GI SLIDE DECK 2021

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esdo european society of digestive oncology

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Letter from ESDO

DEAR COLLEAGUES

It is our pleasure to present this ESDO slide set which has been designed to highlight and summarize key findings in digestive cancers from the major congresses in 2021. This slide set specifically focuses on the **2021 Gastrointestinal Cancers Symposium** and **2021 ASCO® Annual Meeting** 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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european society of digestive oncology

ESDO Medical Oncology Slide Deck
Editors 2021

COLORECTAL CANCERS



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GASTRO-OESOPHAGEAL AND NEUROENDOCRINE TUMOURS



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esdo

Glossary

1L	first-line
5FU	5-fluouracil
ACT	adjuvant chemotherapy
AE	adverse event
ALT	alanine aminotransferase
ARDS	acute respiratory distress syndrome
AST	aspartate aminotransferase
Bev	bevacizumab
BICR	blinded-independent central review
bid	twice daily
BCLC	Barcelona Clinic Liver Cancer
BL	baseline
BOR	best overall response
BSC	best supportive care
cCR	confirmed complete response
CEA	carcinoembryonic antigen
Cet	cetuximab
Chemo	chemotherapy
CI	confidence interval
CPS	combined positive score
CR	complete response
CRC	colorectal cancer
CRT	chemoradiotherapy
CSR	central serous retinopathy
CT	computed tomography
ctDNA	circulating tumor DNA
CXB	contact X-ray brachytherapy
D	day
DCR	disease control rate
DFS	disease-free survival
dMMR	deficient mismatch repair
DoR	duration of response
EBCRT	external beam chemoradiotherapy
ECOG	Eastern Cooperative Oncology Group
ECS	Esophageal Cancer Subscale
EFS	event-free survival
EQ-5D-3L	EuroQol five dimensions questionnaire
ESCC	esophageal squamous cell carcinoma
ETS	early tumor shrinkage
FACT-E	Functional Assessment of Cancer Therapy – Esophageal
FACT-G7	Functional Assessment of Cancer Therapy – General 7-item version
FGFR	fibroblast growth factor receptor
FLOT	5FU + leucovorin + oxaliplatin + docetaxel
FOLFIRI	folinic acid + 5-fluouracil + irinotecan
mFOLFIRINOX	oxaliplatin + irinotecan + leucovorin + 5FU
(m)FOLFOX	(modified) leucovorin + 5-fluorouracil + oxaliplatin
(m)FOLFOXIR	(modified) 5-fluouracil + leucovorin + oxaliplatin + irinotecan
Fx	fractions
G	grade
GEJ	gastro-esophageal junction
GI	gastrointestinal
Gy	Gray
HAIC	hepatic arterial infusion chemotherapy
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HER2	human epidermal growth factor receptor 2
HIGRT	hypofractionated image guided radiotherapy
HR	hazard ratio
HRQoL	health-related quality of life
ICR	independent committee review
IDH1	isocitrated dehydrogenase 1
IPI	ipilimumab
ITT	intent-to-treat
iv	intravenous
LN	lymph node
LV	leucovorin
mCRC	metastatic colorectal cancer
MID	minimally important difference
mo	months
MRD	molecular residual disease
MSI-H	high microsatellite instability
NA	not available
NAR	neoadjuvant rectal (score)
NE	not evaluable/estimable
NGS	next generation sequencing
Nivo	nivolumab
NR	not reached
NSCLC	non-small cell lung cancer
ORR	overall/objective response rate
OR	odds ratio
(m)OS	(median) overall survival
pCR	pathological complete response
PD	progressive disease
PD-L1	programmed death-ligand 1
Pembro	pembrolizumab
(m)PFS	(median) progression-free survival
Pmab	panitumumab
PPE	palmar plantar erythrodysesthesia
po	orally
PR	partial response
PRO	patient-reported outcome
PS	performance status
q(2/3/4/6)w	every (2/3/4/6) week(s)
QoL	quality of life
R	randomized
R0	resection 0
RECIST	Response Evaluation Criteria In Solid Tumors
RFS	relapse-free survival
ROW	rest of world
RPED	retinal pigment epithelial detachment
RPSFT	rank preserving structural failure time
RT	radiotherapy
SAE	serious adverse event
SBRT	stereotactic body radiotherapy
SD	stable disease
SMV/PV	superior mesenteric
TEAE	treatment-emergent adverse event
TKI	tyrosine kinase inhibitor
TME	total mesorectal excision
TRAE	treatment-related adverse event
TTP	time to progression
TTR	time to response
VAS	visual analogue scale
VTE	venous thromboembolism
WBC	white blood cell
WT	wild type
XELOX	oxaliplatin + capecitabine

Contents

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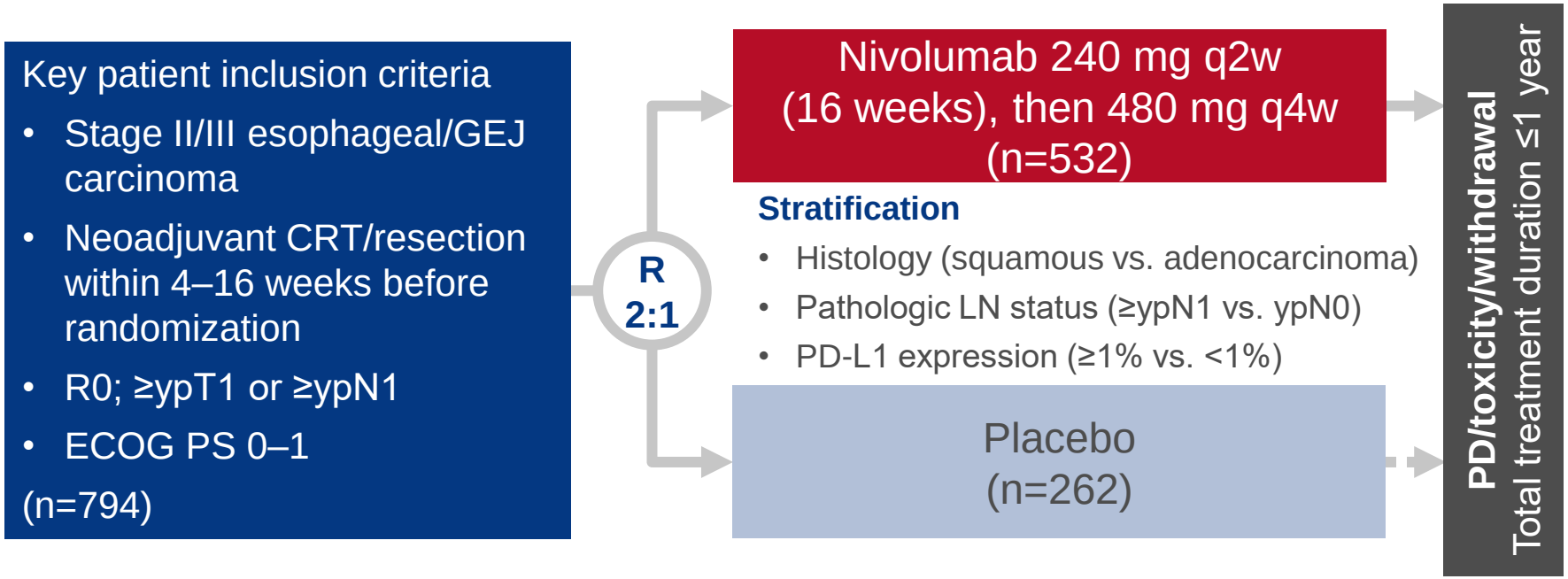
CANCERS OF THE OESOPHAGUS AND STOMACH

167: CheckMate 577: Health-related quality of life (HRQoL) in a randomized, double-blind phase III study of nivolumab (NIVO) versus placebo (PBO) as adjuvant treatment in patients (pts) with resected esophageal or gastroesophageal junction cancer (EC/GEJC) – Van Cutsem E, et al

Study objective

- To evaluate the HRQoL of adjuvant nivolumab in patients with esophageal/GEJ cancer and residual disease after CRT and surgery in the CheckMate 577 study



PRIMARY ENDPOINT

- DFS

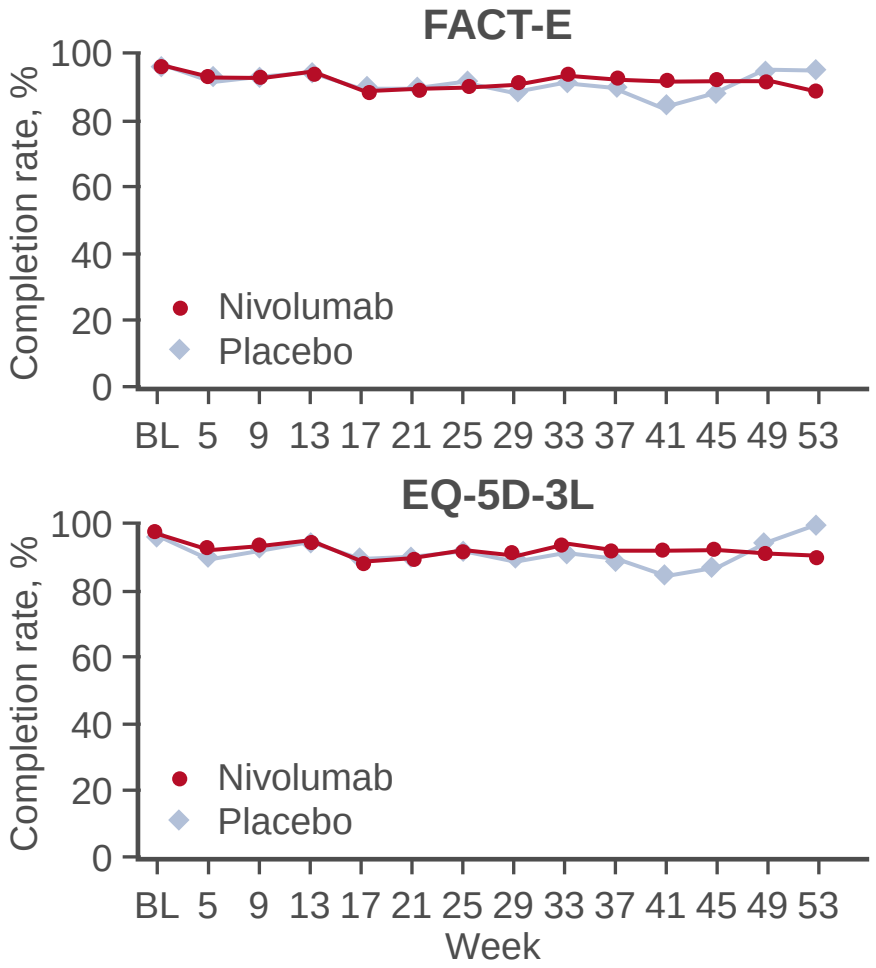
EXPLORATORY ENDPOINTS

- HRQoL: FACT-E, EQ-5D-3L, ECS, FACT-G7

Van Cutsem E, et al. J Clin Oncol 2021;39(suppl):abstr 167

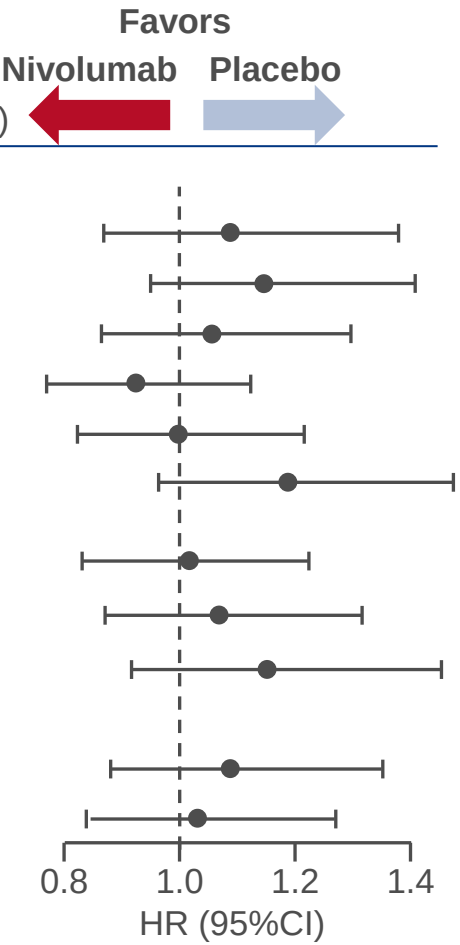
167: CheckMate 577: Health-related quality of life (HRQoL) in a randomized, double-blind phase III study of nivolumab (NIVO) versus placebo (PBO) as adjuvant treatment in patients (pts) with resected esophageal or gastroesophageal junction cancer (EC/GEJC) – Van Cutsem E, et al

Key results



Time to first deterioration in QoL metrics*

PRO measure	Nivolumab (n=532) Events, n (%)	Placebo (n=252) Events, n (%)
FACT-E		
Total score (MID=9.5)	228 (42.9)	109 (41.6)
Physical well-being (MID=2)	309 (58.1)	146 (55.7)
Social / family well-being (MID=2)	284 (53.4)	140 (53.4)
Emotional well-being (MID=2)	301 (56.6)	156 (59.2)
Functional well-being (MID=2)	289 (54.3)	146 (55.7)
Esophageal Cancer Subscale (ECS) (MID=4)	274 (51.5)	121 (46.2)
FACT-G Total score (MID=3)	314 (59.0)	163 (62.2)
FACT-G7 Total score (MID=2.5)	273 (51.3)	130 (49.6)
Trial Outcome Index (MID=6.1)	254 (44.0)	108 (41.2)
EQ-5D-3L		
VAS (MID=7)	266 (50.0)	125 (47.7)
Index score (UK weights) (MID=0.08)	274 (51.5)	135 (51.5)



*Defined as the time from randomization until the first deterioration in PRO score meeting or exceeding the MID/responder definition threshold corresponding to that score

Van Cutsem E, et al. J Clin Oncol 2021;39(suppl):abstr 167

167: CheckMate 577: Health-related quality of life (HRQoL) in a randomized, double-blind phase III study of nivolumab (NIVO) versus placebo (PBO) as adjuvant treatment in patients (pts) with resected esophageal or gastroesophageal junction cancer (EC/GEJC) – Van Cutsem E, et al

Conclusions

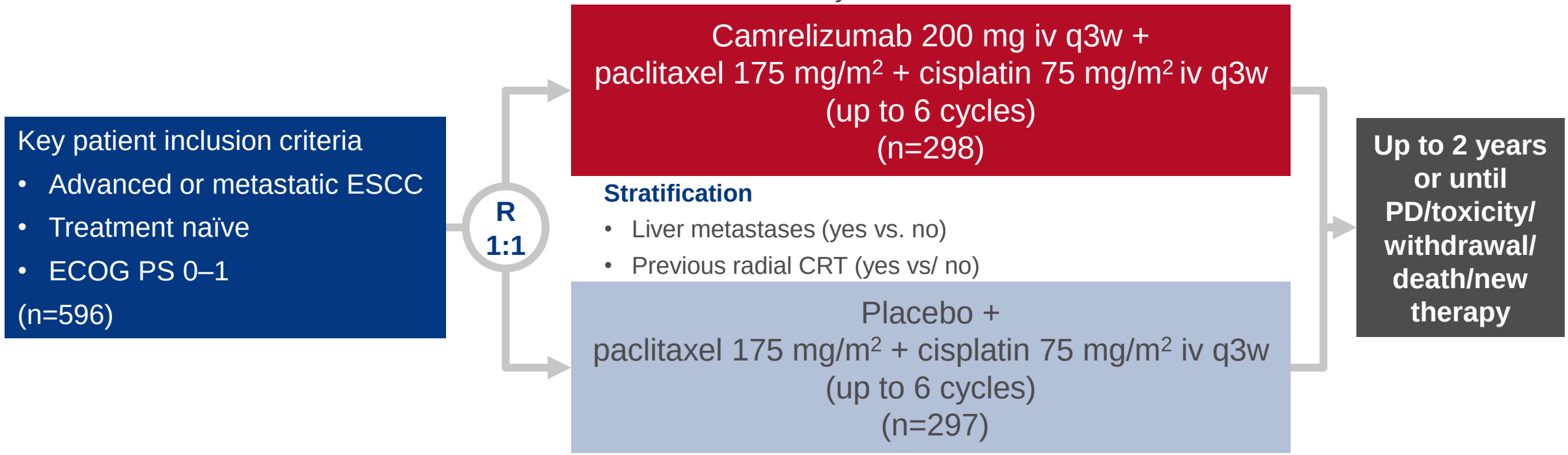
- In patients with resected esophageal or GEJ cancer, nivolumab and placebo both demonstrated trends in improvement and maintenance of HRQoL from baseline and there were no differences between the groups

Van Cutsem E, et al. J Clin Oncol 2021;39(suppl):abstr 167

4000: ESCORT-1st: A randomized, double-blind, placebo-controlled, phase 3 trial of camrelizumab plus chemotherapy versus chemotherapy in patients with untreated advanced or metastatic esophageal squamous cell carcinoma (ESCC) – Xu R, et al

Study objective

- To evaluate the efficacy and safety of camrelizumab (an anti-PD-1) + chemotherapy in treatment-naïve patients with advanced or metastatic ESCC in China in the ESCORT-1st study



CO-PRIMARY ENDPOINTS

- OS, PFS (ICR)

SECONDARY ENDPOINTS

- ORR, DCR, DoR, HRQoL, safety

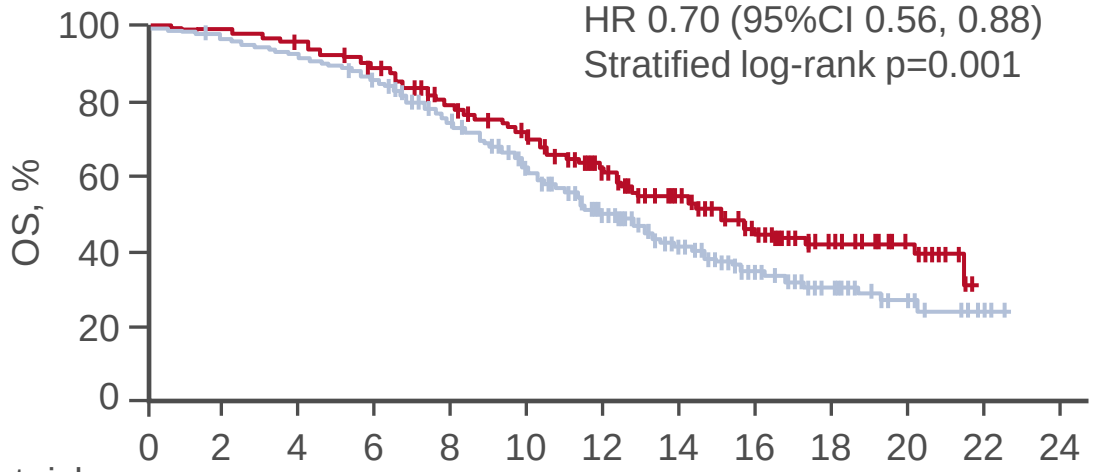
Xu R, et al. J Clin Oncol 2021;39(suppl):abstr 4000

4000: ESCORT-1st: A randomized, double-blind, placebo-controlled, phase 3 trial of camrelizumab plus chemotherapy versus chemotherapy in patients with untreated advanced or metastatic esophageal squamous cell carcinoma (ESCC) – Xu R, et al

Key results

Overall survival

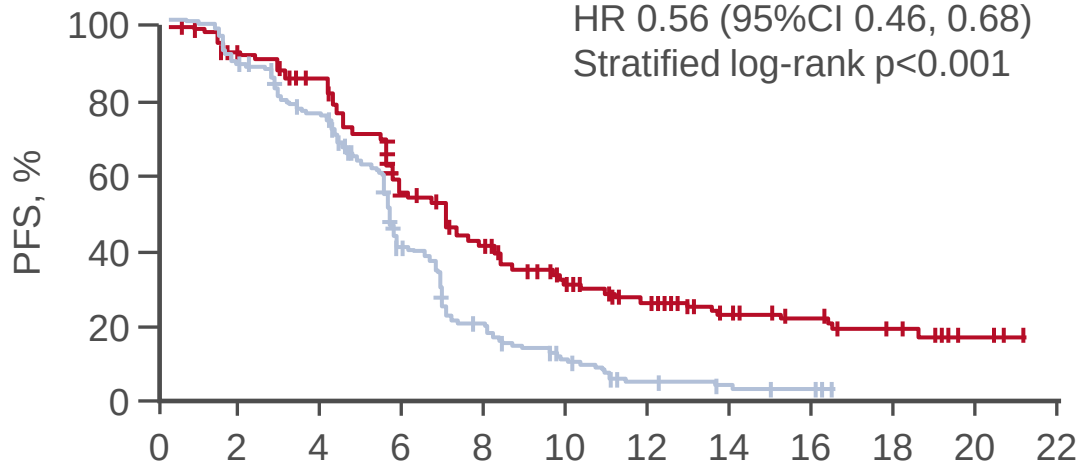
	Camrelizumab-chemo (n=298)	Placebo-chemo (n=298)
Events, n (%)	135 (45.3)	174 (58.4)
mOS, mo (95%CI)	15.3 (12.8, 17.3)	12.0 (11.0, 13.3)



No. at risk													
Camrelizumab-chemo	298	294	285	260	218	180	128	89	51	33	16	0	0
Placebo-chemo	298	289	275	249	203	161	110	72	41	24	11	4	0

Progression-free survival

	Camrelizumab-chemo (n=298)	Placebo-chemo (n=298)
Events, n (%)	199 (66.8)	229 (76.8)
mPFS, mo (95%CI)	6.9 (5.8, 7.4)	5.6 (5.5, 5.7)



No. at risk												
Camrelizumab-chemo	298	263	236	142	100	61	42	24	19	9	3	0
Placebo-chemo	298	243	196	93	45	22	8	5	3	0	0	0

Xu R, et al. J Clin Oncol 2021;39(suppl):abstr 4000

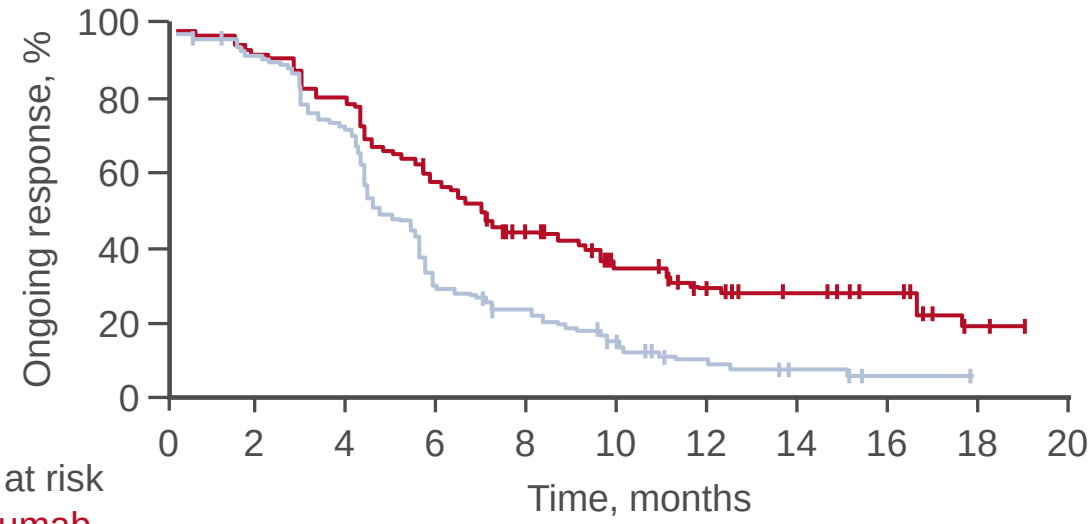
4000: ESCORT-1st: A randomized, double-blind, placebo-controlled, phase 3 trial of camrelizumab plus chemotherapy versus chemotherapy in patients with untreated advanced or metastatic esophageal squamous cell carcinoma (ESCC) – Xu R, et al

Key results (cont.)

	Camrelizumab (n=298)	Placebo (n=298)
BOR, n (%)		
CR	20 (6.7)	11 (3.7)
PR	195 (65.4)	174 (58.4)
SD	57 (19.1)	80 (26.8)
PD	14 (4.7)	15 (5.0)
NE	0 (0)	2 (0.7)
NA	12 (4.0)	16 (5.4)
ORR, n (%) [95%CI]	215 (72.1) [66.7, 77.2]	185 (62.1) [56.3, 67.6]
DCR, n (%) [95%CI]	272 (91.3) [87.5, 94.2]	265 (88.9) [84.8, 92.3]

Duration of response

	Camrelizumab-chemo (n=298)	Placebo-chemo (n=298)
Events, n (%)	131 (44.0)	150 (50.3)
mDoR, mo (95%CI)	7.0 (6.1, 8.9)	4.6 (4.3, 5.5)



No. at risk											
Camrelizumab-chemo	215	190	162	104	74	45	31	23	13	4	0
Placebo-chemo	185	164	122	47	33	18	10	4	1	0	0

Xu R, et al. J Clin Oncol 2021;39(suppl):abstr 4000

4000: ESCORT-1st: A randomized, double-blind, placebo-controlled, phase 3 trial of camrelizumab plus chemotherapy versus chemotherapy in patients with untreated advanced or metastatic esophageal squamous cell carcinoma (ESCC) – Xu R, et al

Key results (cont.)

TRAEs, n (%)	Camrelizumab (n=298)	Placebo (n=297)
Any	296 (99.3)	288 (97.0)
Grade ≥3	189 (63.4)	201 (67.7)
Serious	90 (30.2)	69 (23.2)
Led to treatment interruption of any component	135 (45.3)	71 (23.9)
Camrelizumab or placebo	128 (43.0)	60 (20.2)
Paclitaxel	86 (28.9)	60 (20.2)
Cisplatin	80 (26.8)	60 (20.2)
Led to treatment interruption of any component	36 (12.1)	28 (9.4)
Camrelizumab or placebo	12 (4.0)	16 (5.4)
Paclitaxel	24 (8.1)	22 (7.4)
Cisplatin	25 (8.4)	23 (7.4)
Led to death	9 (3.0)	11 (3.7)

Conclusions

- **In patients with advanced or metastatic ESCC, 1L camrelizumab + chemotherapy demonstrated significant improvement in survival compared with chemotherapy alone and had a manageable safety profile**

Xu R, et al. J Clin Oncol 2021;39(suppl):abstr 4000

LBA4001: Nivolumab (NIVO) plus ipilimumab (IPI) or NIVO plus chemotherapy (chemo) versus chemo as first-line (1L) treatment for advanced esophageal squamous cell carcinoma (ESCC): First results of the CheckMate 648 study – Chau I, et al

Study objective

- To evaluate the efficacy and safety of 1L nivolumab + ipilimumab or chemotherapy in patients with advanced ESCC in the CheckMate 648 study

Key patient inclusion criteria

- Unresectable advanced, recurrent or metastatic ESCC
- Treatment naïve
- Any PD-L1 expression
- ECOG PS 0–1

(n=970)

R 1:1:1

- Nivolumab 3 mg/kg q2w + ipilimumab 1 mg/kg q6w (n=325)
- Nivolumab 240 mg q2w + chemotherapy* (n=321)
- Chemotherapy* (n=324)

PD†/toxicity/ withdrawal

Stratification

- Tumor cell PD-L1 expression (≥1% vs. <1%)
- Region (East Asia vs. rest of Asia vs. ROW)
- ECOG PS (0 vs. 1)
- Number of organs with metastases (≤1 vs. ≥2)

CO-PRIMARY ENDPOINTS

- OS, PFS (BICR) for PD-L1 ≥1%

SECONDARY ENDPOINTS

- ORR, DoR, safety

*5FU 800 mg/m^2 iv D1–5+ cisplatin 80 mg/m^2 iv D1 q4w; †treatment beyond progression permitted for nivolumab + ipilimumab or nivolumab + chemotherapy

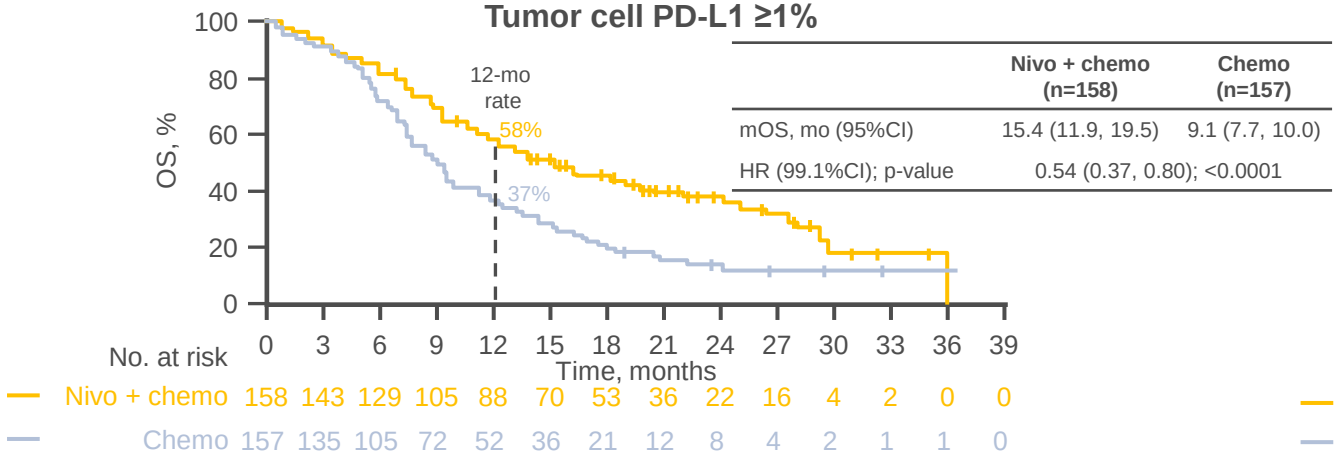
Chau I, et al. J Clin Oncol 2021;39(suppl):abstr LBA4001

LBA4001: Nivolumab (NIVO) plus ipilimumab (IPI) or NIVO plus chemotherapy (chemo) versus chemo as first-line (1L) treatment for advanced esophageal squamous cell carcinoma (ESCC): First results of the CheckMate 648 study – Chau I, et al

Key results

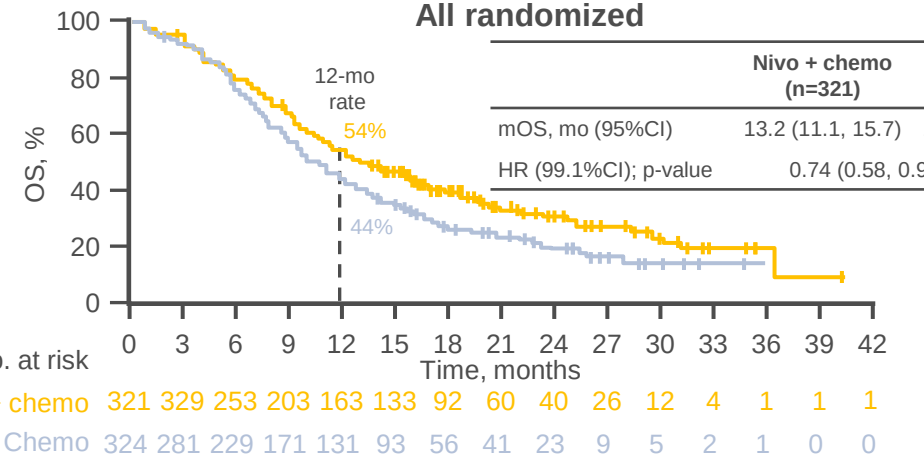
Overall survival

Tumor cell PD-L1 ≥1%



	Nivo + chemo (n=158)	Chemo (n=157)
mOS, mo (95%CI)	15.4 (11.9, 19.5)	9.1 (7.7, 10.0)
HR (99.1%CI); p-value	0.54 (0.37, 0.80); <0.0001	

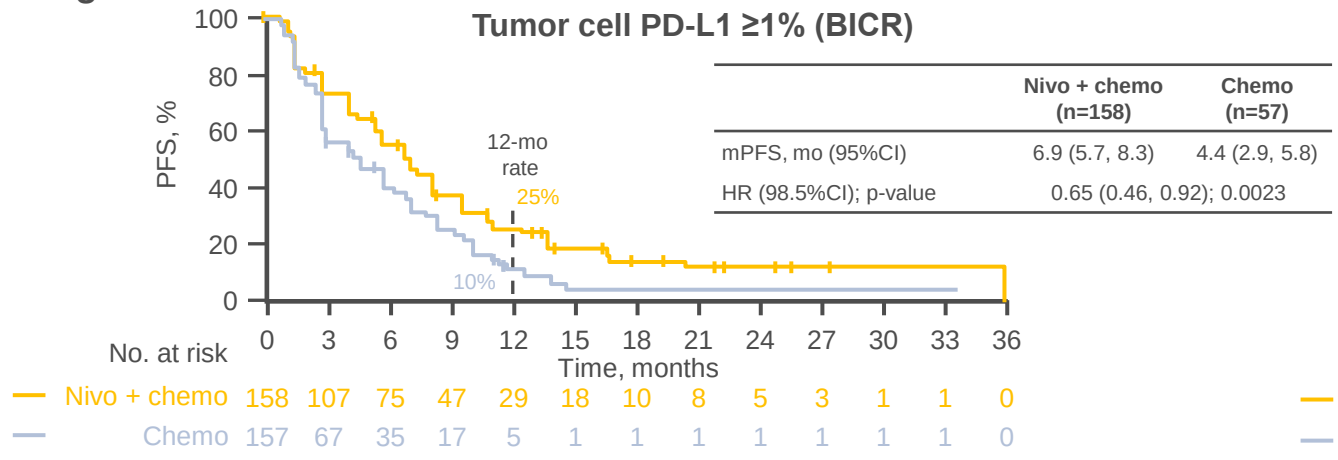
All randomized



	Nivo + chemo (n=321)	Chemo (n=324)
mOS, mo (95%CI)	13.2 (11.1, 15.7)	10.7 (9.4, 11.9)
HR (99.1%CI); p-value	0.74 (0.58, 0.96); 0.0021	

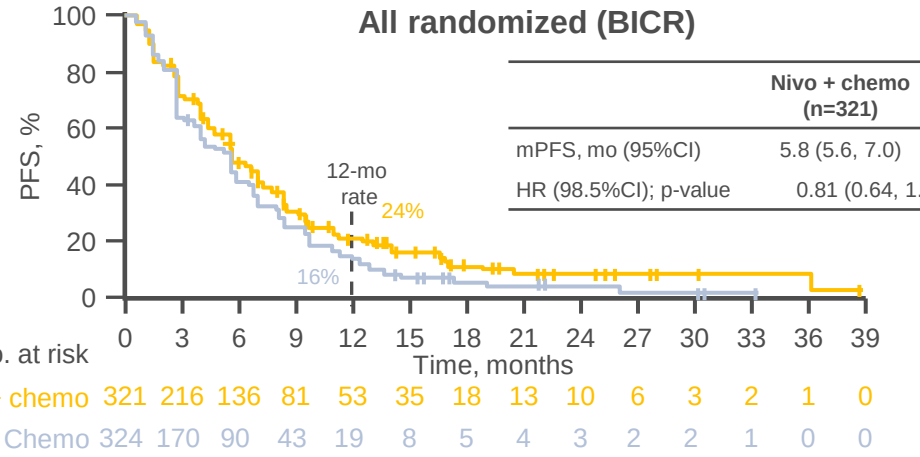
Progression-free survival

Tumor cell PD-L1 ≥1% (BICR)



	Nivo + chemo (n=158)	Chemo (n=57)
mPFS, mo (95%CI)	6.9 (5.7, 8.3)	4.4 (2.9, 5.8)
HR (98.5%CI); p-value	0.65 (0.46, 0.92); 0.0023	

All randomized (BICR)



	Nivo + chemo (n=321)	Chemo (n=324)
mPFS, mo (95%CI)	5.8 (5.6, 7.0)	5.6 (4.3, 5.9)
HR (98.5%CI); p-value	0.81 (0.64, 1.04); 0.0355	

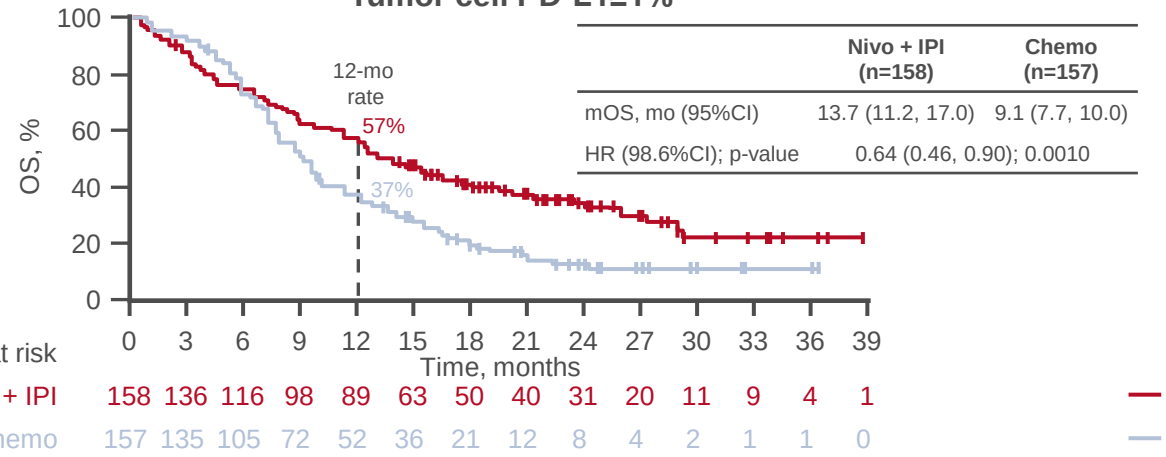
Chau I, et al. J Clin Oncol 2021;39(suppl):abstr LBA4001

LBA4001: Nivolumab (NIVO) plus ipilimumab (IPI) or NIVO plus chemotherapy (chemo) versus chemo as first-line (1L) treatment for advanced esophageal squamous cell carcinoma (ESCC): First results of the CheckMate 648 study – Chau I, et al

Key results (cont.)

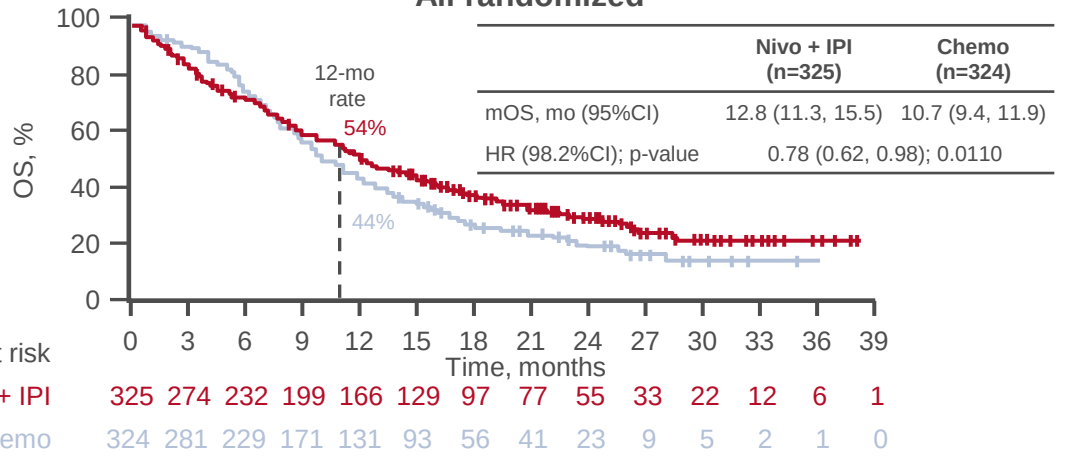
Overall survival

Tumor cell PD-L1≥1%



	Nivo + IPI (n=158)	Chemo (n=157)
mOS, mo (95%CI)	13.7 (11.2, 17.0)	9.1 (7.7, 10.0)
HR (98.6%CI); p-value	0.64 (0.46, 0.90); 0.0010	

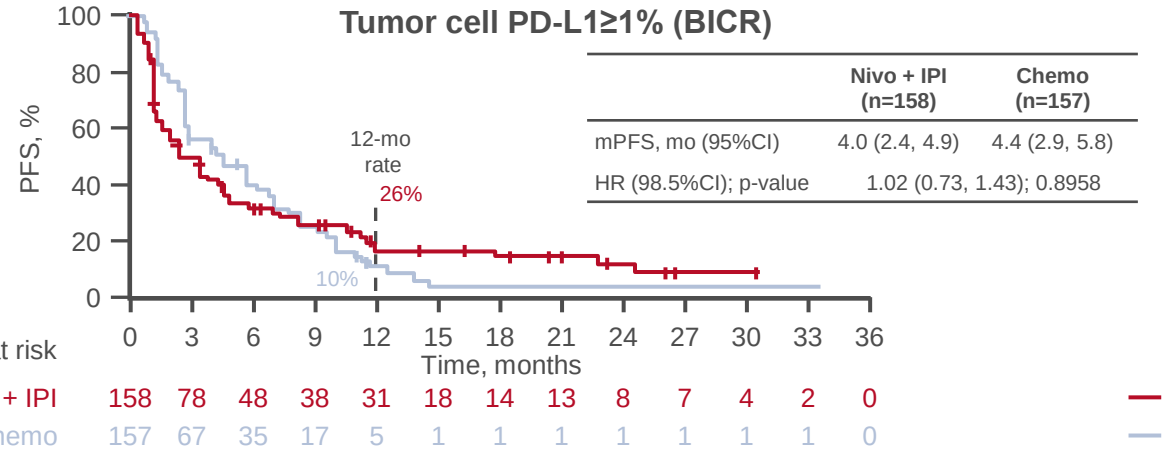
All randomized



	Nivo + IPI (n=325)	Chemo (n=324)
mOS, mo (95%CI)	12.8 (11.3, 15.5)	10.7 (9.4, 11.9)
HR (98.2%CI); p-value	0.78 (0.62, 0.98); 0.0110	

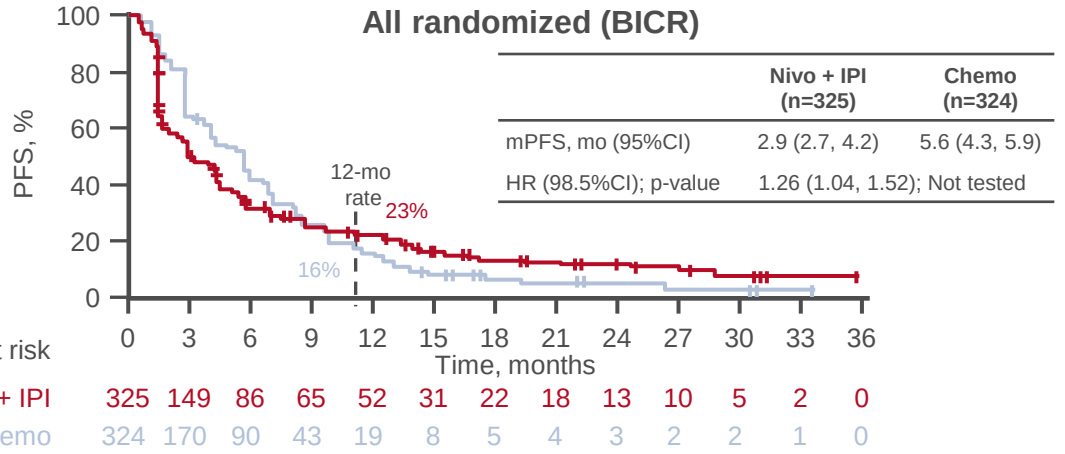
Progression-free survival

Tumor cell PD-L1≥1% (BICR)



	Nivo + IPI (n=158)	Chemo (n=157)
mPFS, mo (95%CI)	4.0 (2.4, 4.9)	4.4 (2.9, 5.8)
HR (98.5%CI); p-value	1.02 (0.73, 1.43); 0.8958	

All randomized (BICR)



	Nivo + IPI (n=325)	Chemo (n=324)
mPFS, mo (95%CI)	2.9 (2.7, 4.2)	5.6 (4.3, 5.9)
HR (98.5%CI); p-value	1.26 (1.04, 1.52); Not tested	

Chau I, et al. J Clin Oncol 2021;39(suppl):abstr LBA4001

LBA4001: Nivolumab (NIVO) plus ipilimumab (IPI) or NIVO plus chemotherapy (chemo) versus chemo as first-line (1L) treatment for advanced esophageal squamous cell carcinoma (ESCC): First results of the CheckMate 648 study – Chau I, et al

Key results (cont.)

Grade 3–4 TRAEs, n (%)	Nivolumab + ipilimumab (n=322)	Nivolumab + chemotherapy (n=310)	Chemotherapy (n=304)
Any	102 (32)	147 (47)	108 (36)
Serious	73 (23)	57 (18)	38 (13)
Led to discontinuation	41 (13)	29 (9)	4 (5)
Deaths	5 (2)	5 (2)	4 (1)

Grade 3–4 TRAEs, n (%)	Nivolumab + ipilimumab (n=322)	Nivolumab + chemotherapy (n=310)	Chemotherapy (n=304)
Endocrine	19 (6)	4 (1)	0 (0)
Gastrointestinal	5 (2)	7 (2)	7 (2)
Hepatic	14 (4)	7 (2)	2 (<1)
Pulmonary	9 (3)	2 (<1)	0 (0)
Renal	2 (<1)	7 (2)	5 (2)
Skin	13 (4)	1 (<1)	0 (0)

Conclusions

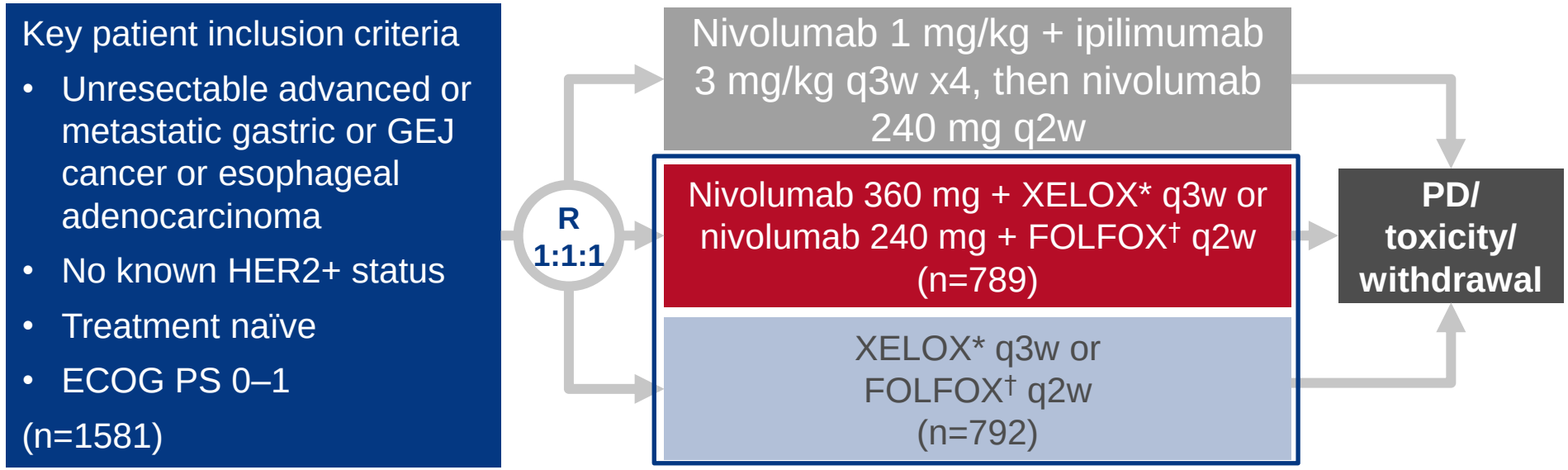
- **In patients with advanced ESCC, 1L nivolumab with either ipilimumab or chemotherapy demonstrated significant improvements in OS and durable responses compared with chemotherapy alone and was generally well-tolerated**

Chau I, et al. J Clin Oncol 2021;39(suppl):abstr LBA4001

4002: First-line (1L) nivolumab (NIVO) plus chemotherapy (chemo) versus chemo in advanced gastric cancer/gastroesophageal junction cancer/esophageal adenocarcinoma (GC/GEJC/EAC): Expanded efficacy and safety data from CheckMate 649 – Moehler MH, et al

Study objective

- To evaluate the efficacy and safety of nivolumab as a 1L treatment for patients with gastric or GEJ cancer or esophageal adenocarcinoma in the CheckMate 649 study



Stratification

- Region, ECOG PS, chemotherapy regimen, PD-L1 expression

CO-PRIMARY ENDPOINTS

- OS and PFS (BICR) in PD-L1 CPS ≥5

SECONDARY ENDPOINTS

- OS, PFS, ORR, safety

*Oxaliplatin 130 mg/m^2 iv D1 + capecitabine 1000 mg/m^2 po bid D1–14; †oxaliplatin 85 mg/m^2, leucovorin 400 mg/m^2 + 5FU 400 mg/m^2 D1 then 5FU 1200 mg/m^2 iv D1–2

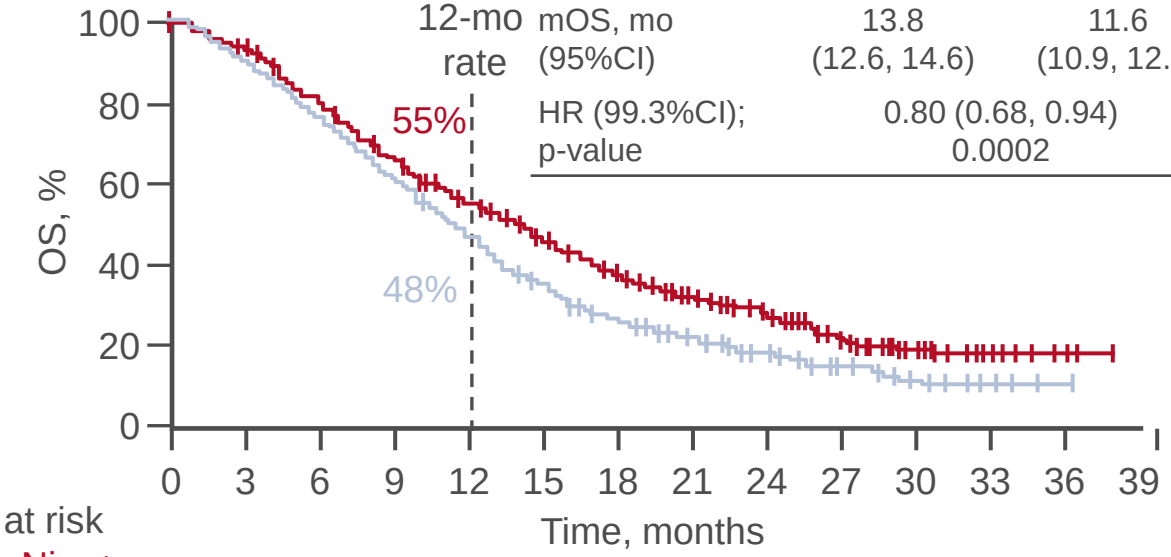
Moehler MH, et al. J Clin Oncol 2021;39(suppl):abstr 4002

4002: First-line (1L) nivolumab (NIVO) plus chemotherapy (chemo) versus chemo in advanced gastric cancer/gastroesophageal junction cancer/esophageal adenocarcinoma (GC/GEJC/EAC): Expanded efficacy and safety data from CheckMate 649 – Moehler MH, et al

Key results

Overall survival

	Nivo + chemo (n=789)	Chemo (n=792)
mOS, mo (95%CI)	13.8 (12.6, 14.6)	11.6 (10.9, 12.5)
HR (99.3%CI); p-value	0.80 (0.68, 0.94) 0.0002	

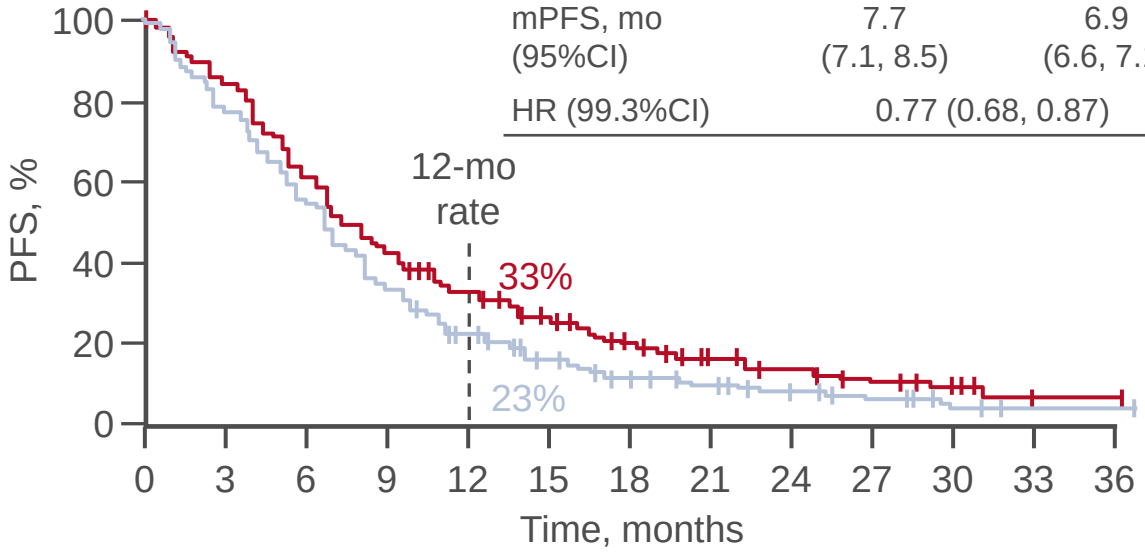


No. at risk

Nivo+ chemo	789	731	621	506	420	308	226	147	100	49	34	14	2	0
Chemo	792	697	586	469	359	239	160	94	59	35	15	7	2	0

Progression-free survival

	Nivo + chemo (n=789)	Chemo (n=792)
mPFS, mo (95%CI)	7.7 (7.1, 8.5)	6.9 (6.6, 7.1)
HR (99.3%CI)	0.77 (0.68, 0.87)	



Nivo+ chemo	789	639	429	287	197	136	83	51	31	15	11	1	0	
Chemo	792	544	351	202	120	65	38	28	18	12	6	1	0	

Moehler MH, et al. J Clin Oncol 2021;39(suppl):abstr 4002

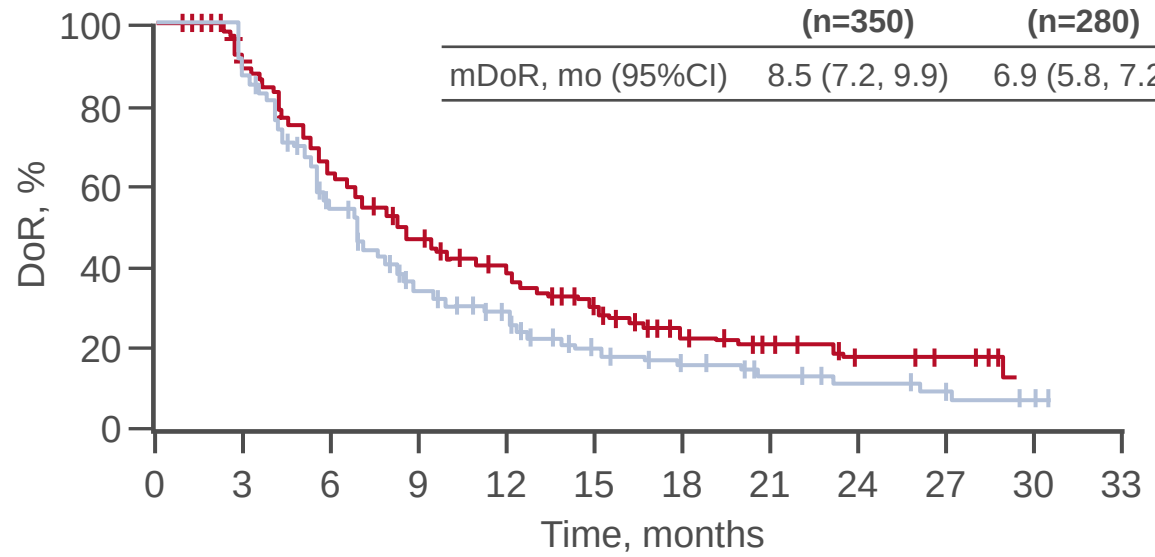
4002: First-line (1L) nivolumab (NIVO) plus chemotherapy (chemo) versus chemo in advanced gastric cancer/gastroesophageal junction cancer/esophageal adenocarcinoma (GC/GEJC/EAC): Expanded efficacy and safety data from CheckMate 649 – Moehler MH, et al

Key results (cont.)

	Nivolumab + chemo (n=603)	Chemo (n=608)
BOR, %		
CR	10	6
PR	48	40
SD	28	33
PD	7	10
NE	7	11
ORR, % (95%CI)	58 (54, 62)	46 (42, 50)
Median TTR, mo (range)	1.5 (0.8–10.9)	1.5 (0.6–7.1)

Duration of response

	Nivo + chemo (n=350)	Chemo (n=280)
mDoR, mo (95%CI)	8.5 (7.2, 9.9)	6.9 (5.8, 7.2)



Nivo+ chemo	350	302	203	143	110	72	40	21	10	7	0	0
Chemo	280	233	137	77	55	30	20	10	7	5	2	0

Moehler MH, et al. J Clin Oncol 2021;39(suppl):abstr 4002

4002: First-line (1L) nivolumab (NIVO) plus chemotherapy (chemo) versus chemo in advanced gastric cancer/gastroesophageal junction cancer/esophageal adenocarcinoma (GC/GEJC/EAC): Expanded efficacy and safety data from CheckMate 649 – Moehler MH, et al

Key results (cont.)

Grade 3–4 TRAEs, n (%)	Nivolumab + chemotherapy (n=782)
Endocrine	5 (<1)
Gastrointestinal	43 (5)
Hepatic	29 (4)
Pulmonary	14 (2)
Renal	6 (<1)
Skin	26 (3)

Conclusions

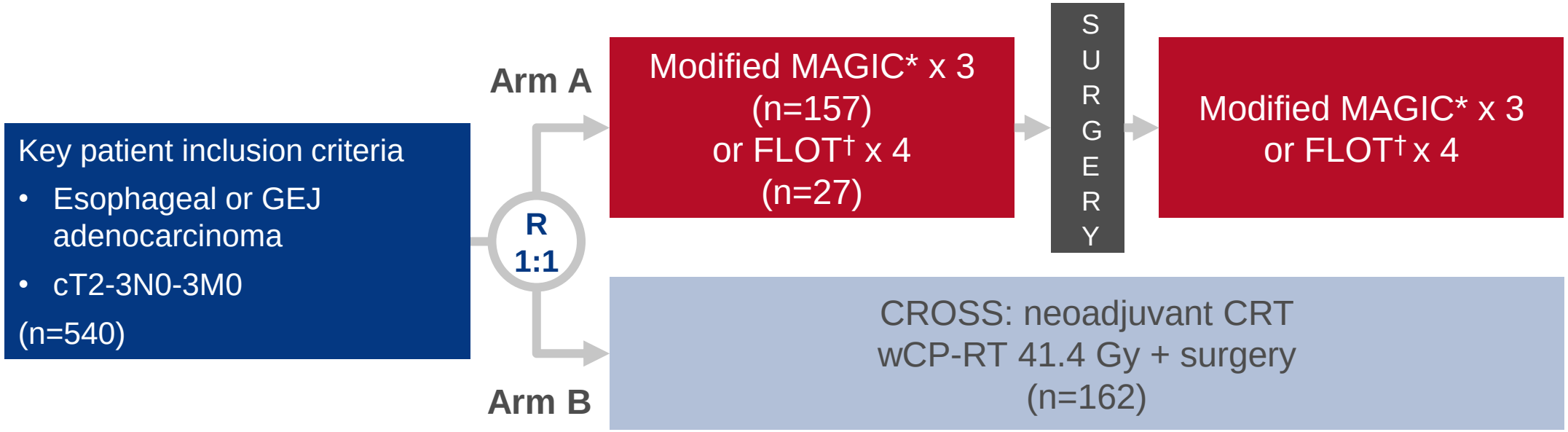
- **In patients with advanced gastric/GEJ cancer or esophageal adenocarcinoma, 1L nivolumab + chemotherapy demonstrated significant improvement in OS and durable responses compared with chemotherapy alone and had an acceptable safety profile**

Moehler MH, et al. J Clin Oncol 2021;39(suppl):abstr 4002

4004: Neo-AEGIS (Neoadjuvant trial in Adenocarcinoma of the Esophagus and Esophago-Gastric Junction International Study): Preliminary results of phase III RCT of CROSS versus perioperative chemotherapy (Modified MAGIC or FLOT protocol) – Reynolds JV, et al

Study objective

- To evaluate the efficacy and safety of the CROSS regimen vs. perioperative chemotherapy (either modified MAGIC or FLOT regimen) in patients with esophageal or GEJ adenocarcinoma in the Neo-AEGIS study



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

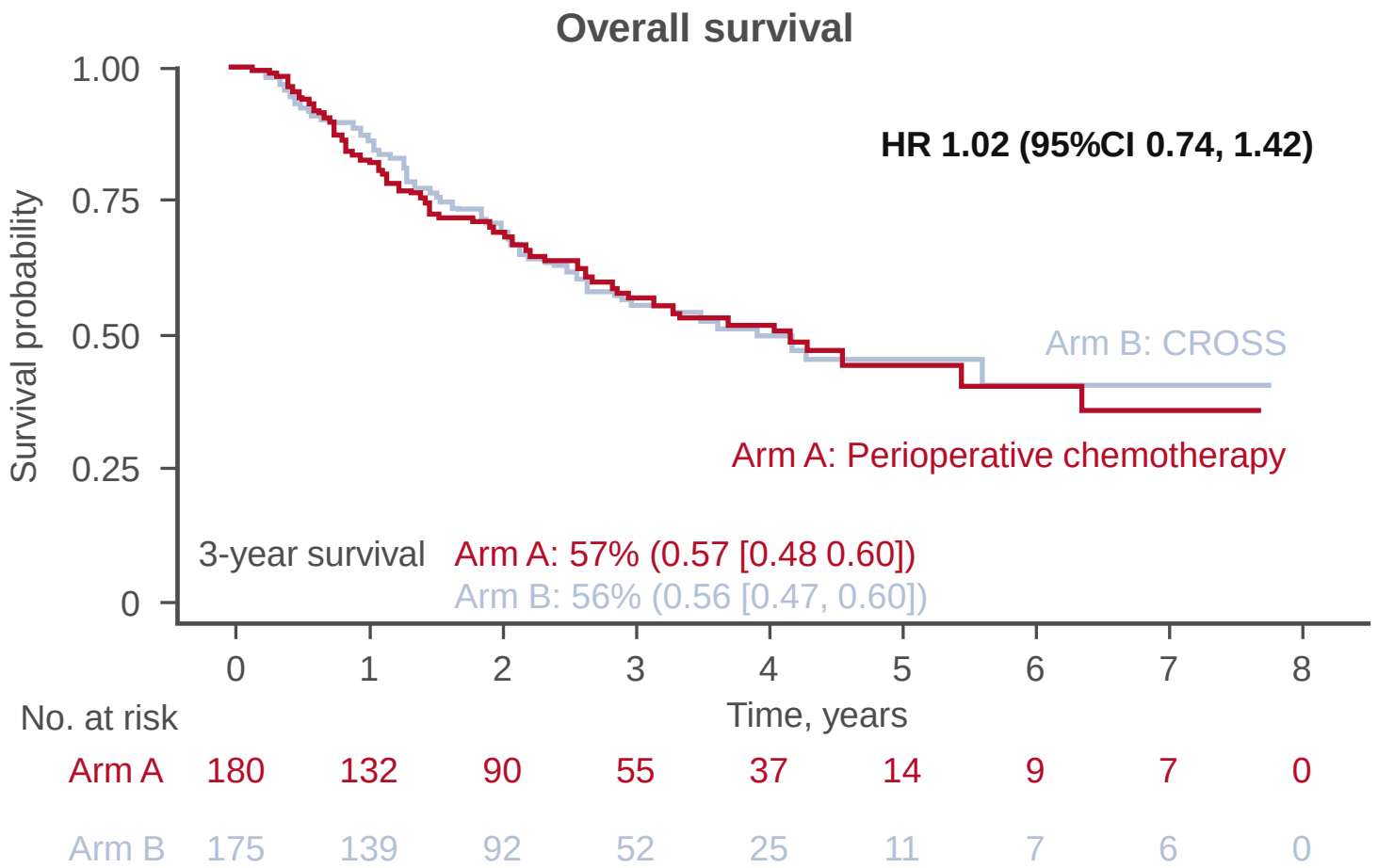
- DFS, TTF, TRG, R0 rate, postoperative complications, HR-QoL, safety

*ECF/ECX/EOF/EOX; †5FU 2600 mg/m^2 iv 24 h infusion D1 + leucovorin 200 mg/m^2 iv D1 + oxaliplatin 85 mg/m^2 iv D1 + docetaxel 50 mg/m^2 iv D1 q2w

Reynolds JV, et al. J Clin Oncol 2021;39(suppl):abstr 4004

4004: Neo-AEGIS (Neoadjuvant trial in Adenocarcinoma of the Esophagus and Esophago-Gastric Junction International Study): Preliminary results of phase III RCT of CROSS versus perioperative chemotherapy (Modified MAGIC or FLOT protocol) – Reynolds JV, et al

Key results



Reynolds JV, et al. J Clin Oncol 2021;39(suppl):abstr 4004

4004: Neo-AEGIS (Neoadjuvant trial in Adenocarcinoma of the Esophagus and Esophago-Gastric Junction International Study): Preliminary results of phase III RCT of CROSS versus perioperative chemotherapy (Modified MAGIC or FLOT protocol) – Reynolds JV, et al

Key results (cont.)

Postoperative complications, %	Arm A: Chemo (n=157)	Arm B: CROSS (n=162)	p-value
Mortality	1.9	3.0	0.723
Anastomotic leaks	12.0	12.0	
Respiratory			
Pneumonia	19.7	16.0	
ARDS	0.6	4.3	0.067
Respiratory failure	7.6	8.0	
VTE	3.8	3.0	
Cardiac			
Atrial fibrillation	12.7	14.2	
Sepsis	5.0	5.0	

Grade 3–4 AEs, %	Arm A: Chemo	Arm B: CROSS	p-value
Death	1.6	3.0	0.497
Neutropenia	14.1	2.8	<0.001
Diarrhea	10.9	0	<0.001
Neutropenic sepsis	2.7	0.6	0.215
Vomiting	7.6	2.8	0.035
Pulmonary embolism	5.4	5.1	0.872

Conclusions

- **In patients with esophageal or GEJ adenocarcinoma, perioperative chemotherapy was non-inferior to the CROSS regimen with no differences in postoperative complications**

Reynolds JV, et al. J Clin Oncol 2021;39(suppl):abstr 4004

CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

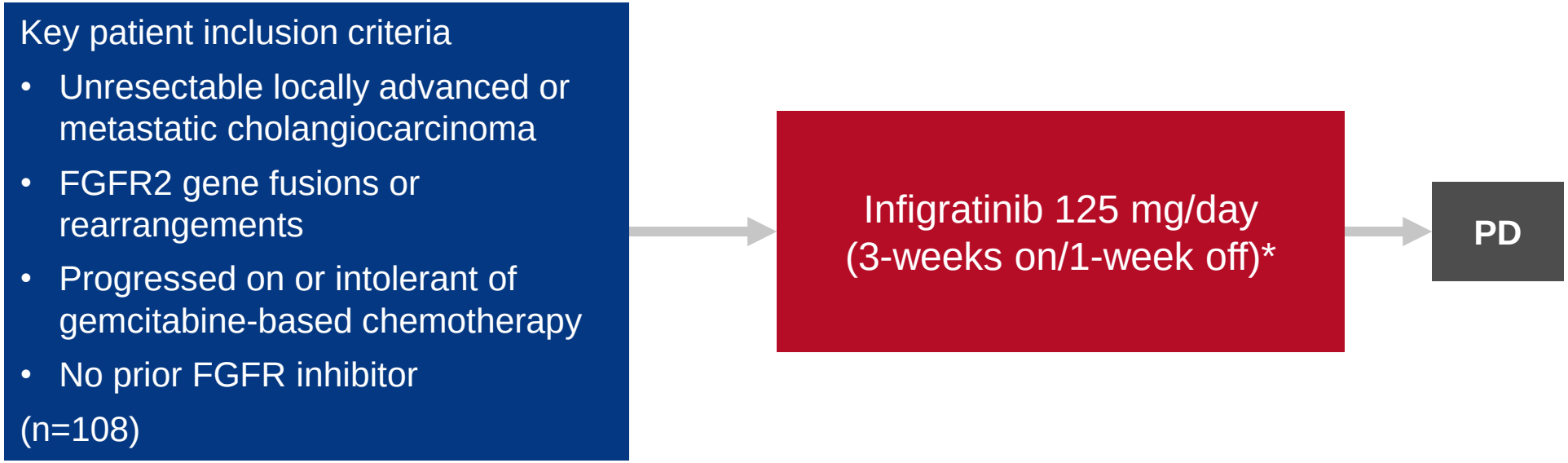
Cancers of the pancreas, small bowel and hepatobiliary tract

PANCREATIC CANCER

265: Final results from a phase II study of infigratinib (BGJ398), an FGFR-selective tyrosine kinase inhibitor, in patients with previously treated advanced cholangiocarcinoma harboring an FGFR2 gene fusion or rearrangement – Javle MM, et al

Study objective

- To evaluate the efficacy and safety of infigratinib, an FGFR1-3 TKI, in previously treated patients with cholangiocarcinoma and FGFR fusions or rearrangements



PRIMARY ENDPOINTS

- ORR (RECIST v1.1, ICR), DoR

SECONDARY ENDPOINTS

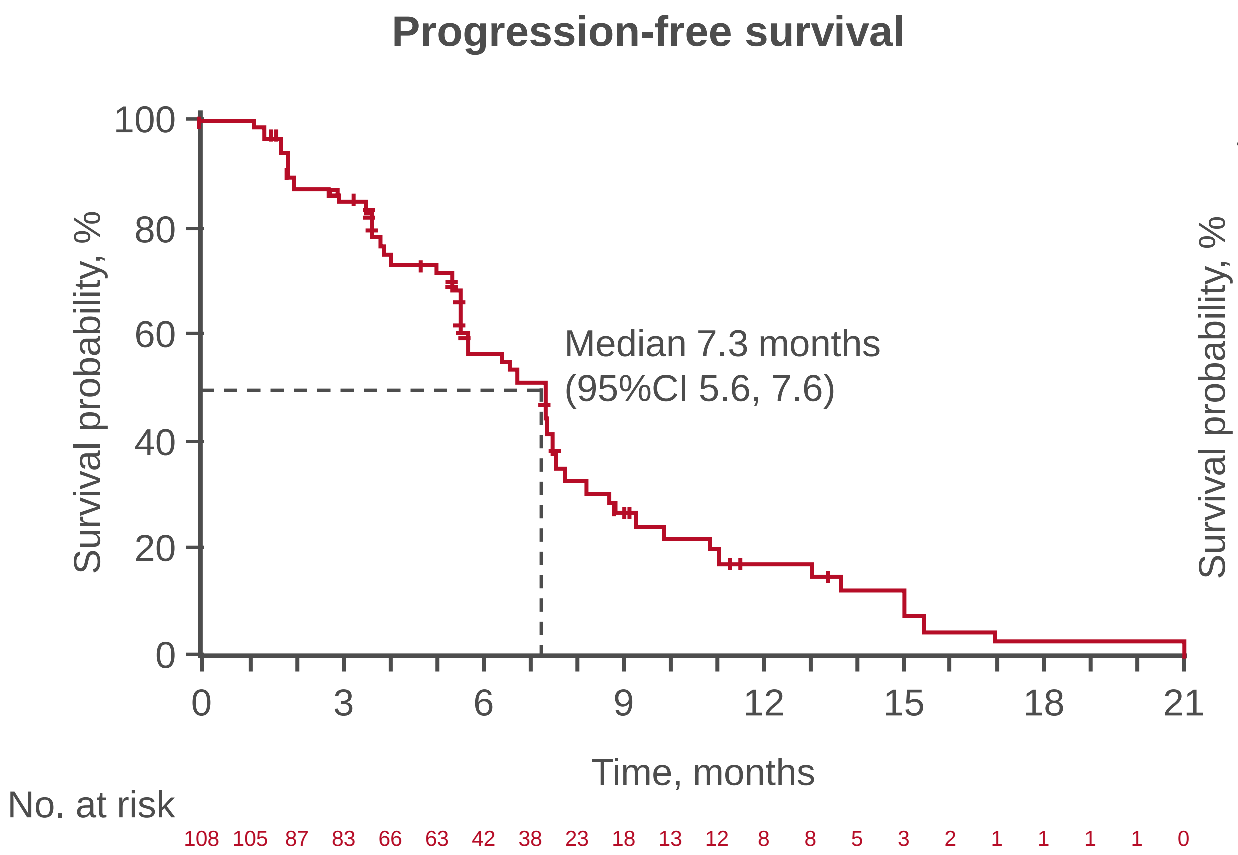
- PFS, DCR, BOR, OS, safety

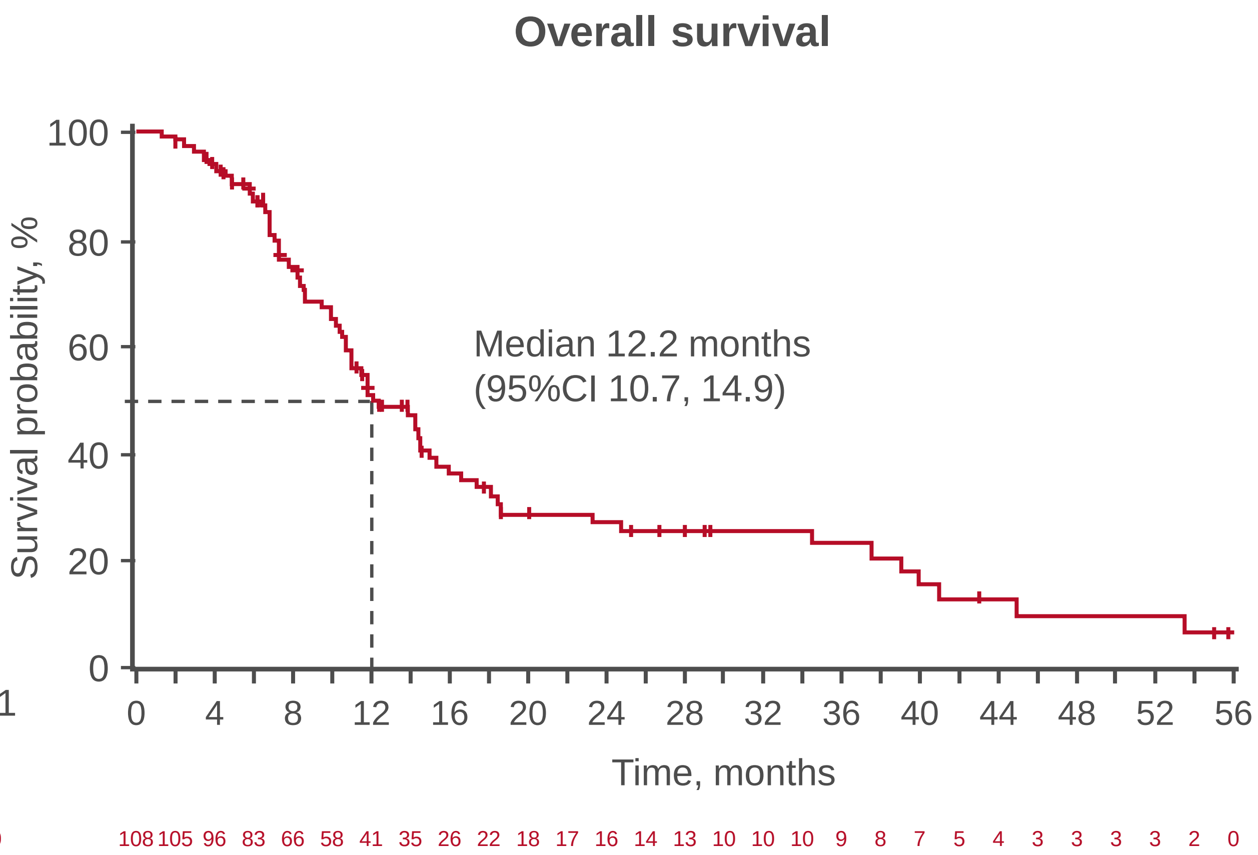
*All patients received prophylactic sevelamer, an oral phosphate binder

Javle MM, et al. J Clin Oncol 2021;39(suppl):abstr 265

265: Final results from a phase II study of infigratinib (BGJ398), an FGFR-selective tyrosine kinase inhibitor, in patients with previously treated advanced cholangiocarcinoma harboring an FGFR2 gene fusion or rearrangement – Javle MM, et al

Key results





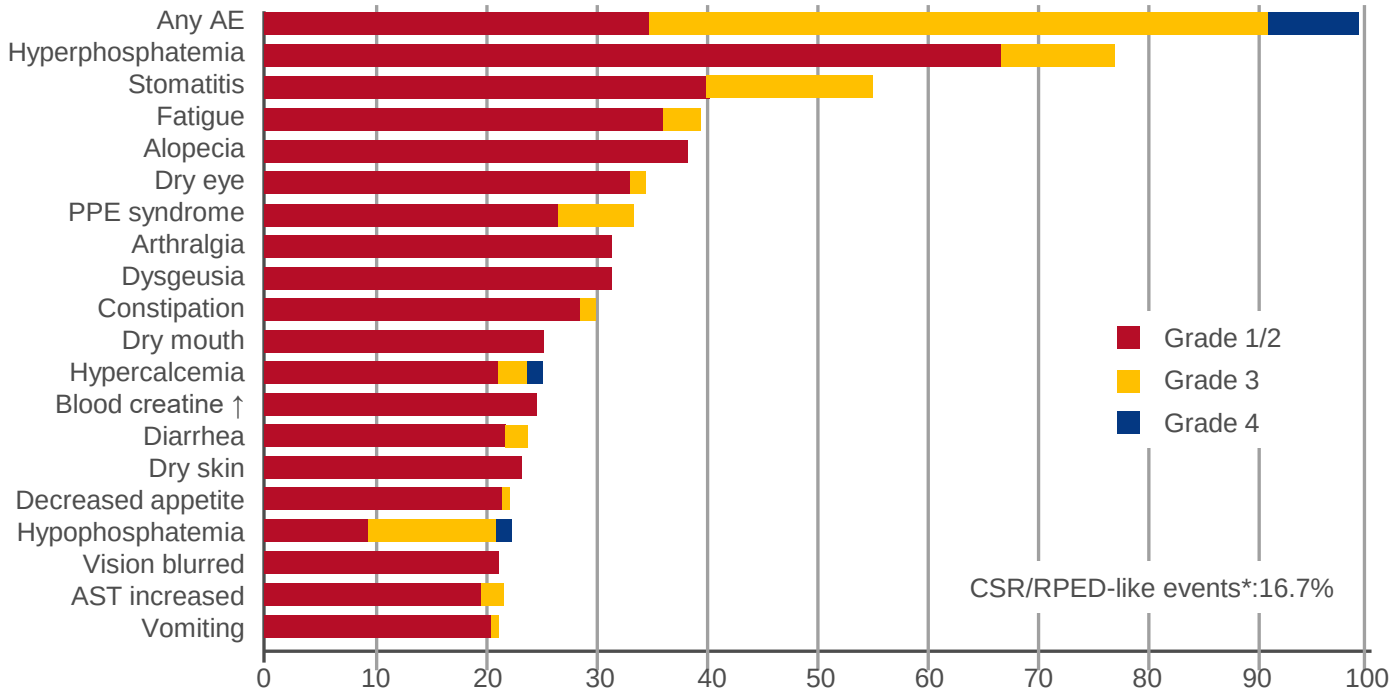
Javle MM, et al. J Clin Oncol 2021;39(suppl):abstr 265

265: Final results from a phase II study of infigratinib (BGJ398), an FGFR-selective tyrosine kinase inhibitor, in patients with previously treated advanced cholangiocarcinoma harboring an FGFR2 gene fusion or rearrangement – Javle MM, et al

Key results (cont.)

	Infigratinib (n=108)
BOR, % (95%CI)	34.3 (25.4, 44.0)
CR	1 (0.9)
PR	24 (22.2)
SD	66 (61.1)
PD	11 (10.2)
Unknown	6 (5.6)
ORR, % (95%CI)	**23.1 (15.6, 32.2)**
DCR, % (95%CI)	84.3 (76.0, 90.6)
Median DoR, months (range)	5.0 (0.9–19.1)

Incidence of treatment-emergent adverse events (n=108)



Conclusions

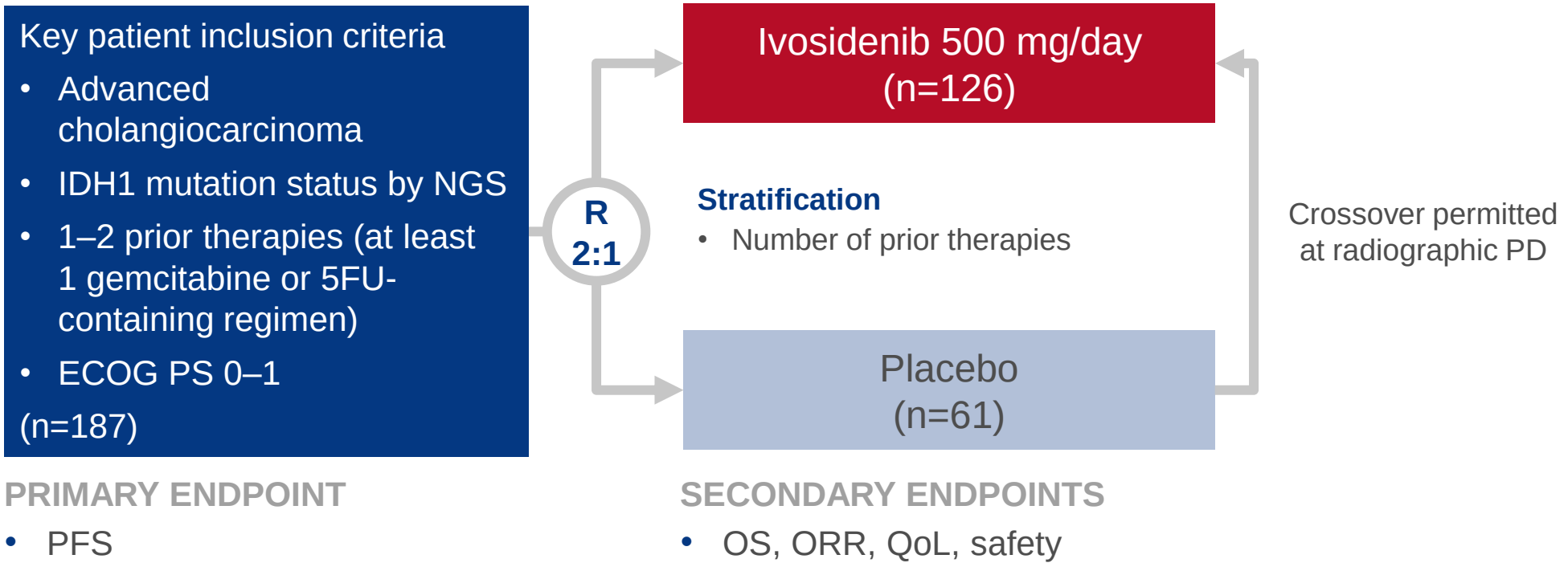
- **In patients with previously treated advanced cholangiocarcinoma and FGFR2 gene fusions and rearrangements, infigratinib demonstrated encouraging clinical activity and was generally well-tolerated**

Javle MM, et al. J Clin Oncol 2021;39(suppl):abstr 265

266: Final results from ClarIDHy, a global, phase III, randomized, double-blind study of ivosidenib (IVO) versus placebo (PBO) in patients (pts) with previously treated cholangiocarcinoma (CCA) and an isocitrate dehydrogenase 1 (IDH1) mutation – Zhu AX, et al

Study objective

- To evaluate the efficacy and safety of ivosidenib in patients with advanced cholangiocarcinoma and an IDH1 mutation in the ClarIDHy study



Zhu AX, et al. J Clin Oncol 2021;39(suppl):abstr 266

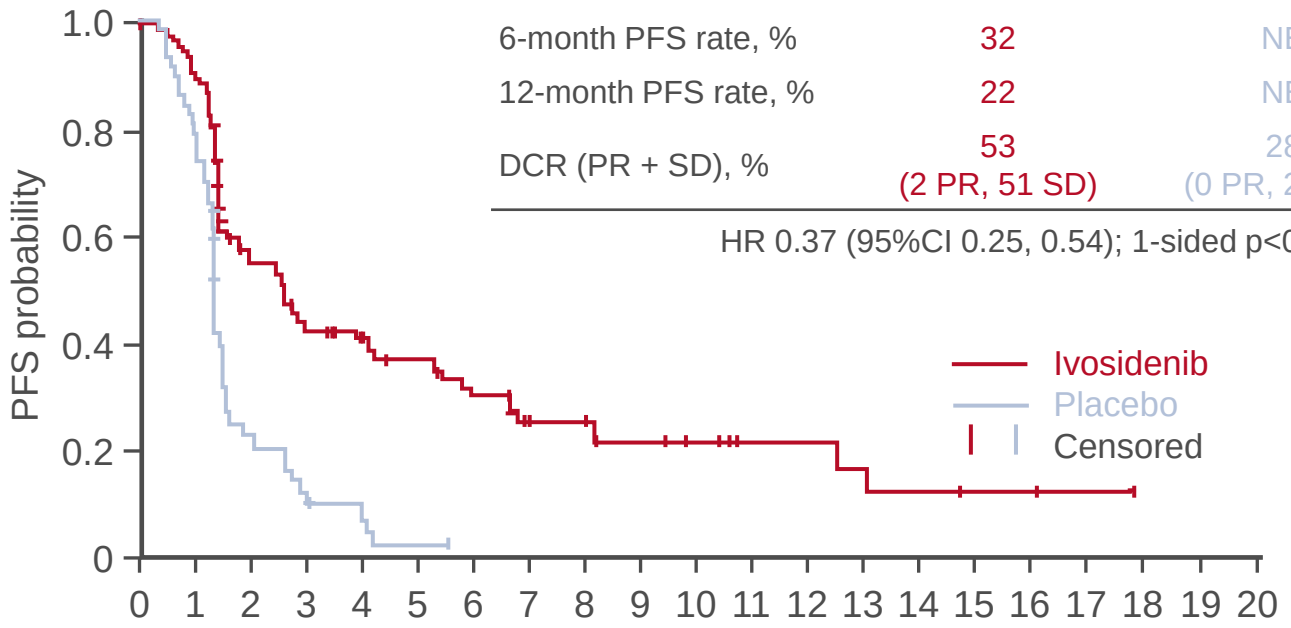
266: Final results from ClarIDHy, a global, phase III, randomized, double-blind study of ivosidenib (IVO) versus placebo (PBO) in patients (pts) with previously treated cholangiocarcinoma (CCA) and an isocitrate dehydrogenase 1 (IDH1) mutation – Zhu AX, et al

Key results

Progression-free survival

	Ivosidenib	Placebo
mPFS, months	2.7	1.4
6-month PFS rate, %	32	NE
12-month PFS rate, %	22	NE
DCR (PR + SD), %	53 (2 PR, 51 SD)	28 (0 PR, 28 SD)

HR 0.37 (95%CI 0.25, 0.54); 1-sided p<0.0001



No. at risk																			
Ivosidenib	124	105	54	40	36	28	22	16	14	10	9	6	5	4	3	3	2	1	1
Placebo	61	46	11	6	4	1													

Zhu AX, et al. J Clin Oncol 2021;39(suppl):abstr 266

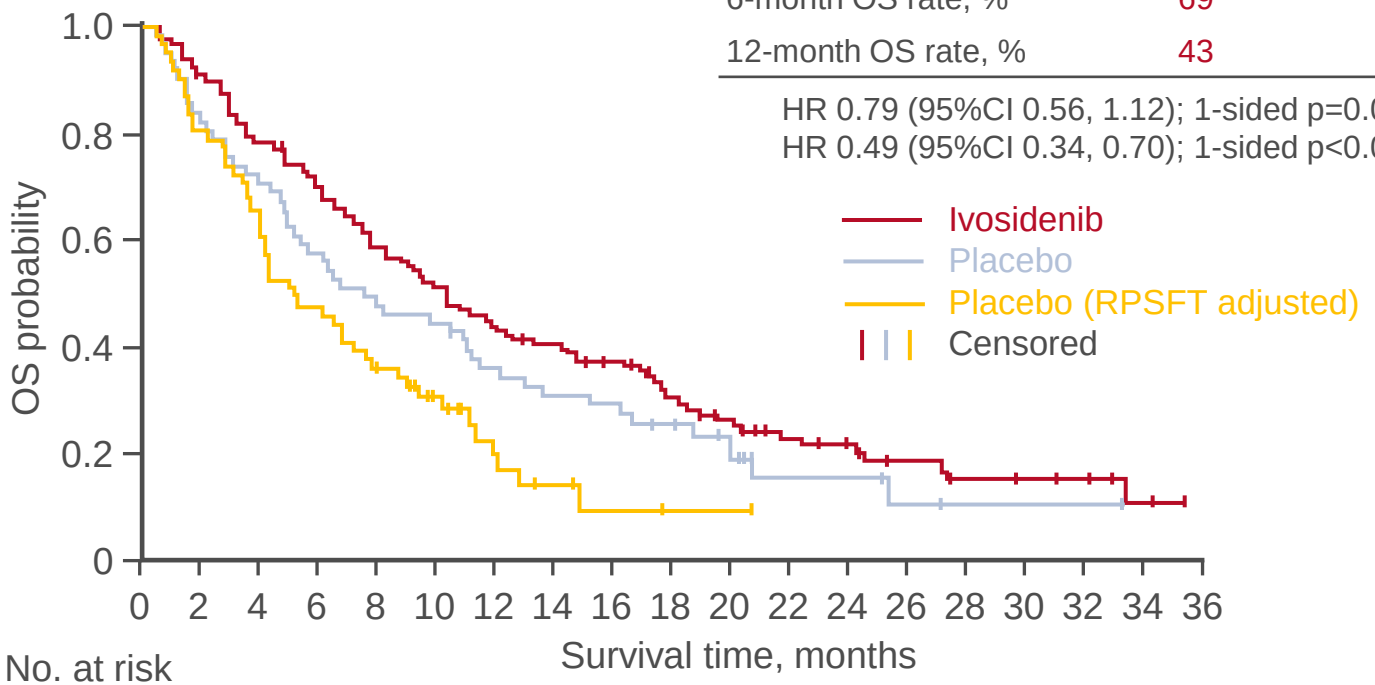
266: Final results from ClarIDHy, a global, phase III, randomized, double-blind study of ivosidenib (IVO) versus placebo (PBO) in patients (pts) with previously treated cholangiocarcinoma (CCA) and an isocitrate dehydrogenase 1 (IDH1) mutation – Zhu AX, et al

Key results (cont.)

Overall survival
Rank preserving structural failure time (RPSFT)

	Ivosidenib	Placebo
mOS, months	10.3	7.5
6-month OS rate, %	69	57
12-month OS rate, %	43	36

HR 0.79 (95%CI 0.56, 1.12); 1-sided p=0.093
HR 0.49 (95%CI 0.34, 0.70); 1-sided p<0.0001 (RPFST adj.)



No. at risk

Ivosidenib	126	113	97	85	72	62	53	48	42	32	25	18	14	10	7	6	5	2
Placebo	61	50	43	35	29	27	21	18	17	12	8	4	4	2	1	1	1	
Placebo (RPSFT adjusted)	61	49	37	29	21	14	6	4	2	1	1							

Zhu AX, et al. J Clin Oncol 2021;39(suppl):abstr 266

266: Final results from ClarIDHy, a global, phase III, randomized, double-blind study of ivosidenib (IVO) versus placebo (PBO) in patients (pts) with previously treated cholangiocarcinoma (CCA) and an isocitrate dehydrogenase 1 (IDH1) mutation – Zhu AX, et al

Key results (cont.)

TEAEs, %	Ivosidenib (n=166)	Placebo (n=59)
Grade ≥3	53.0	37.3
Ascites	9.0	6.8
Anemia	7.2	0
Blood bilirubin increased	5.4	1.7
Led to discontinuation	6.6	8.5
Led to dose reductions	3.0	0
Led to dose interruptions	30.1	18.6

Conclusions

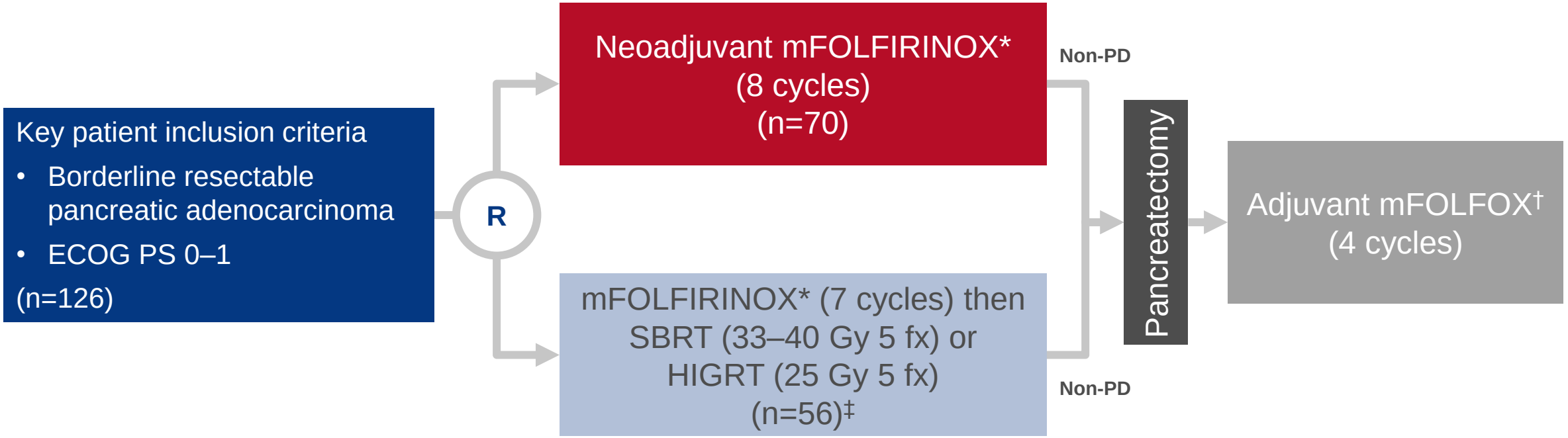
- **In patients with previously treated cholangiocarcinoma and an IDH1 mutation, ivosidenib provided a significant PFS improvement, but only a numerical OS improvement despite a high crossover from placebo arm and was generally well-tolerated**

Zhu AX, et al. J Clin Oncol 2021;39(suppl):abstr 266

377: Alliance A021501: Preoperative mFOLFIRINOX or mFOLFIRINOX plus hypofractionated radiation therapy (RT) for borderline resectable (BR) adenocarcinoma of the pancreas – Katz MHG, et al

Study objective

- To evaluate the efficacy and safety of neoadjuvant mFOLFIRINOX with or without radiotherapy in patients with borderline resectable pancreatic adenocarcinoma



PRIMARY ENDPOINT

- 18-month OS rate

SECONDARY ENDPOINTS

- EFS, R0 rate, pCR rate, safety

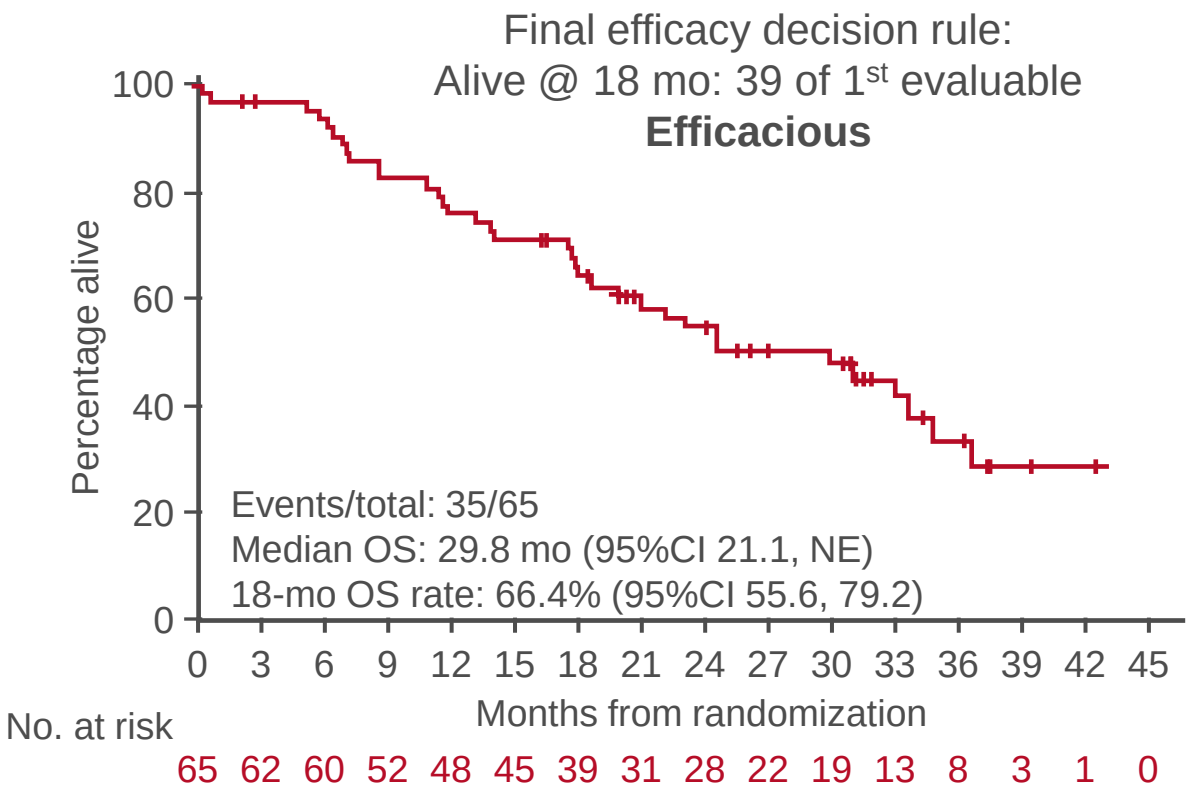
*Oxaliplatin 85 mg/m^2 + irinotecan 180 mg/m^2 + leucovorin 400 mg/m^2 + 5FU 2400 mg/m^2 over 46 h; †oxaliplatin 85 mg/m^2 + leucovorin 400 mg/m^2 + 5FU 2400 mg/m over 46 h; ‡arm closed early at interim analysis due to futility

Katz MHG, et al. J Clin Oncol 2021;39(suppl):abstr 377

377: Alliance A021501: Preoperative mFOLFIRINOX or mFOLFIRINOX plus hypofractionated radiation therapy (RT) for borderline resectable (BR) adenocarcinoma of the pancreas – Katz MHG, et al

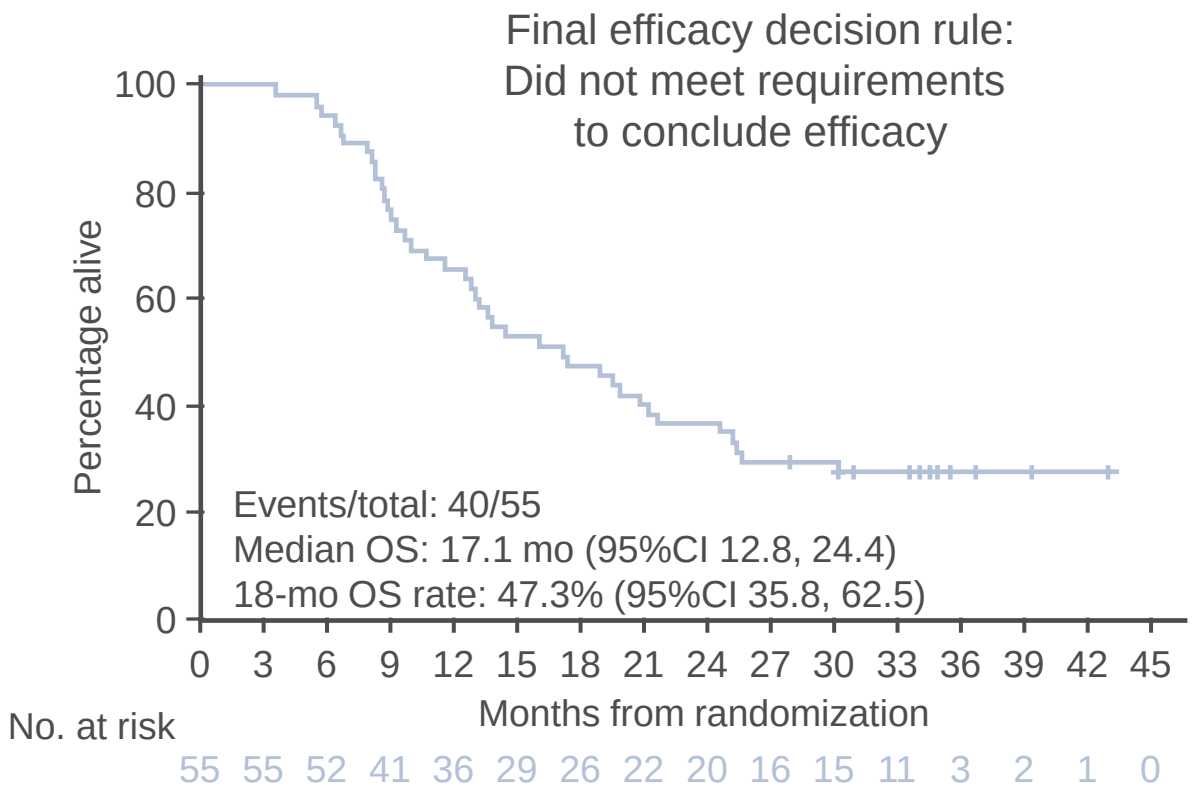
Key results

mFOLFIRINOX



Median EFS: 15.0 months (95%CI 11.2, 21.9)

mFOLFIRINOX → radiotherapy



Median EFS: 10.2 months (95%CI 6.7, 17.3)

Katz MHG, et al. J Clin Oncol 2021;39(suppl):abstr 377

377: Alliance A021501: Preoperative mFOLFIRINOX or mFOLFIRINOX plus hypofractionated radiation therapy (RT) for borderline resectable (BR) adenocarcinoma of the pancreas – Katz MHG, et al

Key results (cont.)

Characteristic, n (%)	mFOLFIRINOX (n=32)	mFOLFIRINOX → RT (n=19)
Pancreatoduodenectomy	30 (94)	18 (95)
SMV/PV resection	12 (38)	6 (32)
Hepatic artery resection	1 (3)	2 (11)
R0	28 (88)	14 (74)
N0	15 (47)	9 (47)
pCR	0 (0)	2 (11)

TRAEs, n (%)	mFOLFIRINOX (n=65)	mFOLFIRINOX → RT (n=55)
Grade 3	37 (57)	35 (64)
During mFOLFIRINOX	37 (57)	35 (64)
During RT*	-	5 (13)
Grade 4	11 (17)†	5 (9)
During mFOLFIRINOX	11 (17)	5 (9)
During RT*	-	0 (0)

Conclusions

- **In patients with borderline resectable pancreatic adenocarcinoma, preoperative mFOLFIRINOX demonstrated favorable OS compared with historical data in this patient population**

*40 patients received RT; †one patient experienced a grade 5 AE (sepsis)

Katz MHG, et al. J Clin Oncol 2021;39(suppl):abstr 377

4016: Preoperative chemoradiotherapy to improve overall survival in pancreatic cancer: Long-term results of the multicenter randomized phase III PREOPANC trial – Van Eijck CH, et al

Study objective

- To evaluate the efficacy and safety of preoperative CRT vs. immediate surgery, both followed by adjuvant chemotherapy, in patients with resectable pancreatic cancer in the PREOPANC study

Key patient inclusion criteria

- Pancreatic cancer proven by cytology
- Resectable or borderline resectable

(n=248)

R

Neoadjuvant CRT arm:
Preoperative CRT* + adjuvant gemcitabine† x4 cycles
(n=119)

→ PD

Stratification

- Resectability
- Institution

Upfront surgery arm:
Immediate surgery + adjuvant gemcitabine† x6 cycles
(n=127)

→ PD

PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- R0 resection rate, DFS, distant metastases locoregional recurrence, safety

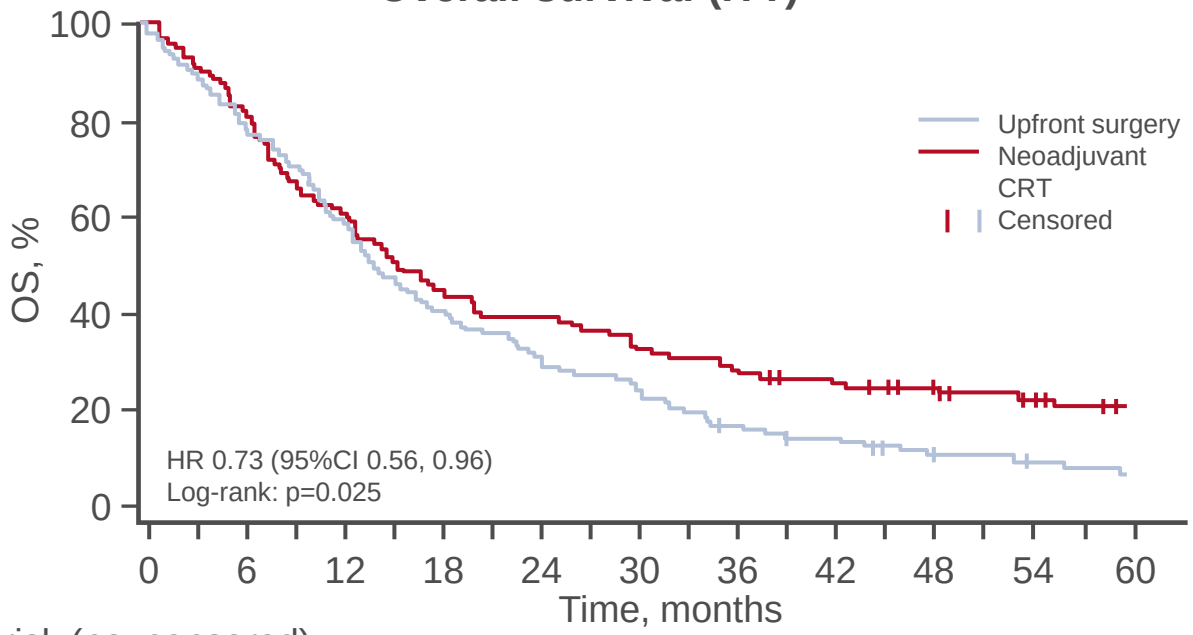
*15 fx 2.4 Gy + gemcitabine 1000 mg/m^2 D1, 8, 15, preceded and followed by gemcitabine 1000 mg/m^2 D1, 8 + 1 wk rest; †gemcitabine 1000 mg/m^2 D1, 8, 15 + 1 wk rest

Van Eijck CH, et al. J Clin Oncol 2021;39(suppl):abstr 4016

4016: Preoperative chemoradiotherapy to improve overall survival in pancreatic cancer: Long-term results of the multicenter randomized phase III PREOPANC trial – Van Eijck CH, et al

Key results

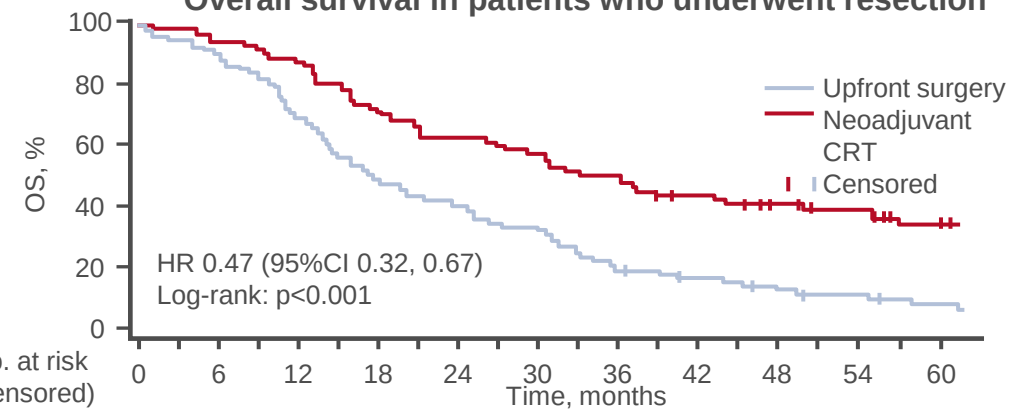
Overall survival (ITT)



No. at risk (no. censored)

Upfront surgery	127 (0)	103 (0)	75 (0)	51 (0)	40 (0)	32 (0)	20 (1)	16 (2)	11 (4)	7 (6)	5 (6)
Neoadjuvant CRT	119 (0)	98 (0)	73 (0)	53 (0)	40 (0)	39 (0)	34 (0)	29 (2)	24 (5)	17 (10)	11 (15)

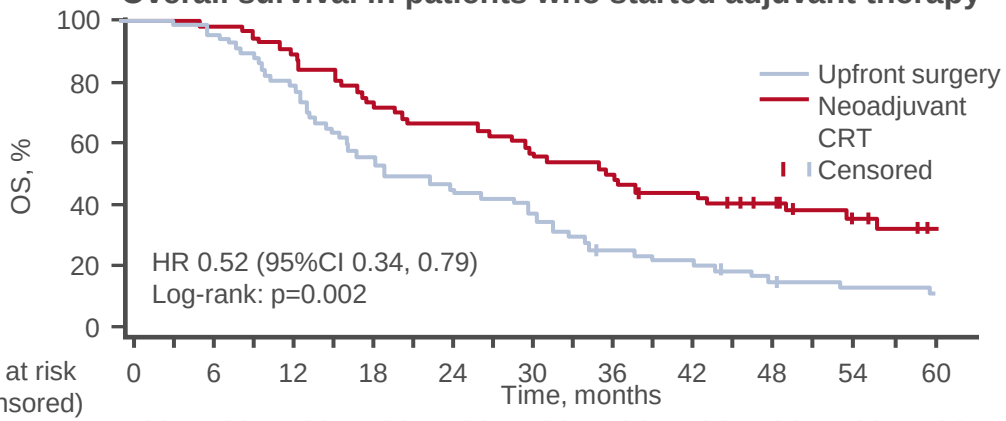
Overall survival in patients who underwent resection



No. at risk (no. censored)

Upfront surgery	92 (0)	84 (0)	64 (0)	45 (0)	38 (0)	30 (0)	18 (1)	15 (2)	11 (3)	7 (5)	5 (5)
Neoadjuvant CRT	72 (0)	68 (0)	63 (0)	50 (0)	45 (0)	39 (0)	34 (0)	29 (2)	24 (5)	17 (10)	11 (15)

Overall survival in patients who started adjuvant therapy



No. at risk (no. censored)

Upfront surgery	65 (0)	64 (0)	52 (0)	36 (0)	30 (0)	26 (0)	15 (1)	13 (1)	9 (2)	6 (3)	5 (3)
Neoadjuvant CRT	55 (0)	54 (0)	50 (0)	40 (0)	36 (0)	31 (0)	27 (0)	23 (1)	18 (4)	11 (9)	6 (13)

Van Eijck CH, et al. J Clin Oncol 2021;39(suppl):abstr 4016

4016: Preoperative chemoradiotherapy to improve overall survival in pancreatic cancer: Long-term results of the multicenter randomized phase III PREOPANC trial – Van Eijck CH, et al

Key results (cont.)

Surgical outcomes, n (%)	Neoadjuvant CRT arm (n=119)	Upfront surgery arm (n=127)	p-value
Underwent surgery	82 (69)	121 (95)	<0.001
Underwent resection	72 (61)	92 (72)	0.058
	n=68	n=82	
R0 resection	49 (72)	35 (43)	<0.001
N0 resection	44 (65)	15 (18)	<0.001

Conclusions

- **In patients with pancreatic cancer, neoadjuvant CRT demonstrated improvement in OS compared with upfront surgery followed by adjuvant gemcitabine**

Van Eijck CH, et al. J Clin Oncol 2021;39(suppl):abstr 4016

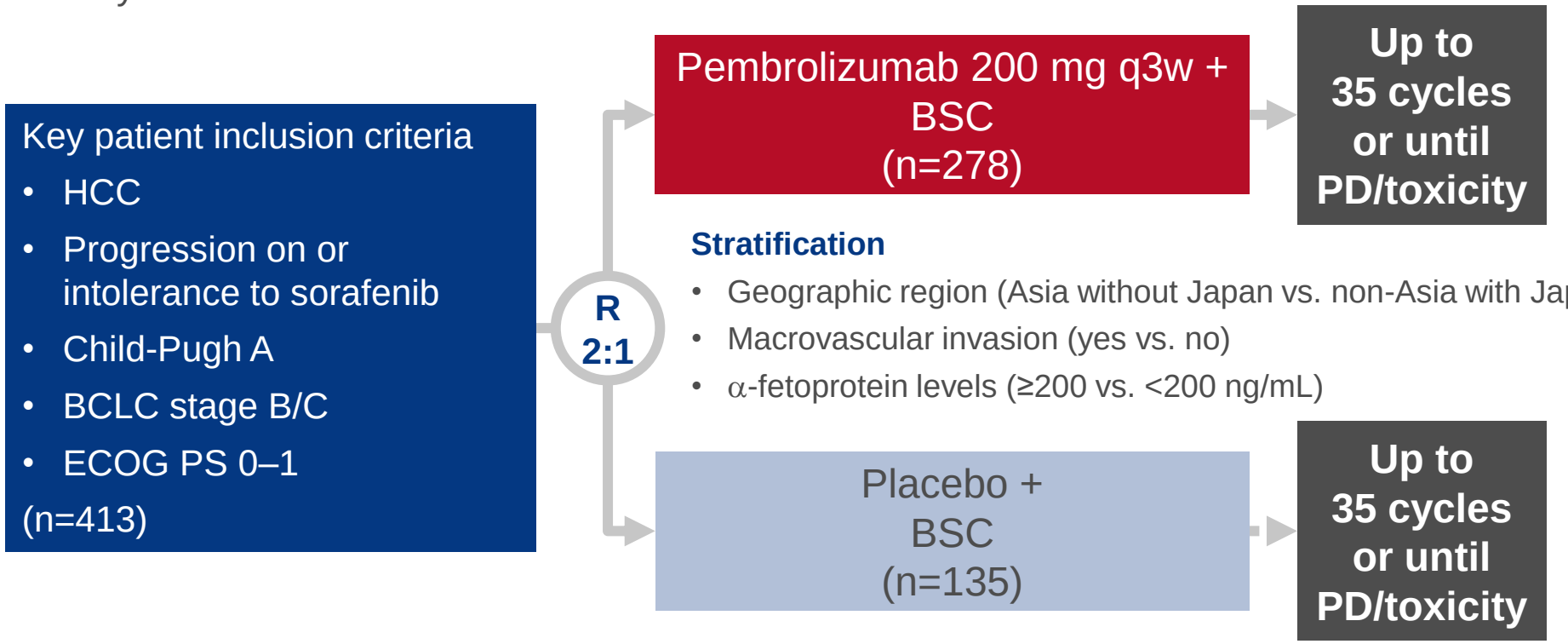
Cancers of the pancreas, small bowel and hepatobiliary tract

HEPATOCELLULAR CARCINOMA

268: Pembrolizumab (pembro) vs placebo (pbo) in patients (pts) with advanced hepatocellular carcinoma (aHCC) previously treated with sorafenib: Updated data from the randomized, phase III KEYNOTE-240 study – Merle P, et al

Study objective

- To evaluate the longer term efficacy and safety of pembrolizumab in patients with previously treated advanced HCC in the KEYNOTE-240 study



CO-PRIMARY ENDPOINTS

- OS, PFS (RECIST v1.1)

SECONDARY ENDPOINTS

- ORR, DoR, DCR, TTP, safety

Data cut-off: July 13, 2020

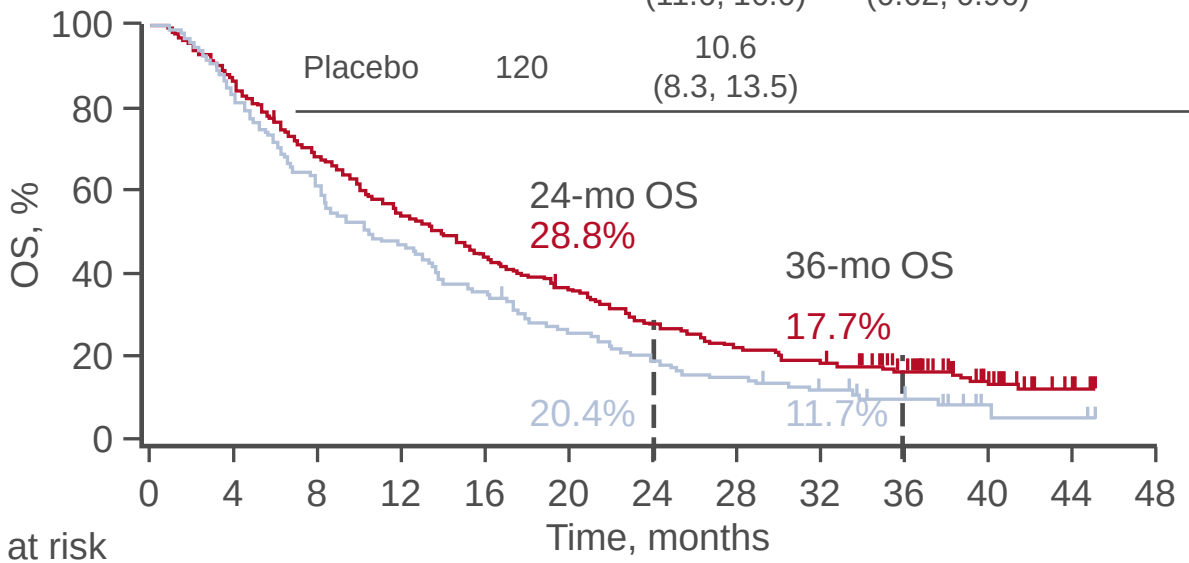
Merle P, et al. J Clin Oncol 2021;39(suppl):abstr 268

268: Pembrolizumab (pembro) vs placebo (pbo) in patients (pts) with advanced hepatocellular carcinoma (aHCC) previously treated with sorafenib: Updated data from the randomized, phase III KEYNOTE-240 study – Merle P, et al

Key results

Overall survival

	Events, n	mOS, months (95%CI)	HR (95%CI)	Nominal p-value
Pembro	232	13.9 (11.6, 16.0)	0.77 (0.62, 0.96)	0.0112
Placebo	120	10.6 (8.3, 13.5)		

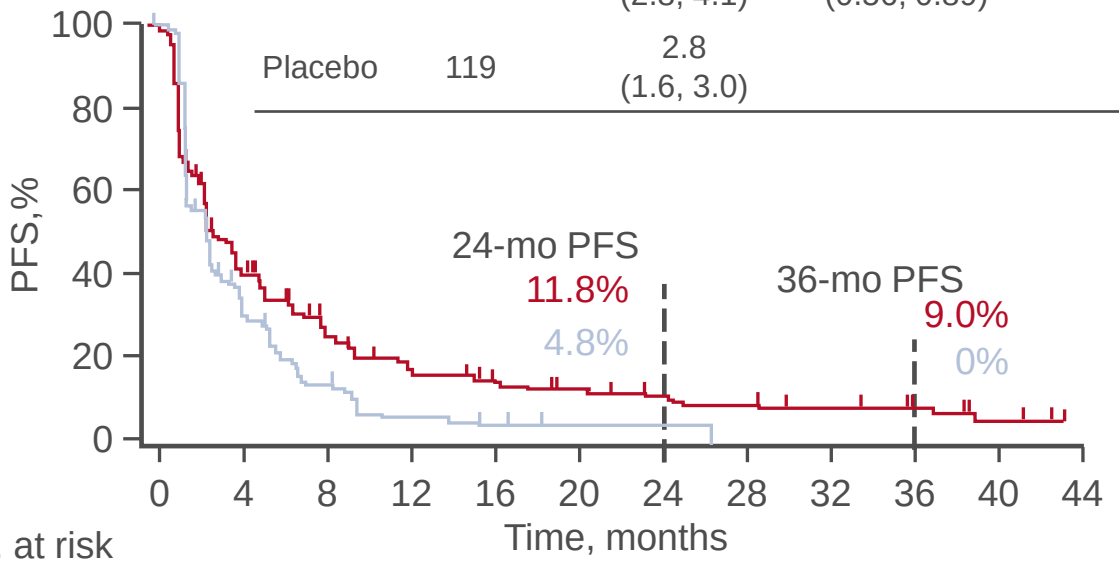


No. at risk

Pembro	278	237	190	152	122	102	79	63	53	37	16	4	0
Placebo	135	113	84	65	49	36	27	22	16	9	2	2	0

Progression-free survival

	Events, n	mPFS, months (95%CI)	HR (95%CI)	Nominal p-value
Pembro	222	3.3 (2.8, 4.1)	0.70 (0.56, 0.89)	0.0011
Placebo	119	2.8 (1.6, 3.0)		



No. at risk

Pembro	278	116	65	38	28	21	17	14	11	9	3	0	
Placebo	135	46	16	7	4	1	1	0	0	0	0	0	

Merle P, et al. J Clin Oncol 2021;39(suppl):abstr 268

268: Pembrolizumab (pembro) vs placebo (pbo) in patients (pts) with advanced hepatocellular carcinoma (aHCC) previously treated with sorafenib: Updated data from the randomized, phase III KEYNOTE-240 study – Merle P, et al

Key results (cont.)

	Pembrolizumab (n=278)	Placebo (n=135)
ORR, n (%)	51 (18.3)	6 (4.4)
BOR, n (%)		
CR	10 (3.6)	0 (0)
PR	41 (14.7)	6 (4.4)
SD	121 (43.5)	66 (48.9)
PD	85 (30.6)	54 (40.0)
NE	4 (1.4)	2 (1.5)
NA	17 (6.1)	7 (5.2)
DCR, n (%)	172 (61.9)	72 (53.3)
Median TTR, months (range)	2.7 (1.2–16.9)	2.9 (1.1–6.9)
Median DoR, months (range)	13.9 (1.5+–41.9+)	15.2 (2.8–21.9)

AEs, n (%)	Pembrolizumab (n=279)	Placebo (n=134)
TRAE	171 (61.3)	65 (48.5)
Grade 3/4	53 (19.0)	10 (7.5)
Led to discontinuation	19 (6.8)	1 (0.7)
Led to death	1 (0.4)*	0 (0)
AEs of special interest	50 (17.9)	11 (8.2)
Grade 3/4	20 (7.2)	1 (0.7)
Led to discontination	10 (3.6)	0 (0)
Immune-mediated hepatitis	10 (3.6)	0 (0)
Received systemic corticosteroid	8 (2.9)	0 (0)

Conclusions

- **In patients with advanced HCC and previously treated with sorafenib, pembrolizumab continued to demonstrate numerical improvements in survival and there were no new or unexpected AEs**

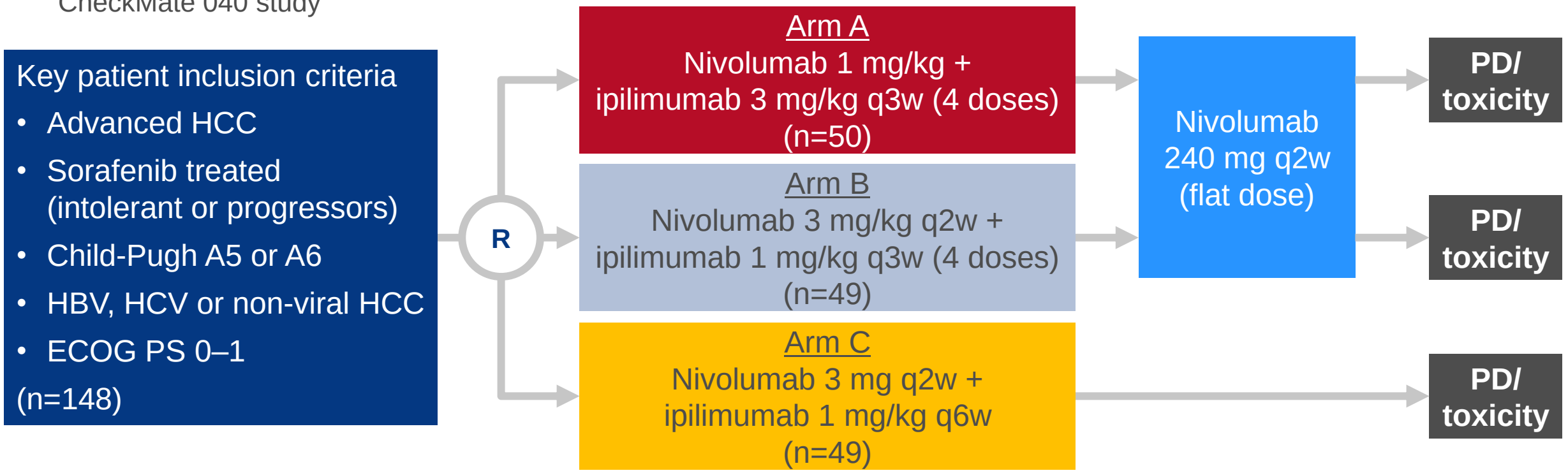
*Attributed to malignant neoplasm progression

Merle P, et al. J Clin Oncol 2021;39(suppl):abstr 268

269: Nivolumab (NIVO) plus ipilimumab (IPI) combination therapy in patients (Pts) with advanced hepatocellular carcinoma (aHCC): Long-term results from CheckMate 040 – El-Khoueiry AB, et al

Study objective

- To evaluate the long-term efficacy and safety of nivolumab ± ipilimumab in patients with advanced HCC in the CheckMate 040 study



PRIMARY ENDPOINTS

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

SECONDARY ENDPOINTS

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

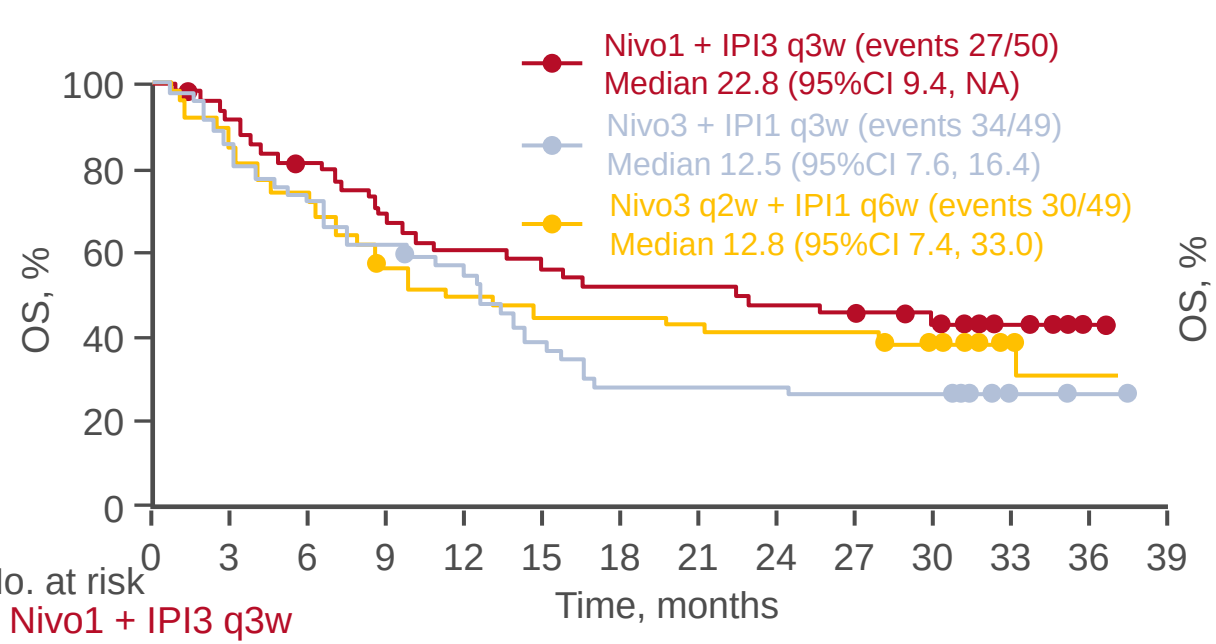
El-Khoueiry AB, et al. J Clin Oncol 2020;39(suppl):abstr 269

269: Nivolumab (NIVO) plus ipilimumab (IPI) combination therapy in patients (Pts) with advanced hepatocellular carcinoma (aHCC): Long-term results from CheckMate 040 – El-Khoueiry AB, et al

Key results

Overall survival

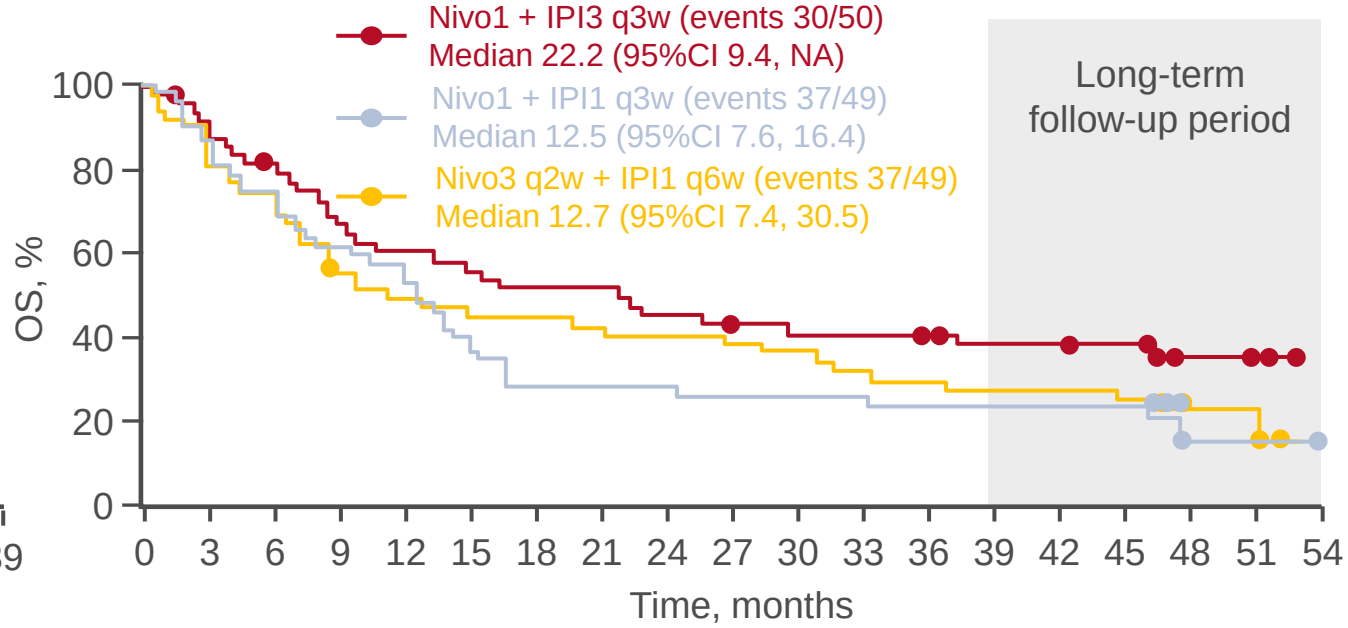
Primary analysis
Median follow-up: 30.7 months



No. at risk

Nivo1 + IPI3 q3w	50	45	39	32	29	27	25	25	23	21	19	7	2	0
Nivo3 + IPI3 q3w	49	41	36	30	26	18	14	14	14	13	13	2	1	0
Nivo3 q2w + IPI1 q6w	49	42	36	27	24	22	22	20	20	20	15	4	2	0

Long-term follow-up
Median follow-up: 46.5 months



Nivo1 + IPI3 q3w	50	45	39	32	29	27	25	25	22	20	19	19	18	16	16	15	6	4	0
Nivo3 + IPI3 q3w	49	41	36	30	26	18	14	14	14	13	13	12	12	12	12	12	2	2	0
Nivo3 q2w + IPI1 q6w	49	42	36	27	24	22	22	20	20	19	18	15	14	14	14	13	38	2	0

El-Khoueiry AB, et al. J Clin Oncol 2020;39(suppl):abstr 269

269: Nivolumab (NIVO) plus ipilimumab (IPI) combination therapy in patients (Pts) with advanced hepatocellular carcinoma (aHCC): Long-term results from CheckMate 040 – El-Khoueiry AB, et al

Key results (cont.)

	Nivo1 + IPI3 q3w (n=50)	Nivo3 + IPI1 q3w (n=49)	Nivo3 + IPI1 q6w (n=49)
ORR, % (95%CI)	32 (20, 47)	31 (18, 45)	31 (18, 45)
CR	4 (8)	3 (6)	1 (2)
PR	12 (24)	12 (24)	14 (29)
SD	9 (18)	5 (10)	9 (18)
PD	20 (40)	24 (49)	21 (43)
Median TTR, months (range)	2.0 (1–13)	2.6 (1–5)	2.7 (1–9)
Median DoR, months (95%CI)	17.5 (8.3, NE)	22.2 (4.4, NE)	16.6 (4.3, NE)
DCR, % (95%CI)	54 (39, 68)	43 (29, 58)	49 (36, 64)

Grade 3/4 TRAEs occurring in ≥5%, n (%)	Nivo1 + IPI3 q3w (n=50)	Nivo3 + IPI1 q3w (n=49)	Nivo3 + IPI1 q6w (n=49)
Any	27 (55)	15 (31)	17 (35)
AST increased	8 (16)	4 (8)	2 (4)
Lipase increased	6 (12)	4 (8)	5 (10)
Hyponatremia	5 (10)	2 (4)	0 (0)
ALT increased	5 (8)	3 (6)	0 (0)

Conclusions

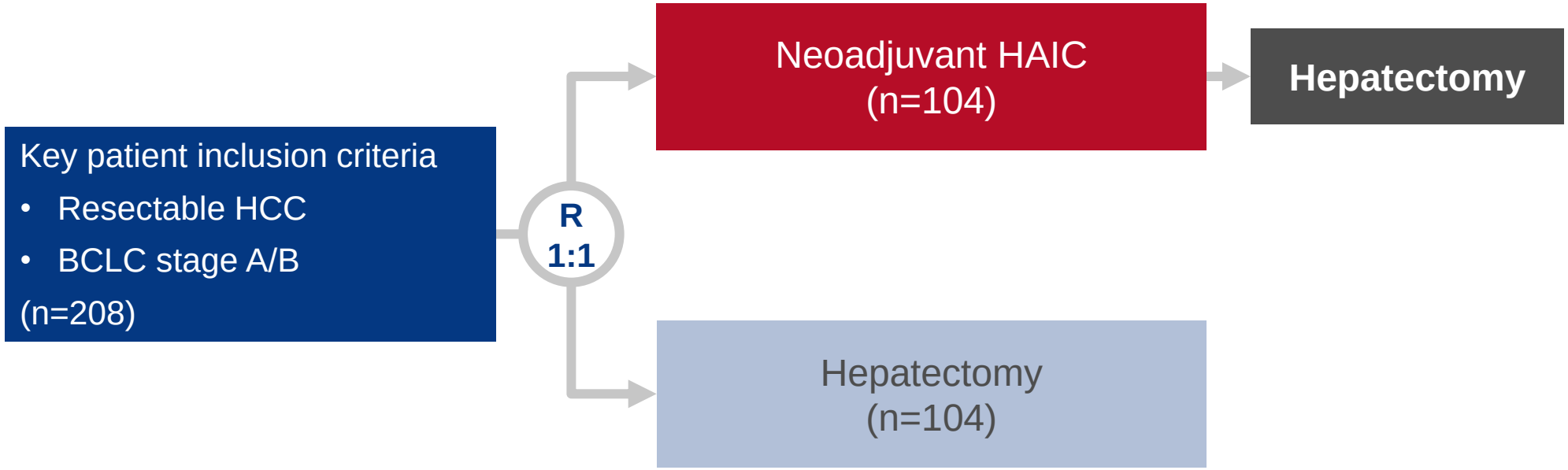
- **In patients with advanced HCC, nivolumab 1 mg/kg + ipilimumab 3 mg/kg demonstrated long-term benefits and had a manageable safety profile**

El-Khoueiry AB, et al. J Clin Oncol 2020;39(suppl):abstr 269

4008: Neoadjuvant transarterial infusion chemotherapy with FOLFOX could improve outcomes of resectable BCLC stage A/B hepatocellular carcinoma patients beyond Milan criteria: An interim analysis of a multi-center, phase 3, randomized, controlled clinical trial – Li S, et al

Study objective

- To evaluate the efficacy and safety of preoperative neoadjuvant HAIC + FOLFOX in patients with resectable BCLC stage A/B HCC beyond the Milan criteria



PRIMARY ENDPOINTS

- OS

SECONDARY ENDPOINTS

- PFS, RFS, safety

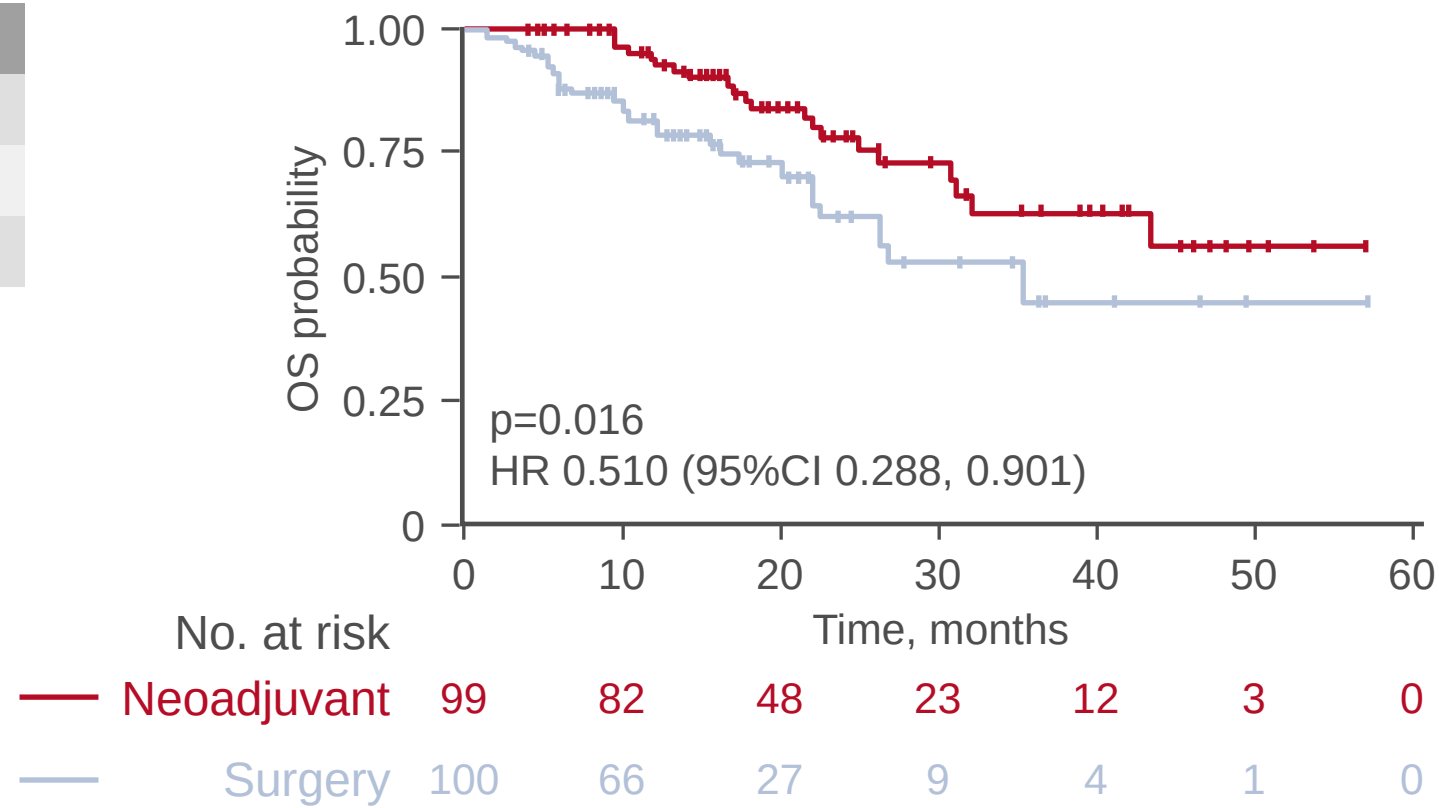
Li S, et al. J Clin Oncol 2021;39(suppl):abstr 4008

4008: Neoadjuvant transarterial infusion chemotherapy with FOLFOX could improve outcomes of resectable BCLC stage A/B hepatocellular carcinoma patients beyond Milan criteria: An interim analysis of a multi-center, phase 3, randomized, controlled clinical trial – Li S, et al

Key results

OS rate, %	Neoadjuvant	Surgery
1 year	92.9	79.5
2 years	78.6	62.0
3 years	63.5	46.3

Overall survival



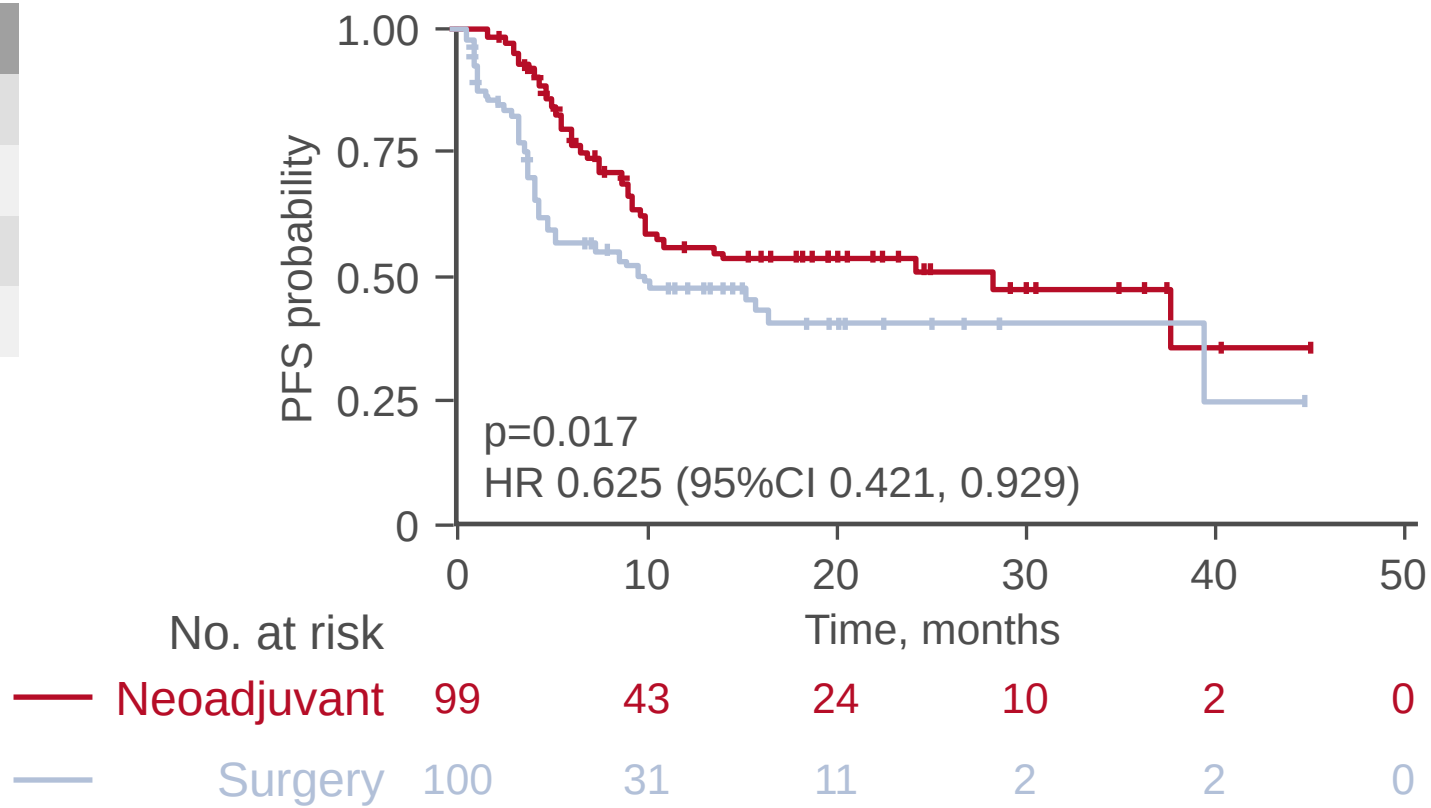
Li S, et al. J Clin Oncol 2021;39(suppl):abstr 4008

4008: Neoadjuvant transarterial infusion chemotherapy with FOLFOX could improve outcomes of resectable BCLC stage A/B hepatocellular carcinoma patients beyond Milan criteria: An interim analysis of a multi-center, phase 3, randomized, controlled clinical trial – Li S, et al

Key results (cont.)

PFS rate, %	Neoadjuvant	Surgery
6 months	77.6	52.7
12 months	50.4	42.8
18 months	47.4	34.8
mPFS, months	14.1	8.9

Progression-free survival



Li S, et al. J Clin Oncol 2021;39(suppl):abstr 4008

4008: Neoadjuvant transarterial infusion chemotherapy with FOLFOX could improve outcomes of resectable BCLC stage A/B hepatocellular carcinoma patients beyond Milan criteria: An interim analysis of a multi-center, phase 3, randomized, controlled clinical trial – Li S, et al

Key results (cont.)

- Incidence of MVI was lower with neoadjuvant HAIC (11.4%) compared with hepatectomy alone (39.0%)
- In the HAIC arm, 88 of 99 patients underwent hepatectomy and ORR was 63.6% and DCR 96.0%
- In the HAIC arm, grade 1 and 2 AEs were experienced by 59 (56.6%) and 26 (26.3%), respectively
- There was no significant difference between the two groups for operation-related AEs

Conclusions

- **In patients with resectable BCLC stage A/B HCC beyond the Milan criteria, neoadjuvant HAIC with FOLFOX was effective and safe with a reduced incidence of MVI**

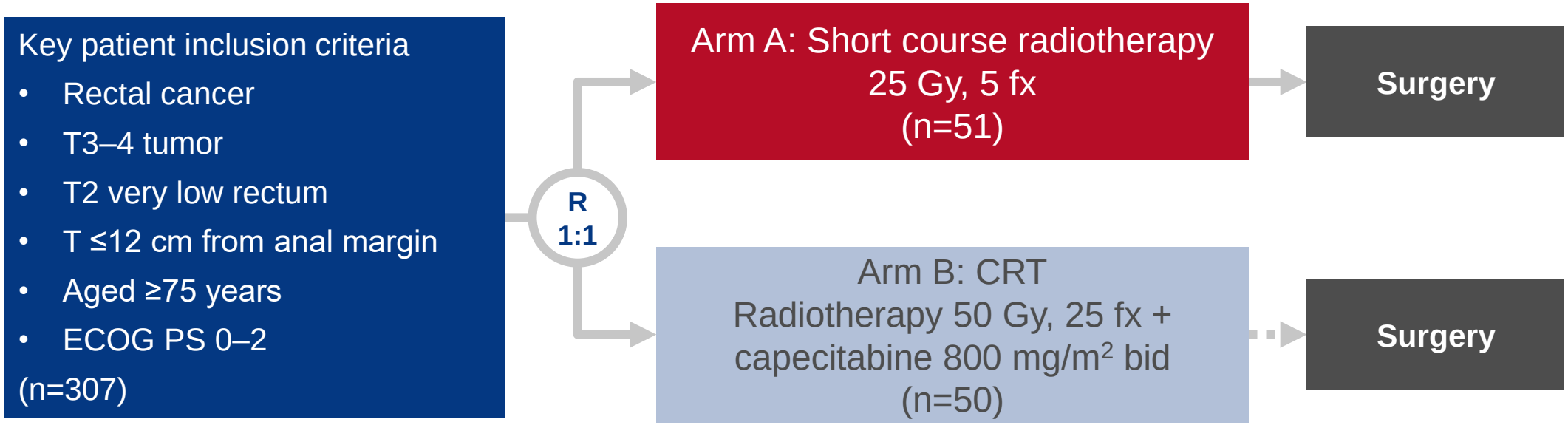
Li S, et al. J Clin Oncol 2021;39(suppl):abstr 4008

CANCERS OF THE COLON, RECTUM AND ANUS

4: NACRE: A randomized study comparing short course radiotherapy with radiochemotherapy for locally advanced rectal cancers in the elderly—Preliminary results – Francois E, et al

Study objective

- To evaluate the efficacy and safety of short course radiotherapy vs. CRT for elderly patients with locally advanced rectal cancers in the NACRE study



CO-PRIMARY ENDPOINTS

- R0 resection rate, preservation of autonomy

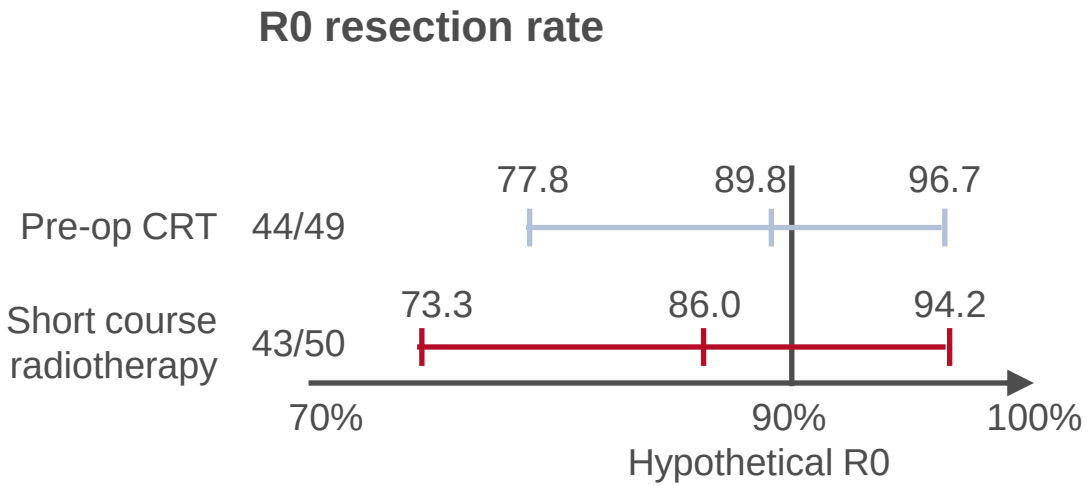
SECONDARY ENDPOINTS

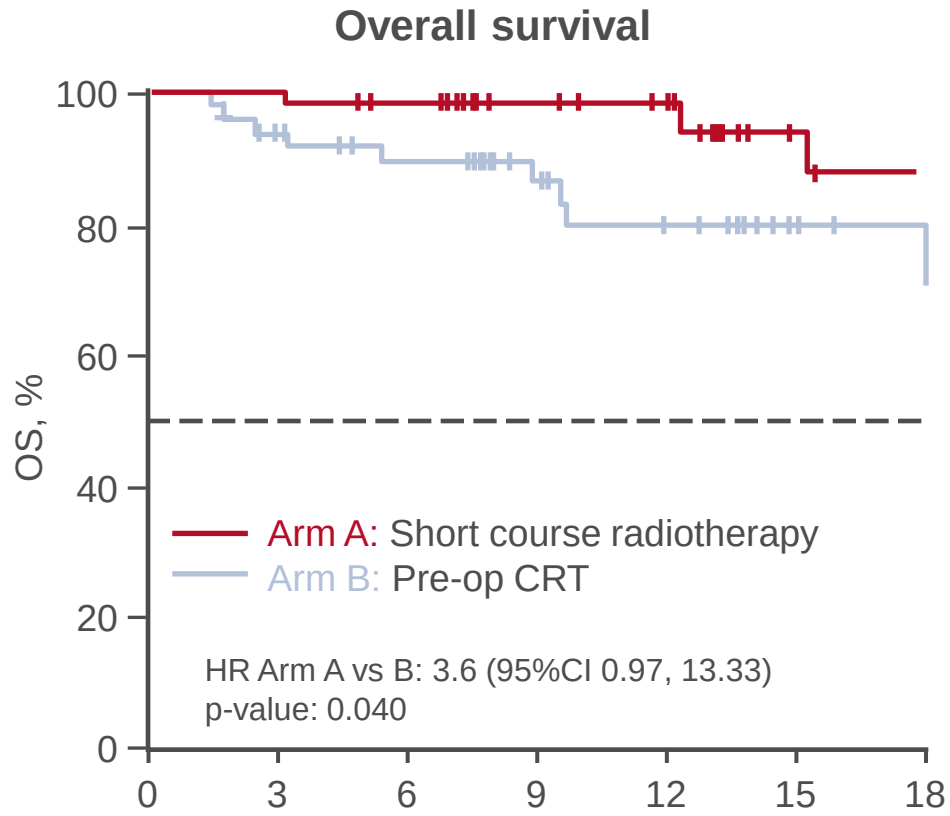
- OS, DFS, RFS, safety

Francois E, et al. J Clin Oncol 2021;39(suppl):abstr 4

4: NACRE: A randomized study comparing short course radiotherapy with radiochemotherapy for locally advanced rectal cancers in the elderly—Preliminary results – Francois E, et al

Key results





Francois E, et al. J Clin Oncol 2021;39(suppl):abstr 4

4: NACRE: A randomized study comparing short course radiotherapy with radiochemotherapy for locally advanced rectal cancers in the elderly—Preliminary results – Francois E, et al

Key results (cont.)

AEs	Arm A: Short course radiotherapy (n=51)	Arm B: CRT (n=50)
All, n (%)	43 (84.3)	48 (96.0)
Severe, n (%)	6 (11.8)	12 (24.0)
Grade ≥3, n	8	7
Digestive	0	2
Hematologic	3	0
Cardiovascular	0	2
Septic	1	1
General condition/biology	0	4
Death	0	1

Conclusions

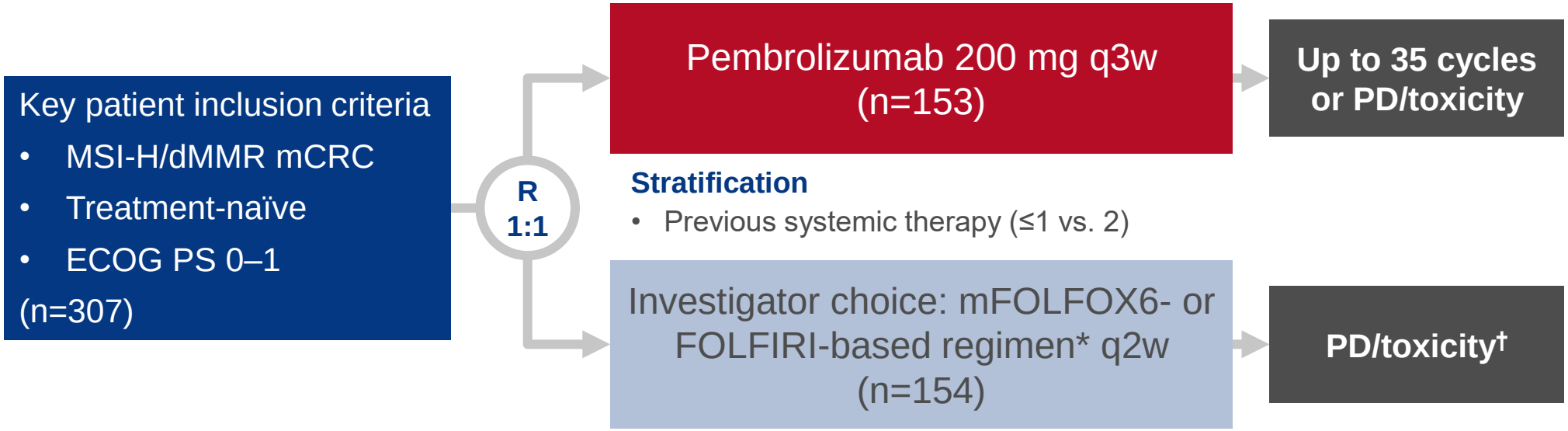
- **In elderly patients with rectal cancers, short course radiotherapy with delayed surgery demonstrated comparable R0 resection to CRT, was associated improvements on OS and was generally better tolerated**

Francois E, et al. J Clin Oncol 2021;39(suppl):abstr 4

6: KEYNOTE-177: Phase III randomized study of pembrolizumab versus chemotherapy for microsatellite instability-high advanced colorectal cancer – Shiu K-K, et al

Study objective

- To evaluate the efficacy and safety of 1L pembrolizumab vs. standard of care chemotherapy in patients with MSI-H/dMMR mCRC in the KEYNOTE-177 study



CO-PRIMARY ENDPOINTS

- PFS (RECIST v1.1, BICR), OS

SECONDARY ENDPOINTS

- ORR (RECIST v1.1, BICR), DoR, TTR, safety

*mFOLFOX6 or FOLFIRI alone or plus bevacizumab 5 mg/kg or plus cetuximab 400 mg/m^2 over 2 h then 250 mg/m^2 over 1 h q1w; †potential for crossover to pembrolizumab for ≤35 cycles after PD

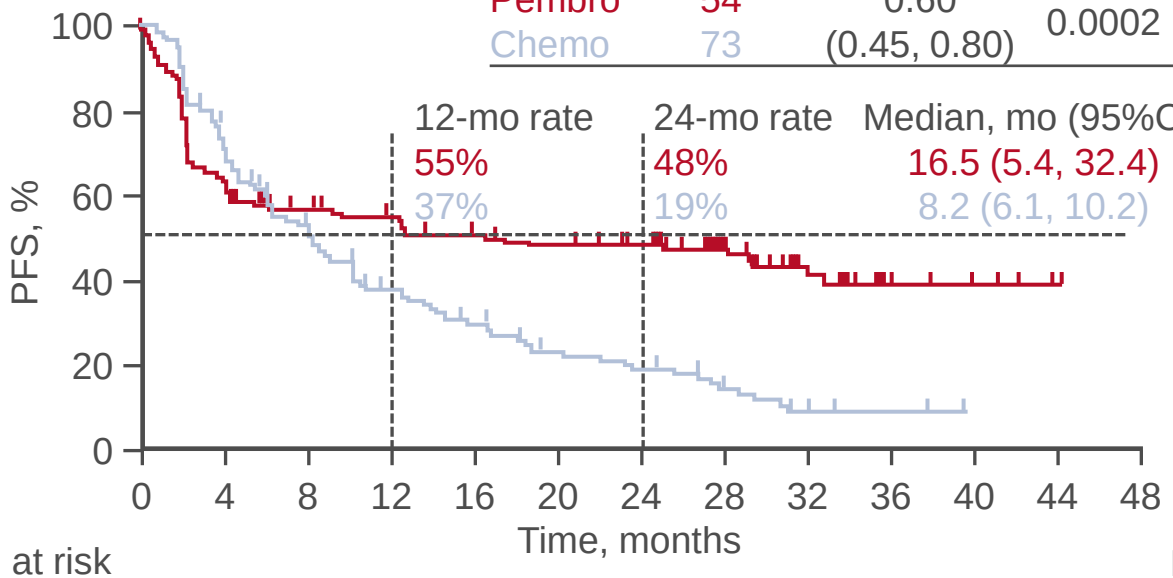
Shiu K-K, et al. J Clin Oncol 2021;39(suppl):abstr 6

6: KEYNOTE-177: Phase III randomized study of pembrolizumab versus chemotherapy for microsatellite instability-high advanced colorectal cancer – Shiu K-K, et al

Key results

Progression-free survival

	Events, %	HR (95%CI)	p-value
Pembro	54	0.60 (0.45, 0.80)	0.0002
Chemo	73		



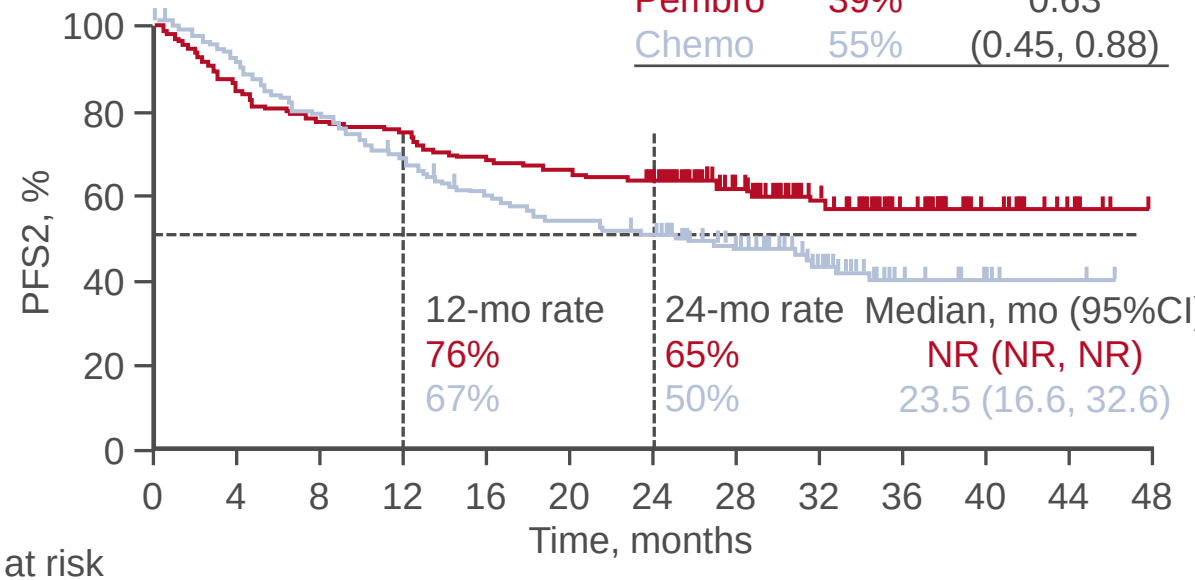
No. at risk

Pembro	153	96	77	72	64	60	55	37	20	7	5	0	0
Chemo	154	100	68	43	33	22	18	11	4	3	0	0	0

Progression-free survival 2

Time from randomization to progression on next line therapy or death of any cause

	Events, %	HR (95%CI)
Pembro	39%	0.63 (0.45, 0.88)
Chemo	55%	



No. at risk

Pembro	153	131	120	116	107	103	98	72	46	25	15	5	0
Chemo	154	136	117	100	86	77	71	51	30	11	5	2	0

	Pembrolizumab	Chemotherapy
Median DoR, months (range)	NR (2.3+ to 41.4+)	10.6 (2.8 to 37.5+)

Shiu K-K, et al. J Clin Oncol 2021;39(suppl):abstr 6

6: KEYNOTE-177: Phase III randomized study of pembrolizumab versus chemotherapy for microsatellite instability-high advanced colorectal cancer – Shiu K-K, et al

Key results (cont.)

	Pembrolizumab (n=153)	Chemotherapy (n=154)
ORR, % (95%CI)	43.8 (35.8, 52.0)	33.1 (25.8, 41.1)
BOR, %		
CR	11.1	3.9
PR	32.7	29.2
SD	20.9	42.2
PD	29.4	12.3
NE/NA	5.9	12.3
Median DoR, months (range)	NR (2.3+ to 41.4+)	10.6 (2.8 to 37.5+)

AEs, %	Pembrolizumab (n=153)	Chemotherapy (n=143)
Any	97	99
TRAE	80	99
Grade ≥3	22	66
Death	0	1*
Led to discontinuation	10	6

Conclusions

- **In patients with MSI-H/dMMR mCRC, pembrolizumab demonstrated significant improvements in PFS and durable responses compared with chemotherapy and had a manageable safety profile**

*One grade 5 event of intestinal perforation

Shiu K-K, et al. J Clin Oncol 2021;39(suppl):abstr 6

11: Circulating tumor DNA analysis for assessment of recurrence risk, benefit of adjuvant therapy, and early relapse detection after treatment in colorectal cancer patients – Henriksen TV, et al

Study objective

- To evaluate the use of ctDNA analysis for detecting MRD and recurrence in patients with CRC

Methods

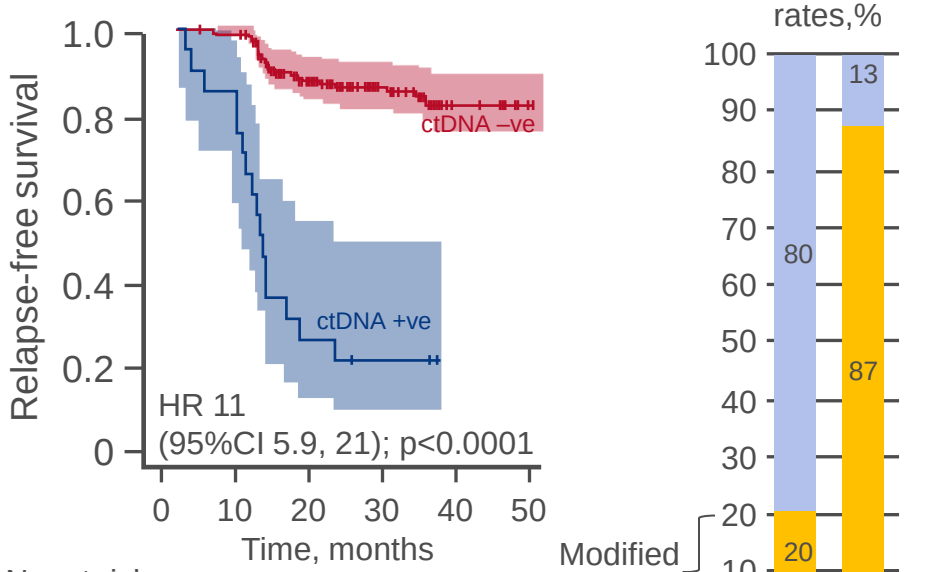
- Tissue samples were collected at the time of surgery and plasma samples were collected every 3 months for 3 years in 260 patients with CRC for tumor and PBC DNA exome sequencing and Signatera ctDNA assay. In addition, CT scans were conducted at the end of year 1 and 3
- MRD was determined and patients stratified according to high or low risk of recurrence
- The relapse risk after therapy was assessed in ctDNA-positive patients
- The lead time of ctDNA detection was compared with CT recurrence

Henriksen TV, et al. J Clin Oncol 2021;39(suppl):abstr 11

11: Circulating tumor DNA analysis for assessment of recurrence risk, benefit of adjuvant therapy, and early relapse detection after treatment in colorectal cancer patients – Henriksen TV, et al

Key results

Postoperative ctDNA detection

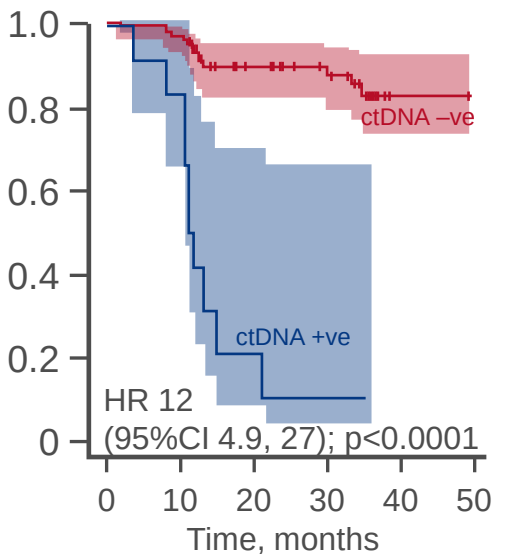


No. at risk

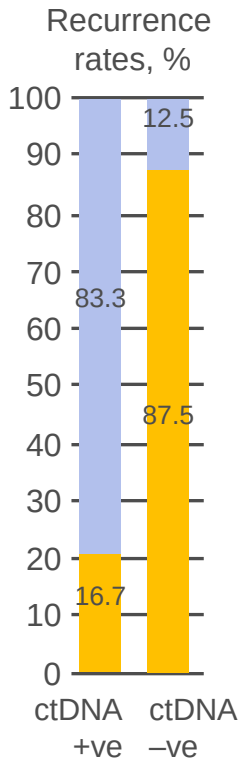
ctDNA –ve	198	194	121	94	7	1
ctDNA +ve	20	13	5	3	0	0

Post-treatment ctDNA detection

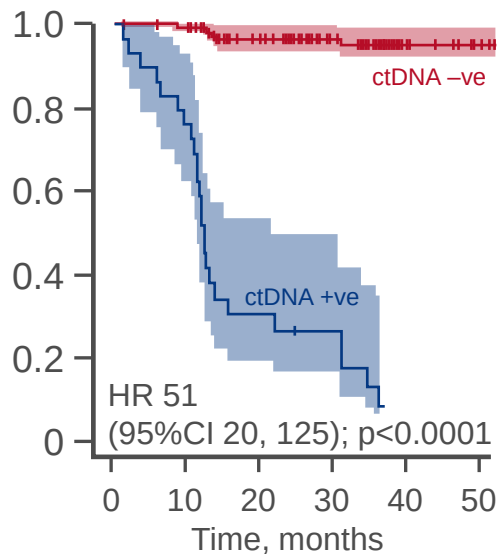
After end of ACT



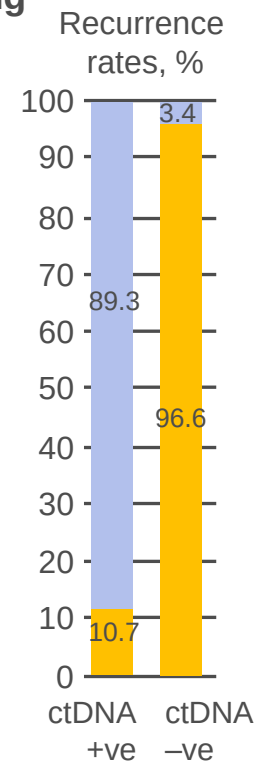
ctDNA –ve	96	93	51	48	1	1
ctDNA +ve	12	10	2	1	0	0



Longitudinal monitoring



ctDNA –ve	174	171	118	92	9	3
ctDNA +ve	28	21	7	5	0	0



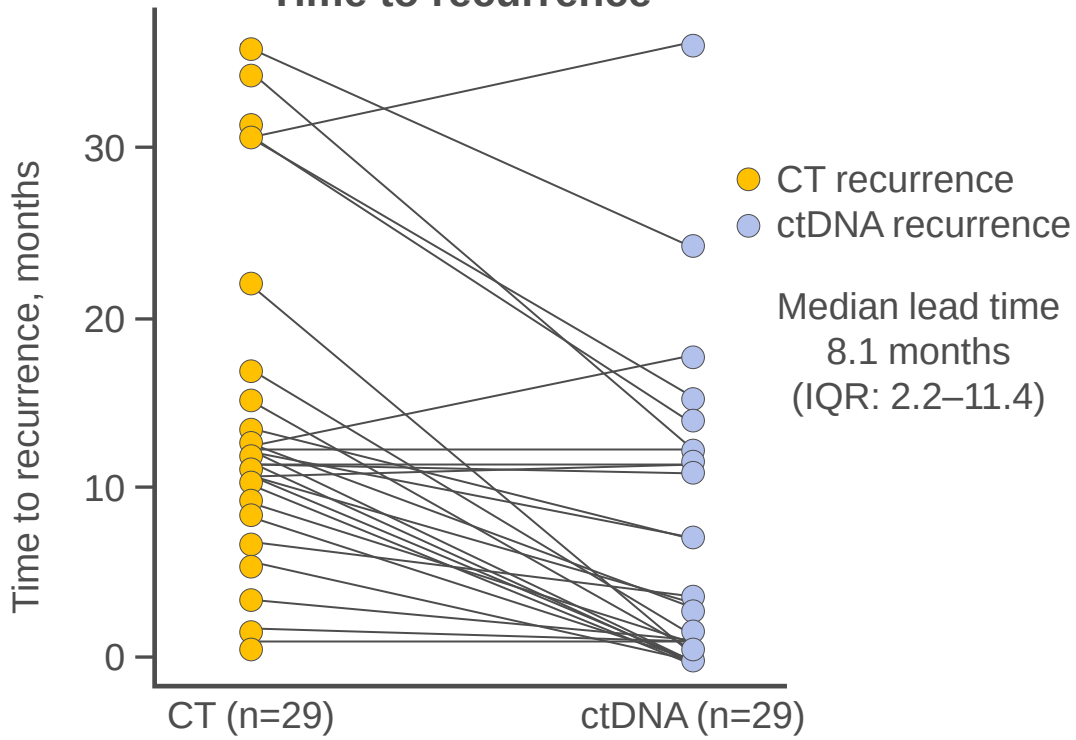
Relapse
No relapse

Henriksen TV, et al. J Clin Oncol 2021;39(suppl):abstr 11

11: Circulating tumor DNA analysis for assessment of recurrence risk, benefit of adjuvant therapy, and early relapse detection after treatment in colorectal cancer patients – Henriksen TV, et al

Key results (cont.)

Time to recurrence



ctDNA vs. CEA levels

	n	Univariate analysis		Multivariate analysis	
		HR (95%CI)	p-value	HR (95%CI)	p-value
CEA post-op	175	1.3 (0.6, 3.2)	0.524		
CEA post-ACT	99	1.4 (0.4, 4.2)	0.596		
CEA longitudinal	197	4.9 (3.2, 15)	<0.0001	1.8 (0.8, 4.0)	0.184
ctDNA longitudinal	197	95.7 (28, 322)	<0.0001	80.6 (23.1, 281)	<0.0001

Conclusions

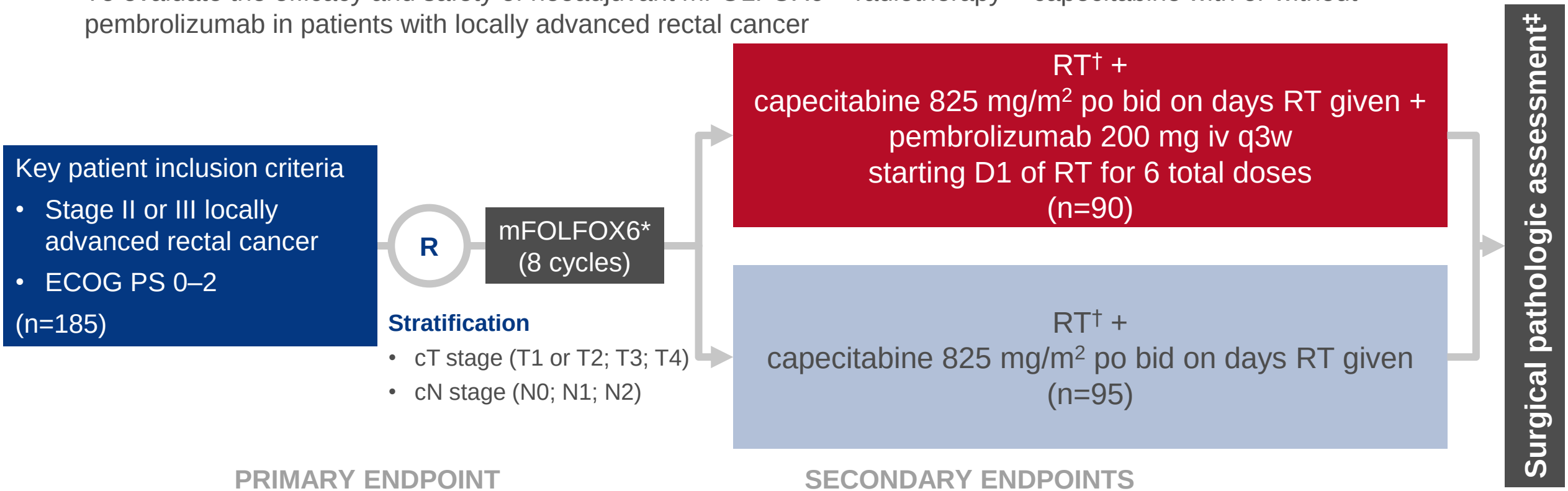
- **In patients with CRC, ctDNA analysis was able to detect patients who were at high risk of recurrence immediately after surgery as well as detecting recurrence much earlier than radiological detection and was better at predicting RFS than CEA levels**

Henriksen TV, et al. J Clin Oncol 2021;39(suppl):abstr 11

8: NRG-GI002: A phase II clinical trial platform using total neoadjuvant therapy (TNT) in locally-advanced rectal cancer (LARC)—Pembrolizumab experimental arm (EA) primary results – Rahma OE, et al

Study objective

- To evaluate the efficacy and safety of neoadjuvant mFOLFOX6 + radiotherapy + capecitabine with or without pembrolizumab in patients with locally advanced rectal cancer



PRIMARY ENDPOINT

- Neoadjuvant rectal (NAR) score

SECONDARY ENDPOINTS

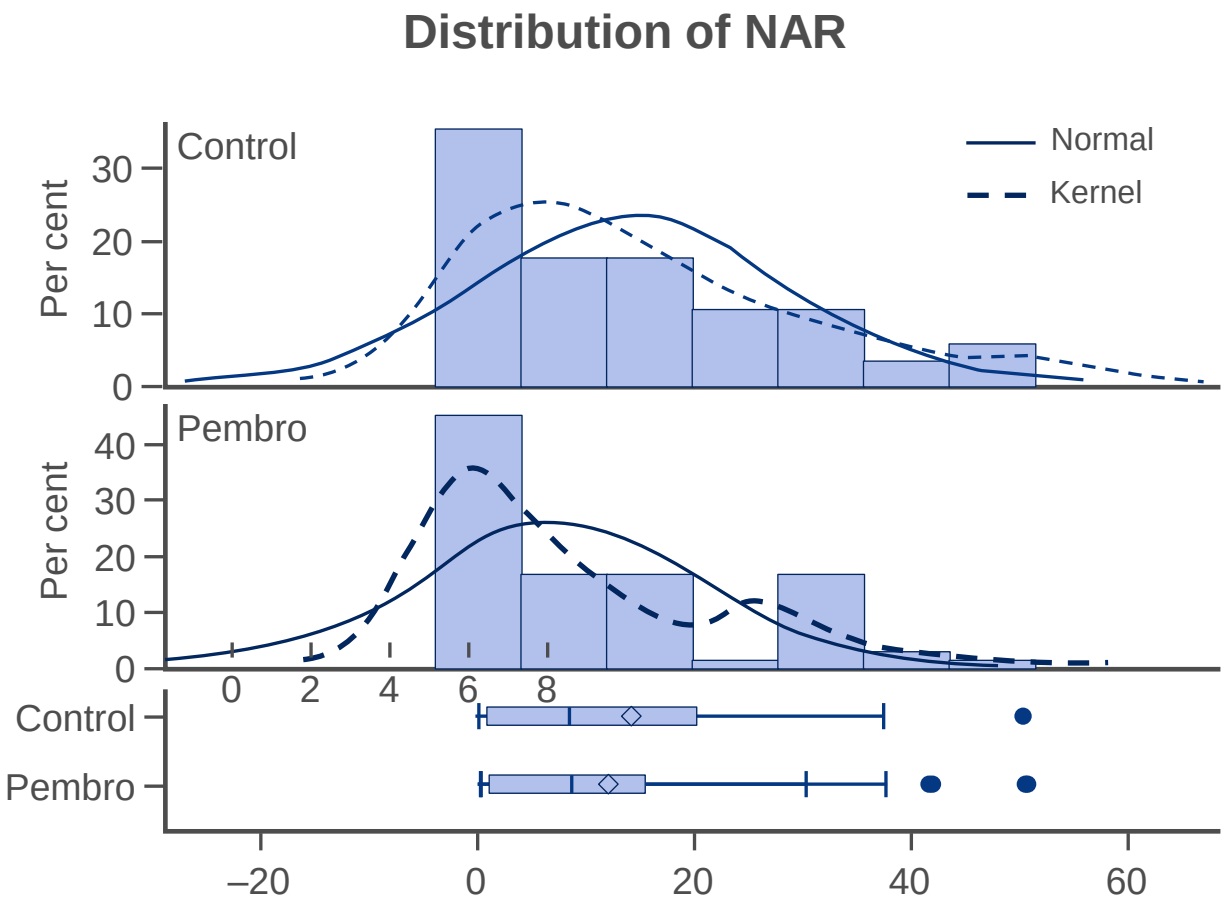
- pCR, cCR, OS, DFS, safety

*Oxaliplatin 85 mg/m^2 iv D1 + leucovorin 400 mg/m^2 iv D1 + 5FU 400 mg/m^2 iv bolus followed by 2400 mg/m^2 continuous infusion (46 h) q2w; †RT 4500 cGy in 25 fx over 5 weeks + 540 cGy boost in 3 fx starts following last dose of mFOLFOX6; ‡performed 8–12 weeks after last RT dose

Rahma OE, et al. J Clin Oncol 2021;39(suppl):abstr 8

8: NRG-GI002: A phase II clinical trial platform using total neoadjuvant therapy (TNT) in locally-advanced rectal cancer (LARC)—Pembrolizumab experimental arm (EA) primary results – Rahma OE, et al

Key results



Treatment	Mean	95%CL mean		p-value
Control	14.08	10.74	17.43	
Pembro	11.53	8.54	14.51	0.26
Diff (1-2)	2.55	–1.89	6.99	

Rahma OE, et al. J Clin Oncol 2021;39(suppl):abstr 8

8: NRG-GI002: A phase II clinical trial platform using total neoadjuvant therapy (TNT) in locally-advanced rectal cancer (LARC)—Pembrolizumab experimental arm (EA) primary results – Rahma OE, et al

Key results (cont.)

	Pembrolizumab	Control	p-value
pCR, %	31.9	29.4	0.75
cCR, %	13.9	13.6	0.95
R0 resection, %	94.0	89.4	0.36
SSS, %	59.4	71.0	0.15

AEs, n (%)	Pembrolizumab (n=90)		Control (n=95)	
	G3/4	G5	G3/4	G5
During chemotherapy	45 (50)	1 (1.1)	38 (40)	1 (1.1)
During CRT	39 (48.2)	0 (0)	31 (37.3)	0 (0)

Conclusions

- **In patients with locally advanced rectal cancer, combining pembrolizumab with CRT after mFOLFOX6 did not provide any improvement in NAR score compared with CRT alone after mFOLFOX6**

Rahma OE, et al. J Clin Oncol 2021;39(suppl):abstr 8

9: Safety and efficacy of anti–PD-1 antibody dostarlimab in patients (pts) with mismatch repair-deficient (dMMR) solid cancers: Results from GARNET study – Andre T, et al

Study objective

- To evaluate the efficacy and safety of dostarlimab, an anti-PD-1 antibody, in a cohort of patients with non-endometrial dMMR or MSI-H pan tumors in the GARNET study

ENDPOINTS

- Antitumor activity, DoR, safety

Andre T, et al. J Clin Oncol 2021;39(suppl):abstr 9

9: Safety and efficacy of anti–PD-1 antibody dostarlimab in patients (pts) with mismatch repair-deficient (dMMR) solid cancers: Results from GARNET study – Andre T, et al

Key results

Tumor type	Patients, n	ORR, n (%) [95%CI]
Overall	106	41 (38.7) [29.4, 48.6]
CRC	69	25 (36.2) [25.0, 48.7]
Non-CRC	37	16 (43.2) [27.1, 60.5]
Small intestinal cancer	12	4 (33.3) [9.9, 65.1]
Gastric + GEJ	8	3 (37.5) [8.5, 75.5]
Pancreatic carcinoma	4	SD, 3 PD
Ovarian cancer	2	PR, SD
HCC	2	PR, PD
Biliary neoplasm	1	CR
Breast cancer	1	CR
Gallbladder	1	CR
Adrenal cortical	1	PR
Genital neoplasm malignant female	1	PR
Pleural	1	PR
Unknown origin	1	PR
Renal cell carcinoma	1	SD
Esophageal cancer	1	PD

Andre T, et al. J Clin Oncol 2021;39(suppl):abstr 9

9: Safety and efficacy of anti–PD-1 antibody dostarlimab in patients (pts) with mismatch repair-deficient (dMMR) solid cancers: Results from GARNET study – Andre T, et al

Key results (cont.)

AEs, n (%)	Dostarlimab (n=144)
Any TEAE	140 (97)
Grade ≥3	61 (42)
Any TRAE	99 (69)
Grade ≥3	12 (8)
SAE	9 (6)
Led to discontinuation	5 (4)

Grade ≥3 immune-related TRAEs, n (%)	Dostarlimab (n=144)
Lipase increased	2 (1)
Adrenal insufficiency	1 (<1)
ALT increased	1 (<1)
AST increased	1 (<1)
Diarrhea	1 (<1)
Hyperthyroidism	1 (<1)
Rash	1 (<1)

Conclusions

- **In patients with non-endometrial dMMR or MSI-H pan tumors, dostarlimab provided promising antitumor activity and was generally well-tolerated**

Andre T, et al. J Clin Oncol 2021;39(suppl):abstr 9

12: Does non-TME surgery of rectal cancer compromise the chance of cure? Preliminary surgical salvage data from OPERA phase III randomized trial – Myint AS, et al

Study objective

- To evaluate the surgical salvage data for treatment failures in patients with rectal adenocarcinoma in the OPERA trial

Key patient inclusion criteria
- Rectal adenocarcinoma
- cT2 or CT3a/b cN0/cN1 (<8 mm)
- Diameter <5 cm
- Within 12 cm from anal verge

(n=148)

R

Arm A:
EBCRT (45 Gy, 25 fx, 5 weeks) +
CXB (Papillon) boost (90 Gy, 3 fx, 4 weeks)
(n=73)

Arm B:
EBCRT (45 Gy, 25 fx, 5 weeks) + capecitabine 825 mg/m^2 + EBRT boost (9 Gy, 5 fx, 5 days)
(n=71)

cCR at 24 weeks use watch and wait or for residual disease surgery (TME or local excision)

PRIMARY ENDPOINT

- Organ preservation (3 years)

Myint MS, et al. J Clin Oncol 2021;39(suppl):abstr 12

12: Does non-TME surgery of rectal cancer compromise the chance of cure? Preliminary surgical salvage data from OPERA phase III randomized trial – Myint AS, et al

Key results

	n=144
Organ preservation, n (%)	116 (80.5)
cCR, n (%)	103 (81)
Surgery with residual disease	49 (34)
Local excision	21 (43)
TME surgery	28 (57)
18-month TME-free suvival, %	76
Tumor <3 cm TME-free survival, %	86*

Conclusions

- **In patients with rectal cancer, using non-TME surgical treatment and a watch & wait approach is feasible in those who are fit and wish to avoid surgery, with patients who failed being offered salvage surgery**

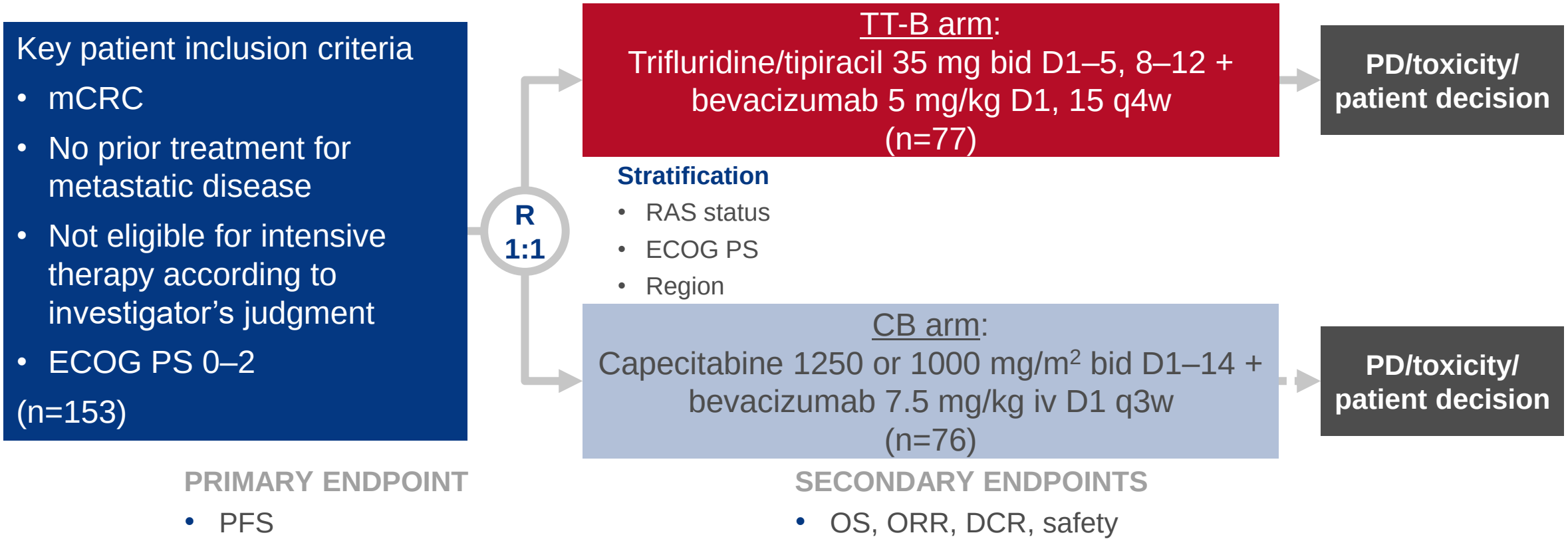
*n=62

Myint MS, et al. J Clin Oncol 2021;39(suppl):abstr 12

14: Phase II study evaluating trifluridine/tipiracil + bevacizumab and capecitabine + bevacizumab in first-line unresectable metastatic colorectal cancer (mCRC) patients who are noneligible for intensive therapy (TASCO1): Results of the final analysis on the overall survival – Van Cutem E, et al

Study objective

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

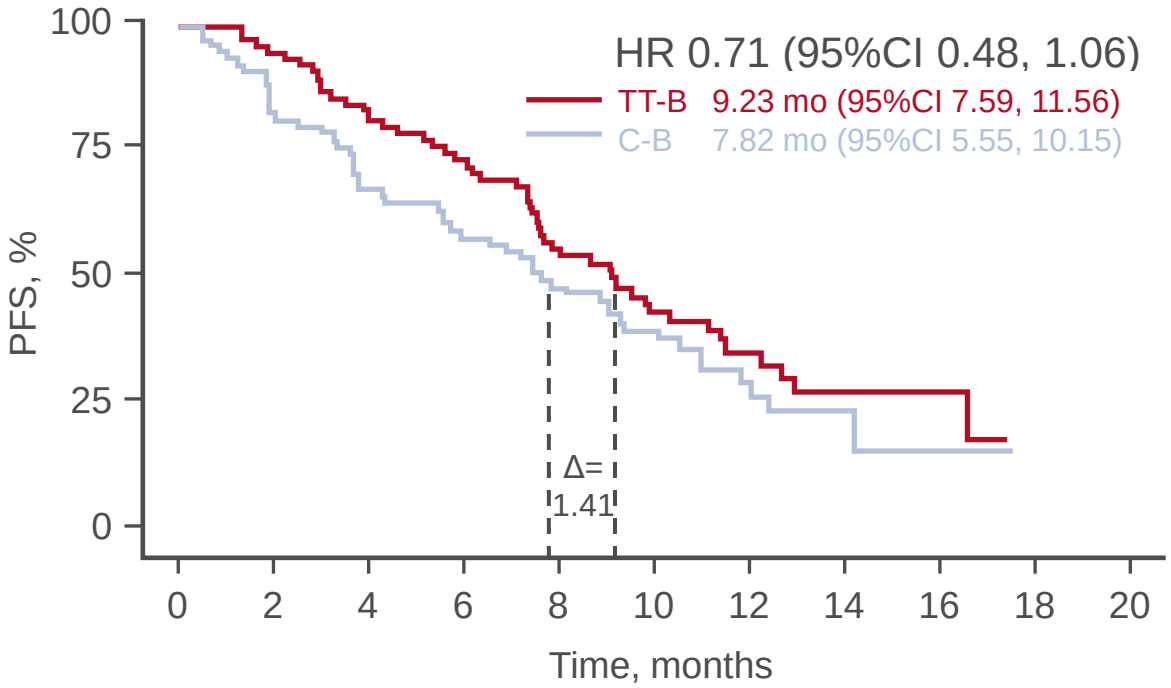


Van Cutsem E, et al. J Clin Oncol 2021;39(suppl):abstr 14

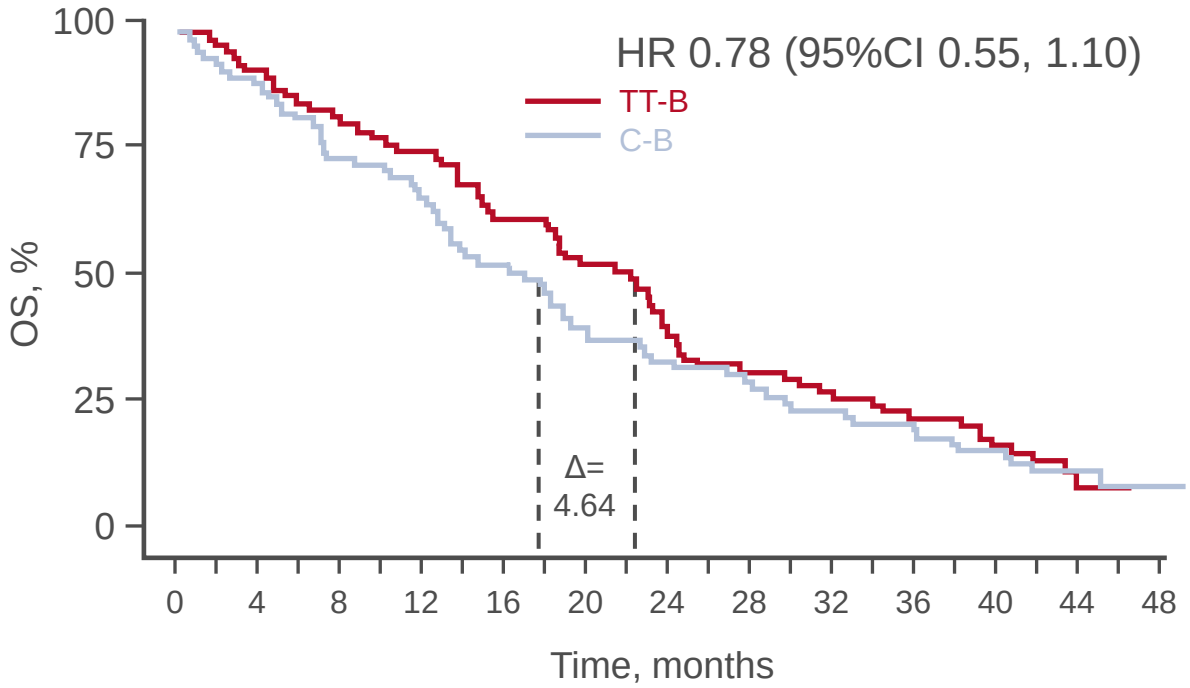
14: Phase II study evaluating trifluridine/tipiracil + bevacizumab and capecitabine + bevacizumab in first-line unresectable metastatic colorectal cancer (mCRC) patients who are noneligible for intensive therapy (TASCO1): Results of the final analysis on the overall survival – Van Cutem E, et al

Key results

Progression-free survival



Overall survival



Van Cutsem E, et al. J Clin Oncol 2021;39(suppl):abstr 14

14: Phase II study evaluating trifluridine/tipiracil + bevacizumab and capecitabine + bevacizumab in first-line unresectable metastatic colorectal cancer (mCRC) patients who are noneligible for intensive therapy (TASCO1): Results of the final analysis on the overall survival – Van Cutem E, et al

Key results (cont.)

Hematologic AEs, %	Trifluridine/tipiracil		Capecitabine	
	G3	G4	G3	G4
Anemia	11.7	1.3	-	-
Neutropenia	20.8	26.0	2.6	2.6
Neutrophil count decreased	13.0	6.5	-	1.3
Leukopenia	3.9	-	2.6	1.3
WBC count decreased	1.3	1.3	1.3	1.3
Thrombocytopenia	3.9	-	1.3	-
Febrile neutropenia	2.6	2.6	2.6	1.3
Serious	3.9	-	3.9	0

Non-hematologic AEs, %	Trifluridine/tipiracil	Capecitabine
	G3-4	G3-4
Diarrhea	1.3	9.2
Nausea	2.6	-
Vomiting	5.2	1.3
Appetite decreased	-	1.3
Stomatitis	1.3	-
Hand-foot syndrome	-	11.8
Hypertension	13.0	3.9

Conclusions

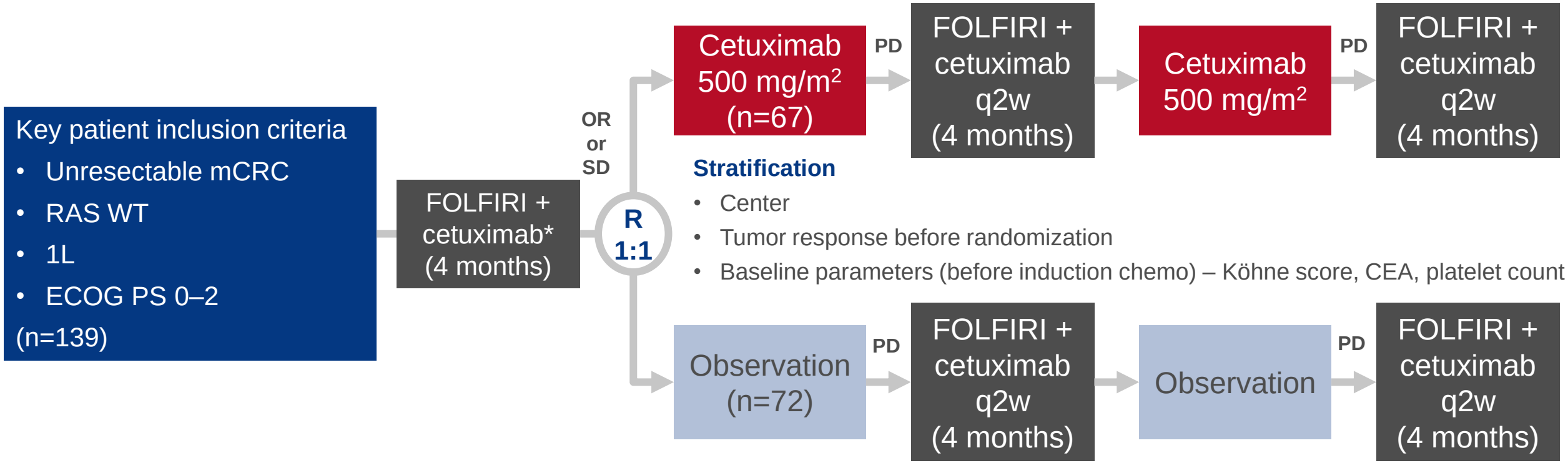
- **In patients with unresectable mCRC, 1L trifluridine/tipiracil + bevacizumab provided numerical improvements in OS over capecitabine + bevacizumab and had a safety profile comparable to previous findings**

Van Cutsem E, et al. J Clin Oncol 2021;39(suppl):abstr 14

15: Maintenance treatment with cetuximab versus observation in RAS wild-type metastatic colorectal cancer: Results of the randomized phase II PRODIGE 28-time UNICANCER study – Boige V, et al

Study objective

- To evaluate the efficacy and safety of maintenance cetuximab in patients with RAS WT mCRC



Stratification

- Center
- Tumor response before randomization
- Baseline parameters (before induction chemo) – Köhne score, CEA, platelet count

PRIMARY ENDPOINT

- 6-month PFS rate

SECONDARY ENDPOINTS

- PFS, ORR, OS, safety

*Cetuximab 500 mg/m^2 + irinotecan 180 mg/m^2 + leucovorin 400 mg/m^2 + 5FU 400 mg/m^2 iv bolus then 2400 mg/m^2, continuous infusion (46 h)

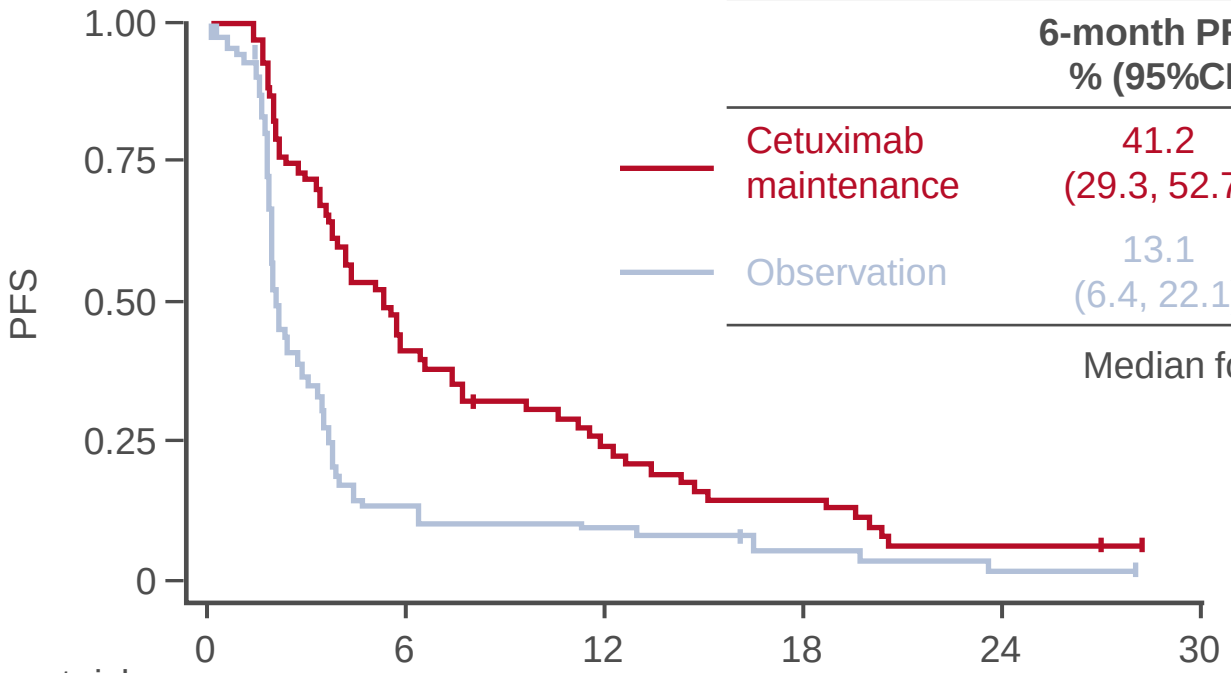
Boige V, et al. J Clin Oncol 2021;39(suppl):abstr 15

15: Maintenance treatment with cetuximab versus observation in RAS wild-type metastatic colorectal cancer: Results of the randomized phase II PRODIGE 28-time UNICANCER study – Boige V, et al

Key results

- 6-month PFS rate was 34.3% (95%CI 23.2, 46.9) in the cetuximab maintenance arm and 6.9% (95%CI 2.3, 15.5) in the observation arm

Progression-free survival



	6-month PFS, % (95%CI)	mPFS, months (95%CI)
Cetuximab maintenance	41.2 (29.3, 52.7)	5.3 (3.7, 6.5)
Observation	13.1 (6.4, 22.1)	2.0 (1.8, 2.8)

Median follow-up: 30 months

Boige V, et al. J Clin Oncol 2021;39(suppl):abstr 15

15: Maintenance treatment with cetuximab versus observation in RAS wild-type metastatic colorectal cancer: Results of the randomized phase II PRODIGE 28-time UNICANCER study – Boige V, et al

Key results (cont.)

Grade ≥3 AEs, n (%)	Cetuximab maintenance (n=67)	Observation (n=72)
Diarrhea	4 (6)	1 (1)
Rash	1 (2)	0 (0)
Hypomagnesemia	3 (5)	0 (0)
Fatigue	2 (3)	2 (3)

Conclusions

- **In patients with RAS WT mCRC, cetuximab maintenance did not demonstrate a significant improvement in 6-month PFS rate compared with observation and there were no new safety findings**

Boige V, et al. J Clin Oncol 2021;39(suppl):abstr 15

3004: MyPathway HER2 basket study: Pertuzumab (P) + trastuzumab (H) treatment of a large, tissue-agnostic cohort of patients with HER2-positive advanced solid tumors – Meric-Bernstam F, et al

Study objective

- To evaluate the efficacy and safety of pertuzumab + trastuzumab in patients with HER2-amplified and/or overexpressed tumors in the MyPathway HER2 basket trial

Key patient inclusion criteria

- HER2-altered tumors*
- No prior HER2-targeted treatment
- No satisfactory alternative treatment option
- Tissue agnostic
- ECOG PS ≤2

(n=258)

→ Pertuzumab 840 mg loading dose then 420 mg iv q3w + trastuzumab 8 mg/kg loading dose then 6 mg/kg iv q3w → **PD/toxicity**

PRIMARY ENDPOINT

- ORR (investigator assessed)

SECONDARY ENDPOINTS

- DCR, DoR, PFS, OS, safety

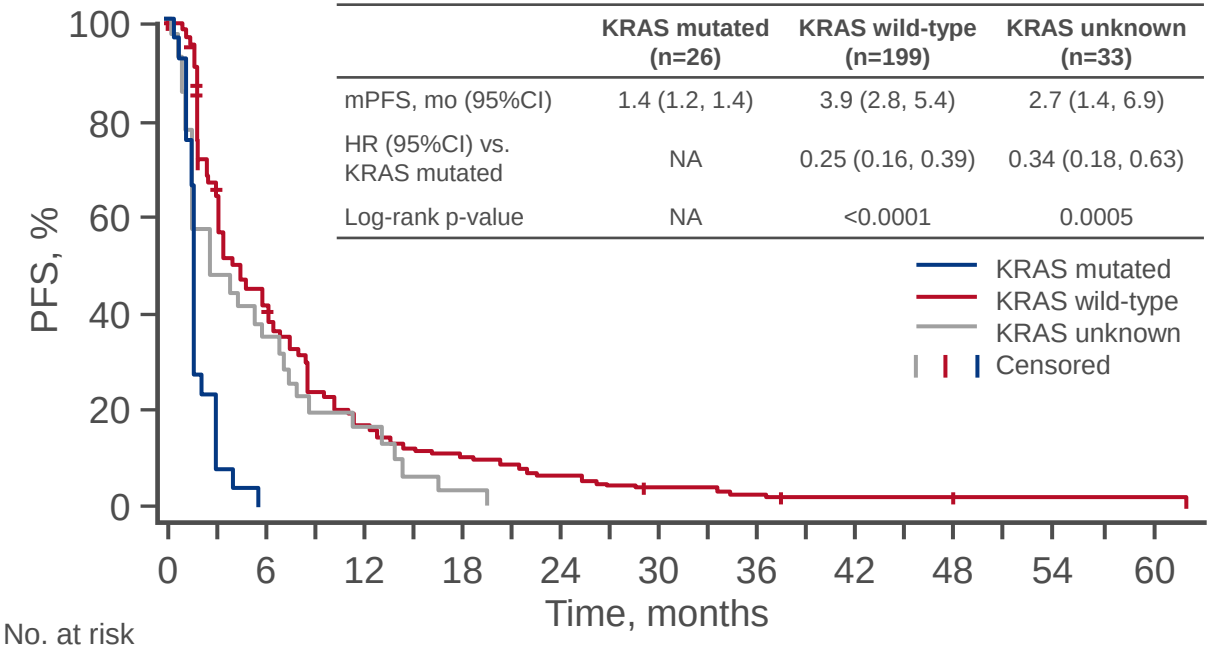
*CRC, n=84; biliary, n=40; NSCLC, n=27; uterine, n=23; urothelial, n=22; salivary, n=18; ovarian, n=12; pancreas, n=10; other, n=22

Meric-Bernstam F, et al. J Clin Oncol 2021;39(suppl):abstr 3004

3004: MyPathway HER2 basket study: Pertuzumab (P) + trastuzumab (H) treatment of a large, tissue-agnostic cohort of patients with HER2-positive advanced solid tumors – Meric-Bernstam F, et al

Key results

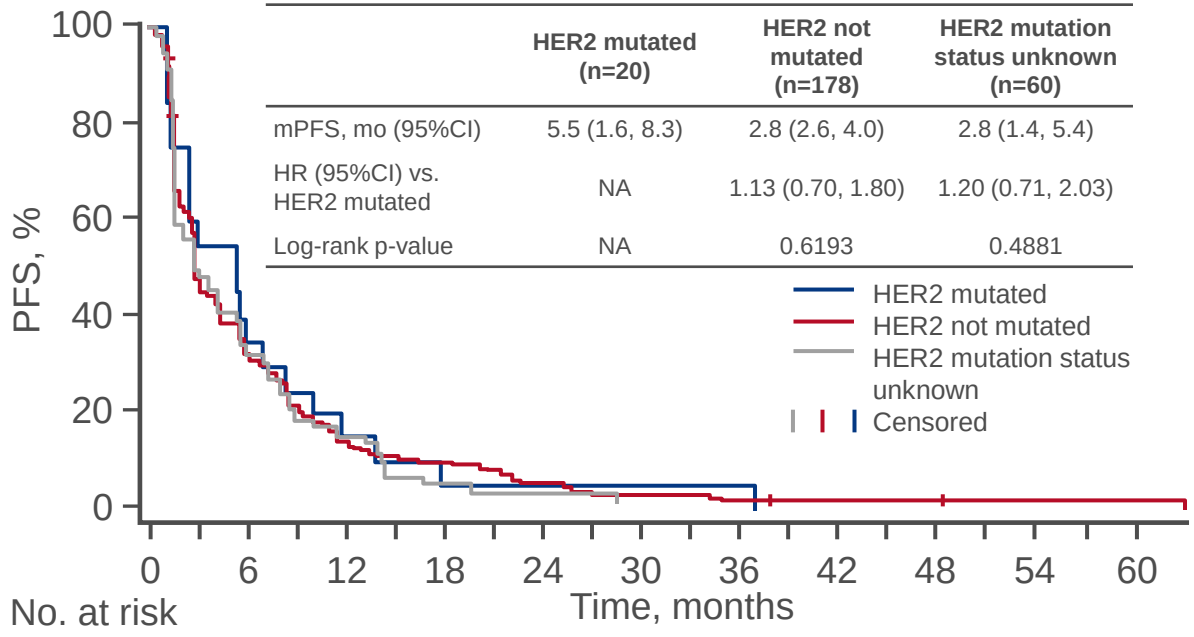
Progression-free survival



	KRAS mutated (n=26)	KRAS wild-type (n=199)	KRAS unknown (n=33)
mPFS, mo (95%CI)	1.4 (1.2, 1.4)	3.9 (2.8, 5.4)	2.7 (1.4, 6.9)
HR (95%CI) vs. KRAS mutated	NA	0.25 (0.16, 0.39)	0.34 (0.18, 0.63)
Log-rank p-value	NA	<0.0001	0.0005

No. at risk

KRAS mutated	26	2	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
KRAS wild-type	199	102	69	43	29	21	18	14	12	8	6	6	3	2	2	2	1	1	1	1	1	
KRAS unknown	33	15	11	6	5	2	1	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE



	HER2 mutated (n=20)	HER2 not mutated (n=178)	HER2 mutation status unknown (n=60)
mPFS, mo (95%CI)	5.5 (1.6, 8.3)	2.8 (2.6, 4.0)	2.8 (1.4, 5.4)
HR (95%CI) vs. HER2 mutated	NA	1.13 (0.70, 1.80)	1.20 (0.71, 2.03)
Log-rank p-value	NA	0.6193	0.4881

No. at risk

HER2 mutated	20	12	7	5	3	2	1	1	1	1	1	1	NE	NE	NE	NE	NE	NE	NE	NE	NE	
HER2 not mutated	178	79	54	33	22	17	15	11	9	5	5	5	3	2	2	2	1	1	1	1	1	
HER2 mutation status unknown	60	28	19	11	9	4	3	2	2	2	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE

Meric-Bernstam F, et al. J Clin Oncol 2021;39(suppl):abstr 3004

3004: MyPathway HER2 basket study: Pertuzumab (P) + trastuzumab (H) treatment of a large, tissue-agnostic cohort of patients with HER2-positive advanced solid tumors – Meric-Bernstam F, et al

Key results (cont.)

Outcome	HER2-amplified/ overexpressed (n=258)	KRAS WT (n=199)	KRAS mutated (n=26)	KRAS unknown (n=33)
Confirmed ORR, n (%) [95%CI]	60 (23.3) [18.2, 28.9]; 5 CR, 55 PR	51 (25.6) [19.7, 32.3]; 4 CR, 47 PR	1 (3.8) [0.1, 19.6]; 1 PR	8 (24.2) [11.1, 43.2]; 1 CR, 7 PR
DCR, n (%) [95%CI]	115 (44.6) [38.4, 50.9]	99 (49.7) [42.6, 56.9]	1 (3.8) [0.1, 19.6]	15 (45.5) [28.1, 63.6]
Median DoR, months (95%CI)	7.9 (6.2, 9.3)	8.3 (6.2, 10.8)	2.7 (1 responder)	6.7 (2.5, 12.7)
mPFS, months (95%CI)	2.8 (2.7, 4.0)	3.9 (2.8, 5.4)	1.4 (1.2, 1.4)	2.7 (1.4, 6.9)
mOS, months (95%CI)	10.9 (9.2, 13.8)	12.6 (10.1, 15.7)	5.7 (3.7, 9.6)	8.3 (6.6, 22.7)

- Most common TRAEs were diarrhea (26.4%), infusion-related reaction (15.9%), nausea (14.3%), chills (13.2%) and fatigue (12.4%)

Conclusions

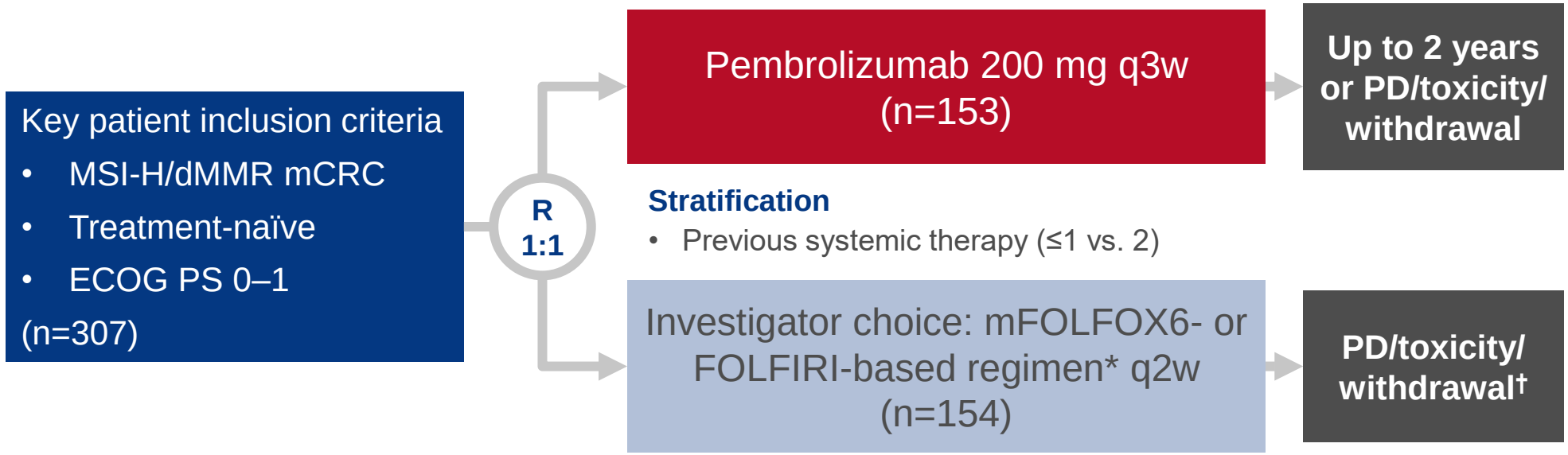
- **In patients with KRAS WT or HER2-amplified/overexpressed advanced solid tumors, pertuzumab + trastuzumab demonstrated encouraging antitumor activity, particularly in KRAS WT CRC, but activity was limited in patients with KRAS-mutated tumors**

Meric-Bernstam F, et al. J Clin Oncol 2021;39(suppl):abstr 3004

3500: Final overall survival for the phase III KN177 study: Pembrolizumab versus chemotherapy in microsatellite instability-high/mismatch repair deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC) – Andre T, et al

Study objective

- To evaluate the final OS of 1L pembrolizumab vs. standard of care chemotherapy in patients with MSI-H/dMMR mCRC in the KEYNOTE-177 study



CO-PRIMARY ENDPOINTS

- PFS (RECIST v1.1, BICR), OS

SECONDARY ENDPOINTS

- ORR (RECIST v1.1, BICR), DoR, TTR, safety

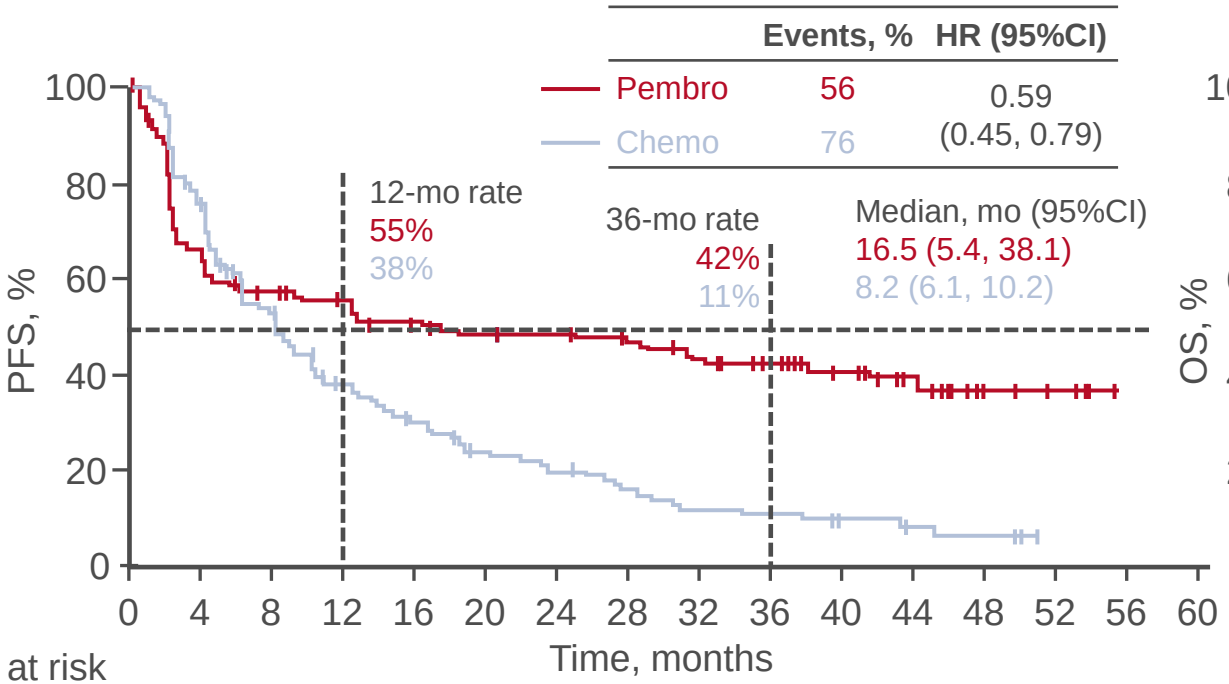
*mFOLFOX6 or FOLFIRI alone or with bevacizumab 5 mg/kg or cetuximab 400 mg/m^2 over 2 h then 250 mg/m^2 over 1 h q1w; †potential for crossover to pembrolizumab for ≤35 cycles after PD

Andre T, et al. J Clin Oncol 2021;39(suppl):abstr 3500

3500: Final overall survival for the phase III KN177 study: Pembrolizumab versus chemotherapy in microsatellite instability-high/mismatch repair deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC) – Andre T, et al

Key results

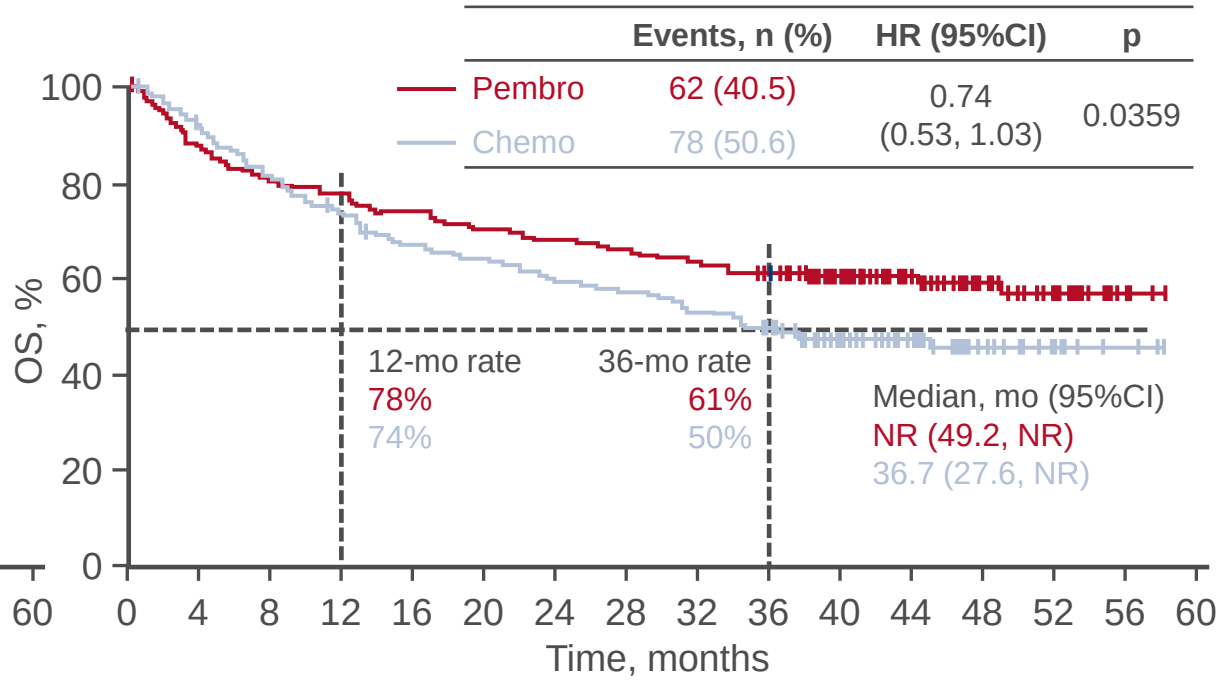
Progression-free survival



No. at risk

Pembro	153	96	77	72	64	60	59	55	50	42	28	16	7	5	0	0
Chemo	154	101	69	45	35	25	21	16	12	11	8	5	3	0	0	0

Overall survival



Pembro	153	134	123	119	112	107	104	101	97	92	70	48	28	16	4	0
Chemo	153	137	121	110	99	95	88	85	79	71	53	36	18	11	3	0

Andre T, et al. J Clin Oncol 2021;39(suppl):abstr 3500

3500: Final overall survival for the phase III KN177 study: Pembrolizumab versus chemotherapy in microsatellite instability-high/mismatch repair deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC) – Andre T, et al

Key results (cont.)

	Pembrolizumab (n=153)	Chemotherapy (n=154)
ORR, n (%)	69 (45.1)	51 (33.1)
BOR, n (%)		
CR	20 (13.1)	6 (3.9)
PR	49 (32.0)	45 (29.2)
SD	30 (19.6)	65 (42.2)
PD	45 (29.4)	19 (12.3)
NE	3 (2.0)	2 (1.3)
NA	6 (3.9)	17 (11.0)
DCR, n (%)	99 (64.7)	116 (75.3)
Median DoR, months (range)	NR (2.3+ to 53.5+)	10.6 (2.8 to 48.3+)

AEs, n (%)	Pembrolizumab (n=153)	Chemotherapy (n=143)
Any	149 (97.4)	142 (99.3)
TRAE	122 (79.7)	141 (98.6)
Grade ≥3	33 (21.6)	95 (66.4)
Death	15 (9.8)	10 (7.0)
Led to discontinuation	0 (0)	1 (0.7)

Conclusions

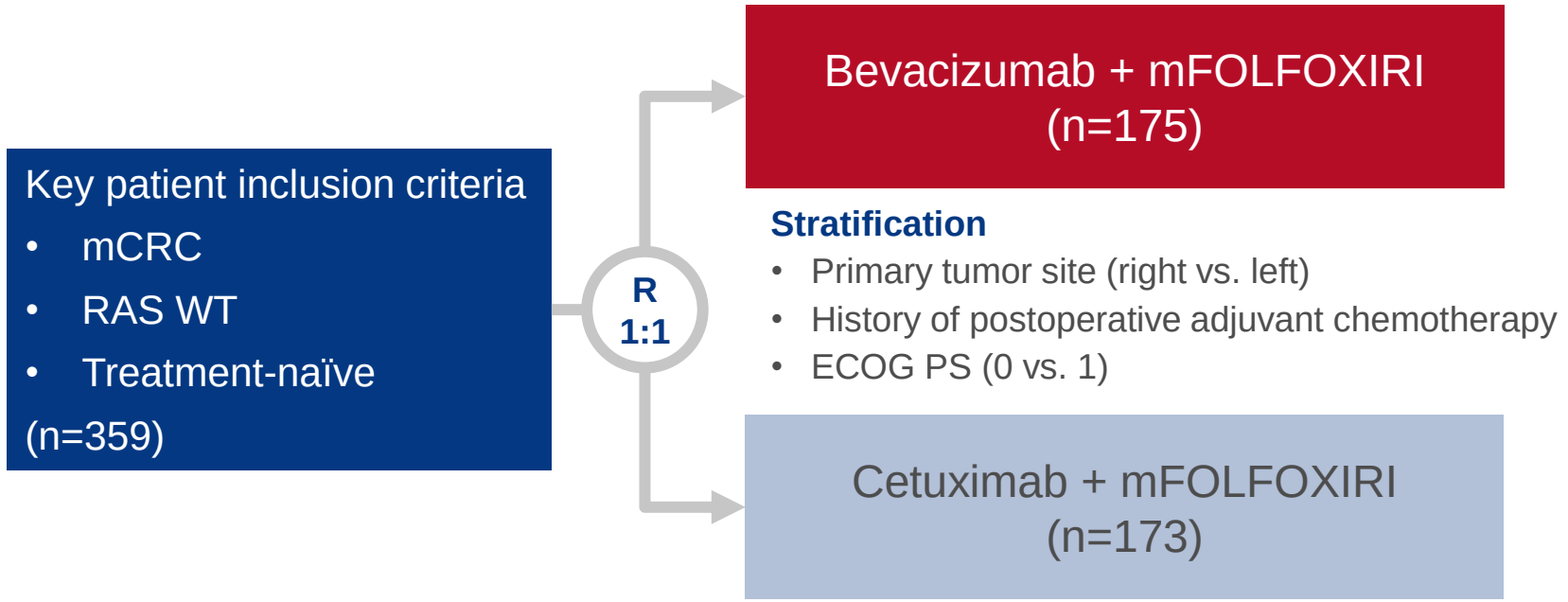
- **In patients with MSI-H/dMMR mCRC, 1L pembrolizumab demonstrated significant improvements in PFS compared with chemotherapy and had a manageable safety profile**

Andre T, et al. J Clin Oncol 2021;39(suppl):abstr 3500

3501: The randomized phase II study of FOLFOXIRI plus cetuximab versus FOLFOXIRI plus bevacizumab as the first-line treatment in metastatic colorectal cancer with RAS wild-type tumors: The DEEPER trial (JACCRO CC-13) – Tsuji A, et al

Study objective

- To evaluate the efficacy and safety of bevacizumab + mFOLFOXIRI vs. cetuximab + mFOLFOXIRI in treatment naïve patients with mCRC and RAS WT tumors in the DEEPER study



PRIMARY ENDPOINT

- Depth of response

SECONDARY ENDPOINTS

- ETS, ORR, PFS, OS, resection rate, safety

Tsuji A, et al. J Clin Oncol 2021;39(suppl):abstr 3501

3501: The randomized phase II study of FOLFOXIRI plus cetuximab versus FOLFOXIRI plus bevacizumab as the first-line treatment in metastatic colorectal cancer with RAS wild-type tumors: The DEEPER trial (JACCRO CC-13) – Tsuji A, et al

Key results

Depth of response	Bevacizumab + mFOLFOXIRI (n=162)	Cetuximab + mFOLFOXIRI (n=158)
Median, % (range)	46.0 (-0.6–100)	57.4 (-15.0–100)
Mean, % (95%CI)	47.3 (44.1, 50.5)	55.8 (51.9, 59.7)
SD (95%CI)	20.53 (18.5, 23.0)	25.06 (22.6, 28.2)
T-test by welch	0.001	

Depth of response by tumor location	Left-sided		Right-sided	
	Bevacizumab + mFOLFOXIRI (n=137)	Cetuximab + mFOLFOXIRI (n=131)	Bevacizumab + mFOLFOXIRI (n=25)	Cetuximab + mFOLFOXIRI (n=27)
Median, % (range)	46.1 (3.2–100)	60.3 (-9.8–100)	41.2 (-0.6–85.6)	50.0 (-15.0–100)
Mean, % (95%CI)	48.2 (44.9, 51.5)	57.5 (53.2, 61.7)	42.5 (32.1, 52.9)	47.7 (37.3, 58.1)
SD (95%CI)	19.55 (17.48, 22.18)	24.59 (21.93, 27.99)	25.17 (19.65, 35.02)	26.19 (20.63, 35.90)
T-test by welch	0.0007		0.4663	

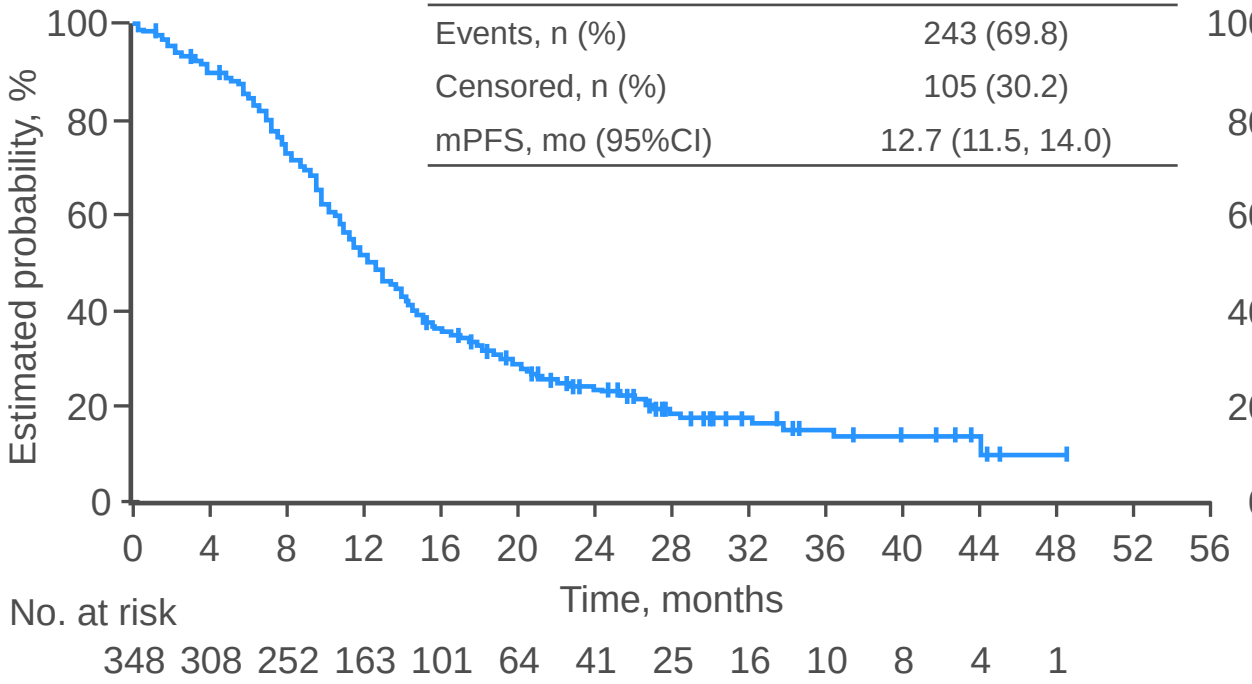
Tsuji A, et al. J Clin Oncol 2021;39(suppl):abstr 3501

3501: The randomized phase II study of FOLFOXIRI plus cetuximab versus FOLFOXIRI plus bevacizumab as the first-line treatment in metastatic colorectal cancer with RAS wild-type tumors: The DEEPER trial (JACCRO CC-13) – Tsuji A, et al

Key results (cont.)

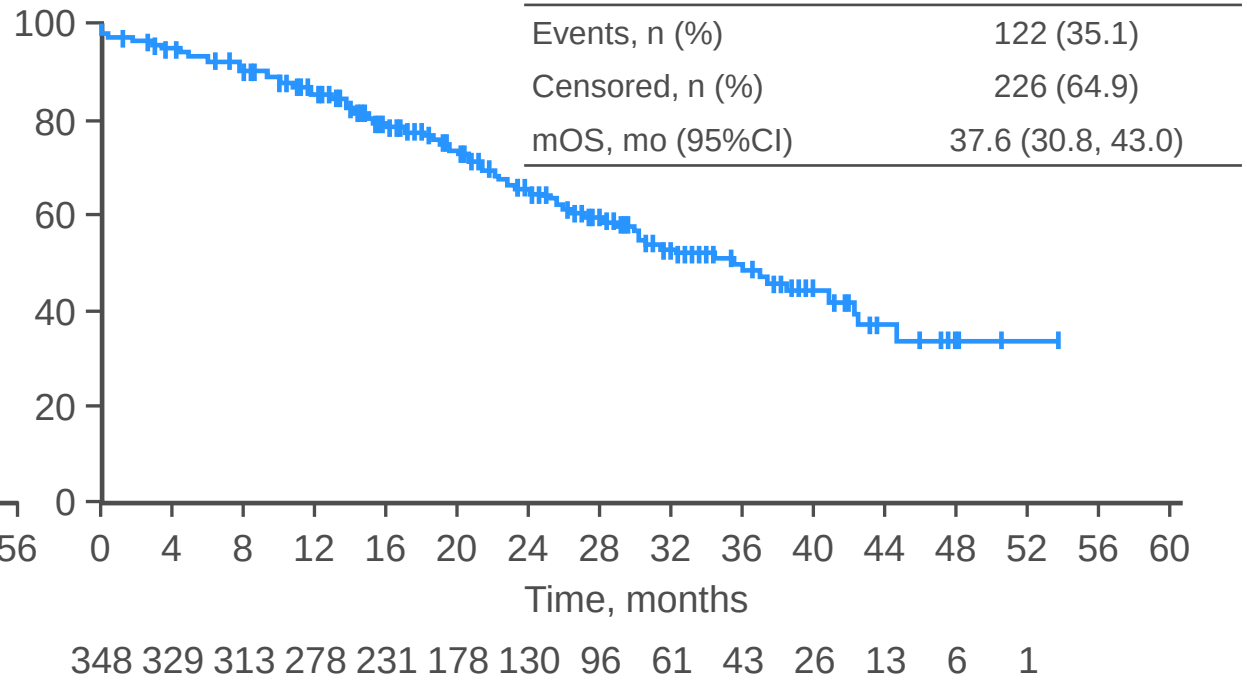
Progression-free survival

	All patients n=348
Events, n (%)	243 (69.8)
Censored, n (%)	105 (30.2)
mPFS, mo (95%CI)	12.7 (11.5, 14.0)



Overall survival

	All patients n=348
Events, n (%)	122 (35.1)
Censored, n (%)	226 (64.9)
mOS, mo (95%CI)	37.6 (30.8, 43.0)



Tsuji A, et al. J Clin Oncol 2021;39(suppl):abstr 3501

3501: The randomized phase II study of FOLFOXIRI plus cetuximab versus FOLFOXIRI plus bevacizumab as the first-line treatment in metastatic colorectal cancer with RAS wild-type tumors: The DEEPER trial (JACCRO CC-13) – Tsuji A, et al

Key results (cont.)

Response	Bevacizumab + mFOLFOXIRI (n=173)	Cetuximab + mFOLFOXIRI (n=175)	p-value
BOR, n (%)			
CR	4 (23)	11 (6.3)	
PR	120 (69.4)	110 (62.9)	
SD	41 (23.7)	38 (21.7)	
PD	3 (1.7)	8 (4.6)	
NE	5 (2.9)	8 (4.6)	
ORR, % (95%CI)	71.7 (65.0, 78.4)	69.1 (62.3, 76.0)	0.6047
DCR, % (95%CI)	95.4 (92.2, 98.5)	90.9 (86.6, 95.1)	0.0963

Grade ≥3 AEs occurring in ≥10%, n (%)	Bevacizumab + mFOLFOXIRI (n=176)	Cetuximab + mFOLFOXIRI (n=175)
Neutropenia	96 (54.5)	96 (54.9)
Hypertension	53 (30.1)	29 (16.6)
Febrile neutropenia	19 (10.8)	15 (8.6)
Anorexia	19 (10.8)	21 (12.0)
Diarrhea	14 (8.0)	21 (12.0)
Rash acneiform	0 (0)	21 (12.0)
Paronychia	0 (0)	20 (11.4)

Conclusions

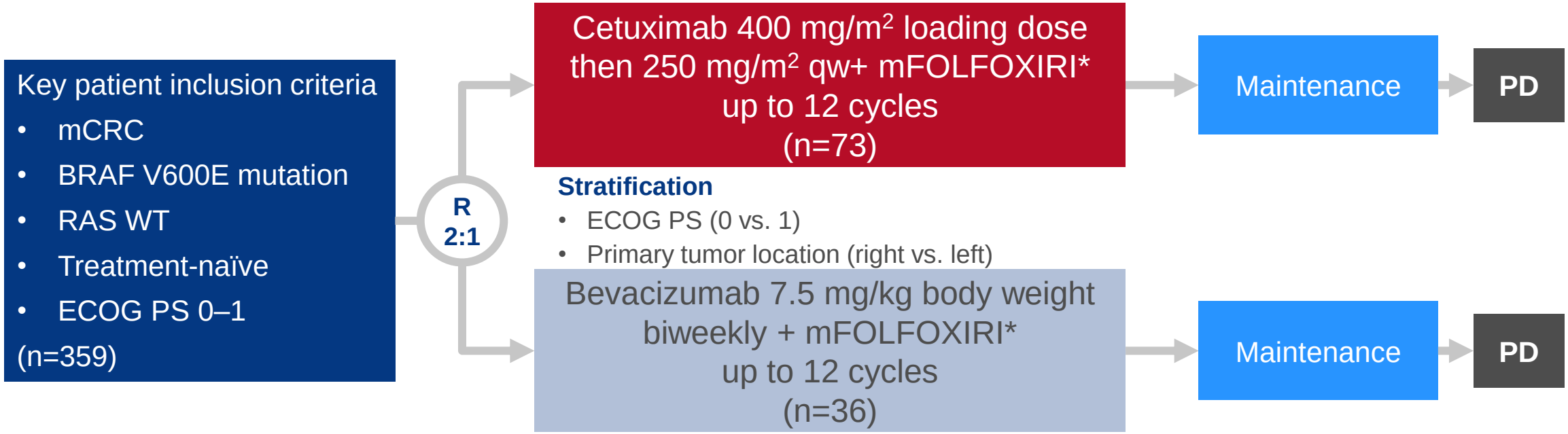
- **In patients with RAS WT mCRC, 1L cetuximab + mFOLFOXIRI demonstrated a superior depth of response compared with bevacizumab + mFOLFOXIRI**

Tsuji A, et al. J Clin Oncol 2021;39(suppl):abstr 3501

3502: Randomized study to investigate FOLFOXIRI plus either bevacizumab or cetuximab as first-line treatment of BRAF V600E-mutant mCRC: The phase-II FIRE-4.5 study (AIO KRK-0116) – Stintzing S, et al

Study objective

- To evaluate the efficacy and safety of bevacizumab + FOLFOXIRI vs. cetuximab + FOLFOXIRI in treatment naïve patients with BRAF V600E-mutant mCRC in the FIRE-4.5 study



PRIMARY ENDPOINT

- ORR (RECIST v1.1)

SECONDARY ENDPOINTS

- PFS, OS, safety

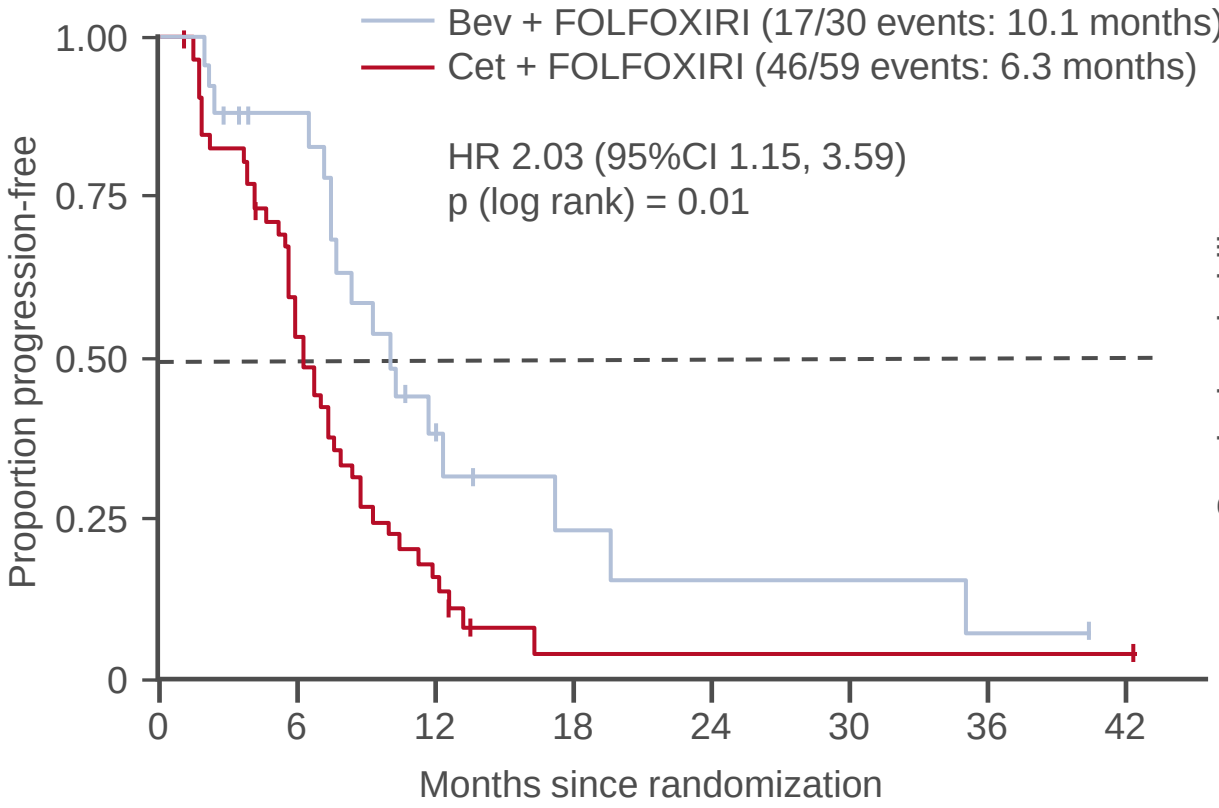
*Irinotecan 150 mg/m² + oxaliplatin 85 mg/m² + folinic acid 400 mg/m² + 5FU 3000 mg/m² within 48 h

Stintzing S, et al. J Clin Oncol 2021;39(suppl):abstr 3502

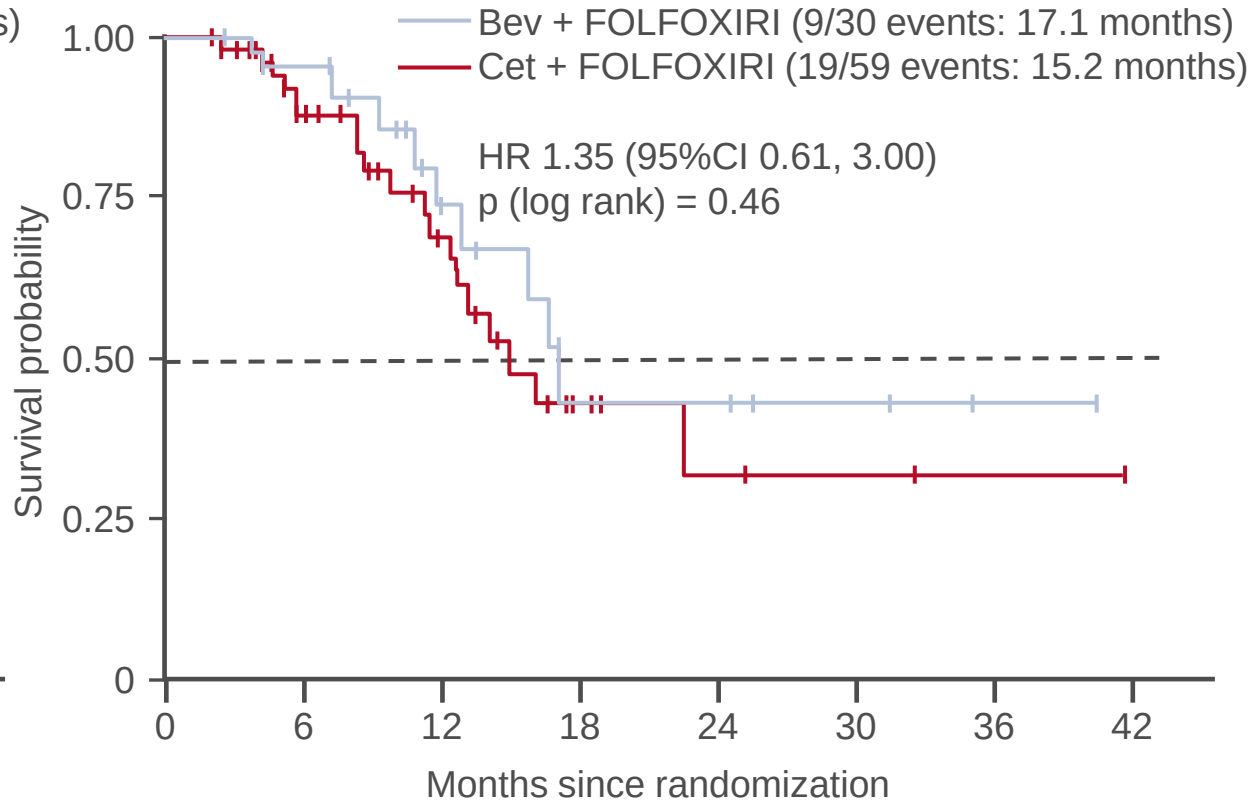
3502: Randomized study to investigate FOLFOXIRI plus either bevacizumab or cetuximab as first-line treatment of BRAF V600E-mutant mCRC: The phase-II FIRE-4.5 study (AIO KRK-0116) – Stintzing S, et al

Key results

Progression-free survival



Overall survival



Stintzing S, et al. J Clin Oncol 2021;39(suppl):abstr 3502

3502: Randomized study to investigate FOLFOXIRI plus either bevacizumab or cetuximab as first-line treatment of BRAF V600E-mutant mCRC: The phase-II FIRE-4.5 study (AIO KRK-0116) – Stintzing S, et al

Key results (cont.)

Response in per protocol population, n (%)	Cetuximab + FOLFOXIRI (n=59)	Bevacizumab + FOLFOXIRI (n=30)
CR	2 (3.5)	2 (6.7)
PR	27 (45.8)	16 (53.3)
SD	19 (32.2)	9 (30.0)
PD	11 (18.6)	3 (10.0)
ORR	29 (49.2)	18 (60.0)
OR (80%CI); p-value	1.55 (0.87, 2.78); 0.33	
DCR	48 (81.4)	27 (90.0)
OR (80%CI); p-value	2.06 (0.53, 8.04); 0.29	

Grade ≥3 AEs occurring in ≥10%, %	Cetuximab + FOLFOXIRI (n=72)	Bevacizumab + FOLFOXIRI (n=35)
Neutropenia	20.9	25.7
Diarrhea	18.1	20.0
Nausea	11.1	2.9
Acneiforme exanthema	11.1	0
Leukopenia	5.6	11.4
Pain	5.6	17.1

Conclusions

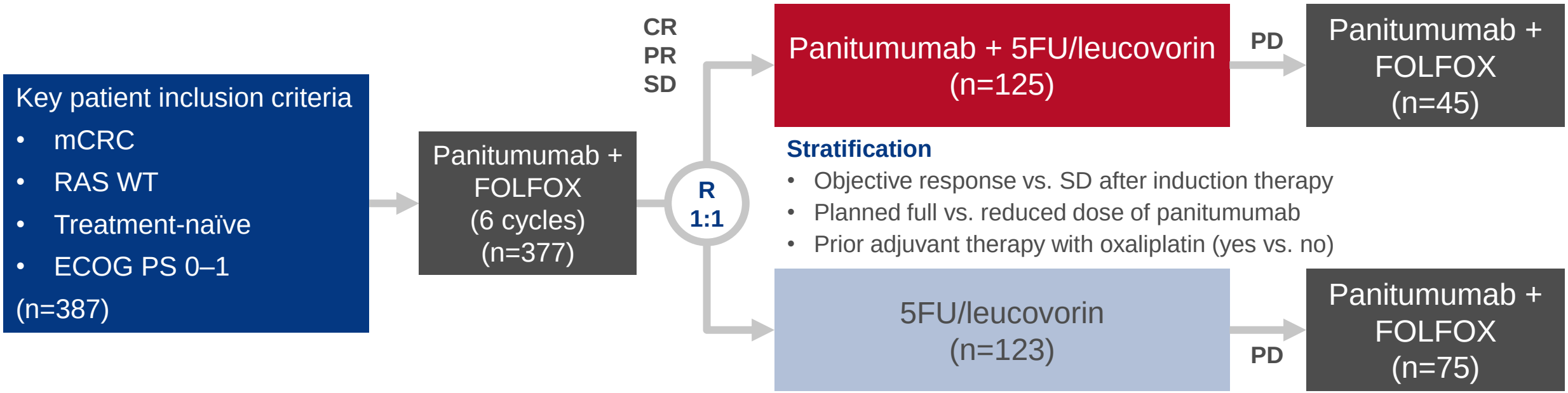
- **In patients with BRAF V600E-mutant mCRC, 1L cetuximab + FOLFOXIRI did not demonstrate additional benefit in ORR or PFS when compared with bevacizumab + FOLFOXIRI**

Stintzing S, et al. J Clin Oncol 2021;39(suppl):abstr 3502

3503: Maintenance therapy with 5-fluoruracil/leucovorin (5FU/LV) plus panitumumab (pmab) or 5FU/LV alone in RAS wild type (WT) metastatic colorectal cancer (mCRC) - the PANAMA trial (AIO KRK 0212) – Modest DP, et al

Study objective

- To evaluate the efficacy and safety of maintenance panitumumab + 5FU/leucovorin in patients with RAS WT mCRC in the PANAMA trial



PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

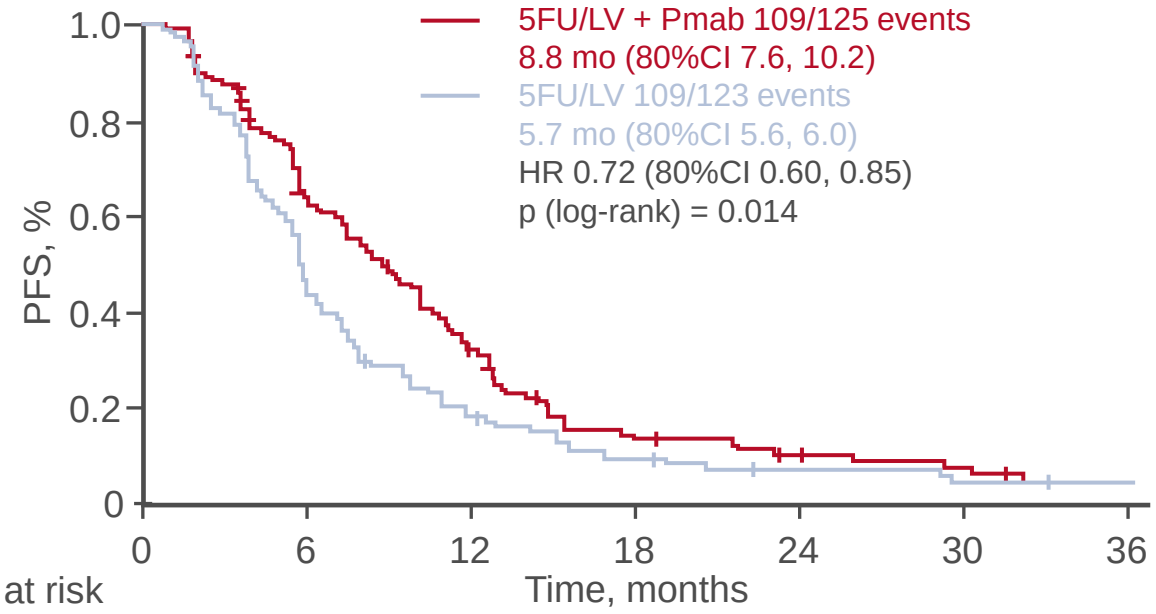
- OS, ORR, QoL, safety

Modest DP, et al. J Clin Oncol 2021;39(suppl):abstr 3503

3503: Maintenance therapy with 5-fluoruracil/leucovorin (5FU/LV) plus panitumumab (pmab) or 5FU/LV alone in RAS wild type (WT) metastatic colorectal cancer (mCRC) - the PANAMA trial (AIO KRK 0212) – Modest DP, et al

Key results

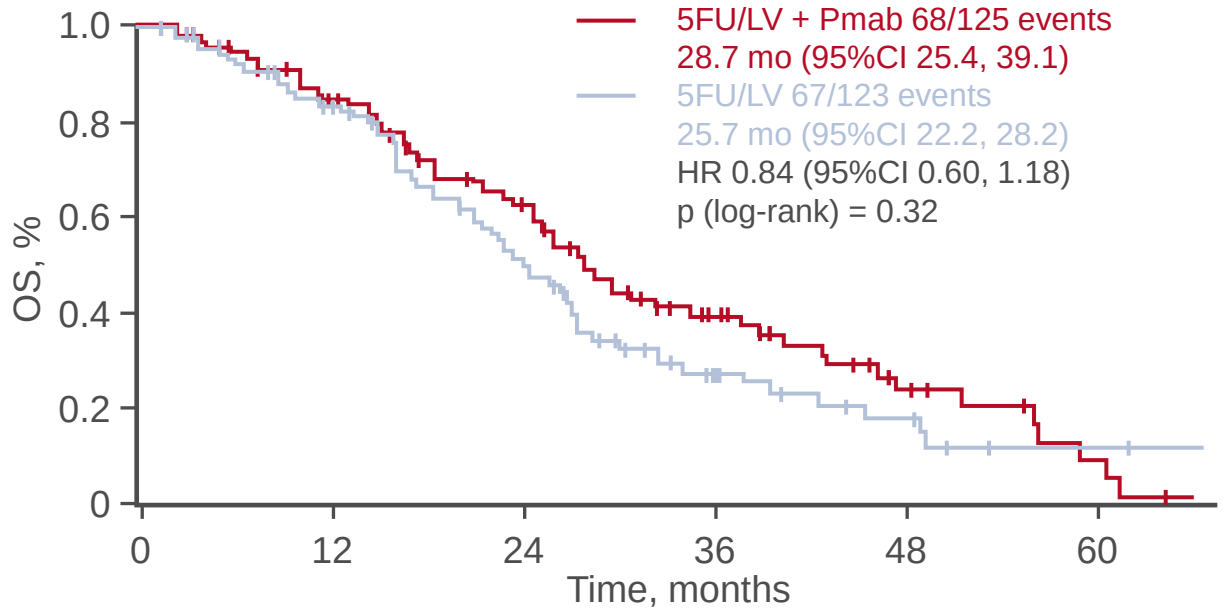
Progression-free survival



No. at risk

5FU/LV + Pmab	125	76	36	15	9	6
5FU/LV	123	54	20	10	6	4

Overall survival



5FU/LV + Pmab	125	92	59	24	11	4
5FU/LV	123	90	42	17	9	3

Modest DP, et al. J Clin Oncol 2021;39(suppl):abstr 3503

3503: Maintenance therapy with 5-fluoruracil/leucovorin (5FU/LV) plus panitumumab (pmab) or 5FU/LV alone in RAS wild type (WT) metastatic colorectal cancer (mCRC) - the PANAMA trial (AIO KRK 0212) – Modest DP, et al

Key results (cont.)

Response, n (%)	Panitumumab + 5FU/LV (n=125)	5FU/LV (n=123)
CR	9 (7.2)	6 (4.9)
PR	42 (33.6)	26 (21.1)
SD	50 (40.0)	52 (42.3)
PD	15 (12.0)	26 (21.1)
NE	9 (7.2)	13 (10.6)
ORR	51 (40.8)	32 (26.0)
OR (95%CI); p-value	1.96 (1.14, 3.36); 0.02	

Grade 3–4 AEs occurring in ≥2%, %	Panitumumab + 5FU/LV (n=125)	5FU/LV (n=123)
Skin rash	7.2	0
Hypomagnesemia	6.4	0
Paronychia	4.8	0
Infections	4.0	0.8
Pain	3.2	4.9
Skin fissures	2.4	0

Conclusions

- **In patients with RAS WT mCRC, combining panitumumab with 5FU/LV maintenance therapy provided additional improvement in PFS and was generally well-tolerated**

Modest DP, et al. J Clin Oncol 2021;39(suppl):abstr 3503