE-NEC trial (GETNE-T1913). A phase II study of nivolumab and platinum-doublet chemotherapy (CT) in untreated advanced G3 neuroendocrine neoplasms (NENs) of gastroenteropancreatic (GEP) or unknown (UK) origin – Riesco MC, et al

Study objective

- To evaluate the final efficacy and safety of 1L nivolumab + platinum-doublet chemotherapy in patients with unresectable, locally advanced or metastatic grade 3 neuroendocrine neoplasms of gastroenteropancreatic or unknown origin in Spanish centres in the NICE-NEC study

Key patient inclusion criteria

- Metastatic or unresectable grade 3 neuroendocrine neoplasms of gastroenteropancreatic or unknown origin
- Treatment naïve
- Ki67 >20%
- ECOG PS ≤2

(n=38)

Induction phase

Nivolumab 360 mg IV D1 + carboplatin AUC5 IV D1 + etoposide 100 mg/m^2/day IV D1–3 q3w (6 cycles)

Maintenance phase

Nivolumab 480 mg IV q4w

PD/toxicity/death/ up to 1 year

PRIMARY ENDPOINTS

- 12-month OS rate

SECONDARY ENDPOINTS

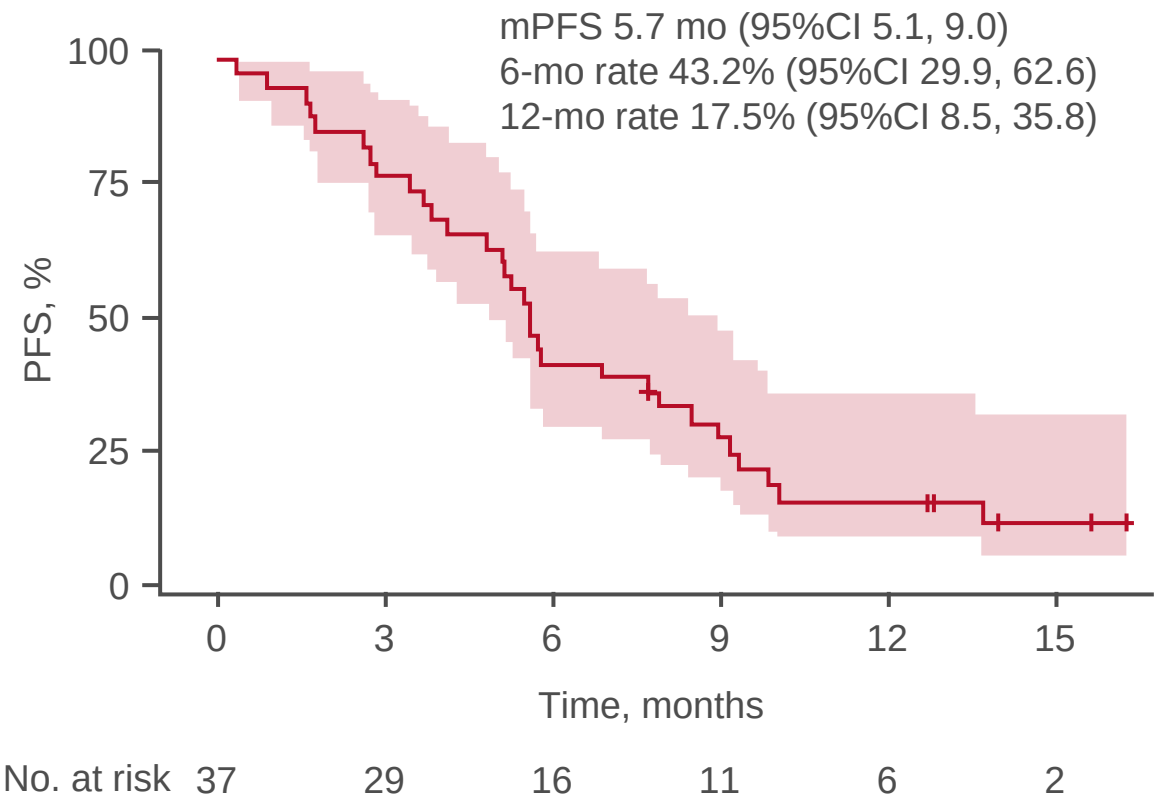
- ORR, DCR, PFS, safety

Presented at ESMO Congress 2022
Riesco MC, et al. Ann Oncol 2022;33(suppl):abstr 496MO

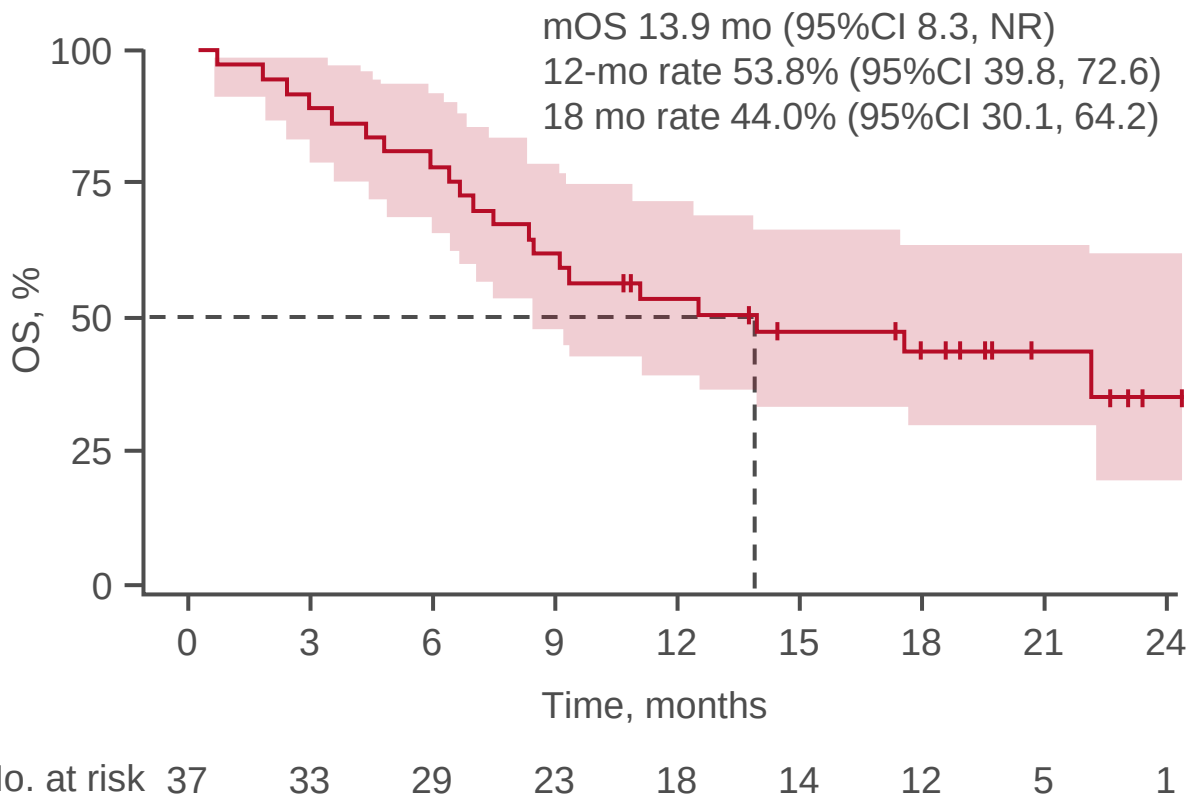
496MO: Final overall survival results from the NICE-NEC trial (GETNE-T1913). A phase II study of nivolumab and platinum-doublet chemotherapy (CT) in untreated advanced G3 neuroendocrine neoplasms (NENs) of gastroenteropancreatic (GEP) or unknown (UK) origin – Riesco MC, et al

Key results

Progression-free survival



Overall survival



Riesco MC, et al. Ann Oncol 2022;33(suppl):abstr 496MO

496MO: Final overall survival results from the NICE-NEC trial (GETNE-T1913). A phase II study of nivolumab and platinum-doublet chemotherapy (CT) in untreated advanced G3 neuroendocrine neoplasms (NENs) of gastroenteropancreatic (GEP) or unknown (UK) origin – Riesco MC, et al

Key results

	n=37
ORR, %	54.1
BOR, n (%)	
PR	20 (54.1)
SD	11 (29.7)
PD	3 (7.9)
NE	3 (7.9)
DCR, %	83.8

		mOS, mo (95%CI)
Tumour differentiation	Well differentiated	NR
	Poorly differentiated	14.6 (8.3, NR)
Ki67 index	≤55	11.0 (3.3, NR)
	>55	17.6 (8.3, NR)
Primary tumour site	Small intestine	NR
	Esophagus/gastric	NR
	Pancreas	14.6 (11.0, NR)
	Colorectum	6.4 (3.3, NR)

Conclusions

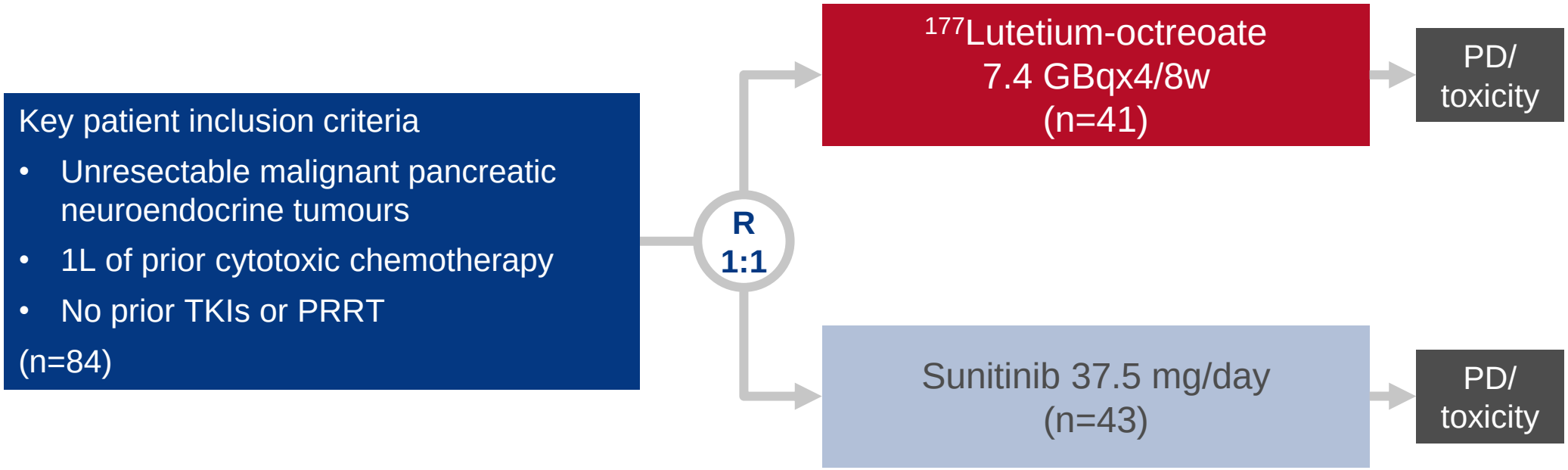
- **In patients with untreated grade 3 neuroendocrine neoplasms of gastroenteropancreatic or unknown origin, 1L nivolumab and platinum-doublet chemotherapy demonstrated encouraging activity particularly in those with non-colorectal grade 3 gastroenteropancreatic neuroendocrine neoplasms**

Riesco MC, et al. Ann Oncol 2022;33(suppl):abstr 496MO

887O: First multicentric randomized phase II trial investigating the antitumor efficacy of peptide receptor radionucleide therapy with 177Lutetium –Octreotate (OCLU) in unresectable progressive neuroendocrine pancreatic tumor: results of the OCLURANDOM trial – Baudin E, et al

Study objective

- To evaluate the efficacy and safety of peptide receptor radionucleide therapy (PRRT) with ^{177}lutetium-octreotate in patients with unresectable neuroendocrine pancreatic tumours in French centres in the phase 2 OCLURANDOM study



PRIMARY ENDPOINT

- 12-mo PFS rate

SECONDARY ENDPOINTS

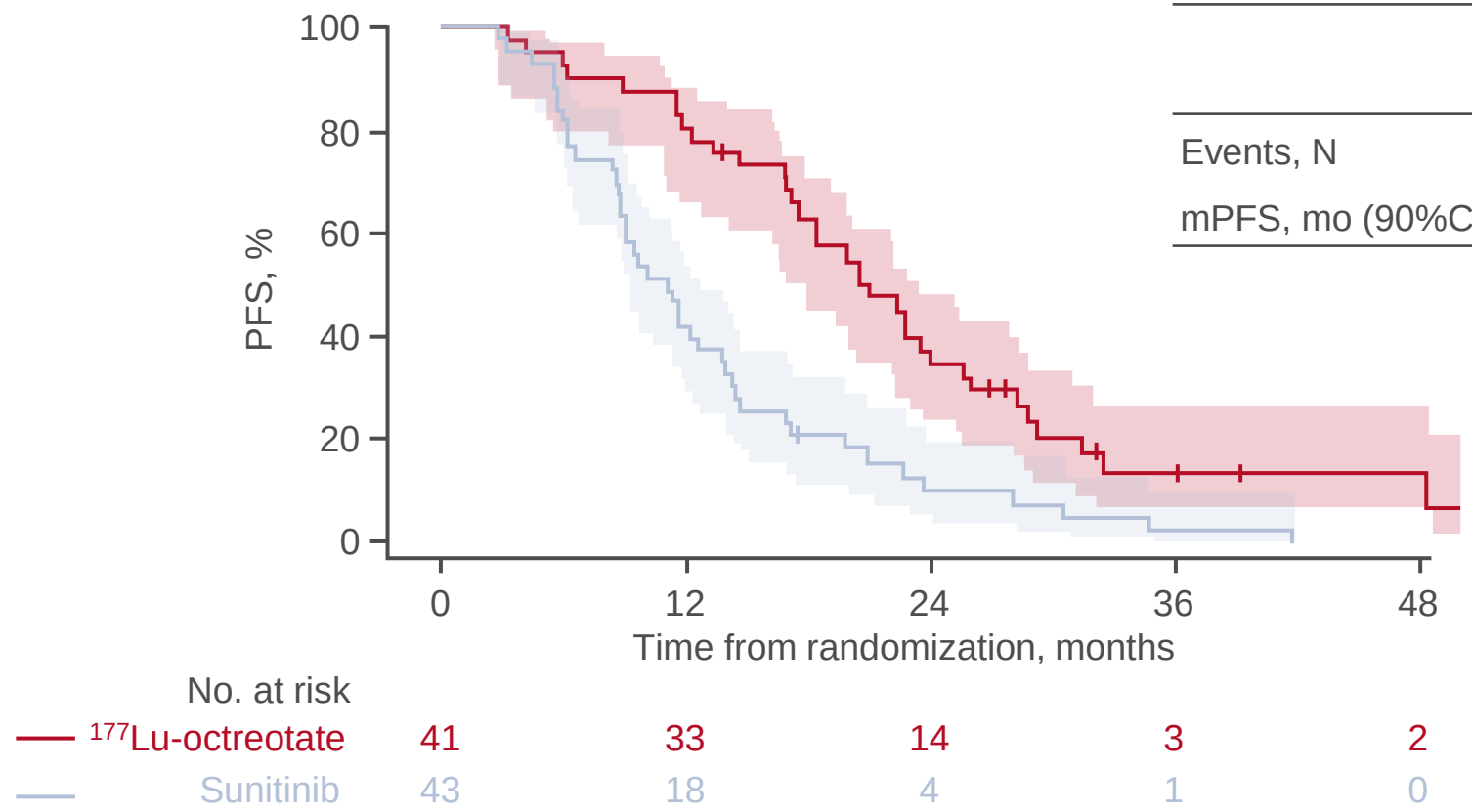
- TTP, BOR, OS, QoL, safety

Presented at ESMO Congress 2022
Baudin E, et al. Ann Oncol 2022;33(suppl):abstr 887O

887O: First multicentric randomized phase II trial investigating the antitumor efficacy of peptide receptor radionucleide therapy with 177Lutetium –Octreotate (OCLU) in unresectable progressive neuroendocrine pancreatic tumor: results of the OCLURANDOM trial – Baudin E, et al

Key results

Progression-free survival



	^{177}Lu-ocreotate (n=41)	Sunitinib (n=43)
Events, N	34	42
mPFS, mo (90%CI)	20.7 (17.2, 23.7)	11.0 (8.8, 12.4)

Baudin E, et al. Ann Oncol 2022;33(suppl):abstr 887O

887O: First multicentric randomized phase II trial investigating the antitumor efficacy of peptide receptor radionucleide therapy with 177Lutetium –Octreotate (OCLU) in unresectable progressive neuroendocrine pancreatic tumor: results of the OCLURANDOM trial – Baudin E, et al

Key results

	^{177}Lu-octreotate (n=41)	Sunitinib (n=43)
12-mo PFS rate, n (%)	33 (80)	18 (42)

Grade 3–4 AEs, n (%)	^{177}Lu-octreotate (n=41)	Sunitinib (n=43)
Any	18 (44)	27 (63)
Blood	5 (12)	10 (23)
Digestive	5 (12)	9 (21)
Fatigue	3 (7)	5 (12)
Hypertension	5 (12)	8 (19)
Led to discontinuation	2 (5)	9 (21)

Conclusions

- **In patients with unresectable progressive pancreatic neuroendocrine tumours, ^{177}Lu-octreotate demonstrated promising antitumor activity and was generally well-tolerated with no new safety signals observed**

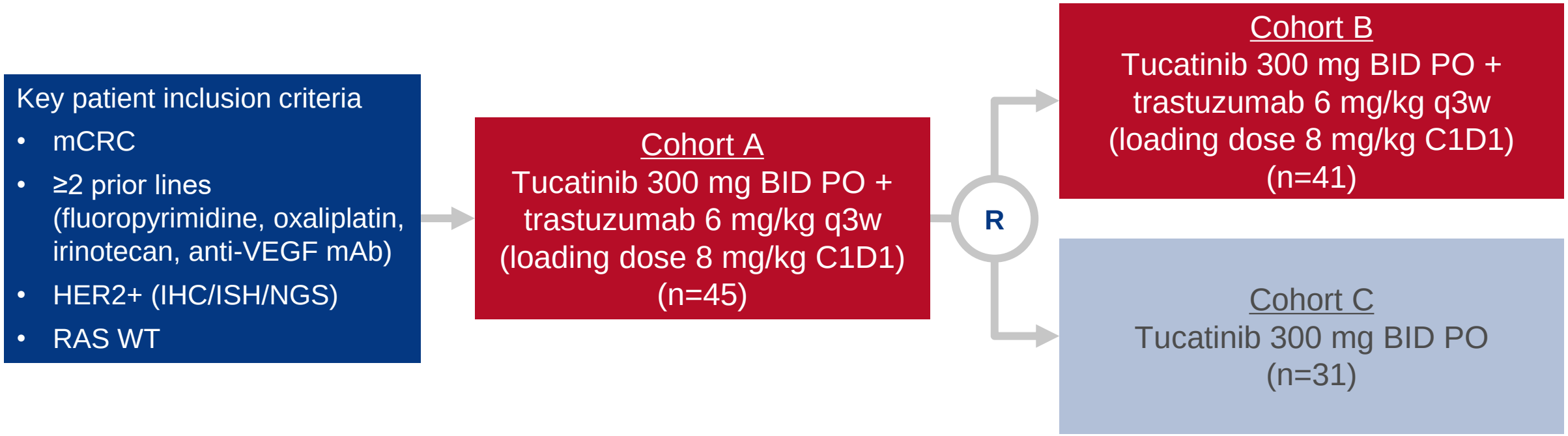
Baudin E, et al. Ann Oncol 2022;33(suppl):abstr 887O

CANCERS OF THE COLON, RECTUM AND ANUS

LBA-2: MOUNTAINEER: Open-label, phase 2 study of tucatinib in combination with trastuzumab for HER2-positive metastatic colorectal cancer (SGNTUC-017) – Strickler J, et al

Study objective

- To evaluate the efficacy and safety of tucatinib with or without trastuzumab in patients with HER2+ RAS WT mCRC in the phase 2 MOUNTAINEER study (Cohort A US and Cohorts B and C global centers)



PRIMARY ENDPOINT

- ORR (RECIST v1.1, BICR)

SECONDARY ENDPOINTS

- DoR, PFS, OS, safety

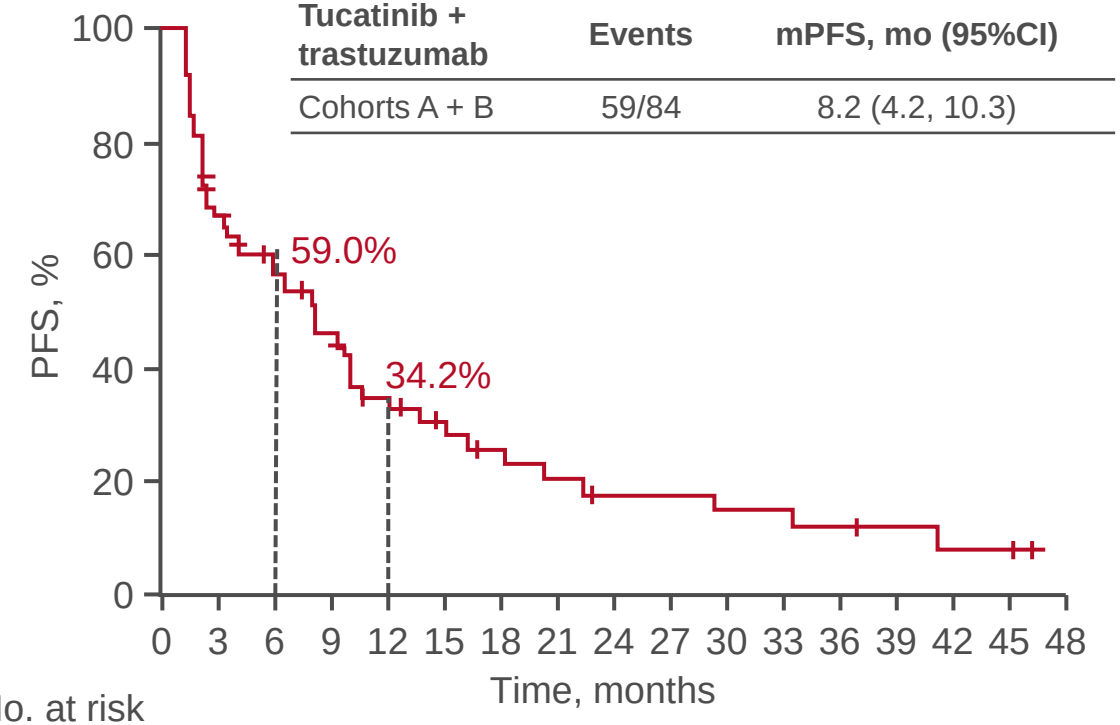
Presented at ESMO WCGC 2022
Strickler J, et al. Ann Oncol 2022;33(suppl):abstr LBA-2

LBA-2: MOUNTAINEER: Open-label, phase 2 study of tucatinib in combination with trastuzumab for HER2-positive metastatic colorectal cancer (SGNTUC-017) – Strickler J, et al

Key results

Progression-free survival

Tucatinib + trastuzumab	Events	mPFS, mo (95%CI)
Cohorts A + B	59/84	8.2 (4.2, 10.3)

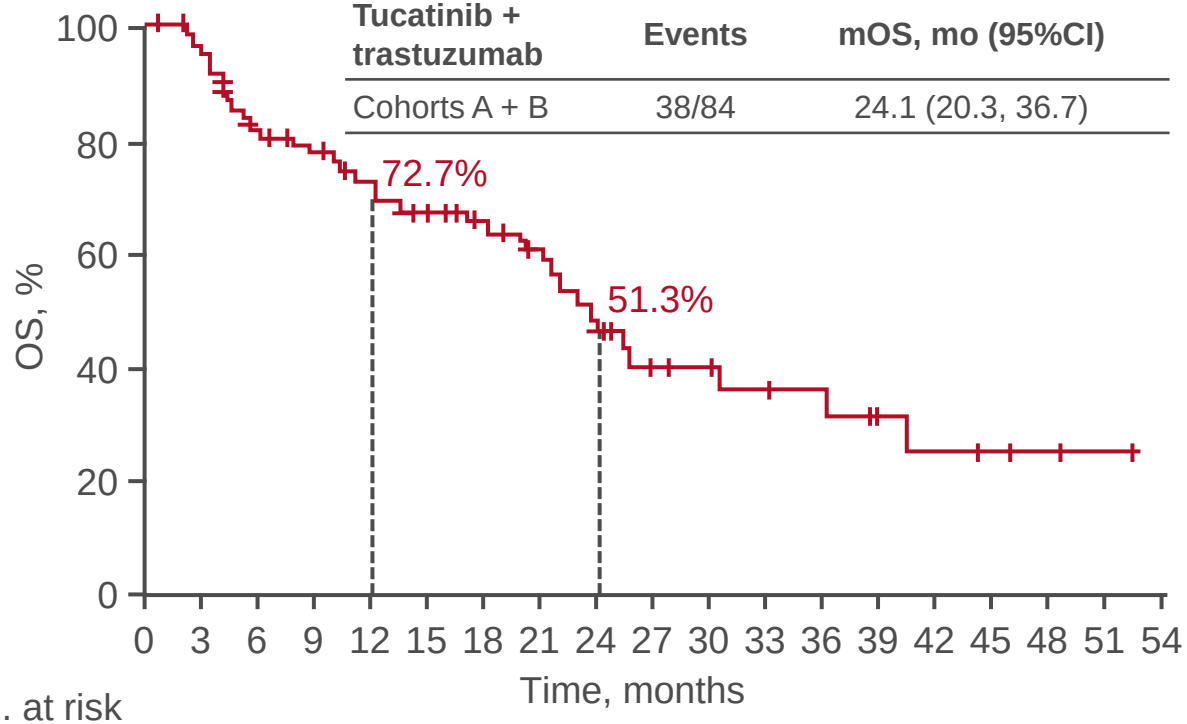


No. at risk

84	52	42	29	19	14	10	8	6	6	5	5	4	3	2	2	0

Overall survival

Tucatinib + trastuzumab	Events	mOS, mo (95%CI)
Cohorts A + B	38/84	24.1 (20.3, 36.7)



No. at risk

84	79	63	55	44	38	29	25	21	13	11	9	8	7	4	4	2	1	0

Strickler J, et al. Ann Oncol 2022;33(suppl):abstr LBA-2

LBA-2: MOUNTAINEER: Open-label, phase 2 study of tucatinib in combination with trastuzumab for HER2-positive metastatic colorectal cancer (SGNTUC-017) – Strickler J, et al

Key results

Outcomes	Tucatinib + trastuzumab Cohorts A + B (n=84)	Tucatinib Cohort C (n=30)
ORR, % (95%CI)	38.1 (27.7, 49.3)	3.3 (0.1, 17.2)
BOR, n (%)		
CR	3 (3.6)	0
PR	29 (34.5)	1 (3.3)
SD	28 (33.3)	23 (76.7)
PD	22 (26.2)	4 (13.3)
NA	2 (2.4)	2 (6.7)
DCR, n (%)	60 (71.4)	24 (80.0)
mDoR, mo (95%CI)	12.4 (8.5, 20.5)	-

TEAEs, n (%)	Tucatinib + trastuzumab Cohorts A + B (n=86)
Any	82 (95.3)
Tucatinib-related	63 (73.3)
Trastuzumab-related	58 (67.4)
Grade ≥3	33 (38.4)
Tucatinib-related	8 (9.3)
Trastuzumab-related	6 (7.0)
SAEs	19 (22.1)
Tucatinib-related	3 (3.5)
Trastuzumab-related	2 (2.3)
Led to discontinuation	5 (5.8)
Led to tucatinib dose modification	22 (25.6)
Led to death	0

Conclusions

- **In previously treated patients with HER2+ RAS WT mCRC, tucatinib + trastuzumab demonstrated promising antitumor activity and was generally well-tolerated**

Strickler J, et al. Ann Oncol 2022;33(suppl):abstr LBA-2

LBA O-9: Botensilimab, a novel innate/adaptive immune activator, plus balstilimab (anti-PD-1) for metastatic heavily pretreated microsatellite stable colorectal cancer – Bullock A, et al

Study objective

- To evaluate the efficacy and safety of botensilimab, an innate/adaptive immune activator, + balstilimab, an anti-PD-1, in a cohort of heavily pretreated patients with MSS mCRC in US centers

Key patient inclusion criteria
- Heavily pretreated mCRC
- MSS
- Prior IO permitted

(n=41)

→ Botensilimab 1 or 2 mg/kg q6w + balstilimab 3 mg/kg q2w

ENDPOINTS

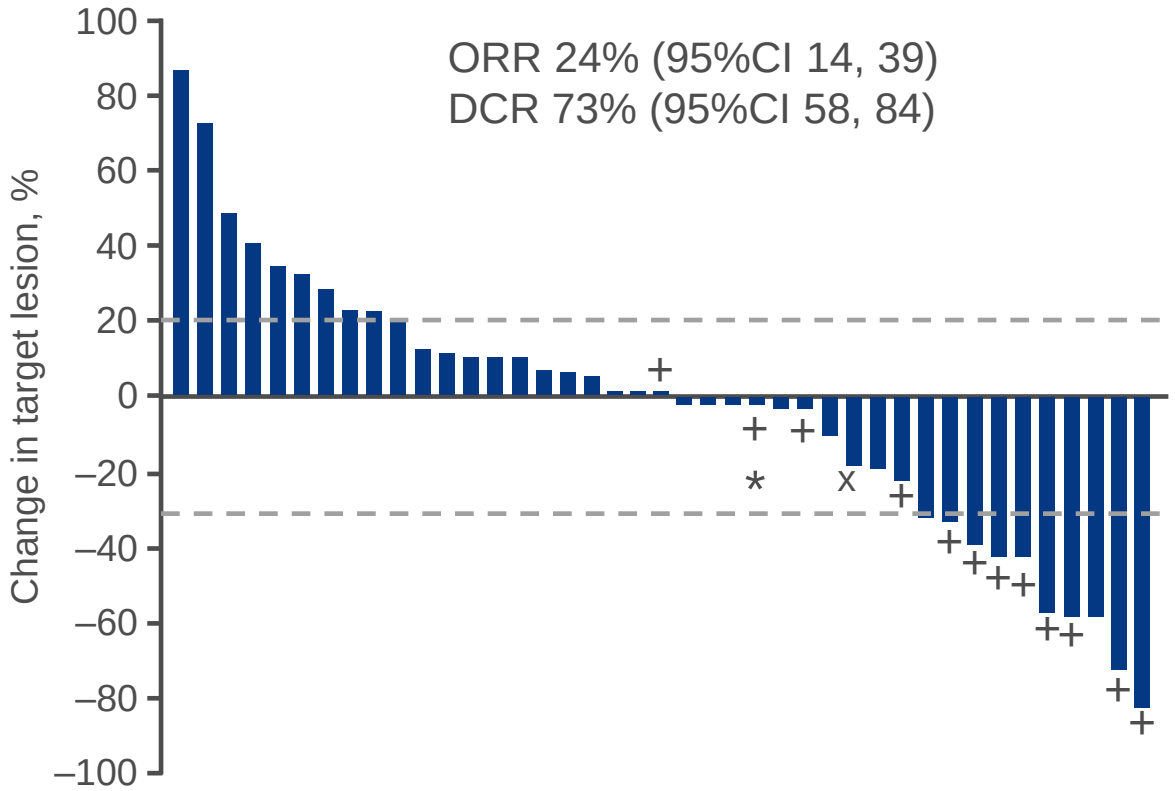
- ORR, DCR, PFS, DoR, OS, safety

Presented at ESMO WCGC 2022
Bullock A, et al. Ann Oncol 2022;33(suppl):abstr LBA O-9

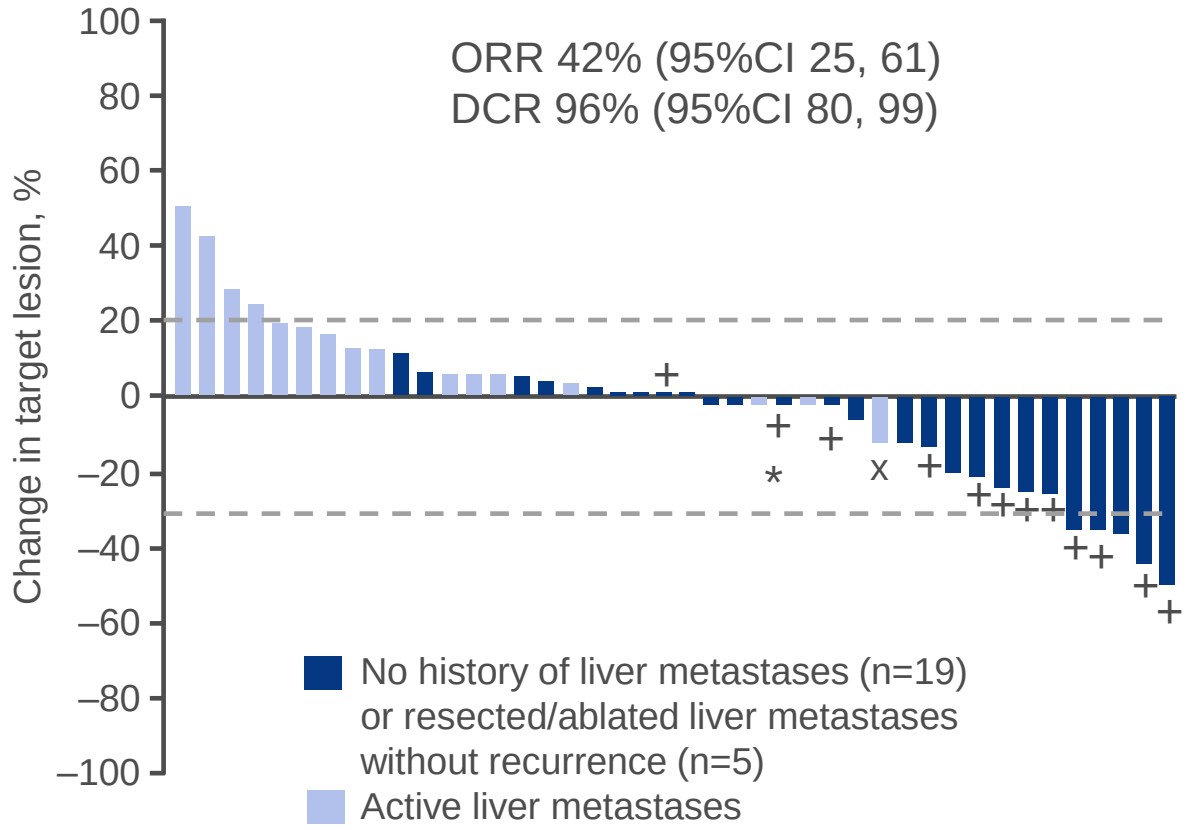
LBA O-9: Botensilimab, a novel innate/adaptive immune activator, plus balstilimab (anti-PD-1) for metastatic heavily pretreated microsatellite stable colorectal cancer – Bullock A, et al

Key results

Best tumour responses



Best tumour responses according to liver involvement



\+ Ongoing PR/SD * Complete metabolic response by PET x Progression of non-target lesions

Bullock A, et al. Ann Oncol 2022;33(suppl):abstr LBA O-9

LBA O-9: Botensilimab, a novel innate/adaptive immune activator, plus balstilimab (anti-PD-1) for metastatic heavily pretreated microsatellite stable colorectal cancer – Bullock A, et al

Key results

Outcomes	Overall (n=41)
ORR, % (95%CI)	24 (14, 39)
BOR, n (%)	
CR	0
PR	10 (24)
SD	20 (49)
PD	11 (27)
DCR, % (95%CI)	73 (58, 84)
Median follow-up, mo (range)	5.8 (1.6–24.4)

Grade 3 TRAEs, n (%)	HCC (n=41)
Any	10 (24)
Diarrhea	4 (10)
Fatigue	1 (2)
Pyrexia	1 (2)
AST increased	1 (2)
Arthralgia	1 (3)

Conclusions

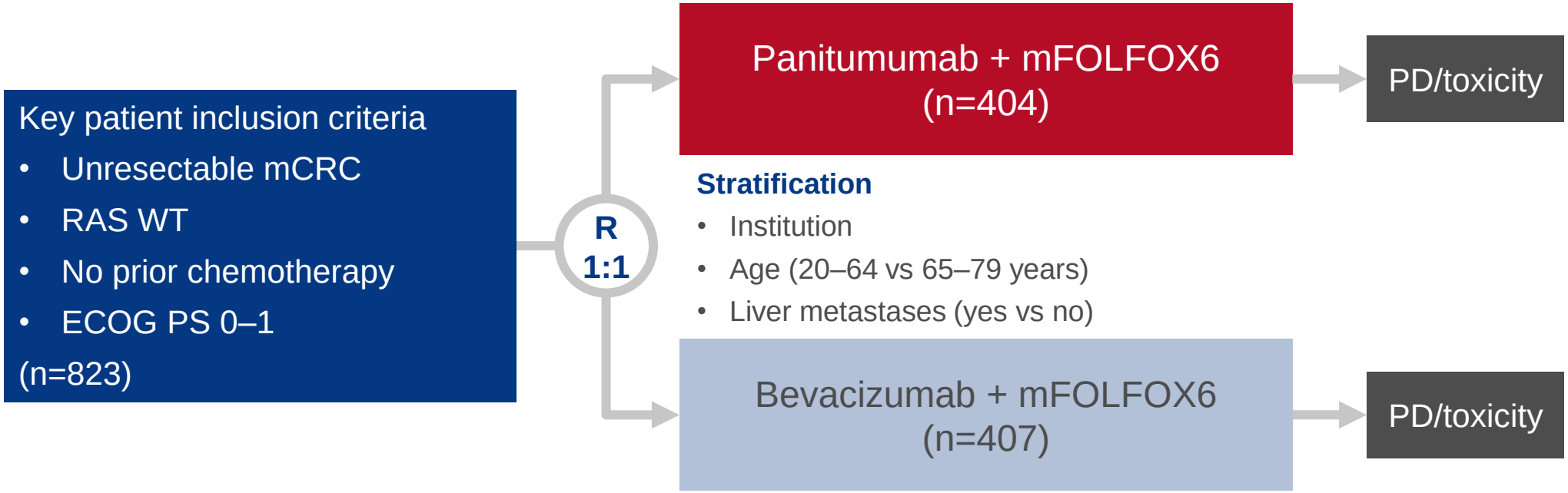
- **In heavily pretreated patients with MSS mCRC, botensilimab + balstilimab demonstrated encouraging clinical activity, particularly in those without active liver metastases, and was generally well-tolerated**

Bullock A, et al. Ann Oncol 2022;33(suppl):abstr LBA O-9

LBA O-10: First-line panitumumab versus bevacizumab in combination with mFOLFOX6 for RAS wild-type metastatic colorectal cancer: PARADIGM trial results – Muro K, et al

Study objective

- To evaluate the efficacy and safety of 1L panitumumab + mFOLFOX6 in patients with RAS WT mCRC in Japanese centers in the PARADIGM study



PRIMARY ENDPOINT

- OS (left-sided population)

SECONDARY ENDPOINTS

- PFS, response rate, DoR, R0 resection, safety

Presented at ESMO WCGC 2022
Muro K, et al. Ann Oncol 2022;33(suppl):abstr LBA O-10

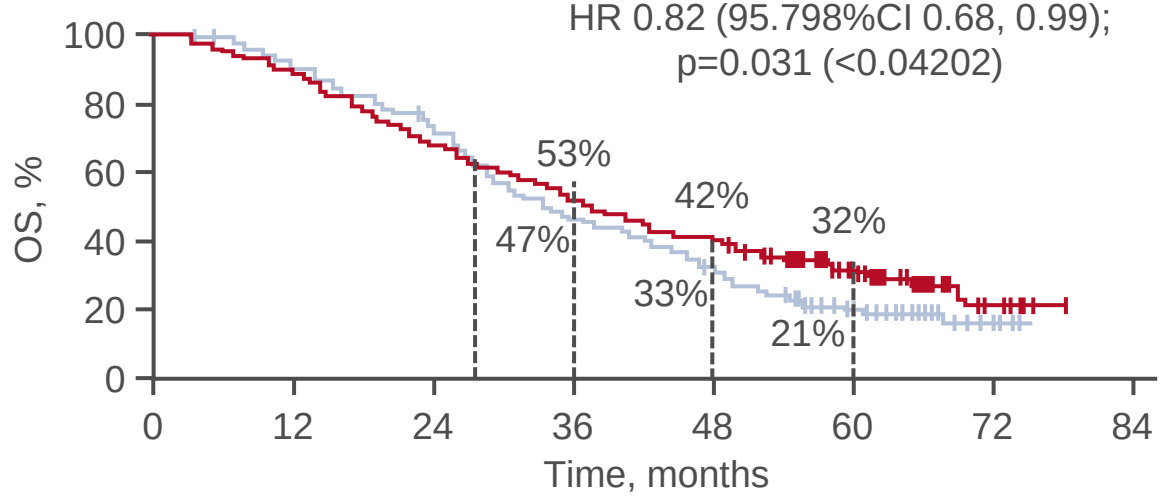
LBA O-10: First-line panitumumab versus bevacizumab in combination with mFOLFOX6 for RAS wild-type metastatic colorectal cancer: PARADIGM trial results – Muro K, et al

Key results

Overall survival

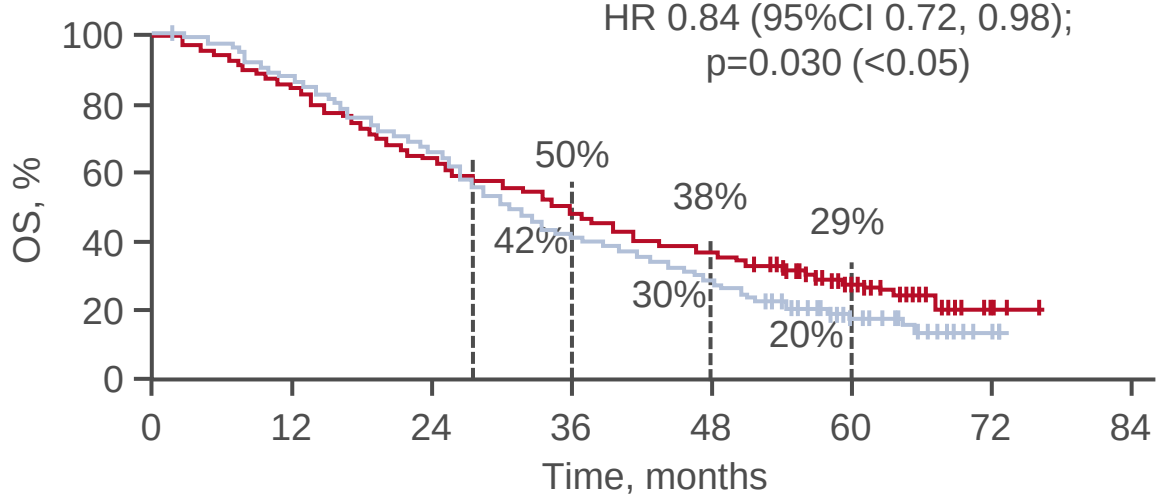
Left-sided population

	Events, n (%)	mOS, mo (95.798%CI)
Pan + mFOLFOX (n=312)	218 (69.9)	37.9 (34.1, 42.6)
Bev + mFOLFOX (n=292)	230 (78.7)	34.3 (30.9, 40.3)



Overall population

	Events, n (%)	mOS, mo (95.798%CI)
Pan + mFOLFOX (n=400)	291 (72.8)	36.2 (32.0, 39.0)
Bev + mFOLFOX (n=402)	322 (80.1)	31.3 (29.3, 34.1)



No. at risk

Panitumumab	312	276	213	166	129	68	5	0
Bevacizumab	292	256	212	136	96	40	5	0

Panitumumab	400	338	253	199	150	80	6	0
Bevacizumab	402	348	265	166	119	54	5	0

Muro K, et al. Ann Oncol 2022;33(suppl):abstr LBA O-10

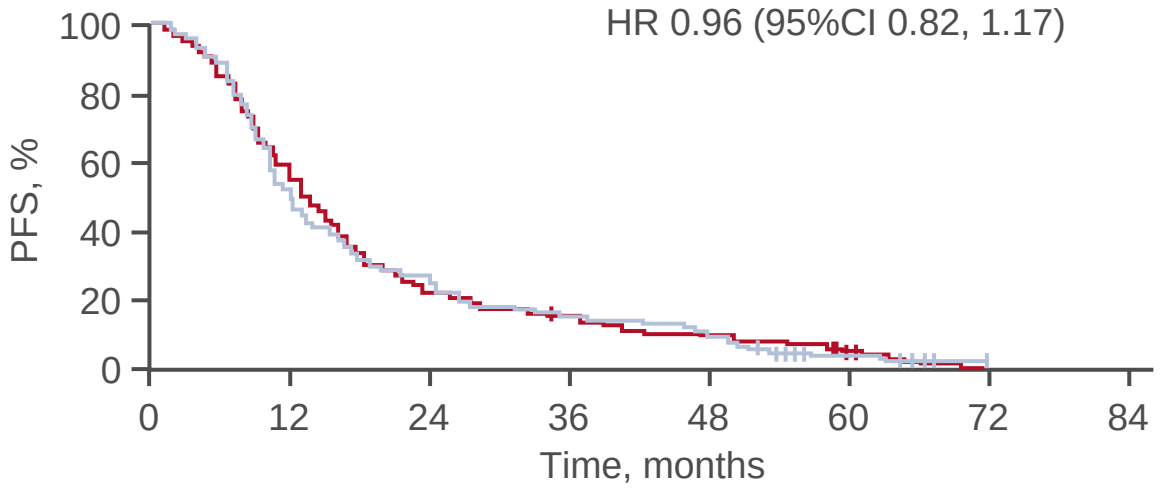
LBA O-10: First-line panitumumab versus bevacizumab in combination with mFOLFOX6 for RAS wild-type metastatic colorectal cancer: PARADIGM trial results – Muro K, et al

Key results

Progression-free survival

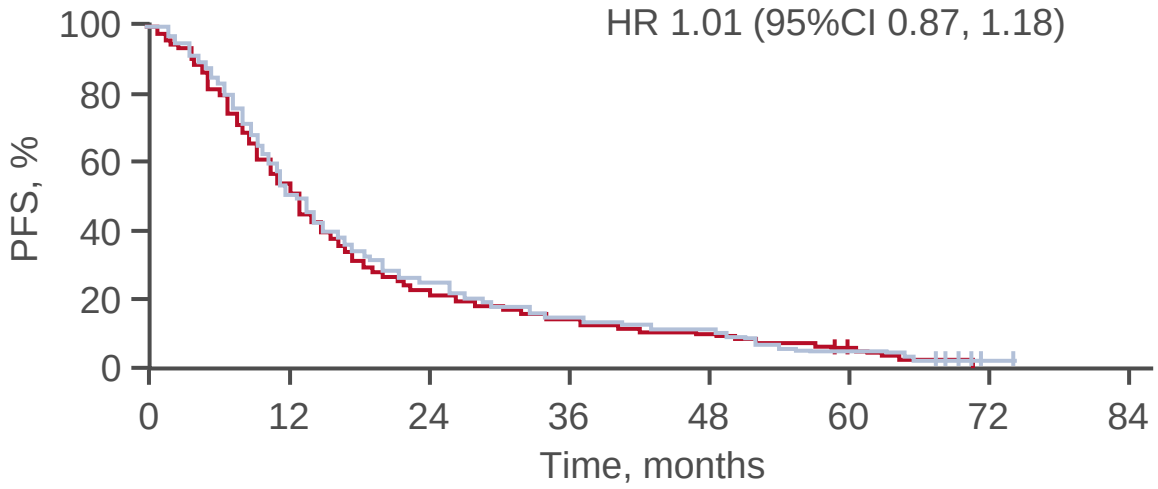
Left-sided population

	Events, n (%)	mPFS, mo (95.798%CI)
Pan + mFOLFOX (n=312)	245 (78.5)	13.7 (12.7, 15.3)
Bev + mFOLFOX (n=292)	252 (86.3)	13.2 (11.4, 14.5)



Overall population

	Events, n (%)	mPFS, mo (95.798%CI)
Pan + mFOLFOX (n=400)	328 (82.0)	12.9 (11.3, 13.6)
Bev + mFOLFOX (n=402)	349 (86.8)	12.0 (11.3, 13.5)



No. at risk

Panitumumab	312	149	59	38	24	13	0	0	400	179	71	43	28	15	0	0
Bevacizumab	292	139	67	40	31	5	1	0	402	182	83	45	35	6	1	0

Muro K, et al. Ann Oncol 2022;33(suppl):abstr LBA O-10

LBA O-10: First-line panitumumab versus bevacizumab in combination with mFOLFOX6 for RAS wild-type metastatic colorectal cancer: PARADIGM trial results – Muro K, et al

Key results

Outcomes	Panitumumab	Bevacizumab
Left-sided population, n	308	287
RR, % (95%CI)	80.2 (75.3)	68.6 (62.9, 74.0)
DCR, % (95%CI)	97.4 (94.9, 98.9)	96.5 (93.7, 98.3)
mDoR, mo (95%CI)	13.1 (11.1, 14.8)	11.2 (9.6, 13.1)
R0 rate, % (95%CI)	18.3 (14.1, 23.0)	11.6 (8.2, 15.9)
Overall population, n	394	397
RR, % (95%CI)	74.9 (70.3, 79.1)	67.3 (62.4, 71.9)
DCR, % (95%CI)	94.9 (92.3, 96.9)	95.5 (92.9, 97.3)
mDoR, mo (95%CI)	11.9 (10.5, 13.4)	10.7 (9.5, 12.2)
R0 rate, % (95%CI)	16.5 (13.0, 20.5)	10.9 (8.1, 17.1)
Right-sided population, n	82	103
RR, % (95%CI)	54.9 (43.5, 65.9)	63.1 (53.0, 72.4)
DCR, % (95%CI)	85.4 (75.8, 92.2)	92.2 (85.3, 96.6)
mDoR, mo (95%CI)	8.8 (5.8, 11.1)	9.7 (6.7, 14.3)
R0 rate, % (95%CI)	10.7 (5.0, 19.4)	9.7 (4.8, 17.1)
mOS, mo (95%CI)	20.2 (15.2, 32.0)	23.2 (18.5, 29.1)
mPFS, mo (95%CI)	7.7 (6.3, 10.6)	10.6 (7.6, 13.0)

Grade ≥3 AEs, %	Panitumumab	Bevacizumab
Acne-like dermatitis	17	0
Peripheral sensory neuropathy	9	10
Stomatitis	7	2
Appetite decreased	8	4
Paronychia	9	<1
Neutrophil count decreased	32	35
Dry skin	8	<1
Nausea	2	3
Fatigue	5	4
Diarrhea	6	3
Hypomagnesemia	8	0
Constipation	0	1
Platelet count decreased	2	1

Conclusions

- **In patients with RAS WT mCRC, 1L panitumumab + mFOLFOX6 demonstrated benefits in OS, response rates and R0 resection rates compared with bevacizumab + mFOLFOX6 and had a manageable safety profile**

Muro K, et al. Ann Oncol 2022;33(suppl):abstr LBA O-10

O-7: Evidence of therapeutic effectiveness of III line cetuximab rechallenge in appropriately selected patients: finding from long-term follow-up of CRICKET and CAVE trials – Martinelli E, et al

Study objective

- To evaluate the long-term efficacy and safety of 3L cetuximab rechallenge in appropriately selected patients with RAS/BRAF WT mCRC in Italian centers in a combined analysis of CRICKET and CAVE studies

Methods

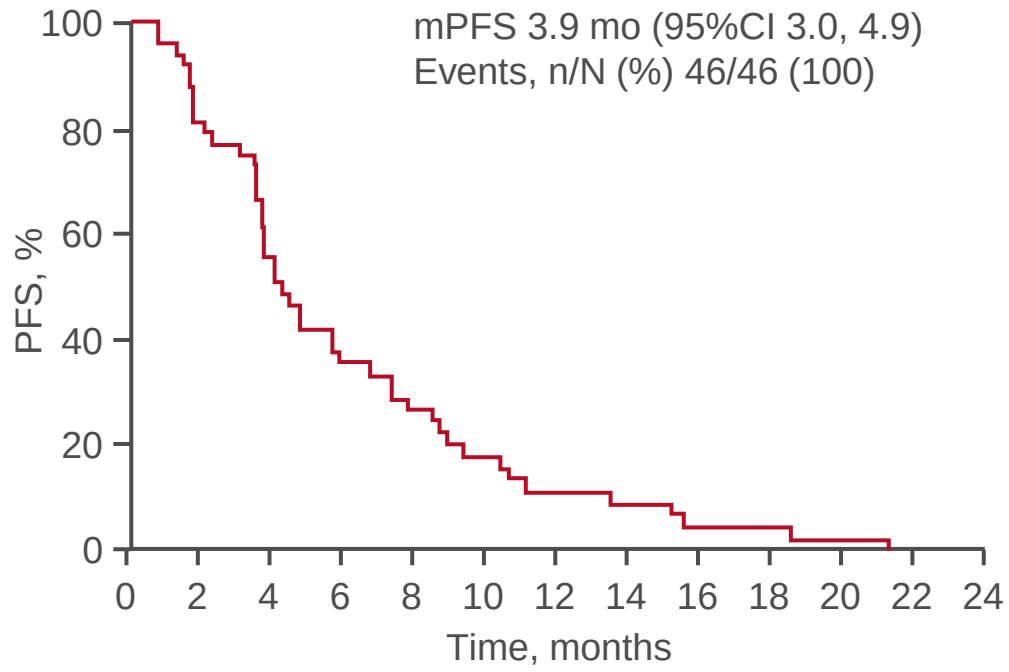
- Patients with RAS/BRAF WT mCRC who received 3L cetuximab rechallenge combined with irinotecan in CRICKET (n=13) and combined with avelumab in CAVE (n=33) were assessed for PFS, OS and safety

Presented at ESMO WCGC 2022
Martinelli E, et al. Ann Oncol 2022;33(suppl):abstr O-7

O-7: Evidence of therapeutic effectiveness of III line cetuximab rechallenge in appropriately selected patients: finding from long-term follow-up of CRICKET and CAVE trials – Martinelli E, et al

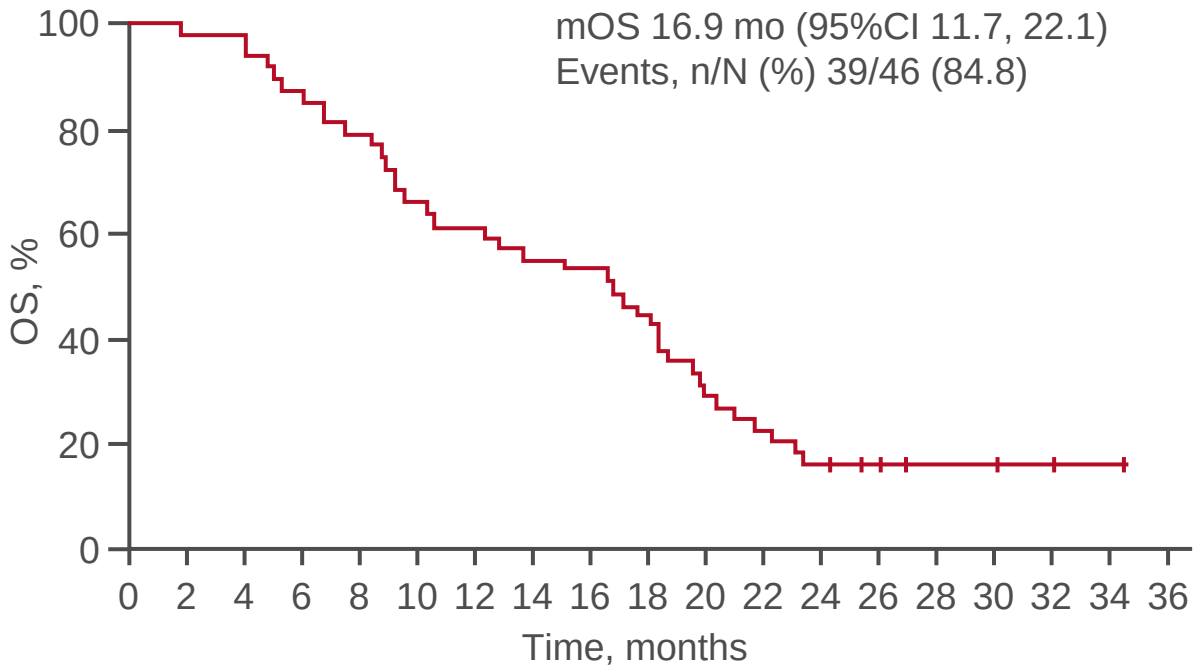
Key results

Progression free survival



No. at risk	46	36	23	16	12	8	5	4	2	2	1	0
(No. censored)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Overall survival



No. at risk	46	45	45	40	36	30	28	25	24	20	14	10	7	5	3	3	2	1	0
(No. censored)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)	(1)	(1)	(1)

Martinelli E, et al. Ann Oncol 2022;33(suppl):abstr O-7

O-7: Evidence of therapeutic effectiveness of III line cetuximab rechallenge in appropriately selected patients: finding from long-term follow-up of CRICKET and CAVE trials – Martinelli E, et al

Key results

Outcomes	CRICKET (n=13)	CAVE (n=33)
ORR, n (%) [95%CI]	5 (38.5) [13.9, 85.4]	3 (9.1) [1.9, 24.3]
BOR, n (%) [95%CI]		
CR	0 (0) [0, 24.7]	1 (3) [0.1, 15.8]
PR	5 (38.5) [13.9, 68.4]	2 (6.1) [0.7, 20.2]
SD	5 (38.5) [13.9, 68.4]	21 (63.6) [45.1, 79.6]
PD	3 (23.1) [5.0, 53.8]	9 (27.3) [13.3, 65.4]
DCR, n (%) [95%CI]	10 (77.0) [46.2, 95.0]	24 (72.7) [54.5, 86.7]
SD >6 mo, n (%) [95%CI]	1 (7.7) [0.2, 36.0]	10 (30.3) [15.6, 48.7]
mPFS, mo (95%CI)	3.9 (1.7, 6.2)	4.1 (3.0, 5.2)
mOS, mo (95%CI)	13.1 (7.3, 18.9)	18.6 (11.7, 25.4)

AEs, n (%)	Pooled (n=46)	CRICKET (n=13)	CAVE (n=33)	p-value
Skin toxicity	33 (71.7)	4 (30.8)	29 (87.9)	0.001
Hematologic toxicity	2 (4.3)	2 (15.4)	0	0.075
Non-hematologic toxicity	11 (23.9)	7 (53.8)	4 (12.1)	0.003
Dose reduction	9 (19.6)	5 (61.5)	4 (12.1)	0.043

Conclusions

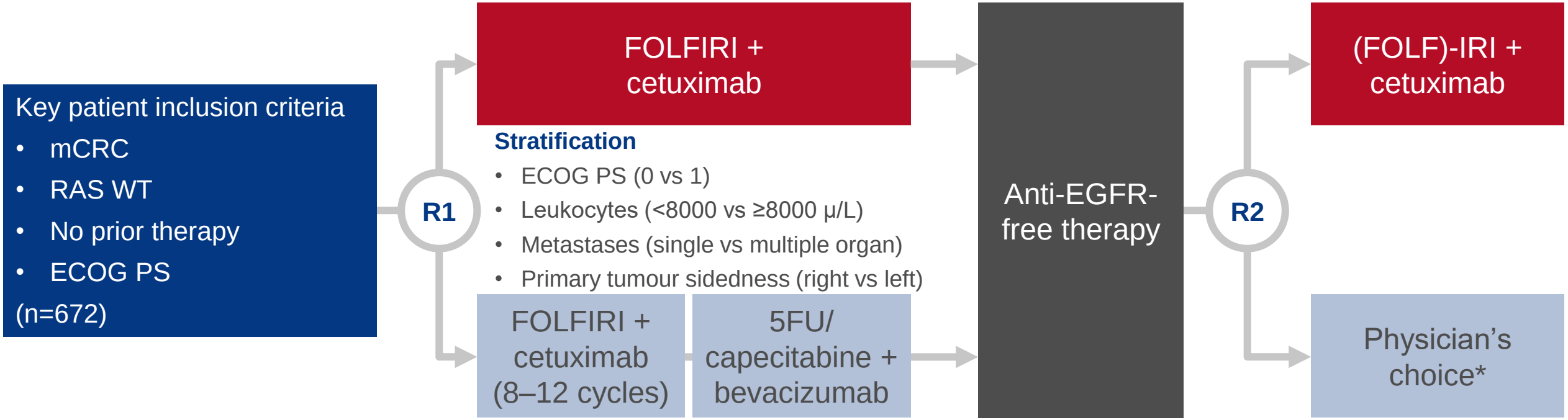
- **In appropriately selected patients with RAS/BRAF WT mCRC, 3L cetuximab with irinotecan or avelumab was effective and generally well-tolerated with cetuximab + irinotecan providing higher cytotoxic responses and cetuximab + avelumab providing longer survival**

Martinelli E, et al. Ann Oncol 2022;33(suppl):abstr O-7

SO-16: FIRE-4 (AIO-KRK-0114): Randomized study for a switch maintenance concept with 5-FU plus bevacizumab after induction treatment with FOLFIRI plus cetuximab versus continued treatment with FOLFIRI plus cetuximab-secondary endpoint – Heinemann V, et al

Study objective

- To evaluate the efficacy and safety of switch maintenance with 5FU + bevacizumab after induction FOLFIRI + cetuximab compared with continued FOLFIRI + cetuximab in patients with RAS WT mCRC in German and Austrian centers in the FIRE-4 study



PRIMARY ENDPOINT

- OS (after randomization 2)

SECONDARY ENDPOINTS

- PFS, ORR, safety

*No anti-EGFR therapies

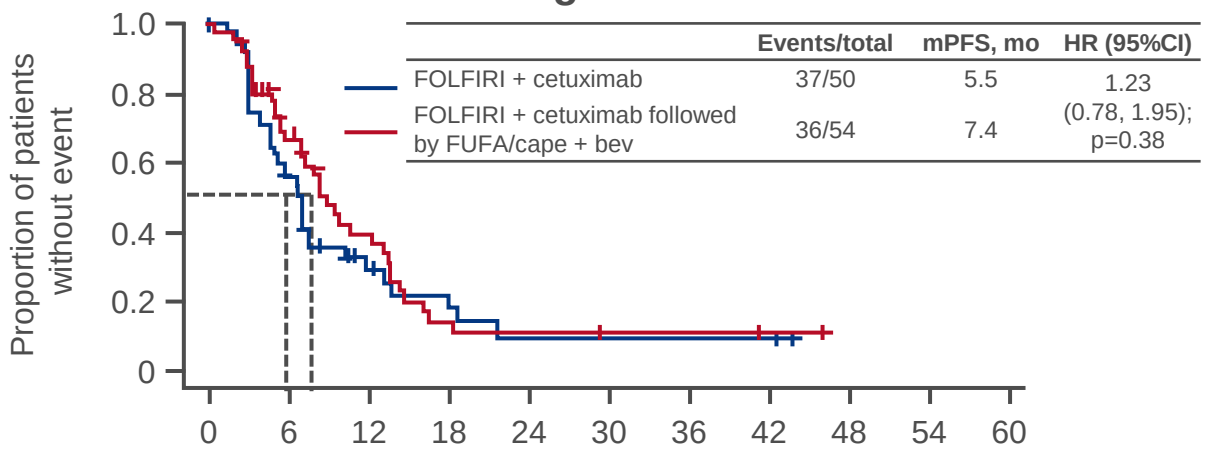
Presented at ESMO WCGC 2022
Heinemann V, et al. Ann Oncol 2022;33(suppl):abstr SO-16

SO-16: FIRE-4 (AIO-KRK-0114): Randomized study for a switch maintenance concept with 5-FU plus bevacizumab after induction treatment with FOLFIRI plus cetuximab versus continued treatment with FOLFIRI plus cetuximab-secondary endpoint – Heinemann V, et al

Key results

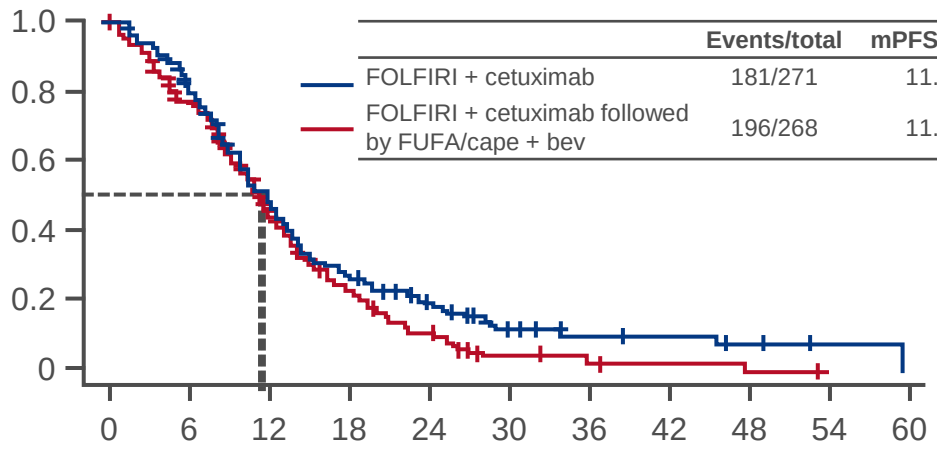
PFS

Right sided



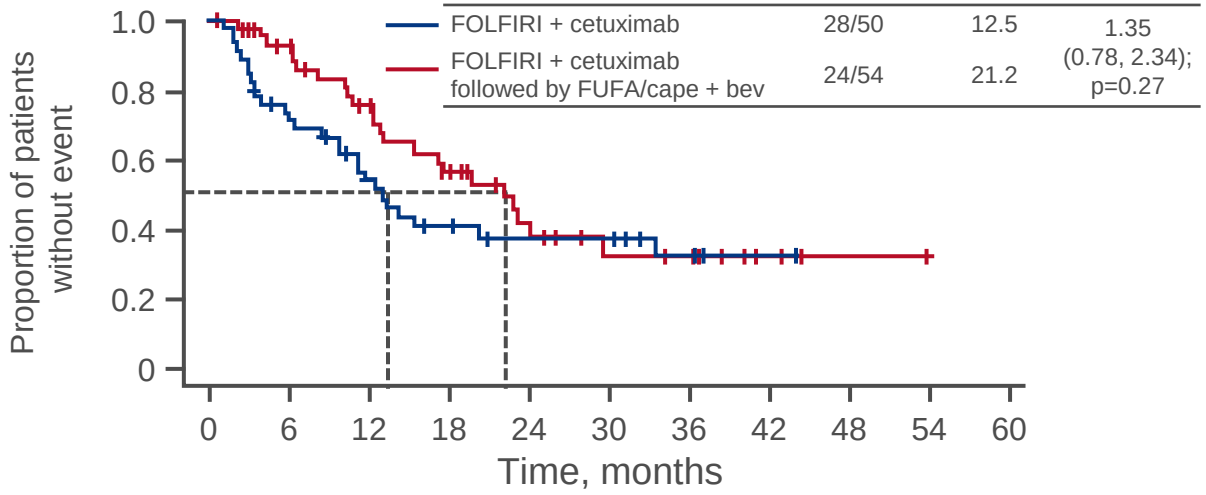
	Events/total	mPFS, mo	HR (95%CI)
FOLFIRI + cetuximab	37/50	5.5	1.23 (0.78, 1.95); p=0.38
FOLFIRI + cetuximab followed by FUFA/cape + bev	36/54	7.4	

Left sided

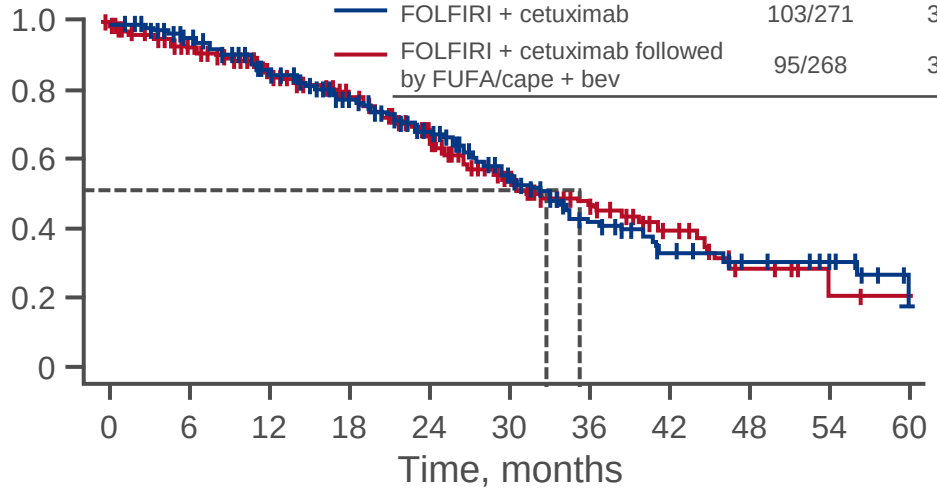


	Events/total	mPFS, mo	HR (95%CI)
FOLFIRI + cetuximab	181/271	11.5	0.87 (0.71, 1.06); p=0.17
FOLFIRI + cetuximab followed by FUFA/cape + bev	196/268	11.6	

OS



	Events/total	mOS, mo	HR (95%CI)
FOLFIRI + cetuximab	28/50	12.5	1.35 (0.78, 2.34); p=0.27
FOLFIRI + cetuximab followed by FUFA/cape + bev	24/54	21.2	



	Events/total	mOS, mo	HR (95%CI)
FOLFIRI + cetuximab	103/271	33.2	0.99 (0.75, 1.32); p=0.96
FOLFIRI + cetuximab followed by FUFA/cape + bev	95/268	35.6	

Heinemann V, et al. Ann Oncol 2022;33(suppl):abstr SO-16

SO-16: FIRE-4 (AIO-KRK-0114): Randomized study for a switch maintenance concept with 5-FU plus bevacizumab after induction treatment with FOLFIRI plus cetuximab versus continued treatment with FOLFIRI plus cetuximab-secondary endpoint – Heinemann V, et al

Key results

Outcomes	Overall population		Right-sided		Left-sided	
	Cetuximab continuation (n=327)	Switch maintenance (n=329)	Cetuximab continuation (n=50)	Switch maintenance (n=54)	Cetuximab continuation (n=271)	Switch maintenance (n=268)
ORR, n (%)	196 (59.9)	193 (58.7)	21 (42.0)	19 (35.2)	171 (63.1)	170 (63.4)
OR (95%CI); p-value	1.05 (0.77, 1.44); 0.75		-		-	
BOR, n (%)						
CR	9 (2.8)	17 (5.2)	1 (2.0)	1 (1.9)	6 (2.2)	16 (6.0)
PR	187 (57.2)	176 (53.5)	20 (40.0)	18 (33.3)	165 (61.1)	154 (57.5)
SD	49 (15.0)	54 (16.4)	12 (24.0)	17 (31.5)	36 (13.3)	37 (13.8)
PD	14 (4.3)	20 (6.1)	4 (8.0)	9 (16.7)	10 (3.7)	11 (4.1)
NE	68 (20.8)	62 (18.8)	13 (26.0)	9 (16.7)	54 (19.9)	50 (18.7)
DCR, n (%)	245 (74.9)	247 (75.1)	33 (66.0)	36 (66.7)	207 (76.4)	207 (77.2)
OR (95%CI); p-value	0.99 (0.70, 1.41); >0.99		-		-	
mPFS, mo (95%CI)	10.7 (9.7, 12.2)	11.3 (10.2, 12.0)	5.5	7.4	11.5	11.6
HR (95%CI); p-value	0.92; 0.36		1.23 (0.78, 1.95); 0.38		0.87 (0.71, 1.06); 0.17	
mOS, mo (95%CI)	32.5 (28.6, 36.3)	31.3 (27.0, 40.0)	12.5	21.2	33.2	35.6
HR (95%CI); p-value	1.03; 0.81		1.35 (0.78, 2.34); 0.27		0.99 (0.75, 1.32); 0.96	

Conclusions

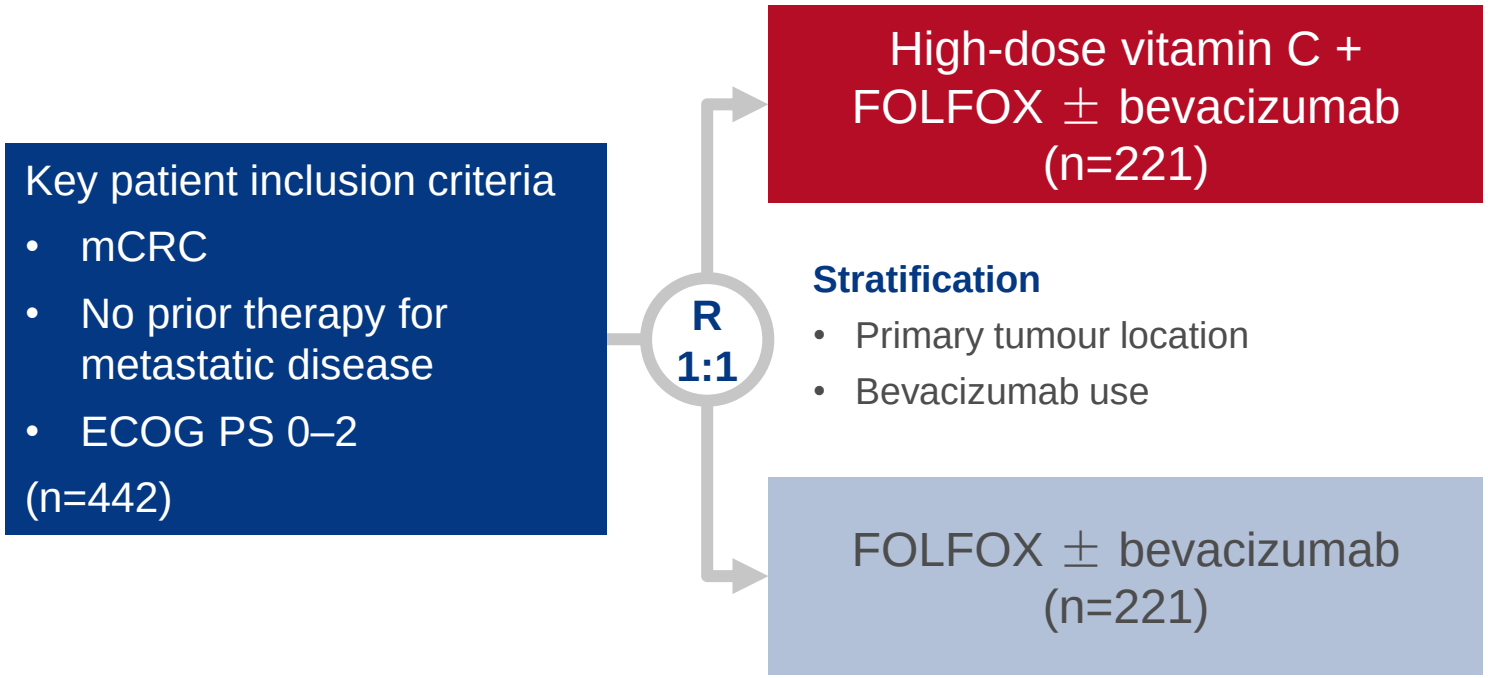
- **In patients with RAS WT mCRC, 1L FOLFIRI + cetuximab demonstrated clinical activity, but switching to maintenance 5FU + bevacizumab did not provide any additional benefit over continuation of cetuximab**

Heinemann V, et al. Ann Oncol 2022;33(suppl):abstr SO-16

SO-17: A randomized, open-label, multicenter, phase 3 study of high-dose vitamin C plus FOLFOX +/- bevacizumab versus FOLFOX +/- bevacizumab as first-line treatment in patients with unresectable metastatic colorectal cancer – Wang F, et al

Study objective

- To evaluate the efficacy and safety of high-dose vitamin C + FOLFOX ± bevacizumab in patients with unresectable mCRC in Chinese centers



PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

- ORR, OS, safety

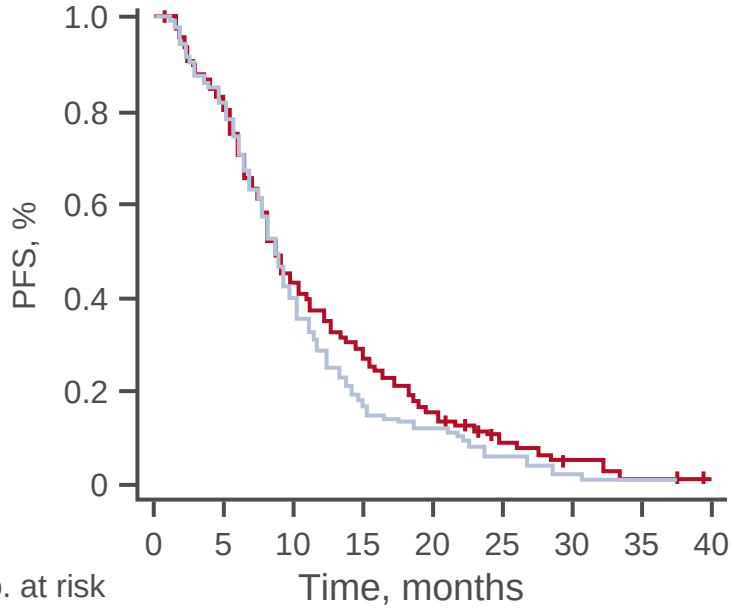
Presented at ESMO WCGC 2022
Wang F, et al. Ann Oncol 2022;33(suppl):abstr SO-17

SO-17: A randomized, open-label, multicenter, phase 3 study of high-dose vitamin C plus FOLFOX +/- bevacizumab versus FOLFOX +/- bevacizumab as first-line treatment in patients with unresectable metastatic colorectal cancer – Wang F, et al

Key results

Progression-free survival

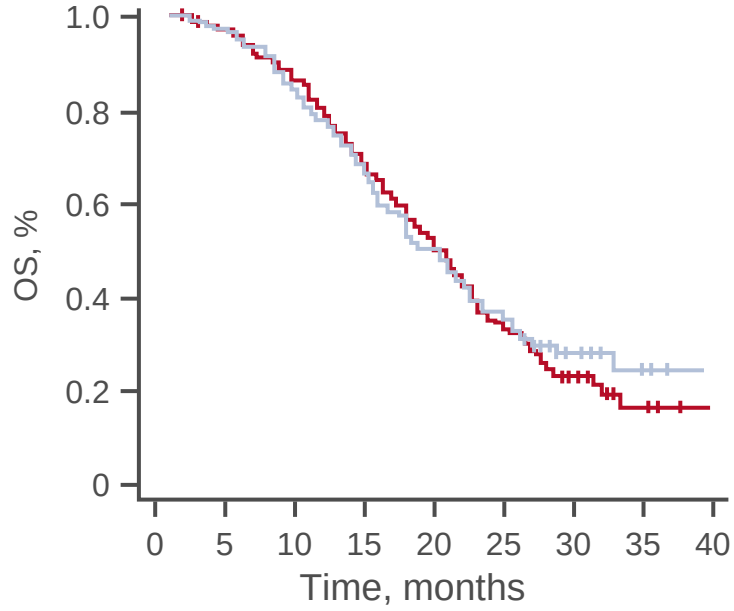
	Experimental arm	Control arm
mPFS, mo (95%CI)	8.6 (7.7, 10.0)	8.3 (7.9, 9.1)
HR (95%CI); p-value	0.86 (0.70, 1.05); 0.1	



No. at risk									
Control arm	221	164	76	33	20	9	3	2	0
Experimental arm	221	172	91	55	24	9	4	2	0

Overall survival

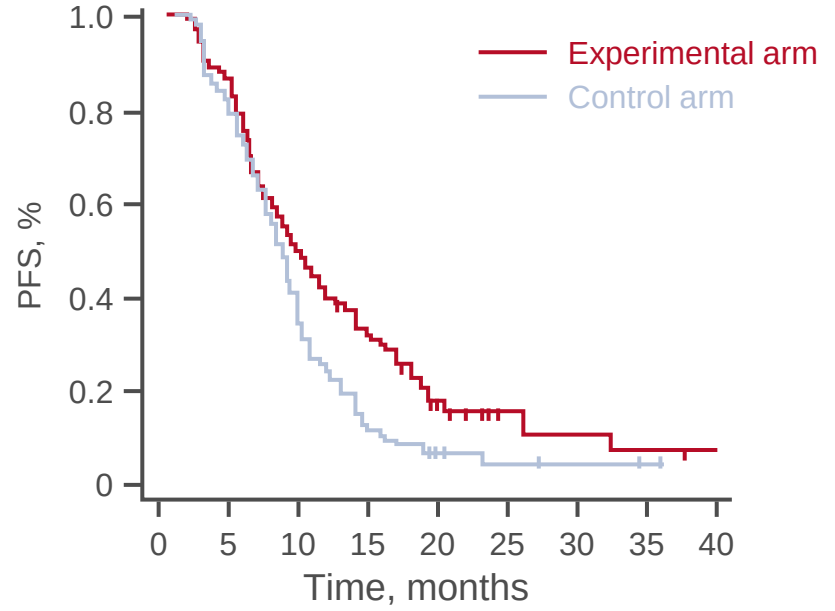
	Experimental arm	Control arm
mOS, mo (95%CI)	20.7 (18.6, 23.0)	19.7 (18.2, 23.0)
HR (95%CI); p-value	1.04 (0.81, 1.33); 0.7	



Control arm	221	204	171	130	72	36	18	8	1
Experimental arm	221	208	177	132	87	40	22	6	1

Progression-free survival in RAS mutant

	Experimental arm	Control arm
mPFS, mo (95%CI)	9.2 (7.6, 12.1)	7.8 (6.5, 8.8)
HR (95%CI); p-value	0.67 (0.50, 0.91); 0.01	



Control arm	100	73	27	11	4	3	2	2	0
Experimental arm	103	77	44	28	10	4	3	2	0

Wang F, et al. Ann Oncol 2022;33(suppl):abstr SO-17

SO-17: A randomized, open-label, multicenter, phase 3 study of high-dose vitamin C plus FOLFOX +/- bevacizumab versus FOLFOX +/- bevacizumab as first-line treatment in patients with unresectable metastatic colorectal cancer – Wang F, et al

Key results

Outcomes	High-dose vitamin C + FOLFOX ± bevacizumab (n=221)	FOLFOX ± bevacizumab (n=221)
ORR, n (%) [95%CI]	98 (44.3) [37.7, 51.2]	93 (42.1) [35.5, 48.9]
DCR, n (%) [95%CI]	186 (84.2) [78.5, 88.6]	180 (81.4) [75.6, 86.2]

Grade ≥3 TRAEs, n (%)	High-dose vitamin C + FOLFOX ± bevacizumab (n=221)	FOLFOX ± bevacizumab (n=221)
Any	74 (33.5)	67 (30.3)
Neutropenia	33 (14.9)	34 (15.4)
Anemia	11 (5.0)	5 (2.3)
Leukopenia	7 (3.2)	8 (3.6)
Nausea	2 (0.9)	1 (0.5)
Transaminase increased	6 (2.7)	2 (0.9)
Vomiting	7 (3.2)	4 (1.8)
Peripheral neuropathy	2 (0.9)	0
Thrombocytopenia	4 (1.8)	4 (1.8)
Appetite decreased	0	1 (0.5)
Diarrhea	7 (3.2)	6 (2.7)

Conclusions

- **In patients with unresectable mCRC, the addition of high-dose vitamin C to 1L FOLFOX ± bevacizumab did not provide any additional benefit in outcomes**

Wang F, et al. Ann Oncol 2022;33(suppl):abstr SO-17

SO-26: Identification and quantification of the microbiome in colorectal cancer metastases – Stevens P, et al

Study objective

- To evaluate the microbiome in patients with CRC metastases and compare it with normal adjacent tissue as well as any potential bacterial transfer from the primary tumour to metastases in Belgian centers

Methods

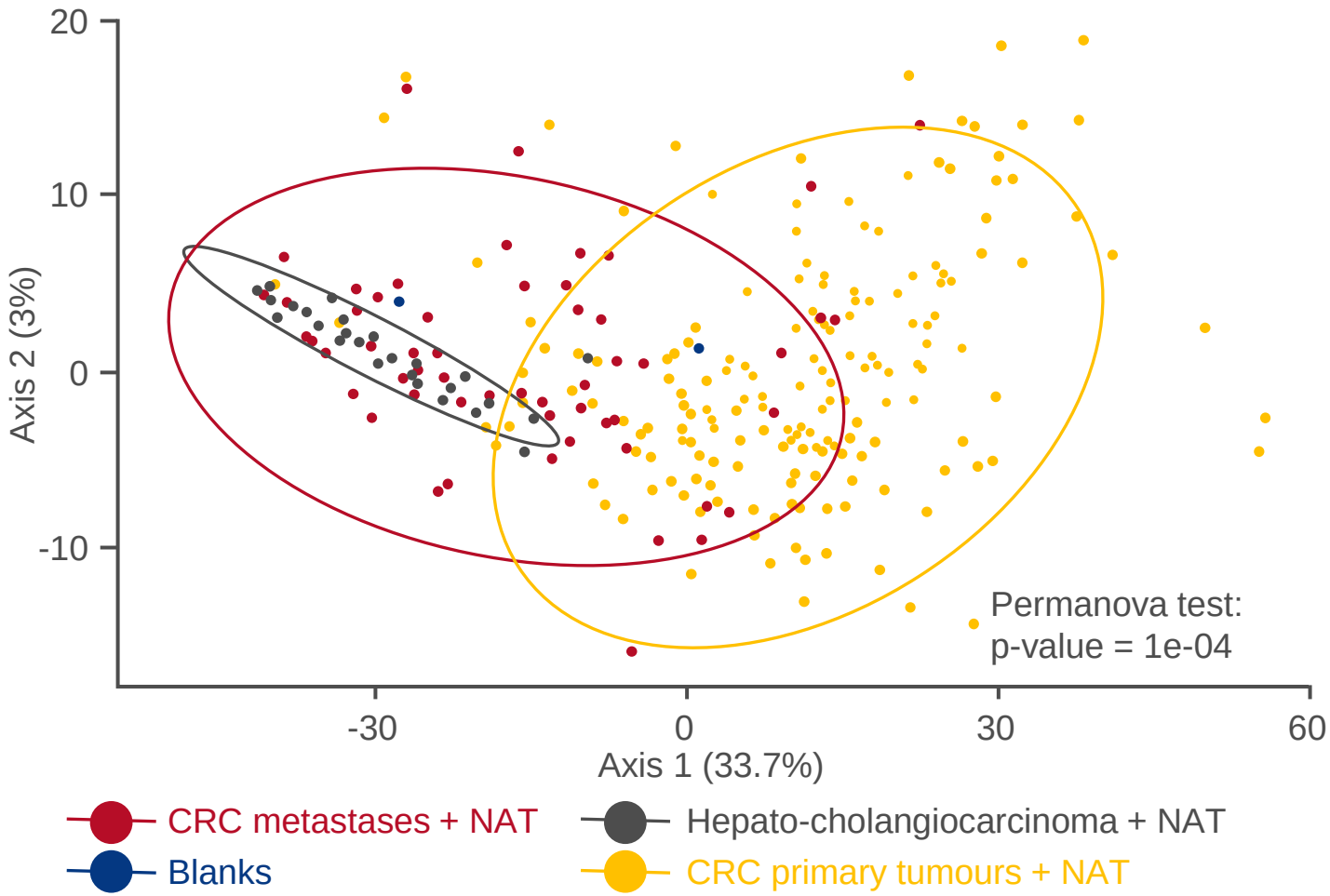
- Samples from patients with CRC (n=99) and 133 metastases (98 liver, 18 lung, 9 peritoneum and 7 brain) or 104 patient-matched primary tumours and associated normal adjacent tissue (NAT) were collected from 7 biobanks in Belgium and examined by amplification (PCR) and sequencing (MiSeq Illumina) of 16S bacterial gene
- A comparison cohort included 27 patients with HCC or cholangiocarcinoma

Presented at ESMO WCGC 2022
Stevens P, et al. Ann Oncol 2022;33(suppl):abstr SO-26

SO-26: Identification and quantification of the microbiome in colorectal cancer metastases – Stevens P, et al

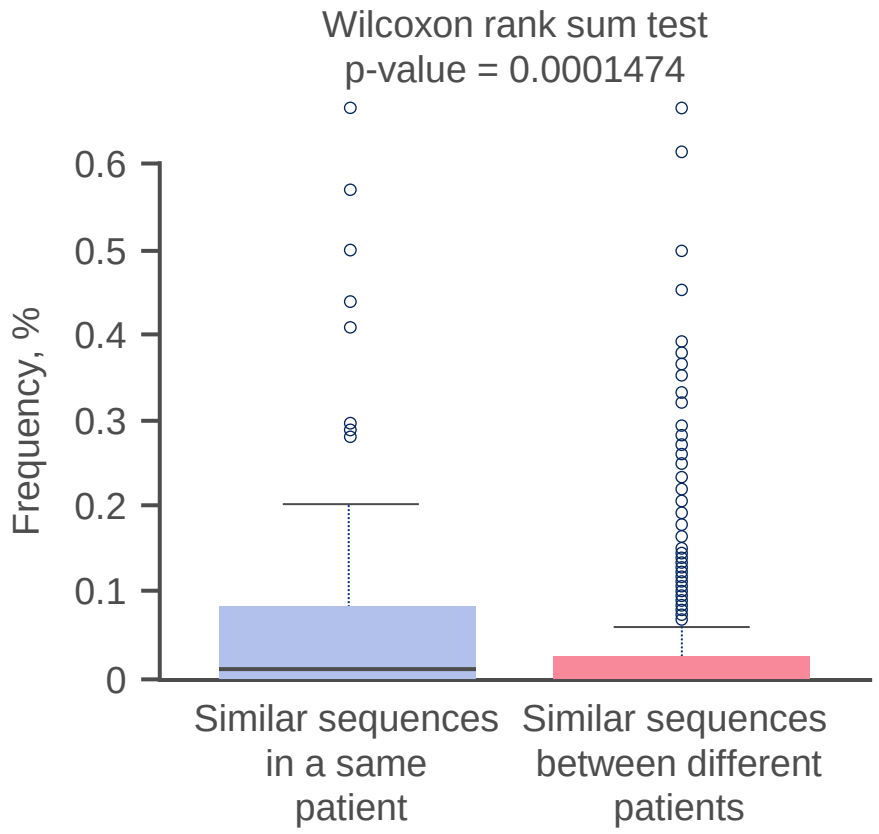
Key results

Bacterial composition



Bacterial transfer

% of bacterial DNA sequence with similarity between primary and metastases



Stevens P, et al. Ann Oncol 2022;33(suppl):abstr SO-26

SO-26: Identification and quantification of the microbiome in colorectal cancer metastases – Stevens P, et al

Conclusions

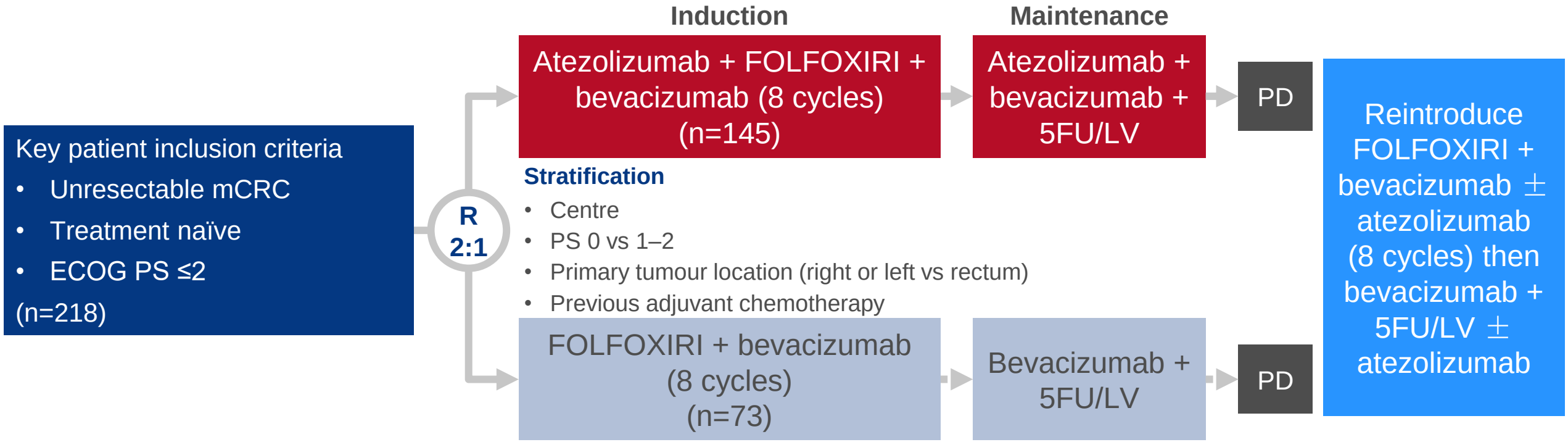
- **In patients with CRC metastases, bacterial identity and diversity are patient dependent. In CRC metastases, there was a low tissue biomass observed that may originate from the primary tumours, while the primary tumours tended to have a much higher tissue bacterial biomass**

Stevens P, et al. Ann Oncol 2022;33(suppl):abstr SO-26

SO-36: An immune-related gene expression profile predicts the efficacy of adding atezolizumab to first-line FOLFOXIRI/bevacizumab in metastatic colorectal cancer: a translational analysis of the phase II randomized AtezoTRIBE study – Antoniotti C, et al

Study objective

- To evaluate whether an immune-related gene expression profile (DetermalO signature) is predictive for adding atezolizumab to 1L FOLFOXIRI + bevacizumab in patients with mCRC in the phase 2 AtezoTRIBE study



PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

- Response, resection rate, safety

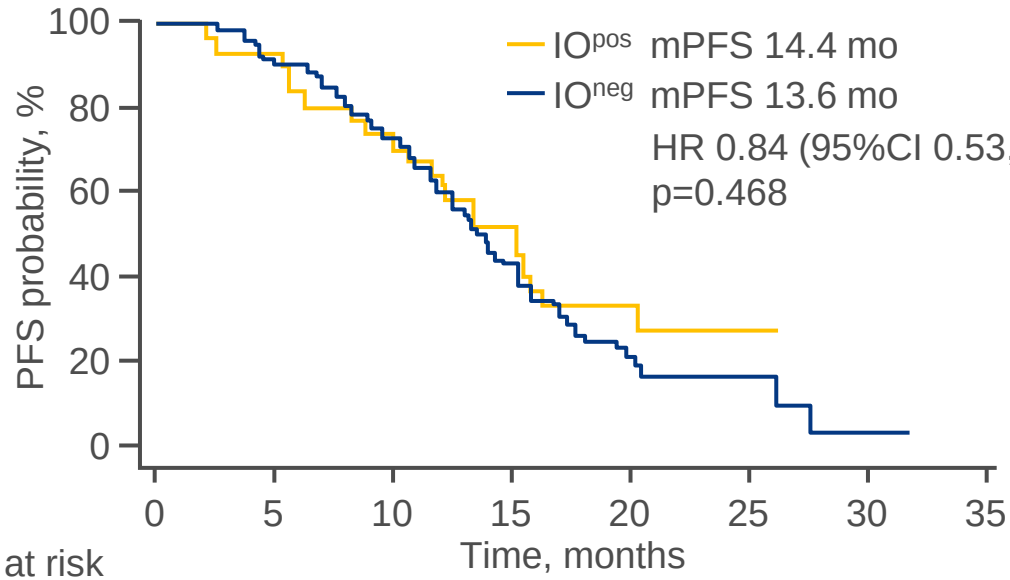
Presented at ESMO WCGC 2022
Antoniotti C, et al. Ann Oncol 2022;33(suppl):abstr SO-36

SO-36: An immune-related gene expression profile predicts the efficacy of adding atezolizumab to first-line FOLFOXIRI/bevacizumab in metastatic colorectal cancer: a translational analysis of the phase II randomized AtezoTRIBE study – Antoniotti C, et al

Key results

Progression-free survival

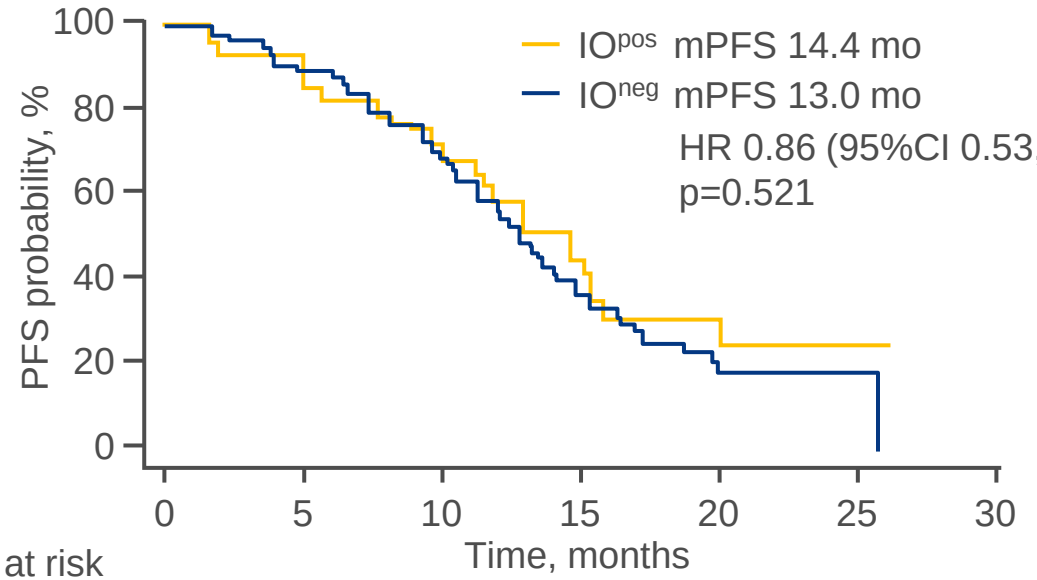
Overall population (n=122)



No. at risk

IO^{pos}	33	28	23	14	5	1	0	0
IO^{neg}	89	77	62	34	12	6	1	0

pMMR subgroup (n=110)



No. at risk

IO^{pos}	30	26	21	12	4	1	0
IO^{neg}	80	69	54	28	10	4	0

IO^{opt} status	Overall population (n=122)		pMMR subgroup (n=110)	
	IO opt^{pos} (n=16)	IO opt^{neg} (n=106)	IO opt^{pos} (n=12)	IO opt^{neg} (n=98)
PFS, mo	14.8	13.3	14.8	12.9
HR (95%CI); p-value	0.50 (0.28, 0.87); 0.053		0.45 (0.25, 0.84); 0.054	

Antoniotti C, et al. Ann Oncol 2022;33(suppl):abstr SO-36

SO-36: An immune-related gene expression profile predicts the efficacy of adding atezolizumab to first-line FOLFOXIRI/bevacizumab in metastatic colorectal cancer: a translational analysis of the phase II randomized AtezoTRIBE study – Antoniotti C, et al

Key results

	IO status				IO^{opt} status			
	Overall population (n=122)		pMMR subgroup (n=110)		Overall population (n=122)		pMMR subgroup (n=110)	
	Atezolizumab + FOLFOXIRI + bevacizumab	FOLFOXIRI + bevacizumab	Atezolizumab + FOLFOXIRI + bevacizumab	FOLFOXIRI + bevacizumab	Atezolizumab + FOLFOXIRI + bevacizumab	FOLFOXIRI + bevacizumab	Atezolizumab + FOLFOXIRI + bevacizumab	FOLFOXIRI + bevacizumab
IO-negative, n	54	35	48	32	67	39	61	37
PFS, mo	13.6	13.0	13.3	13.0	13.5	13.0	12.9	13.0
HR (95%CI); p-value	0.83 (0.50, 1.35); 0.434		0.93 (0.56, 1.55); 0.771		0.85 (0.54, 1.33); 0.463		0.93 (0.58, 1.48); 0.753	
IO-positive, n	23	10	21	9	10	6	8	4
PFS, mo	19.8	12.6	15.1	12.6	NR	11.5	NR	11.5
HR (95%CI); p-value	0.39 (0.15, 1.02); 0.018		0.47 (0.18, 1.25); 0.070		0.10 (0.02, 0.52); <0.001		0.13 (0.02, 0.95); 0.004	

Conclusions

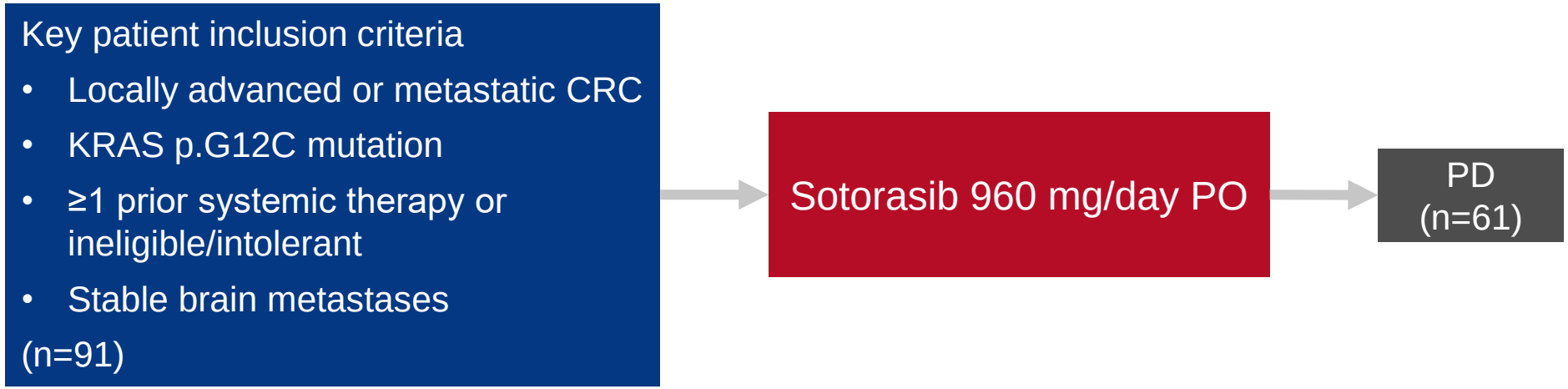
- **In patients with mCRC, use of the DetermaIO signature may be able to identify patients who would benefit from the addition of atezolizumab to 1L FOLFOXIRI/bevacizumab including among pMMR tumours, although the optimized IO cut-point will need to validated**

Antoniotti C, et al. Ann Oncol 2022;33(suppl):abstr SO-36

SO-39: Evaluation of acquired resistance to sotorasib in KRAS p.G12C-mutated colorectal cancer: Exploratory plasma biomarker analysis of CodeBreaK 100 – Prenen H, et al

Study objective

- To evaluate the mechanisms of acquired resistance to sotorasib in patients with KRAS p.G12C-mutated CRC in the CodeBreak 100 study



PRIMARY ENDPOINT

- ORR (RECIST v1.1, central review)

EXPLORATORY ENDPOINTS

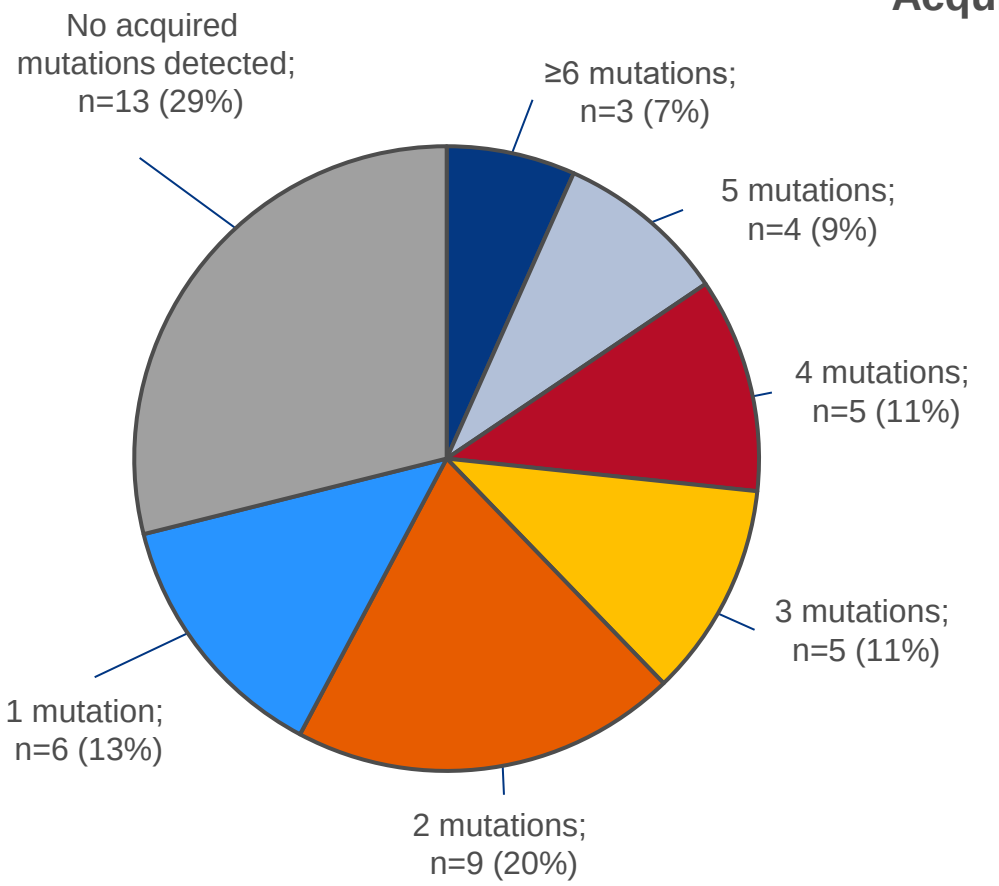
- Acquired genomic alterations at PD*

*74 gene Guardant 360 ctDNA test

Presented at ESMO WCGC 2022
Prenen H, et al. Ann Oncol 2022;33(suppl):abstr SO-39

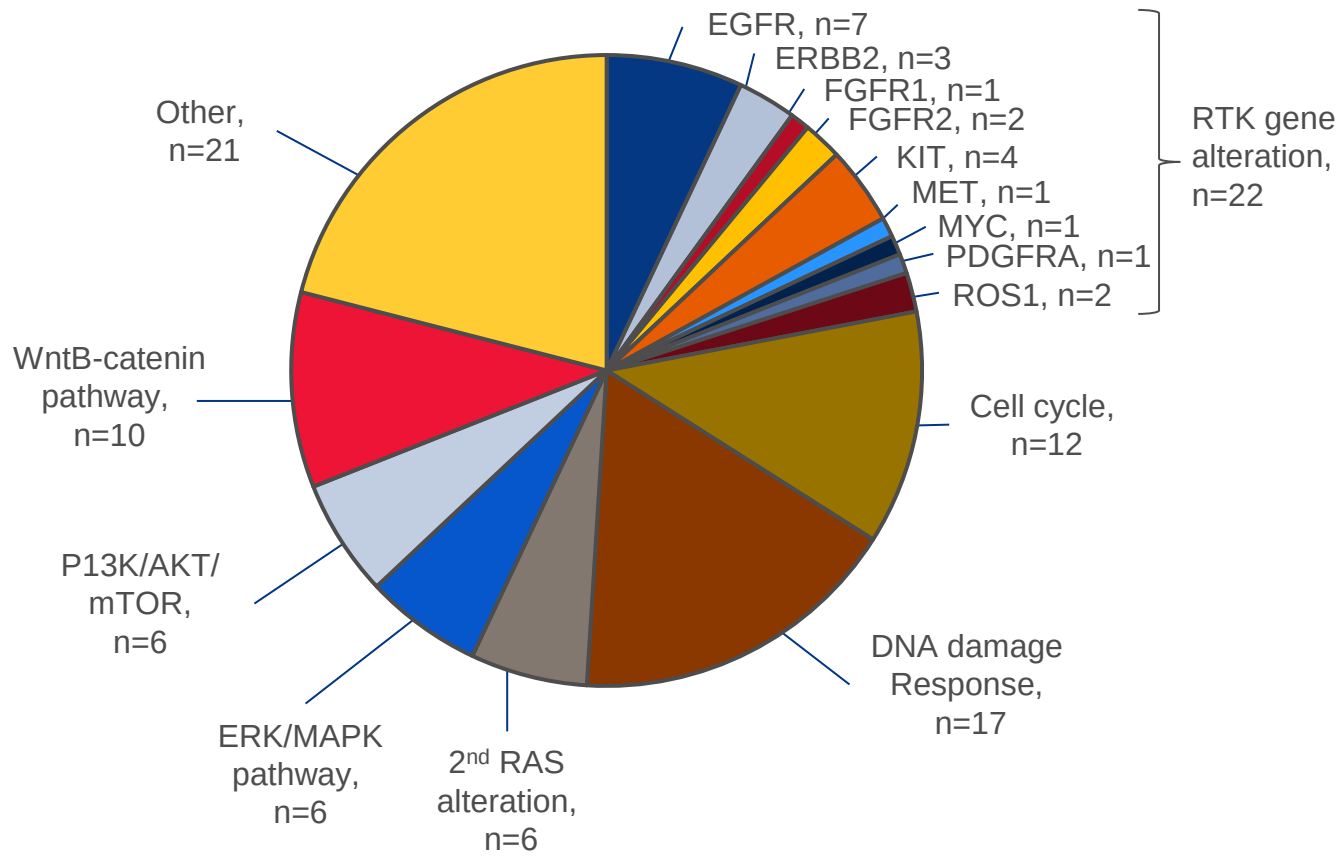
SO-39: Evaluation of acquired resistance to sotorasib in KRAS p.G12C-mutated colorectal cancer: Exploratory plasma biomarker analysis of CodeBreaK 100 – Prenen H, et al

Key results



32 (71%) patients had an acquired genomic alteration

Acquired genomic alterations



100 acquired alterations were detected

Prenen H, et al. Ann Oncol 2022;33(suppl):abstr SO-39

SO-39: Evaluation of acquired resistance to sotorasib in KRAS p.G12C-mutated colorectal cancer: Exploratory plasma biomarker analysis of CodeBreaK 100 – Prenen H, et al

Key results

- There were 16/100 potentially targetable alterations
- There was a higher incidence of secondary RAS variants in patients with CRC vs NSCLC
- The most common acquired genomic alteration was in the RTK gene in 12/45 (27%) followed by ERK/MAPK pathway (13%), secondary RAS genomic alterations (13%) and PI3K/AKT/mTOR mutations (11%)
- In fast progressors, 5/7 EGFR alterations were observed, while 4/6 KRAS alterations and 3/3 ERBB2 mutations were not observed
- In slow progressors, 2/2 SMAD4 truncation mutations were observed

Conclusions

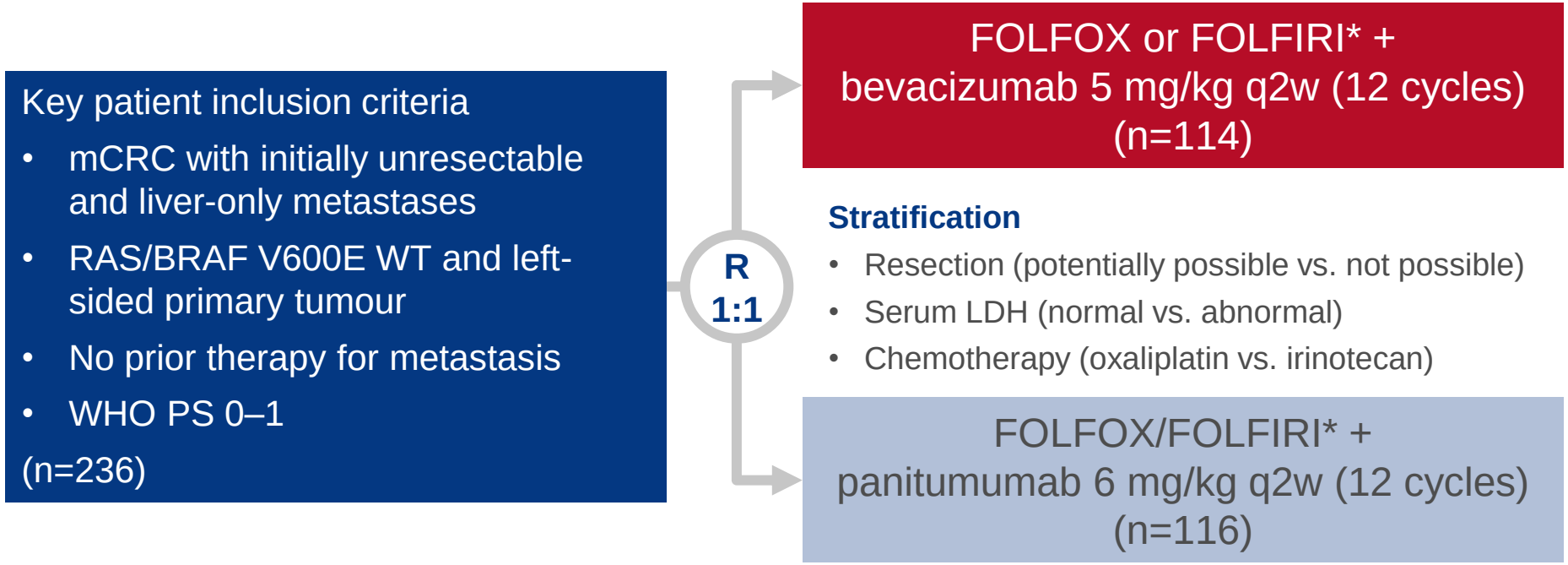
- **In patients with KRAS p.G12C-mutated CRC, the putative mechanisms of resistance to sotorasib were diverse with ≥1 acquired genomic alteration commonly observed and new RTK alterations frequently emerging at progression**

Prenen H, et al. Ann Oncol 2022;33(suppl):abstr SO-39

LBA21: FOLFOX/FOLFIRI plus either bevacizumab or panitumumab in patients with initially unresectable colorectal liver metastases (CRLM) and left-sided and RAS/BRAFV600E wild-type tumour: phase III CAIRO5 study of the Dutch Colorectal Cancer Group – Bond MJ, et al

Study objective

- To evaluate the efficacy and safety of FOLFOXIRI + bevacizumab or panitumumab in patients with initially unresectable colorectal liver metastases, left-sided and/or RAS/BRAF V600E WT tumours in Dutch centres in the phase 3 CAIRO5 study



PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

- OS, ORR, R0/1 rate, postoperative morbidity, safety

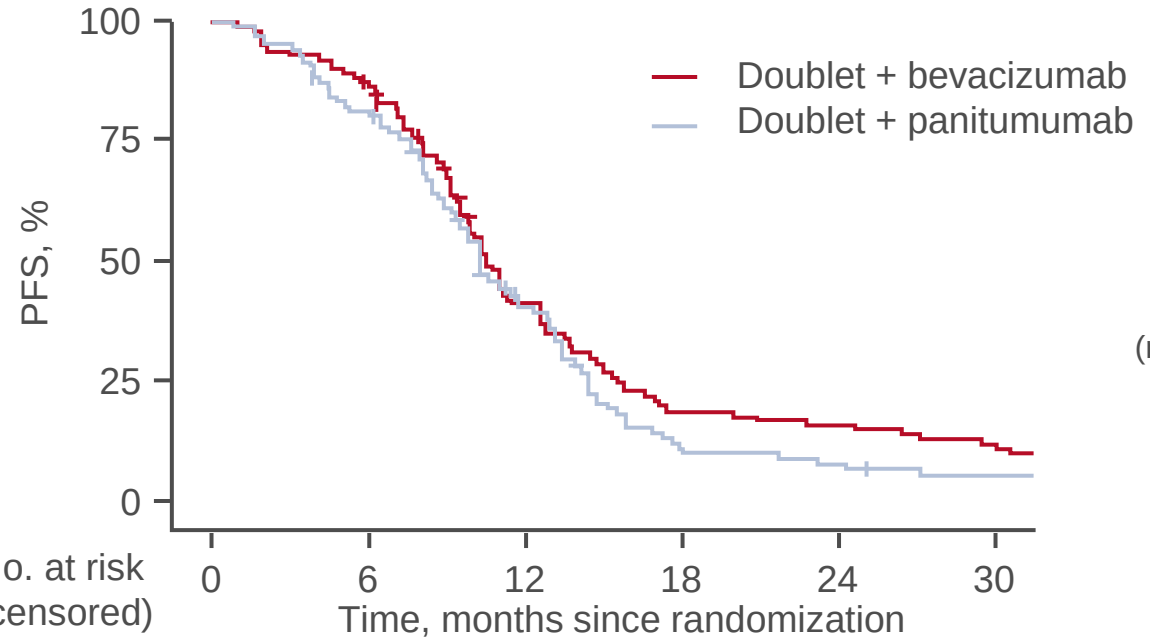
*Patient preference, oxaliplatin 85 mg/m^2 or irinotecan 180 mg/m^2 + LV 400 mg/m^2 + 5FU 400 mg/m^2 bolus then 2400 mg/m^2

Presented at ESMO Congress 2022
Bond MJ, et al. Ann Oncol 2022;33(suppl):abstr LBA21

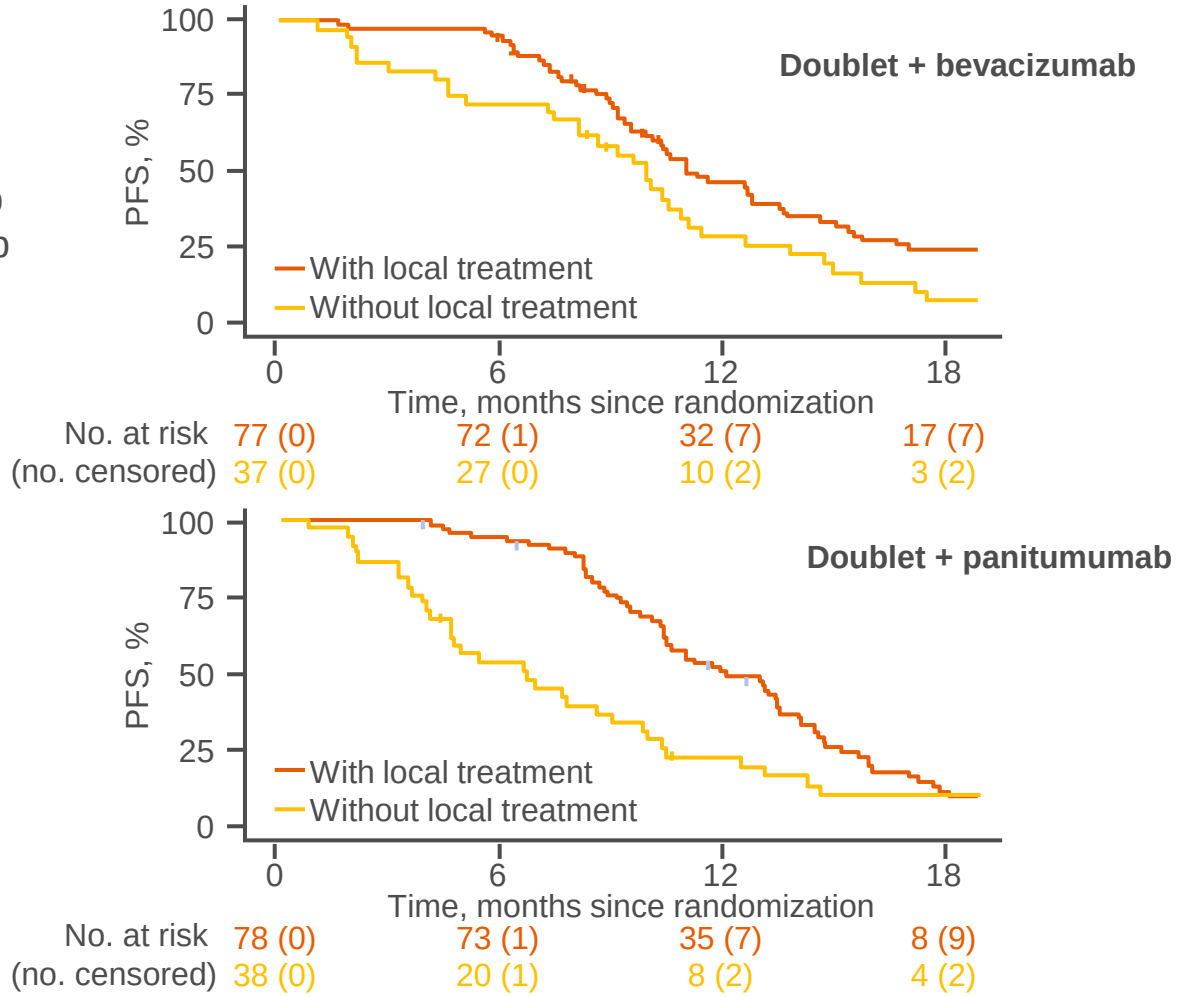
LBA21: FOLFOX/FOLFIRI plus either bevacizumab or panitumumab in patients with initially unresectable colorectal liver metastases (CRLM) and left-sided and RAS/BRAFV600E wild-type tumour: phase III CAIRO5 study of the Dutch Colorectal Cancer Group – Bond MJ, et al

Key results

Progression-free survival



PFS according to resections ± ablations



Bond MJ, et al. Ann Oncol 2022;33(suppl):abstr LBA21

LBA21: FOLFOX/FOLFIRI plus either bevacizumab or panitumumab in patients with initially unresectable colorectal liver metastases (CRLM) and left-sided and RAS/BRAFV600E wild-type tumour: phase III CAIRO5 study of the Dutch Colorectal Cancer Group – Bond MJ, et al

Key results

Systemic treatment	FOLFOX/FOLFIRI + bevacizumab (n=114)	FOLFOX/FOLFIRI + panitumumab (n=116)	p-value
Median cycles, n (IQR)	7 (5–10)	6 (5–9)	
ORR, %	52	76	<0.001
Median depth of response, %	33	49	<0.001
Grade ≥3 AEs, %			
Any	52	69	0.01
Skin toxicity	1	25	<0.001
Hypertension	18	7	0.02
Diarrhea	4	16	0.01
Death	0	1.7	

Local treatments	FOLFOX/FOLFIRI + bevacizumab (n=114)	FOLFOX/FOLFIRI + panitumumab (n=116)	p-value
Resection ± ablation, %	68	67	1
Postoperative complications	42	41	1
Clavien Dindo			
Grade ≥3	21	14	0.3
Grade 5	0.9	0.9	
Median induction cycles, n (IQR)	6 (5–8)	6 (5–9)	
Adjuvant chemotherapy, %	36	42	
R0/1 resection ± ablation rate, %	58	56	0.79

Conclusions

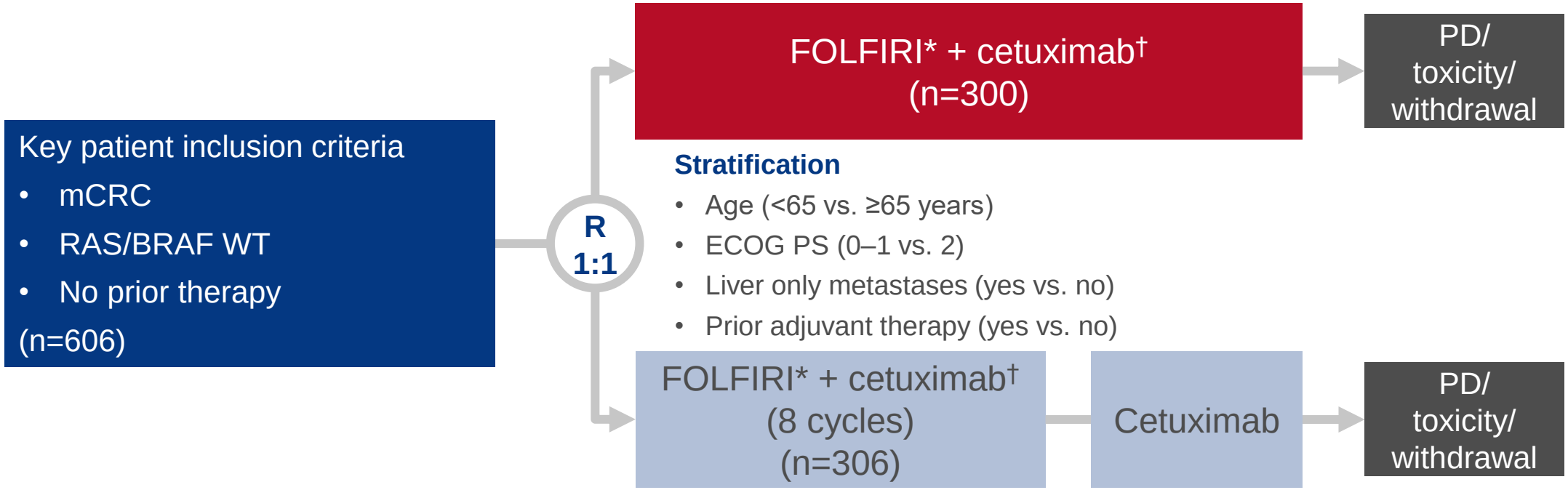
- **In patients with initially unresectable colorectal liver metastases and left-sided, RAS/BRAF V600E WT tumours, there was no difference in survival for 1L FOLFOX/FOLFIRI combined with either bevacizumab or panitumumab, however, the addition of panitumumab resulted in higher rates of toxicity, but improved responses**

Bond MJ, et al. Ann Oncol 2022;33(suppl):abstr LBA21

LBA22: Phase III study with FOLFIRI/cetuximab versus FOLFIRI/cetuximab followed by cetuximab (Cet) alone in first-line therapy of RAS and BRAF wild-type (wt) metastatic colorectal cancer (mCRC) patients: the ERMES Study (NCT02484833) – Orlandi A, et al

Study objective

- To evaluate the efficacy and safety of 1L FOLFIRI + cetuximab followed cetuximab in patients with RAS/BRAF WT mCRC in the phase 3 ERMES study



PRIMARY ENDPOINTS

- PFS, safety

SECONDARY ENDPOINTS

- OS, ORR, QoL

*Irinotecan 180 mg/m^2 D1 q2w + LV 200 mg/m^2 + 5FU 400 mg/m^2 bolus D1 then 1200 mg/m^2 D1, 2 q2w; †cetuximab 400 mg/m^2 loading dose then 250 mg/m^2 qw

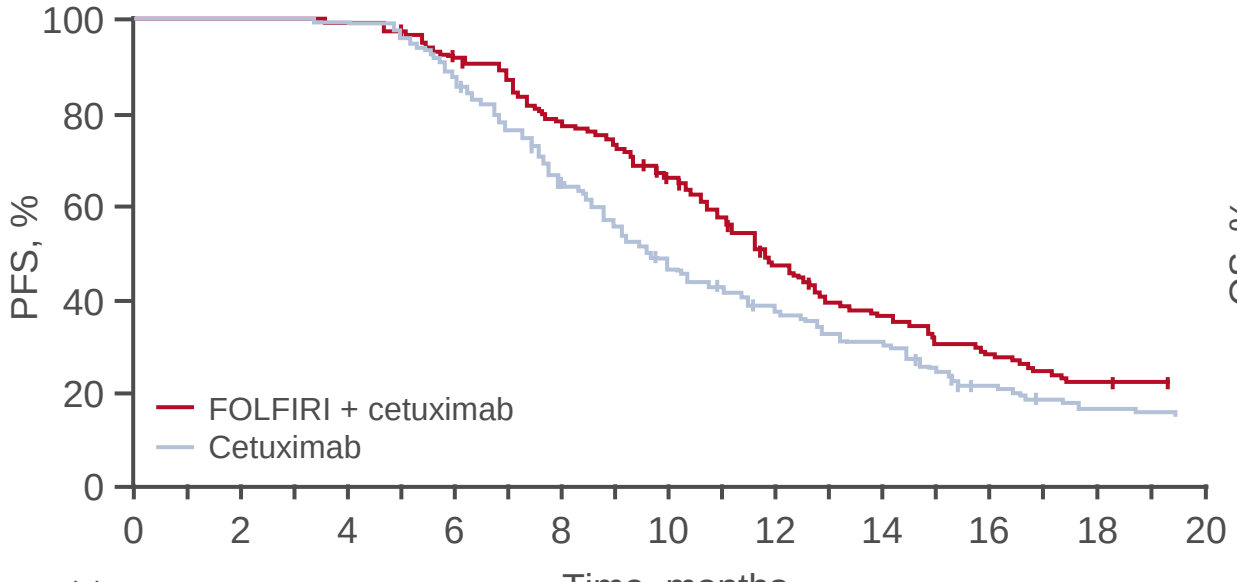
Presented at ESMO Congress 2022
Orlandi A, et al. Ann Oncol 2022;33(suppl):abstr LBA22

LBA22: Phase III study with FOLFIRI/cetuximab versus FOLFIRI/cetuximab followed by cetuximab (Cet) alone in first-line therapy of RAS and BRAF wild-type (wt) metastatic colorectal cancer (mCRC) patients: the ERMES Study (NCT02484833) – Orlandi A, et al

Key results

Progression-free survival (mPP)

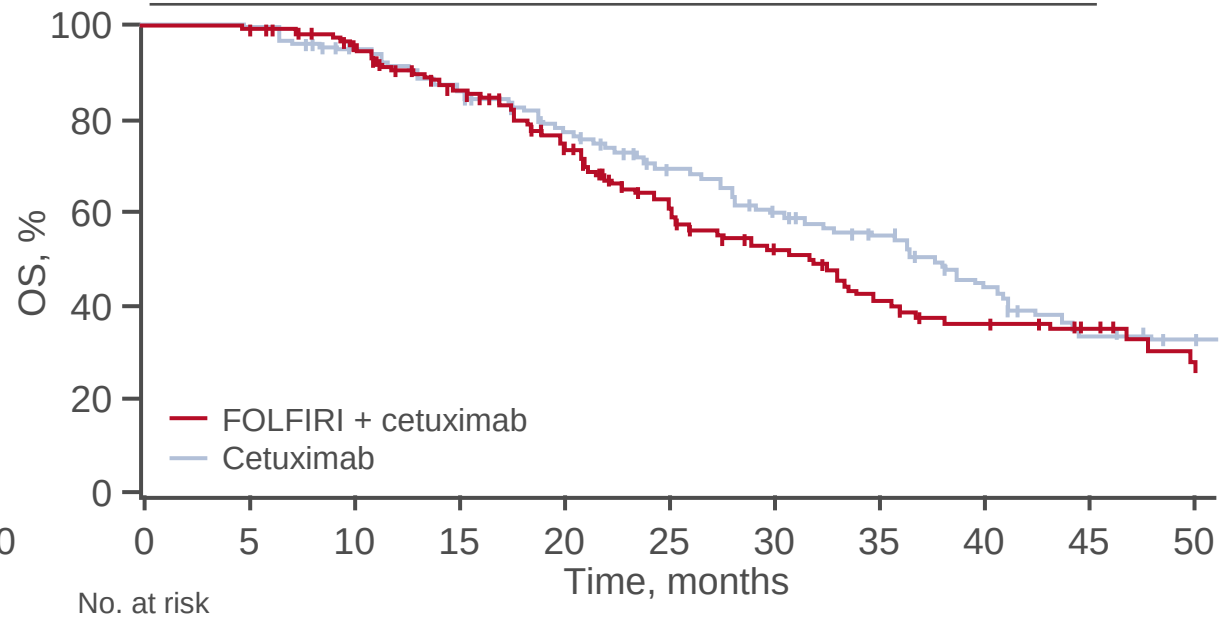
	Cetuximab (n=183)	FOLFIRI + cetuximab (n=154)
Events,	159	132
mPFS, mo (95%CI)	10.0 (9.18, 11.28)	12.2 (11.28, 13.19)
HR (95%CI); p-value	1.30 (1.03, 1.64); 0.43	



No. at risk																				
Cetuximab	183	183	183	183	182	180	161	142	120	104	86	77	67	61	53	46	35	31	27	25	23
FOLFIRI + cetuximab	154	154	154	154	153	150	141	137	119	114	103	89	73	61	53	48	43	38	32	31	30

Overall survival (mPP)

	Cetuximab (n=183)	FOLFIRI + cetuximab (n=154)
Events,	93	83
mOS, mo (95%CI)	36.64 (30.56, 40.16)	30.76 (25.10, 33.88)
HR (95%CI); p-value	0.81 (0.60, 1.09); 0.157	



No. at risk											
Cetuximab	183	183	162	139	109	88	72	61	43	30	21
FOLFIRI + cetuximab	154	153	143	112	86	61	46	34	28	22	13

Orlandi A, et al. Ann Oncol 2022;33(suppl):abstr LBA22

LBA22: Phase III study with FOLFIRI/cetuximab versus FOLFIRI/cetuximab followed by cetuximab (Cet) alone in first-line therapy of RAS and BRAF wild-type (wt) metastatic colorectal cancer (mCRC) patients: the ERMES Study (NCT02484833) – Orlandi A, et al

Key results

	FOLFIRI + cetuximab	Cetuximab	p-value
ORR mPP, % (95%CI)	67.5 (59.5, 74.9)	71.6 (64.5, 78.0)	
BOR mPP, % CR PR	 10.5 56.6	 8.8 62.6	
Right-sided mPP, n mPFS, mo (95%CI)	32 11.73 (9.31, 17.20)	33 8.29 (7.17, 9.70)	0.007
Left-sided mPP, n mPFS, mo (95%CI)	103 12.27 (11.09, 13.19)	135 10.39 (9.31, 12.30)	0.301
mITT, n mPFS, mo (95%CI)	296 10.72 (9.64, 11.41)	297 9.01 (8.16, 9.87)	0.305
mITT, n mOS, mo (95%CI)	296 25.36 (22.04, 32.96)	297 31.09 (26.91, 35.56)	0.327

AEs, %	FOLFIRI + cetuximab (n=154)		Cetuximab (n=183)	
	Whole period	Maintenance period	Whole period	Maintenance period
Any	44.2	23.4	39.9	16.4
Anemia	0.7	0	1.1	1.1
Febrile neutropenia	5.2	1.3	2.7	0
Neutrophil count decreased	14.9	7.1	9.8	0.6
Diarrhea	11.0	5.2	8.2	1.1
Oral mucositis	5.2	2.0	1.6	0.6
Fatigue	4.6	3.3	0.6	0
Hypomagnesemia	2.0	1.3	1.6	0.6
Skin disorders	20.1	9.7	18.0	10.4

Conclusions

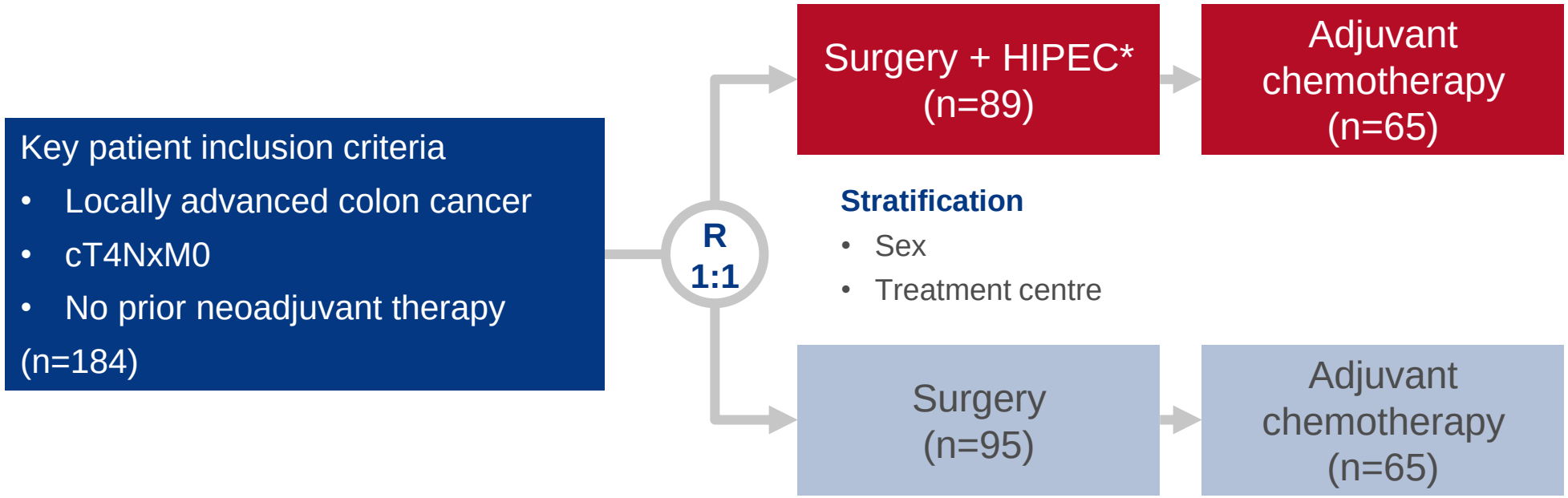
- **In patients with RAS/BRAF WT mCRC, FOLFIRI + cetuximab followed by cetuximab maintenance did not demonstrate non-inferiority to continued FOLFIRI + cetuximab and there were particularly encouraging findings in those with left-sided tumours, but there was a higher than expected dropout rate (40% vs. 20%) that may have confounded the results**

Orlandi A, et al. Ann Oncol 2022;33(suppl):abstr LBA22

314O: Adjuvant hyperthermic intraperitoneal chemotherapy in locally advanced colon cancer (HIPECT4): a randomized,phase 3 study – Arjona-Sanchez A, et al

Study objective

- To evaluate the efficacy and safety of adjuvant hyperthermic intraperitoneal chemotherapy in patients with locally advanced colon cancer in Spanish centres in the phase 3 HIPECT4 study



PRIMARY ENDPOINT

- 3-yr locoregional control rate†

SECONDARY ENDPOINTS

- DFS, OS, safety

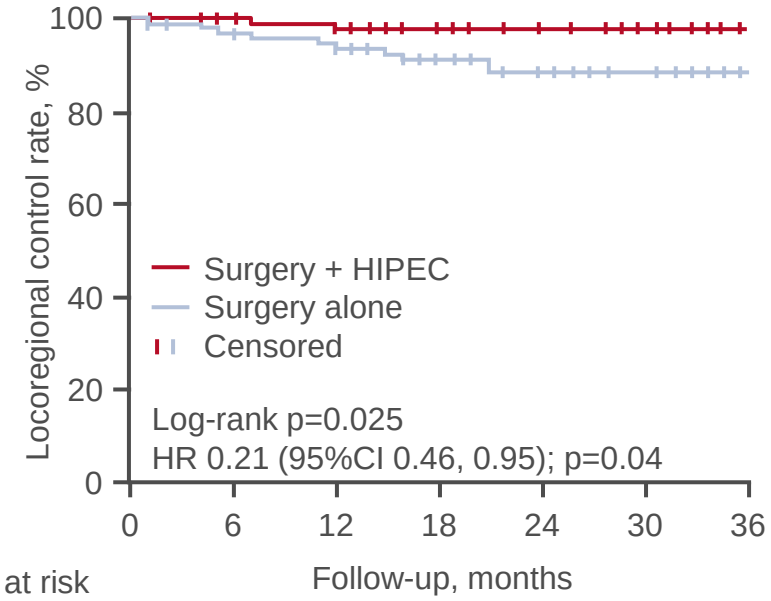
*Mitomycin C 30 mg/m^2; †defined as time from treatment to peritoneal disease recurrence or death from any cause

Presented at ESMO Congress 2022
Arjona-Sanchez A, et al. Ann Oncol 2022;33(suppl):abstr 314O

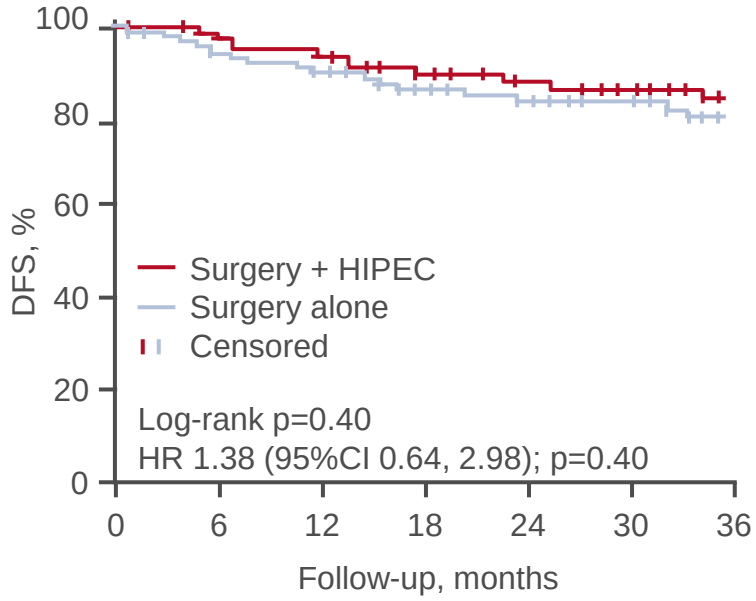
314O: Adjuvant hyperthermic intraperitoneal chemotherapy in locally advanced colon cancer (HIPECT4): a randomized,phase 3 study – Arjona-Sanchez A, et al

Key results

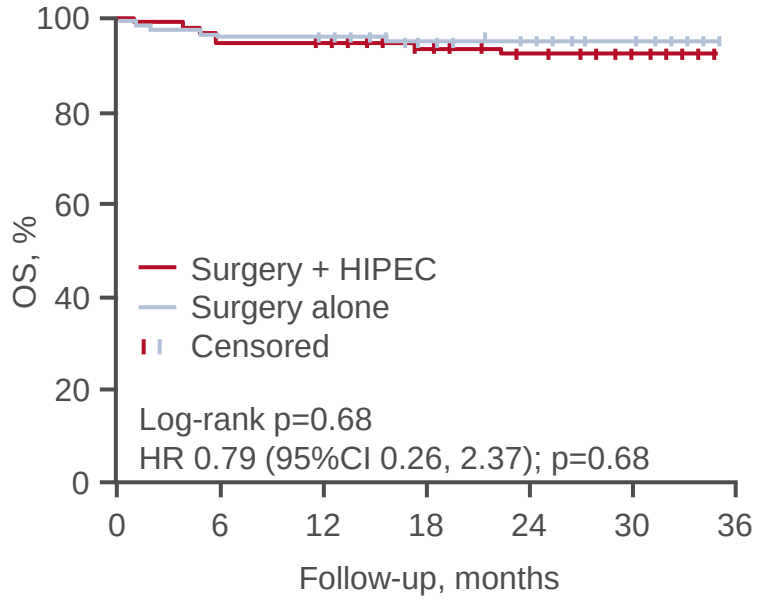
Locoregional control rate



Disease-free survival



Overall survival



No. at risk (censored)												
Surgery alone	95	86 (4)	66 (15)	47 (19)	95	83 (3)	63 (13)	42 (18)	95	90 (0)	74 (15)	53 (20)
HIPEC	89	82 (5)	65 (17)	49 (16)	89	80 (4)	59 (17)	43 (12)	89	83 (0)	65 (16)	49 (16)

Arjona-Sanchez A, et al. Ann Oncol 2022;33(suppl):abstr 314O

314O: Adjuvant hyperthermic intraperitoneal chemotherapy in locally advanced colon cancer (HIPECT4): a randomized,phase 3 study – Arjona-Sanchez A, et al

Key results

Morbidity, n (%)	Surgery + HIPEC (n=89)	Surgery (n=61)	p-value
Ostomy	4 (4.5)	8 (8.5)	0.24
Grade 3 anemia	7 (8.0)	5 (5.3)	0.71
Grade 4 neutropenia	1 (1.1)	0	0.14
Grade 1 thrombocytopenia	2 (2.3)	0	0.27
Renal failure (RIFLE) Risk Injury	 1 (1.1) 1 (1.1)	 1 (1.1) 0	0.54
Re-intervention	11 (12.0)	11 (11.0)	0.89
Major morbidity 30 days 60 days	 21 (23.6) 23 (25.8)	 17 (18.1) 17 (18.1)	 0.35 0.20
Mortality 30 days	1 (1.1)	2 (2.1)	0.60

Conclusions

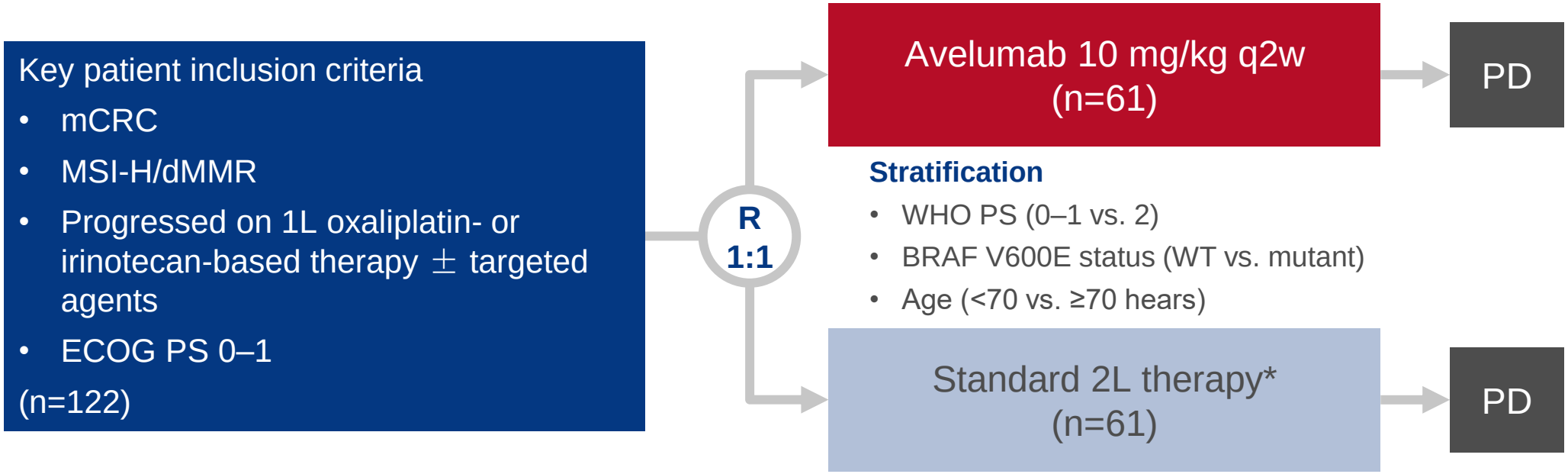
- **In patients with locally advanced colon cancer, adjuvant hyperthermic intraperitoneal chemotherapy demonstrated improved locoregional control rate without increasing morbidity, however, there were no significant improvements observed in DFS or OS**

Arjona-Sanchez A, et al. Ann Oncol 2022;33(suppl):abstr 314O

LBA23: Avelumab versus standard second-line treatment chemotherapy in metastatic colorectal cancer (mCRC) patients with microsatellite instability (MSI): the SAMCO-PRODIGE 54 randomised phase II trial – Taieb J, et al

Study objective

- To evaluate the efficacy and safety of 2L avelumab in patients with mCRC and MSI in French centres in the phase 2 SAMCO-PRODIGE 54 study



PRIMARY ENDPOINT

- PFS (RECIST v1.1)

SECONDARY ENDPOINTS

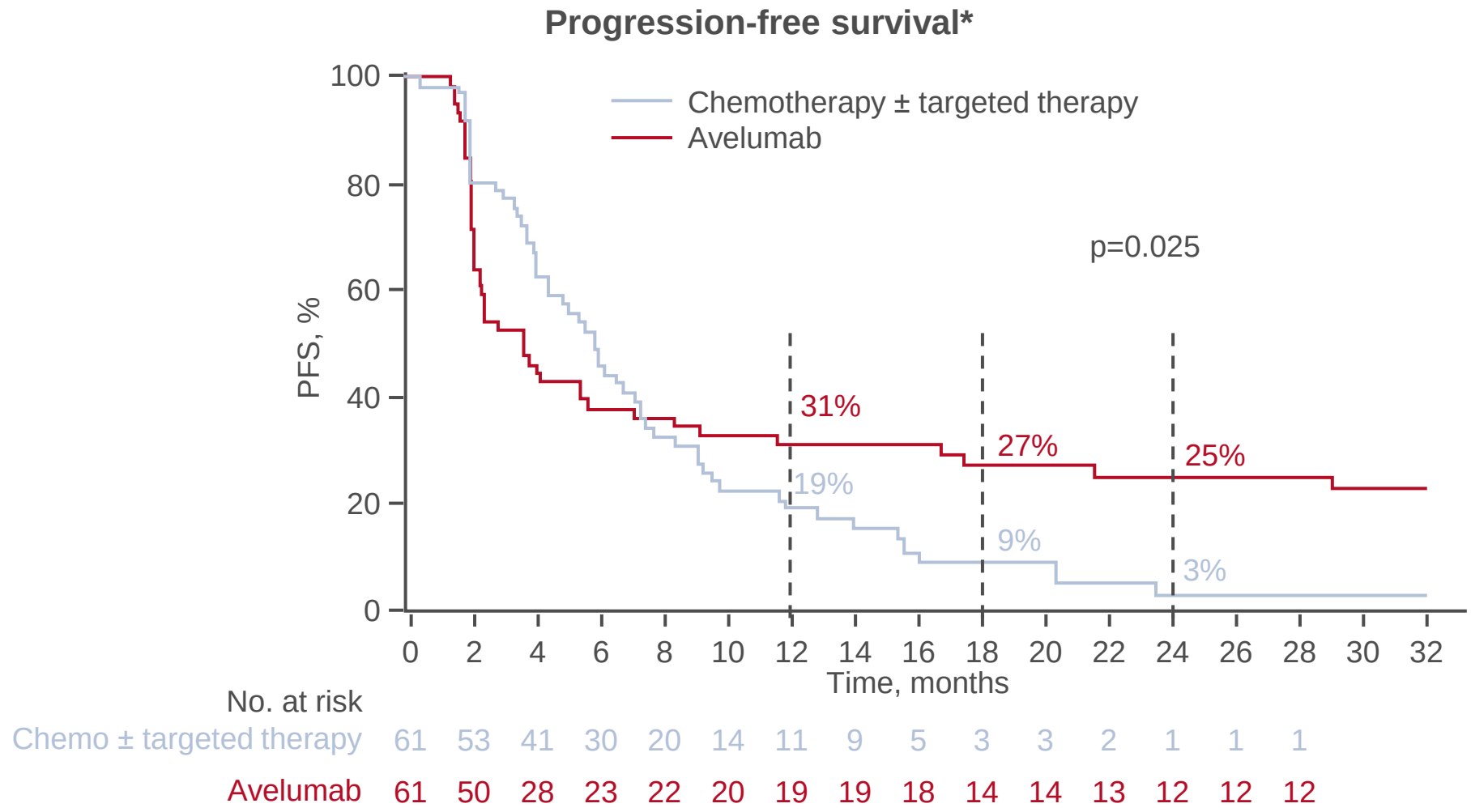
- ORR, DCR, OS, safety

*FOLFOX or FOLFIRI depending on 1L regimen ± targeted therapy (bevacizumab, aflibercept, ramucirumab, panitumumab or cetuximab)

Presented at ESMO Congress 2022
Taieb J, et al. Ann Oncol 2022;33(suppl):abstr LBA23

LBA23: Avelumab versus standard second-line treatment chemotherapy in metastatic colorectal cancer (mCRC) patients with microsatellite instability (MSI): the SAMCO-PRODIGE 54 randomised phase II trial – Taieb J, et al

Key results



*The log-rank test and HE of treatment are not valid as the Kaplan-Meier curved crossed at 7.3 months

Taieb J, et al. Ann Oncol 2022;33(suppl):abstr LBA23

LBA23: Avelumab versus standard second-line treatment chemotherapy in metastatic colorectal cancer (mCRC) patients with microsatellite instability (MSI): the SAMCO-PRODIGE 54 randomised phase II trial – Taieb J, et al

Key results

	Avelumab (n=61)	Chemotherapy (n=61)
ORR, n (%)	18 (29.5)	16 (26.3)
BOR, n (%)		
CR	4 (6.5)	3 (5.0)
PR	14 (23.0)	13 (21.3)
SD	25 (41.0)	31 (51.0)
PD	17 (28.0)	10 (16.5)
Time to best response, mo	2.99	1.94

Grade 3–4 AEs, %	Avelumab (n=63)	Chemotherapy (n=64)
Any	31.7	53.1
Nausea	0	3.0
Vomiting	1.0	2.0
Diarrhea	5.0	8.0
Stomatitis	0	3.0
Neutropenia	0	19.0
Neurotoxicity	4.0	2.0
Fatigue	0	11.0
Hypertension	1.6	11.0
Abnormal liver tests	9.5	1.6

Conclusions

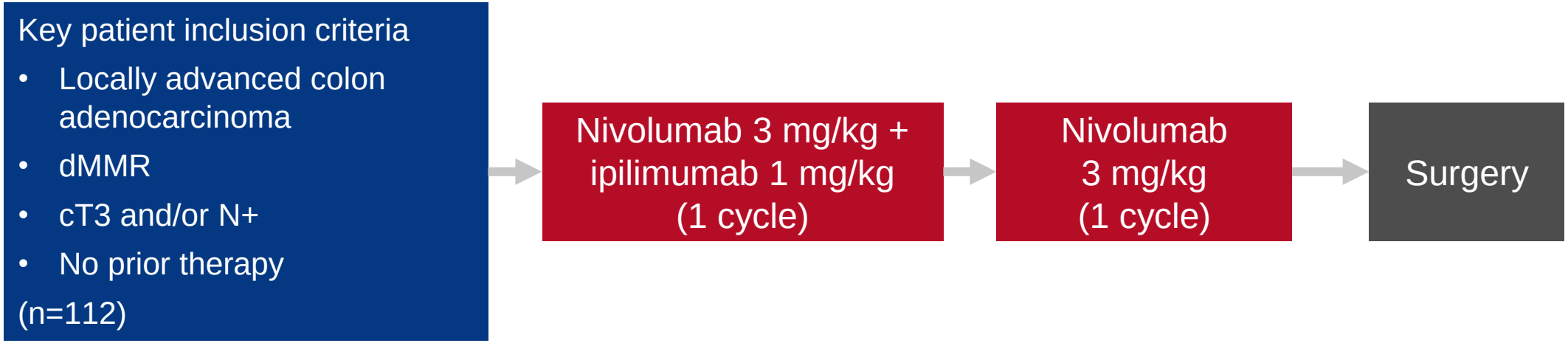
- **In patients with MSI-H mCRC, 2L avelumab demonstrated significant improvement in the 12- ,18- and 24-month PFS rates compared with standard therapy and was generally well-tolerated**

Taieb J, et al. Ann Oncol 2022;33(suppl):abstr LBA23

LBA7: Neoadjuvant immune checkpoint inhibition in locally advanced MMR-deficient colon cancer: the NICHE-2 study – Chalabi M, et al

Study objective

- To evaluate the efficacy and safety of neoadjuvant nivolumab + ipilimumab in patients with locally advanced dMMR colon cancer in the NICHE-2 study



PRIMARY ENDPOINTS

- 3-yr DFS, safety

SECONDARY ENDPOINTS

- MPR, pCR

Presented at ESMO Congress 2022
Chalabi M, et al. Ann Oncol 2022;33(suppl):abstr LBA7

LBA7: Neoadjuvant immune checkpoint inhibition in locally advanced MMR-deficient colon cancer: the NICHE-2 study – Chalabi M, et al

Key results

irAEs, n (%)	n=112
Any	68 (61)
Grade ≥3*	4 (4)
Amylase increased	1 (G3)
Lipase increased	1 (G4)
Hepatitis	1 (G3)
Myositis	1 (G3)
Rash	1 (G3)
Led to ≥2 week delay in surgery	2 (2)

Response	n=107
MPR, %	95
pCR, %	67
Pathologic response (RVT), n (%)	
Yes (≤50%)	106 (99)
Major (≤10%)	102 (95)
Complete (0%)	72 (67)
Partial (10–50%)	4 (4)
No (≥50%)	1 (1)

Adjuvant chemotherapy, n	
Patients with ypN+ disease	14
Received adjuvant chemotherapy	3
Aged >70 years	5
Patients refused treatment	6

Disease recurrence	
Median follow-up, mo (range)	13.1 (1.4–57.4)
Disease recurrence	0

pCR rate, n (%)	Sporadic tumour (n=65)	Lynch syndrome (n=32)	p-value
No pCR	27 (42)	7 (22)	0.056
pCR	38 (58)	25 (78)	

Conclusions

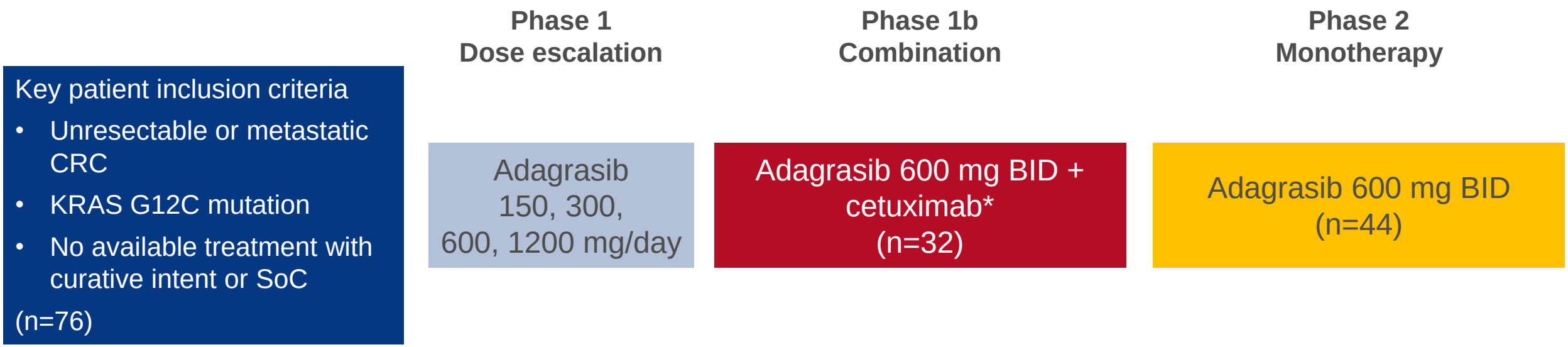
- **In patients with locally advanced dMMR colon cancer, neoadjuvant nivolumab + ipilimumab demonstrated high rates of MPR with no disease recurrences to date and was generally well-tolerated**

Chalabi M, et al. Ann Oncol 2022;33(suppl):abstr LBA7

LBA24: KRYSTAL-1: updated efficacy and safety of adagrasib (MRTX849) with or without cetuximab in patients with advanced colorectal cancer (CRC) harboring a KRASG12C mutation – Klempner SJ, et al

Study objective

- To evaluate the updated efficacy and safety of adagrasib in the cohort of previously treated patients with unresectable or metastatic CRC and harbouring a KRAS G12C mutation in US centres in the phase 2 portion of the KRYSTAL-1 study



PRIMARY ENDPOINT

- Phase 1: RP2D, safety
- Phase 2: ORR (RECIST v1.1)

SECONDARY ENDPOINTS

- Phase 2: DoR, PFS, OS, safety

*Cetuximab 400 mg/m^2 followed by 250 mg/m^2 qw or 500 mg/m^2 q2w

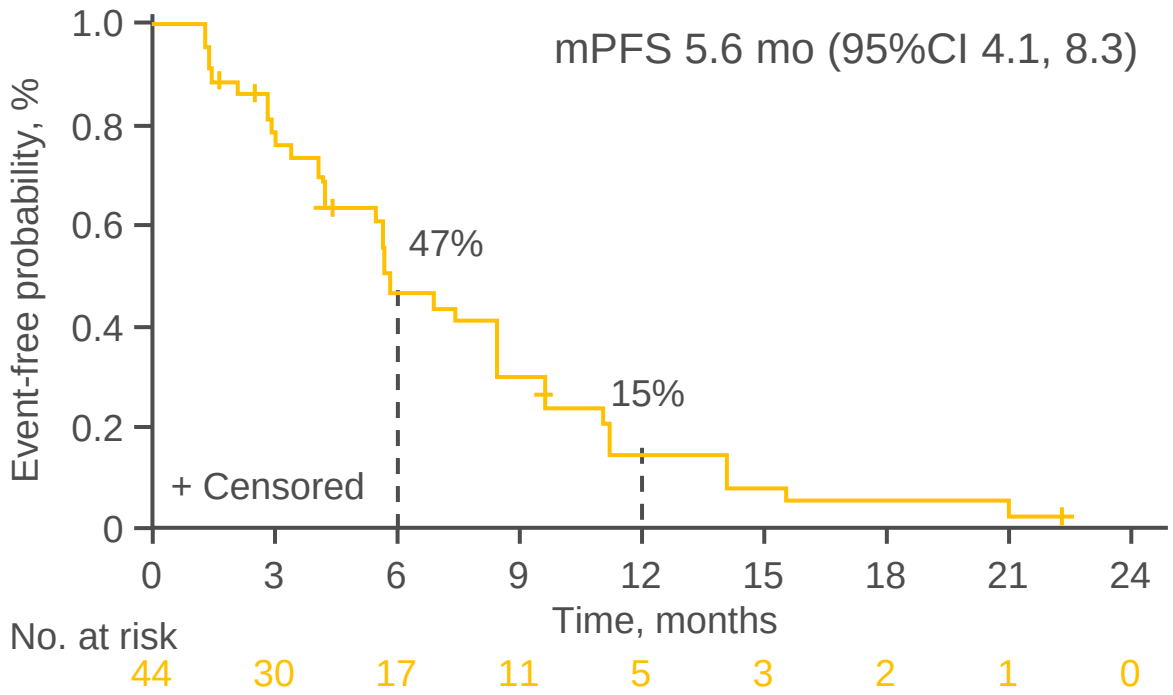
Presented at ESMO Congress 2022
Klempner SJ, et al. Ann Oncol 2022;33(suppl):abstr LBA24

LBA24: KRYSTAL-1: updated efficacy and safety of adagrasib (MRTX849) with or without cetuximab in patients with advanced colorectal cancer (CRC) harboring a KRASG12C mutation – Klempner SJ, et al

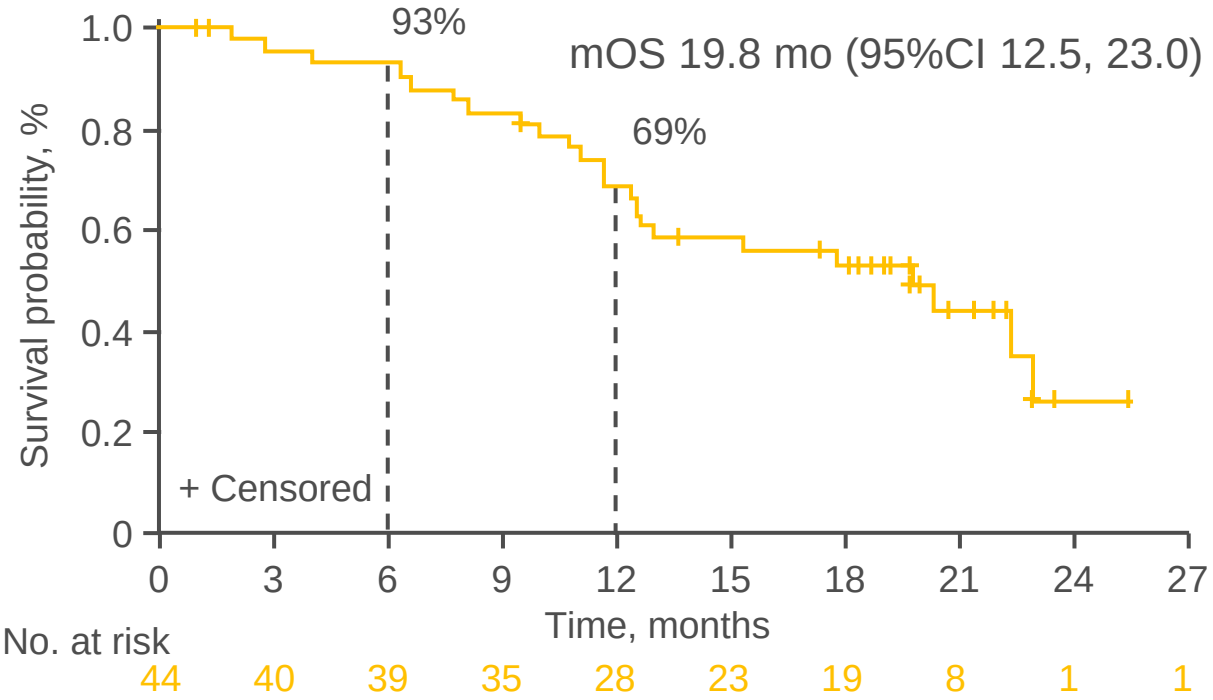
Key results

Adagrasib monotherapy

Progression-free survival



Overall survival



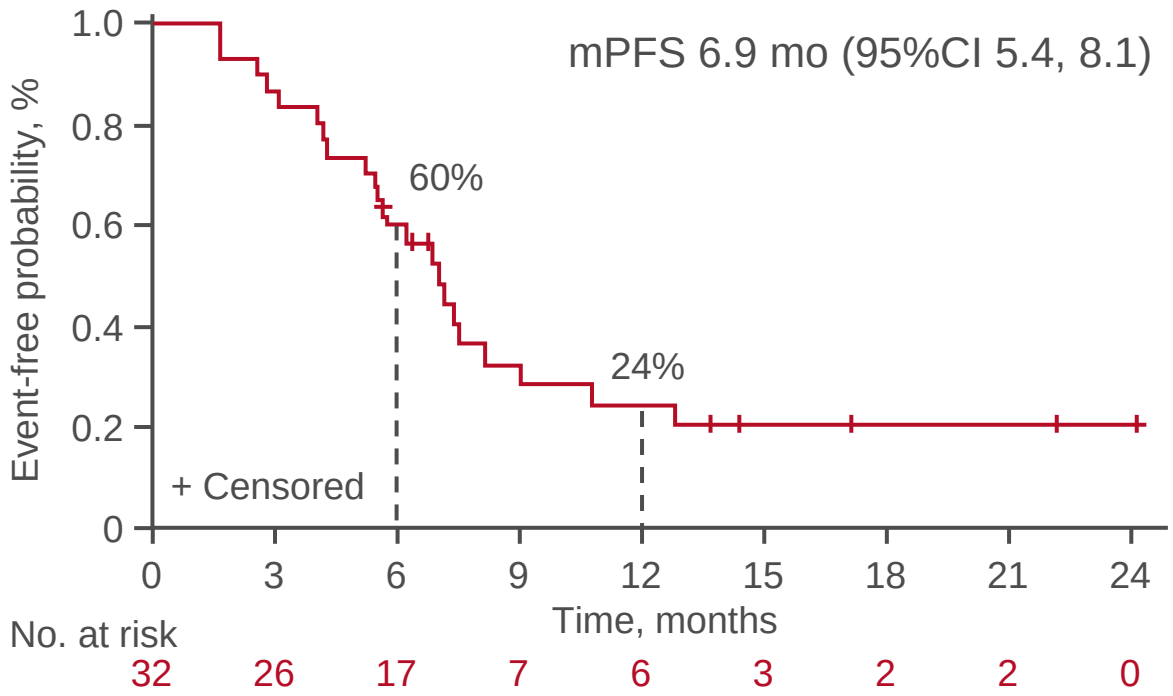
Klempner SJ, et al. Ann Oncol 2022;33(suppl):abstr LBA24

LBA24: KRYSTAL-1: updated efficacy and safety of adagrasib (MRTX849) with or without cetuximab in patients with advanced colorectal cancer (CRC) harboring a KRASG12C mutation – Klempner SJ, et al

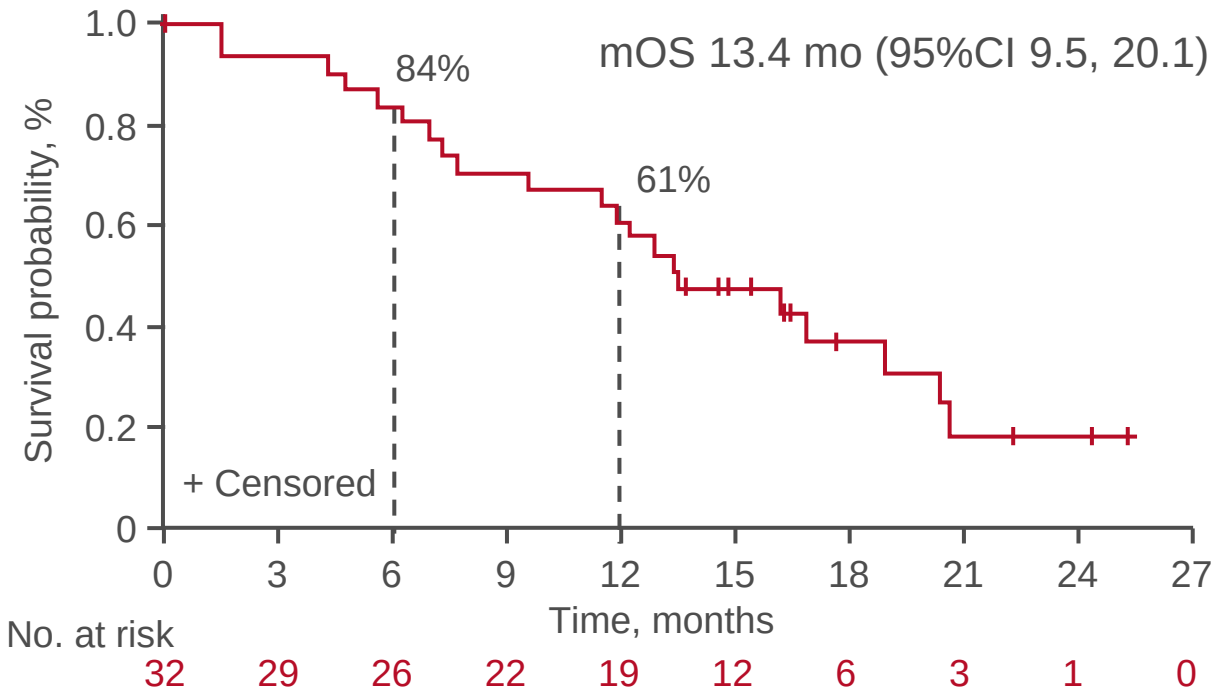
Key results

Adagrasib + cetuximab

Progression-free survival



Overall survival



Klempner SJ, et al. Ann Oncol 2022;33(suppl):abstr LBA24

LBA24: KRYSTAL-1: updated efficacy and safety of adagrasib (MRTX849) with or without cetuximab in patients with advanced colorectal cancer (CRC) harboring a KRASG12C mutation – Klempner SJ, et al

Key results

	Adagrasib (n=43)	Adagrasib + cetuximab (n=28)
ORR, n (%)	8 (19)	13 (46)
DCR, n (%)	37 (86)	28 (100)
Occurrence of tumour shrinkage, %	79	93
mDoR, mo	4.3	7.6
mTTR, mo	1.5	1.4

TRAEs, %	Adagrasib (n=43)	Adagrasib + cetuximab (n=28)
Grade 3	30	9
Grade 4	5	7
Led to dose reduction of adagrasib	39	31
Led to dose interruption of adagrasib	46	44
Led to discontinuation		
Adagrasib	0	0
Cetuximab	-	16

Conclusions

- **In heavily pretreated patients with KRAS G12C-mutant mCRC, adagrasib ± cetuximab demonstrated promising antitumor activity and had a manageable safety profile**

Klempner SJ, et al. Ann Oncol 2022;33(suppl):abstr LBA24

315O: Sotorasib in combination with panitumumab in refractory KRAS G12C-mutated colorectal cancer: safety and efficacy for phase 1b full expansion cohort – Kuboki Y, et al

Study objective

- To evaluate the efficacy and safety of sotorasib + panitumumab in patients with refractory KRAS G12C-mutated mCRC in the phase 1b expansion cohort of the CodeBreaK 101 study

Key patient inclusion criteria

- Refractory mCRC
- KRAS G12C mutation (molecular testing)
- Progressed on or after fluoropyrimidine, oxaliplatin, irinotecan and anti-angiogenic agent
- No prior KRAS G12C inhibitor

(n=40)

Dose exploration

Sotorasib PO daily + panitumumab 6 mg/kg IV q2w

Dose expansion

Sotorasib 960 mg/day PO + panitumumab 6 mg/kg IV q2w (n=40)

PRIMARY ENDPOINT

- Safety

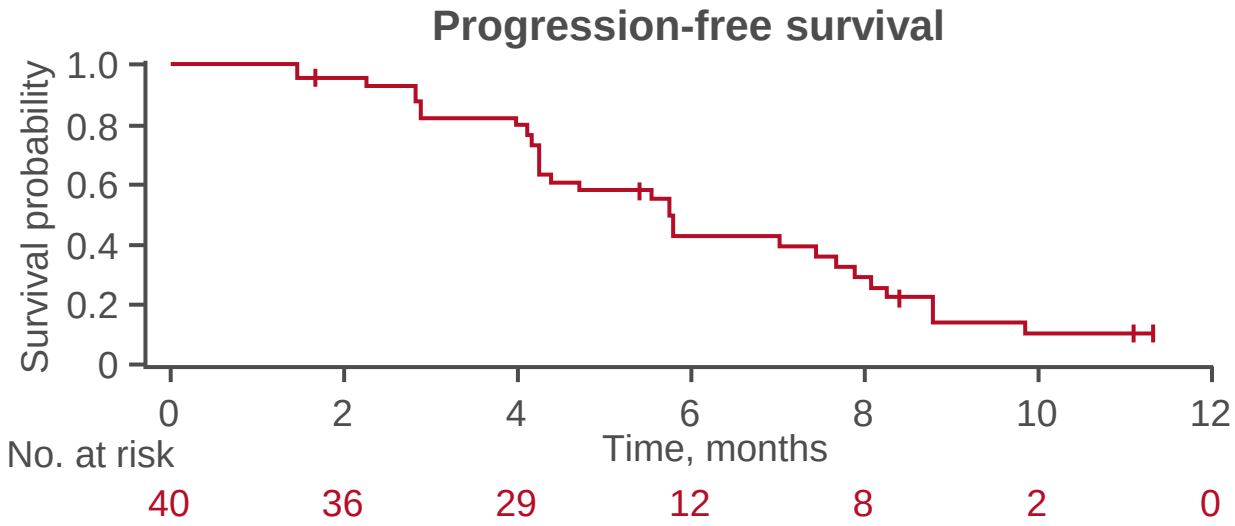
SECONDARY ENDPOINTS

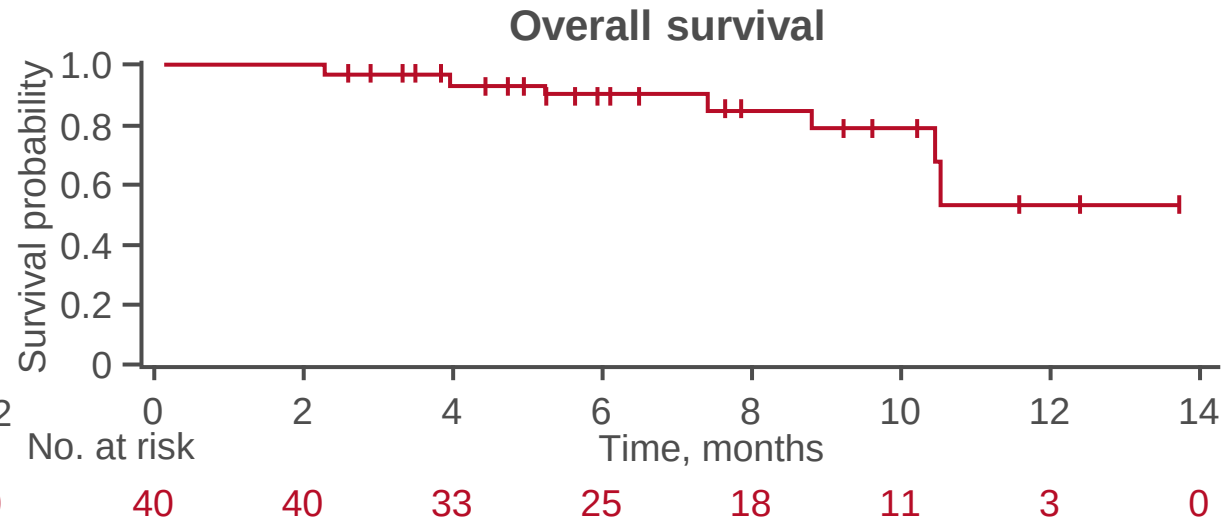
- ORR, DCR, TTR, PFS, OS

Presented at ESMO Congress 2022
Kuboki Y, et al. Ann Oncol 2022;33(suppl):abstr 315O

315O: Sotorasib in combination with panitumumab in refractory KRAS G12C-mutated colorectal cancer: safety and efficacy for phase 1b full expansion cohort – Kuboki Y, et al

Key results





PFS	n=40
mPFS, mo (95%CI)	5.7 (4.2, 7.6)
Left-sided primary	5.8 (4.2, 7.8)
Right-sided primary	5.5 (3.9, 8.2)
PFS rate, % (95%CI)	
3 months	81.7 (65.4, 90.9)
6 months	41.1 (24.7, 56.7)
9 months	12.3 (3.4, 27.2)

OS	n=40
mOS, mo (95%CI)	NE (10.4, NE)
Left-sided primary	NE (10.4, NE)
Right-sided primary	NE (8.7, NE)
OS rate, % (95%CI)	
3 months	97.5 (83.6, 99.6)
6 months	91.5 (75.7, 97.2)
9 months	82.5 (61.8, 92.6)

Kuboki Y, et al. Ann Oncol 2022;33(suppl):abstr 315O

315O: Sotorasib in combination with panitumumab in refractory KRAS G12C-mutated colorectal cancer: safety and efficacy for phase 1b full expansion cohort – Kuboki Y, et al

Key results

	n=40
ORR, n (%) [95%CI]	12 (30) [16.6, 46.5]
BOR, n (%)	
CR	0
PR	12 (30)
SD	25 (63)
PD	3 (8)
DCR, n (%) [95%CI]	37 (93) [79.6, 98.4]
DoR, mo (95%CI)	4.4 (2.8, 7.4)
ORR, %	
Left-sided (n=27)	30
Right-sided (n=13)	31

TRAEs, n (%)	n=40
Any	37 (93)
Attributed to sotorasib	26 (65)
Attributed to panitumumab	37 (93)
Grade 3	9 (23)
Led to dose modification	
Attributed to sotorasib	6 (15)
Attributed to panitumumab	10 (25)
Led to discontinuation of either treatment	0

Conclusions

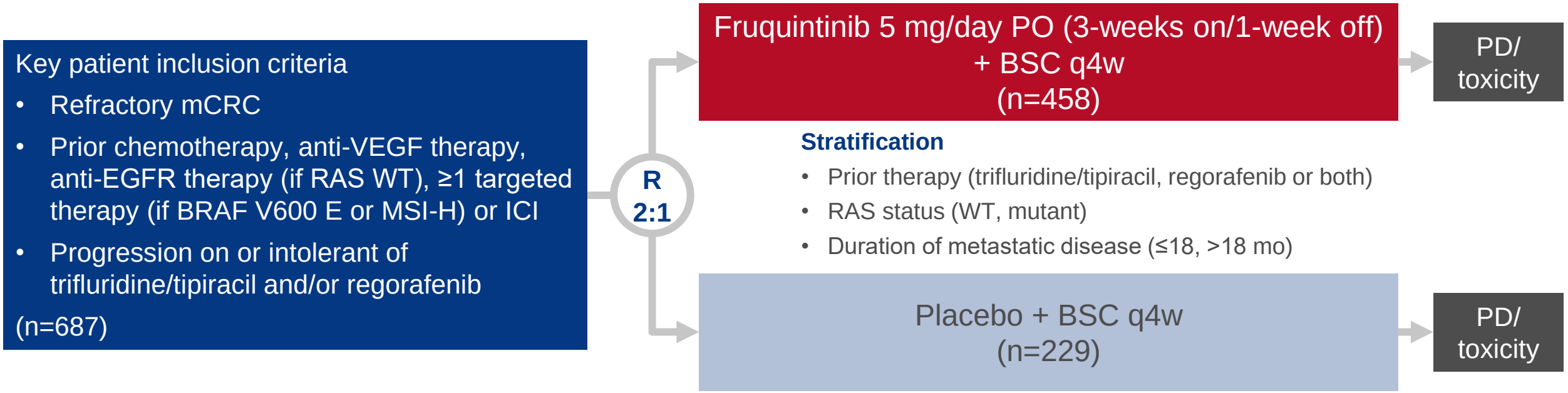
- **In patients with refractory KRAS G12C-mutated CRC, sotorasib + panitumumab demonstrated promising antitumor activity and had an acceptable safety profile**

Kuboki Y, et al. Ann Oncol 2022;33(suppl):abstr 315O

LBA25: FRESCO-2: A global phase 3 multiregional clinical trial (MRCT) evaluating the efficacy and safety of fruquintinib in patients with refractory metastatic colorectal cancer – Dasari NA, et al

Study objective

- To evaluate the efficacy and safety of fruquintinib in patients with refractory mCRC in the global phase 3 FRESCO-2 study



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR, DCR, safety

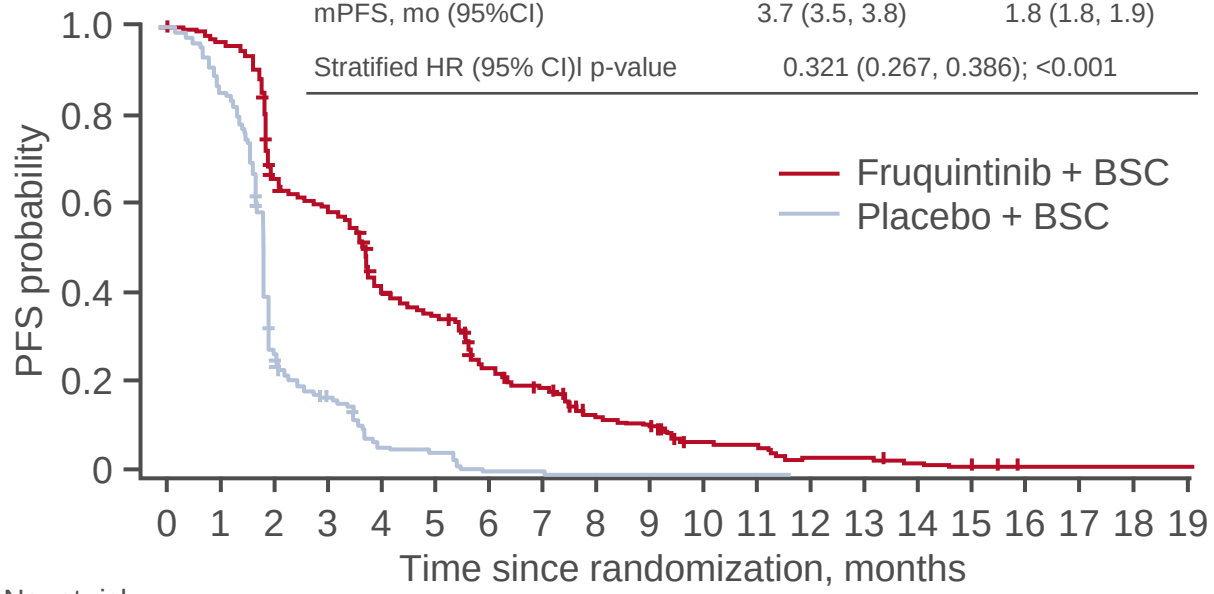
Presented at ESMO Congress 2022
Dasari NA, et al. Ann Oncol 2022;33(suppl):abstr LBA25

LBA25: FRESCO-2: A global phase 3 multiregional clinical trial (MRCT) evaluating the efficacy and safety of fruquintinib in patients with refractory metastatic colorectal cancer – Dasari NA, et al

Key results

Progression-free survival

	Fruquintinib (n=461)	Placebo (n=230)
Events, n (%)	392 (85.0)	213 (92.6)
mPFS, mo (95%CI)	3.7 (3.5, 3.8)	1.8 (1.8, 1.9)
Stratified HR (95% CI)l p-value	0.321 (0.267, 0.386); <0.001	

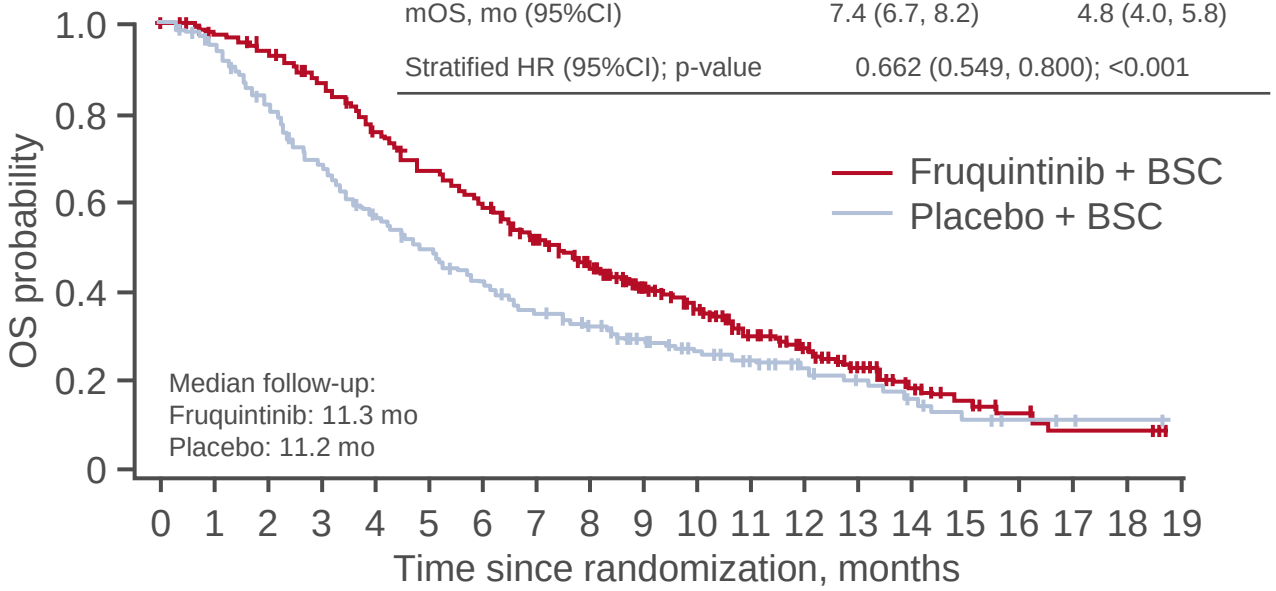


No. at risk

Fruquintinib	461	430	291	256	170	146	89	71	43	36	21	17	10	9	6	4	2	2	2	
Placebo	230	194	60	36	12	10	2	2	1	1	1	1								

Overall survival

	Fruquintinib (n=461)	Placebo (n=230)
Events, n (%)	317 (68.8)	173 (75.2)
mOS, mo (95%CI)	7.4 (6.7, 8.2)	4.8 (4.0, 5.8)
Stratified HR (95%CI); p-value	0.662 (0.549, 0.800); <0.001	



Fruquintinib	461	449	429	395	349	297	266	224	184	143	113	79	58	41	23	14	7	4	4	0
Placebo	230	216	184	153	125	105	89	73	63	45	37	31	20	15	10	6	3	2	1	0

Dasari NA, et al. Ann Oncol 2022;33(suppl):abstr LBA25

LBA25: FRESCO-2: A global phase 3 multiregional clinical trial (MRCT) evaluating the efficacy and safety of fruquintinib in patients with refractory metastatic colorectal cancer – Dasari NA, et al

Key results

	Fruquintinib (n=641)	Placebo (n=230)
ORR, n (%)	7 (1.5)	0
Adjusted difference (95%CI); p-value	1.5 (0.4, 2.7); 0.059	
DCR, n (%)	256 (55.5)	37 (16.1)
Adjusted difference (95%CI); p-value	39.4 (32.8, 46.0); <0.001	

TEAEs, n (%)	Fruquintinib (n=456)	Placebo (n=230)
Any	451 (98.9)	213 (92.6)
Grade ≥3	286 (62.7)	116 (50.4)
Grade ≥3 TRAEs	164 (36.0)	26 (11.3)
Led to death	48 (10.5)	45 (19.6)
Serious	171 (37.5)	88 (38.3)
Grade ≥3	162 (35.5)	85 (37.0)
Led to dose interruption	247 (54.2)	70 (30.4)
Led to dose reduction	110 (24.1)	9 (3.9)
Led to discontinuation	93 (20.4)	49 (21.3)

Conclusions

- **In patients with refractory mCRC, fruquintinib + BSC demonstrated significant improvement in survival compared with BSC alone and was generally well-tolerated**

Dasari NA, et al. Ann Oncol 2022;33(suppl):abstr LBA25

316O: Genomic mechanisms of acquired resistance of patients (pts) with BRAF V600E-mutant (mt) metastatic colorectal cancer (mCRC) treated in the BEACON study – Kopetz S, et al

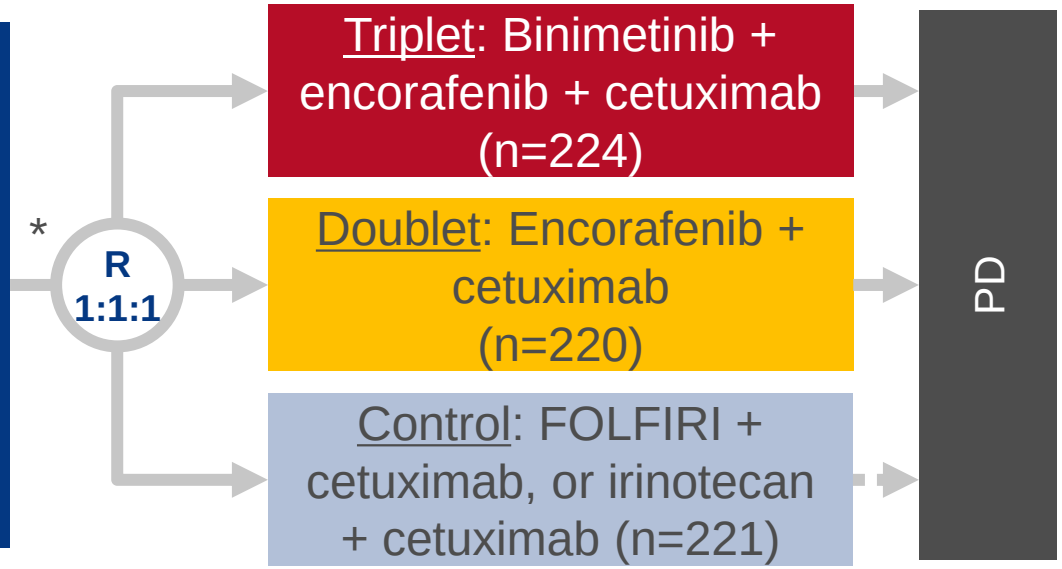
Study objective

- To evaluate the genomic mechanisms of acquired resistance in previously treated patients with BRAF V600E-mutant mCRC in the BEACON study

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)



CO-PRIMARY ENDPOINTS

- OS, ORR (BICR)†

BIOMARKER ENDPOINTS

- Identify genomic alterations of resistance in ctDNA analysis of baseline set (n=544) and paired set (n=320) using GuardantOMNI

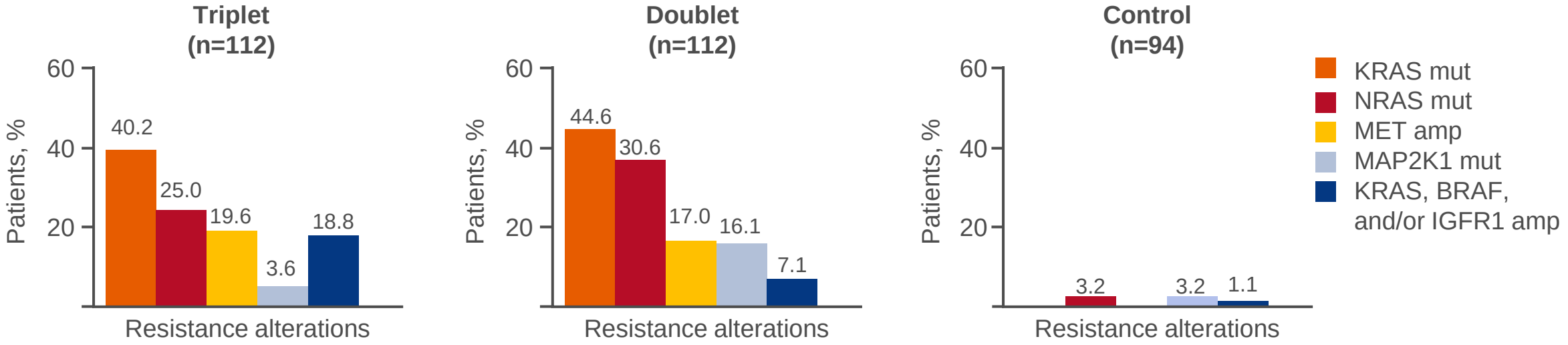
*Safety lead-in (n=30): binimetinib 45 mg bid + encorafenib 300 mg/day + cetuximab 400 mg/m^2 (initial) then 250 mg/m^2 qw; †data previously presented at ESMO WCGC 2019

Presented at ESMO Congress 2022
Kopetz S, et al. Ann Oncol 2022;33(suppl):abstr 316O

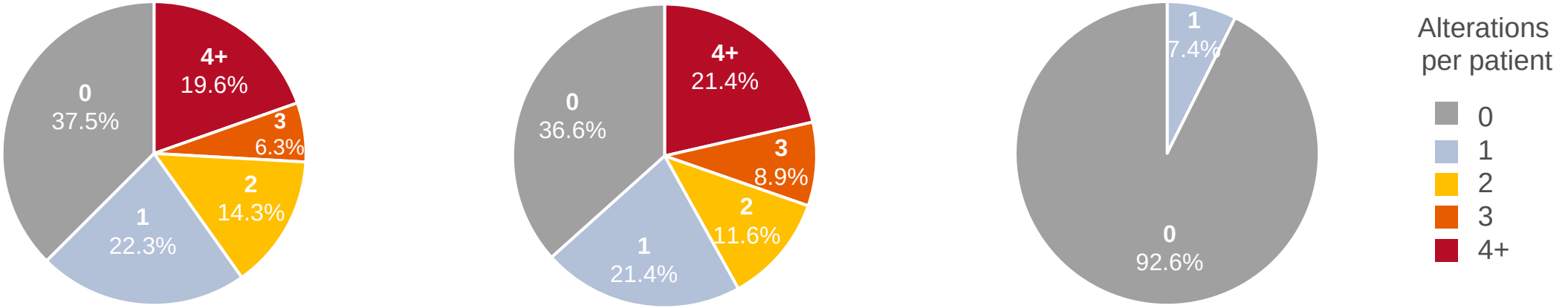
316O: Genomic mechanisms of acquired resistance of patients (pts) with BRAF V600E-mutant (mt) metastatic colorectal cancer (mCRC) treated in the BEACON study – Kopetz S, et al

Key results

Frequency of acquired resistance alterations



Co-occurrence of acquired resistance mechanisms



Kopetz S, et al. Ann Oncol 2022;33(suppl):abstr 316O

316O: Genomic mechanisms of acquired resistance of patients (pts) with BRAF V600E-mutant (mt) metastatic colorectal cancer (mCRC) treated in the BEACON study – Kopetz S, et al

Key results

- KRAS, NRAS and MAP2K1 mutations and MET amplification were the key acquired resistance mutations identified
- In patients receiving doublet or triplet therapy, the most commonly acquired resistance alterations were KRAS and NRAS mutations, which were mainly absent in the control arm
- In patients receiving doublet therapy, 16.1% acquired MAP2K1 mutations compared with 3.6% in those receiving triplet therapy ($p<0.01$)
- Acquired alterations were commonly subclonal

MAP2K1 mutations	RAF dependent	RAF independent	Unknown
Triplet (n=4)	2	0	2
Doublet (n=18)	13*	0	5
Control (n=3)	0	1	2

Conclusions

- **In patients with BRAF V600E-mutant mCRC, the most commonly found acquired resistance alterations were KRAS and NRAS mutations plus MET amplification and MAP2K1/MEK occurred more commonly in the doublet vs. triplet arm**

*Multiple MAP2K1 mutations occurred

Kopetz S, et al. Ann Oncol 2022;33(suppl):abstr 316O

317MO: Efficacy of oxaliplatin-based adjuvant chemotherapy in older patients with stage III colon cancer: an ACCENT/IDEA pooled analysis of 12 trials – Gallois C, et al

Study objective

- To evaluate the efficacy of oxaliplatin-based adjuvant chemotherapy in older patients with stage III colon cancer in a pooled analysis of 12 trials in ACCENT/IDEA

Methods

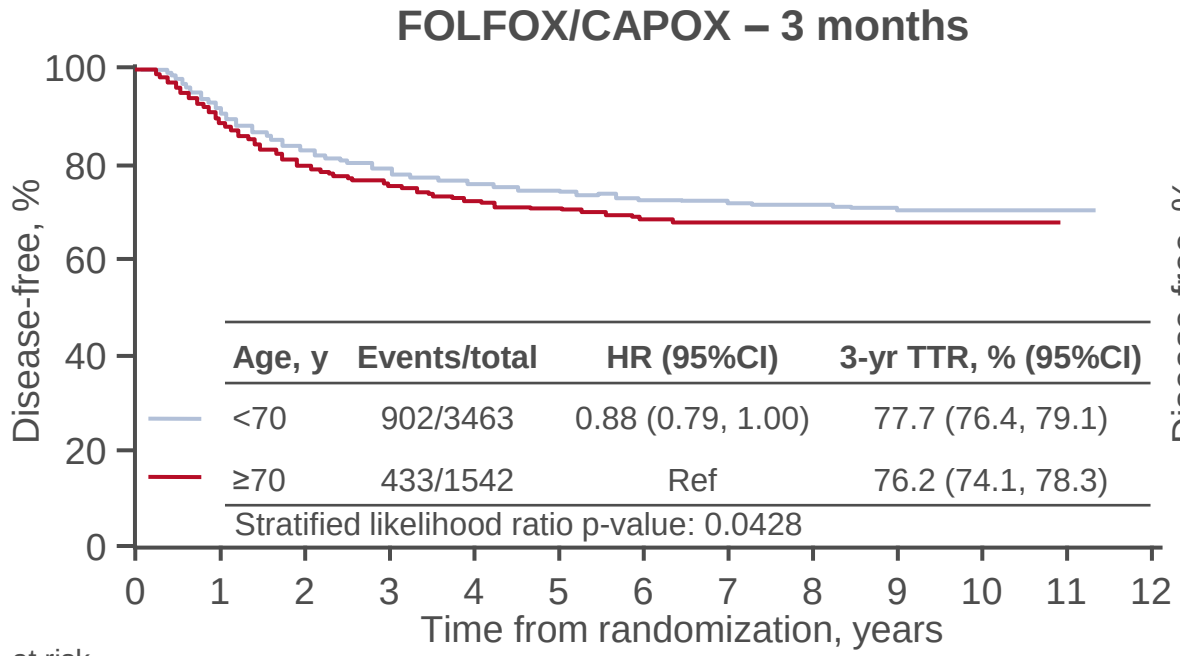
- Data from 12 clinical trials in the ACCENT and IDEA databases were collected for patients with stage III colon cancer (n=17,608) who were due to receive 3 or 6 months of adjuvant fluoropyrimidine + oxaliplatin (FOLFOX or CAPOX)
- The prognostic impact of age in those aged ≥70 years (n=4278) vs. those aged <70 years (n=13,330) and treatment adherence/toxicity patterns were examined
- A Cox model or competing risk model was used to assess associations between age and survival outcomes including TTR, DFS, OS, survival after recurrence and cancer-specific survival and were stratified by studies and adjusted for gender, performance status, T and N stage and enrolment year

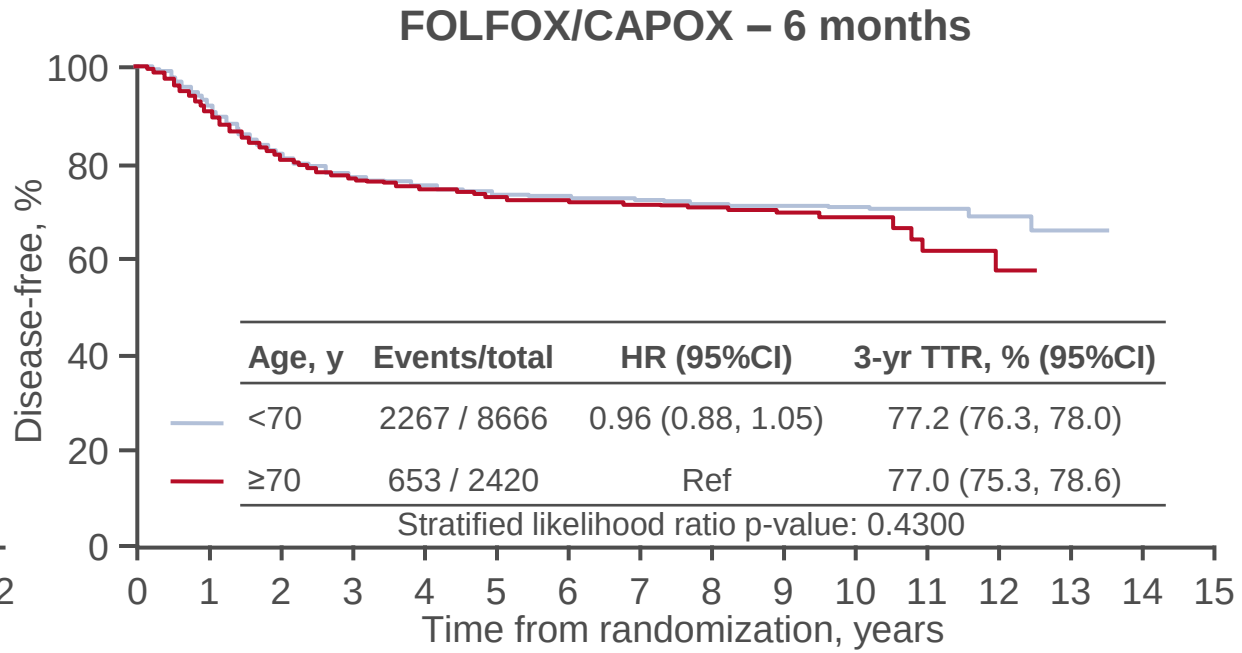
Presented at ESMO Congress 2022
Gallois C, et al. Ann Oncol 2022;33(suppl):abstr 317MO

317MO: Efficacy of oxaliplatin-based adjuvant chemotherapy in older patients with stage III colon cancer: an ACCENT/IDEA pooled analysis of 12 trials – Gallois C, et al

Key results

Time to disease recurrence
(deaths without recurrence censored at the time of death)





No. at risk

<70 y	3463	3074	2713	2180	1824	1459	1025	665	322	104	18	1	0
≥70 y	1542	1347	1161	943	768	600	413	259	129	47	3	0	

<70 y	8666	7768	6743	5916	5154	4157	2994	1743	828	382	183	85	29	5	0
≥70 y	2420	2146	1846	1558	1334	1048	727	442	227	96	32	16	6	0	

Gallois C, et al. Ann Oncol 2022;33(suppl):abstr 317MO

317MO: Efficacy of oxaliplatin-based adjuvant chemotherapy in older patients with stage III colon cancer: an ACCENT/IDEA pooled analysis of 12 trials – Gallois C, et al

Key results

Compliance and tolerance	≥70 years	<70 years	p-value
Early treatment discontinuation, %	21.9	15.2	<0.001
RDI, %			
Fluoropyrimidine	39.6	28.6	<0.001
Oxaliplatin	52.7	42.9	<0.001
Grade 3–4 AEs			
FOLFOX			
Thrombocytopenia	2.5	1.7	0.04
CAPOX			
Diarrhea	14.2	11.3	0.02
Mucositis	1.1	0.3	0.02
Neutropenia	12.1	9.6	0.03

	≥70 years	<70 years	HR (95%CI); p-value
3-mo FOLFOX/CAPOX			
3-yr DFS rate, % (95%CI)	75.5 (73.5, 77.6)	78.0 (76.7, 79.3)	0.80 (0.72, 0.88) <0.0001
5-yr OS rate, % (95%CI)	79.3 (77.3, 81.2)	84.9 (83.7, 86.1)	0.69 (0.61, 0.78) <0.0001
6-mo FOLFOX/CAPOX			
3-yr DFS rate, % (95%CI)	75.1 (73.4, 76.7)	76.7 (75.9, 77.6)	0.83 (0.77, 0.90) <0.001
5-yr OS rate, % (95%CI)	77.5 (75.9, 79.2)	83.4 (82.6, 84.2)	0.69 (0.63, 0.76) <0.0001

Conclusions

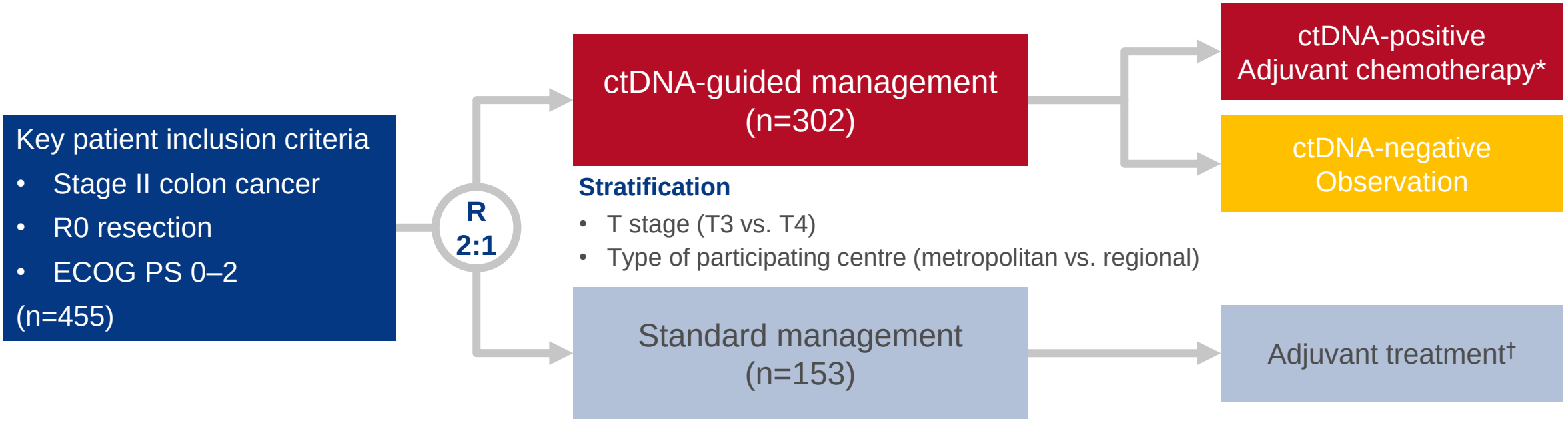
- **In patients aged ≥70 years with stage III colon cancer, FOLFOX and CAPOX were generally well-tolerated although there were more dose decreases and early discontinuations compared with those aged <70 years. Age had no impact on time to recurrence, but those aged ≥70 years had poorer overall outcomes**

Gallois C, et al. Ann Oncol 2022;33(suppl):abstr 317MO

318MO: Circulating tumour DNA (ctDNA) dynamics, CEA and sites of recurrence for the randomised DYNAMIC study: Adjuvant chemotherapy (ACT) guided by ctDNA analysis in stage II colon cancer (CC) – Tie J, et al

Study objective

- To evaluate the efficacy and safety of adjuvant chemotherapy guided by ctDNA analysis in patients with stage II colon cancer in Australian centres in the DYNAMIC study



PRIMARY ENDPOINT

- 2-year RFS rate

SECONDARY ENDPOINTS

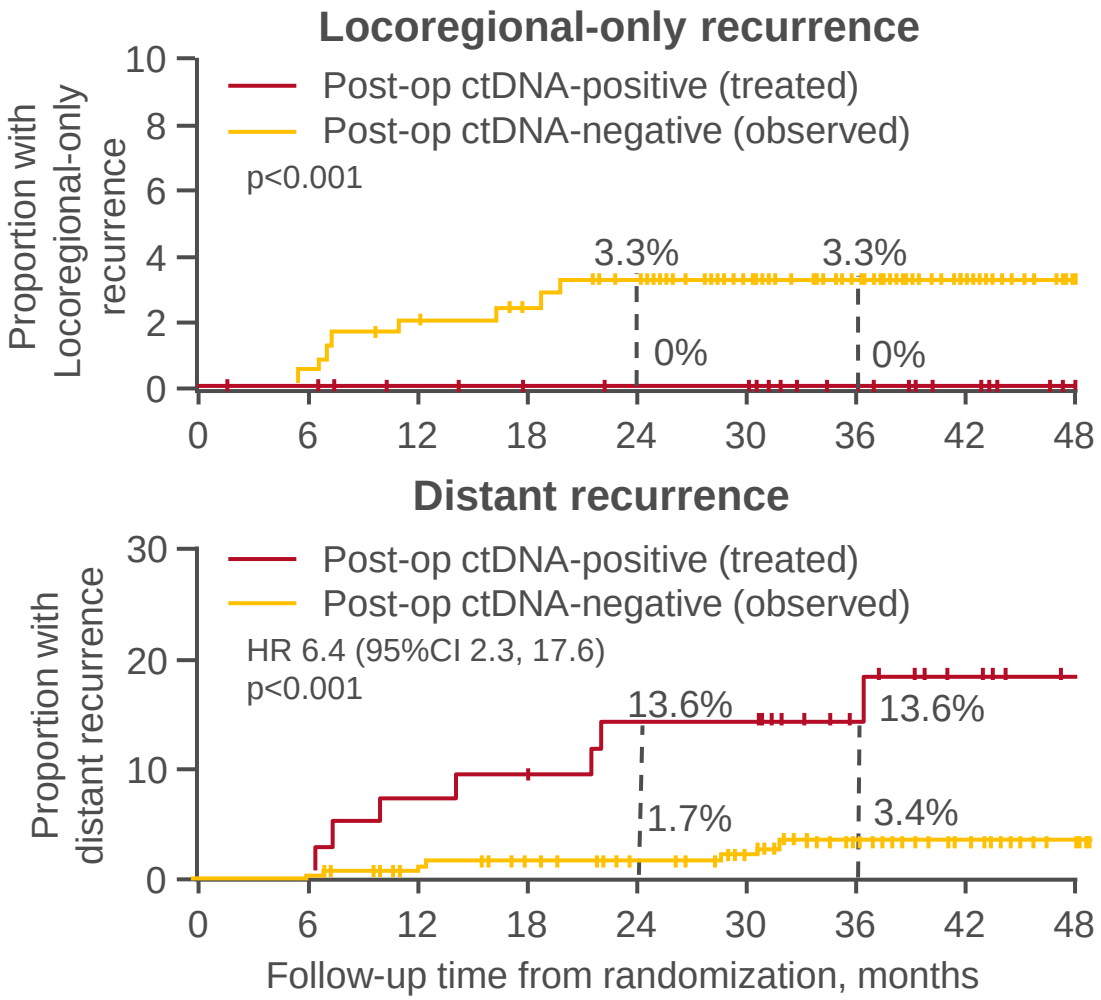
- Proportion receiving adjuvant chemotherapy, TTR, OS, safety

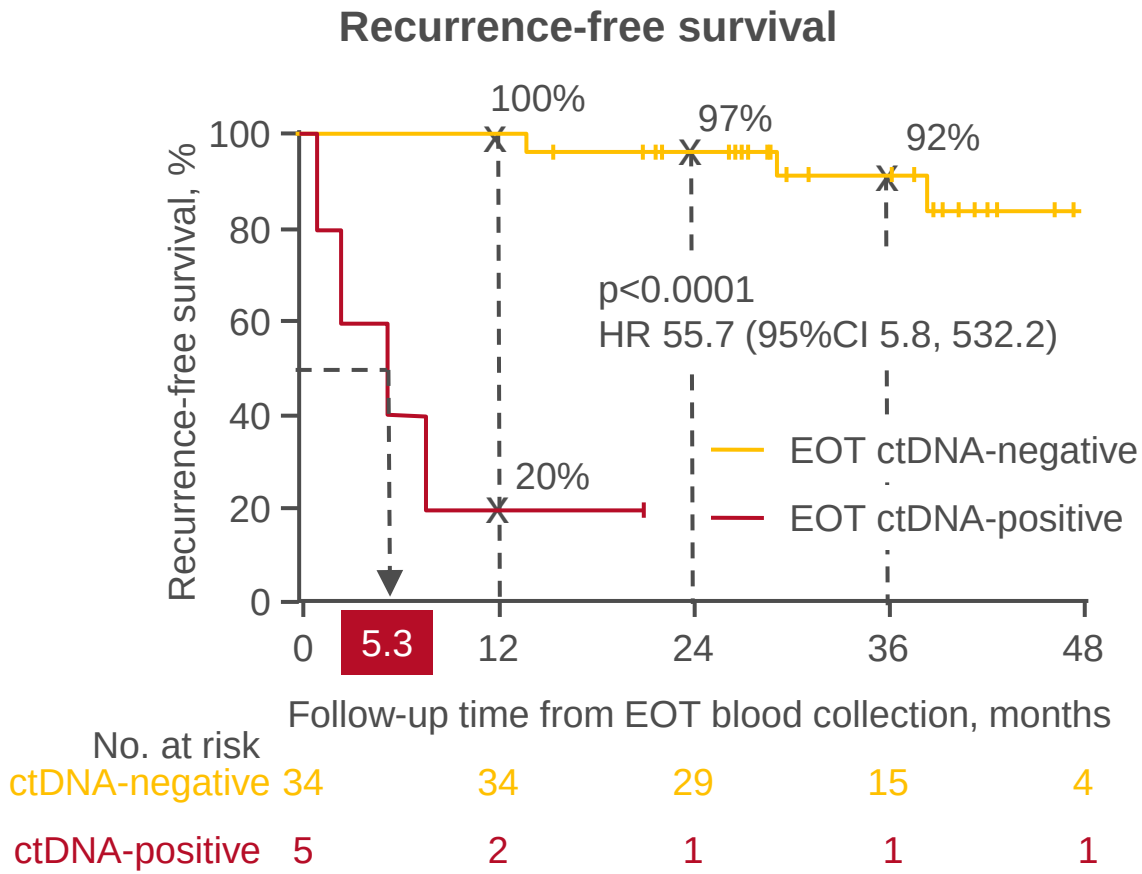
*Oxaliplatin-based or single agent fluoropyrimidine;
†based on conventional clinicopathological criteria

Presented at ESMO Congress 2022
Tie J, et al. Ann Oncol 2022;33(suppl):abstr 318MO

318MO: Circulating tumour DNA (ctDNA) dynamics, CEA and sites of recurrence for the randomised DYNAMIC study: Adjuvant chemotherapy (ACT) guided by ctDNA analysis in stage II colon cancer (CC) – Tie J, et al

Key results





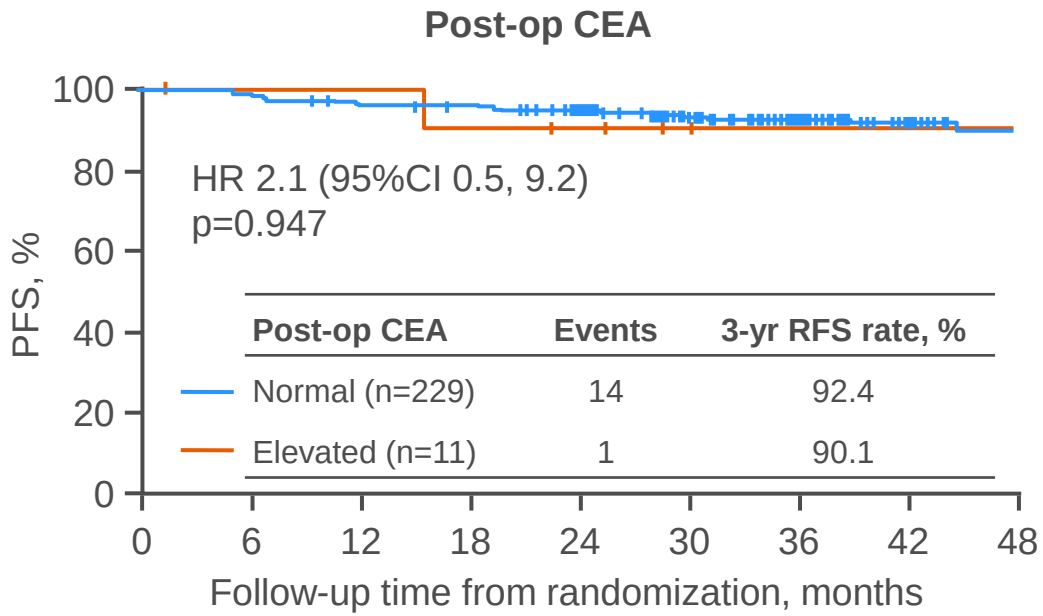
No. at risk					
ctDNA-negative	34	34	29	15	4
ctDNA-positive	5	2	1	1	1

Tie J, et al. Ann Oncol 2022;33(suppl):abstr 318MO

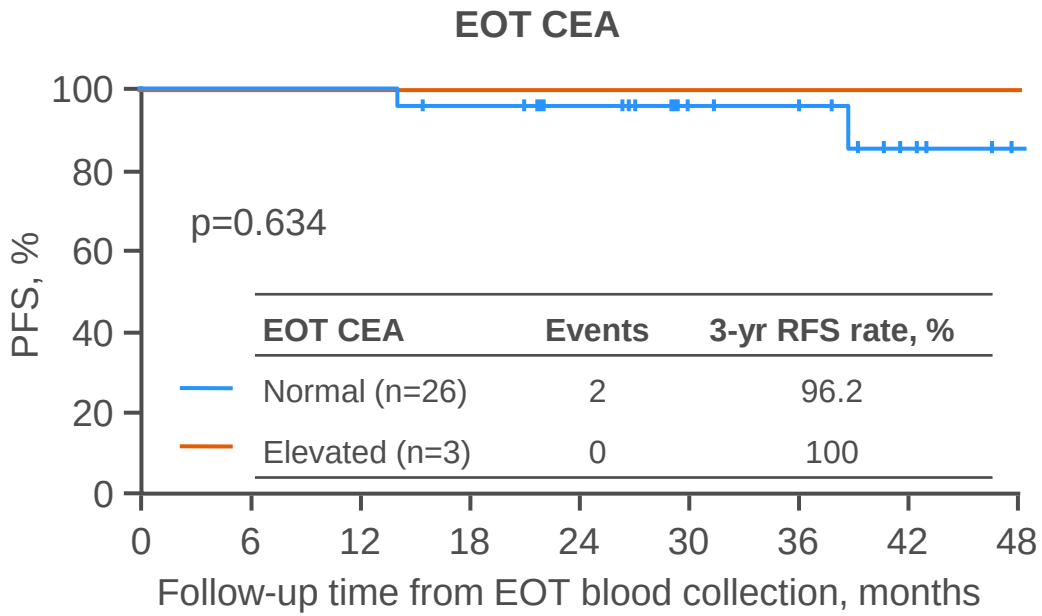
318MO: Circulating tumour DNA (ctDNA) dynamics, CEA and sites of recurrence for the randomised DYNAMIC study: Adjuvant chemotherapy (ACT) guided by ctDNA analysis in stage II colon cancer (CC) – Tie J, et al

Key results

Post-op ctDNA-negative



Post-op ctDNA-positive → EOT ctDNA-negative



Conclusions

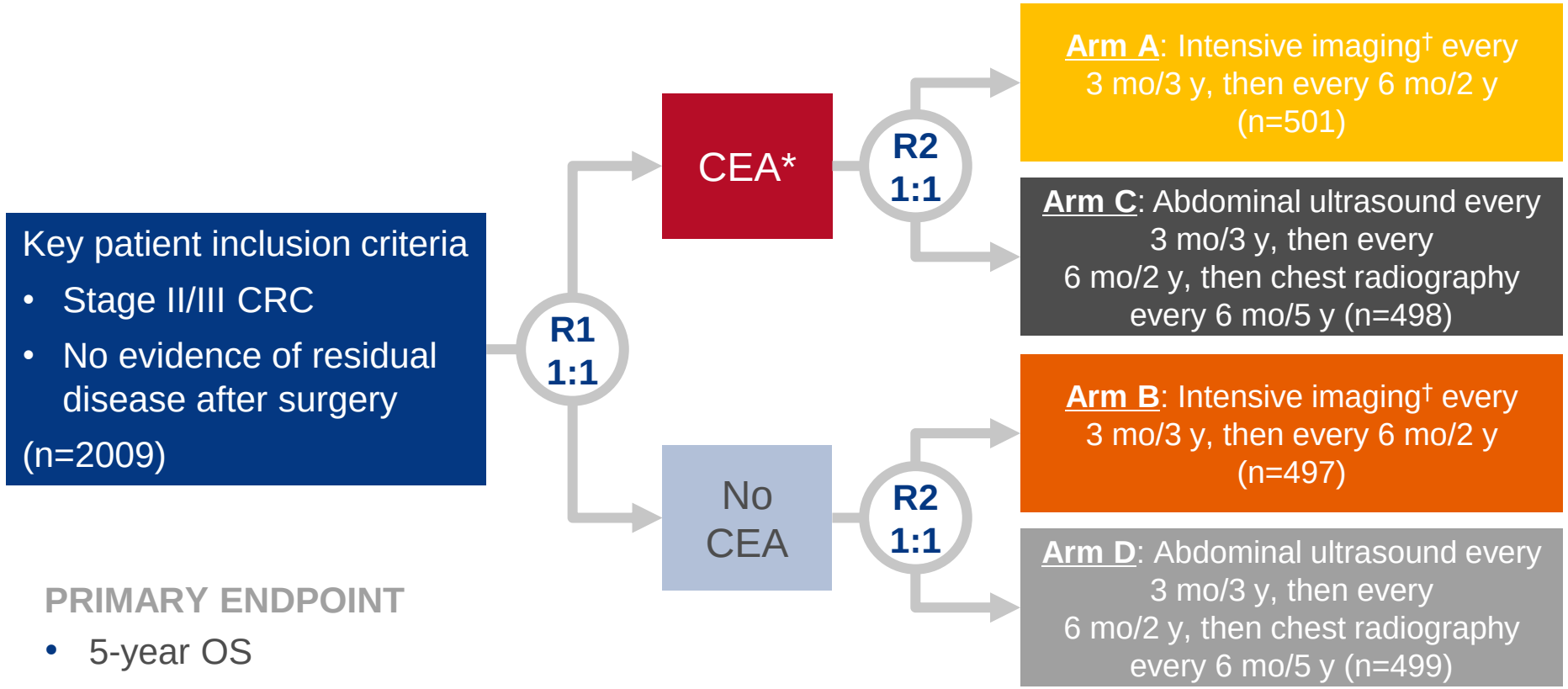
- **In patients with stage II colon cancer, post-operative ctDNA better predicted distant rather than locoregional recurrences and a high proportion of ctDNA-positive patients achieved ctDNA clearance with adjuvant chemotherapy, but in ctDNA-negative patients CEA provided no additional prognostic value**

Tie J, et al. Ann Oncol 2022;33(suppl):abstr 318MO

LBA28: Prognostic effect of imaging and CEA follow-up in resected colorectal cancer (CRC): final results and relapse free survival (RFS) - PRODIGE 13 a FFCD phase III trial – Lepage C, et al

Study objective

- To evaluate the impact of intensive radiological monitoring and CEA assessment in the post-operative surveillance of patients with resected stage II/III CRC in French centres in the phase 3 PRODIGE 13 study



PRIMARY ENDPOINT

- 5-year OS

*Every 3 mo for 2 years, then every 6 mo for 3 years; †intensive imaging: computed tomography alternating with abdominal ultrasound

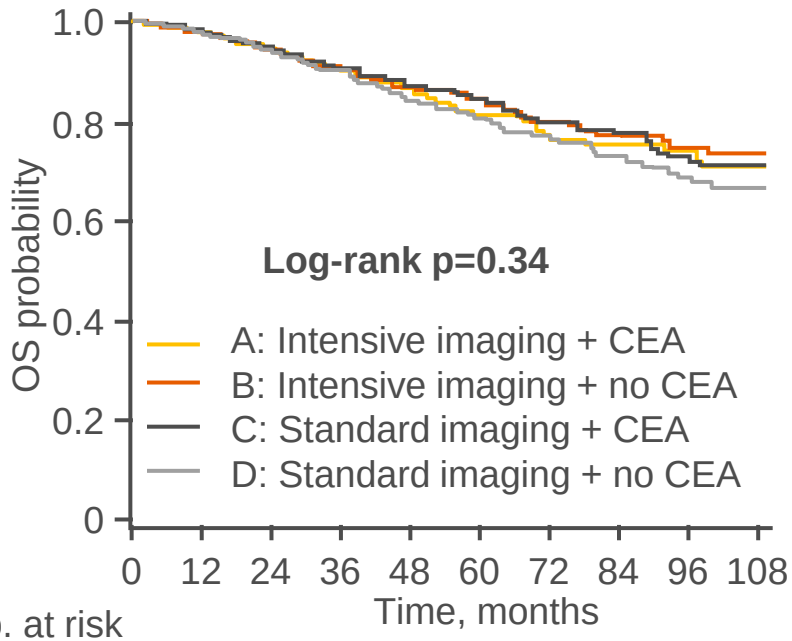
Presented at ESMO Congress 2022
Lepage C, et al. Ann Oncol 2022;33(suppl):abstr LBA28

LBA28: Prognostic effect of imaging and CEA follow-up in resected colorectal cancer (CRC): final results and relapse free survival (RFS) - PRODIGE 13 a FFCD phase III trial – Lepage C, et al

Key results

Overall survival

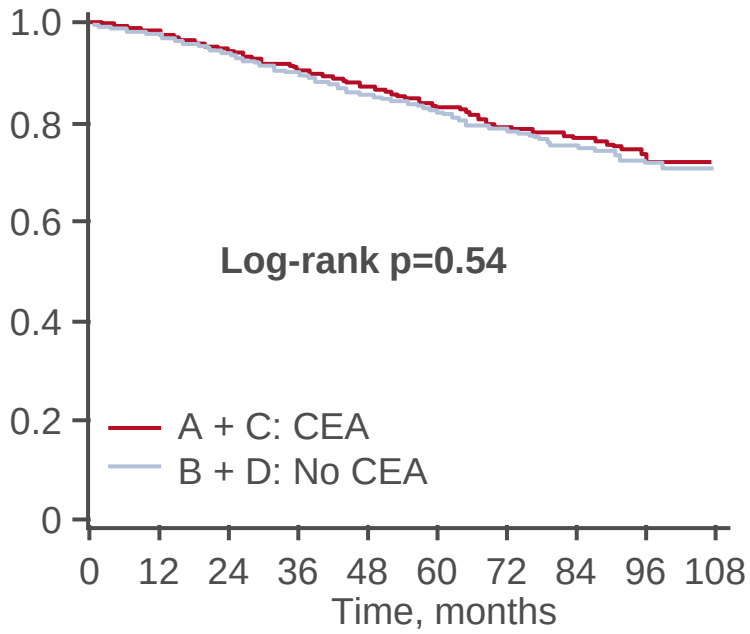
By randomization arm



No. at risk

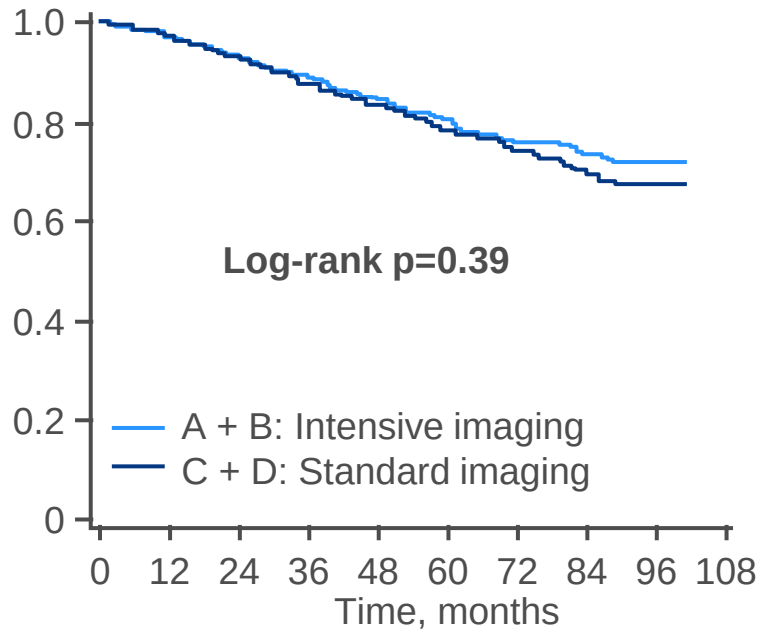
Arm A	501	487	471	449	408	310	216	145	75	11
Arm B	497	482	467	446	411	316	242	152	70	10
Arm C	498	484	465	448	415	315	235	143	66	7
Arm D	499	487	466	447	396	311	227	139	65	10

By CEA surveillance



A + C	999	971	936	897	823	625	451	288	141	18
B + D	996	969	933	893	807	627	469	291	135	20

By CT scan surveillance



A + B	998	969	938	895	819	626	458	297	145	21
C + D	997	971	931	895	811	626	462	282	131	17

Lepage C, et al. Ann Oncol 2022;33(suppl):abstr LBA28

LBA28: Prognostic effect of imaging and CEA follow-up in resected colorectal cancer (CRC): final results and relapse free survival (RFS) - PRODIGE 13 a FFCD phase III trial – Lepage C, et al

Key results

Recurrence and treatment %		Arm A CT scan + CEA (n=501)	Arm B CT scan (n=497)	Arm C Standard + CEA (n=498)	Arm D Standard (n=499)	p-value
Recurrence	n	109	97	111	129	
	Total	21.8	19.5	22.3	25.9	
	Locoregional	2.2	1.4	2.2	3.6	0.584
	Metastatic	15.4	14.5	16.3	19.0	
	Both	4.2	3.6	3.8	3.2	
Treatment	n	104	91	110	117	
Surgery	R0	39.4	36.3	49.1	32.5	
	No R0 resection	21.2	19.7	16.4	15.4	0.012
	No surgery	39.4	44.0	34.5	52.1	
Chemotherapy	After R0 resection	22.1	26.4	32.7	17.1	
	Palliative	52.9	57.1	50.9	61.5	0.120
	Other palliative therapy	25.0	16.5	16.4	21.4	

Conclusions

- **In patients with resected CRC, there were no differences in OS between any of the surveillance arms, therefore, standard of care should remain based on regular semiological assessment with ultrasound and chest radiographs**

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