GI SLIDE DECK 2022
Selected abstracts from:

2022 ASCO® GI Cancers Symposium
20–22 January 2022

2022 ASCO® Annual Meeting
3–7 June 2022

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 ASCO® GI Cancers Symposium** and **2022 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 2022

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esdo

Glossary

1L	first-line
2L	second-line
5FU	5-fluouracil
ACT	adjuvant chemotherapy
AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
Atezo	atezolizumab
Bev	bevacizumab
BID	twice daily
BCLC	Barcelona Clinic Liver Cancer
BOR	best overall response
BSC	best supportive care
CAPOX	capecitabine + oxaliplatin
Cetux	cetuximab
CBR	clinical benefit rate
CF	5-fluorouracil + cisplatin
Chemo	chemotherapy
CI	confidence interval
Cis	cisplatin
CPS	combined positive score
CR	complete response
CRC	colorectal cancer
CRM	circumferential resection margin
CRT	chemoradiotherapy
CT	chemotherapy
ctDNA	circulating tumor DNA
D	day
DCF	docetaxel + cisplatin + 5-fluorouracil
DCR	disease control rate
(m)DDC	(median) duration of disease control
DFS	disease-free survival
dMMR	deficient mismatch repair
(m)DoR	(median) duration of response
Durv	durvalumab
ECOG	Eastern Cooperative Oncology Group
EFS	event-free survival
EGFR	epidermal growth factor receptor
EOD	early oxaliplatin discontinuation
EP	etoposide + cisplatin
ETD	early treatment discontinuation
FLOT	docetaxel + oxaliplatin + leucovorin + 5-fluouraci
FOLFIRI	irinotecan + 5-fluouracil + folinic acid
(m)FOLFIRINOX [or mFFX]	(modified) oxaliplatin + irinotecan+ leucovorin + 5-fluorouracil
(m)FOLFOX	(modified) leucovorin + 5-fluorouracil + oxaliplatin
(m)FOLFOXIRI	(modified) oxaliplatin + irinotecan + 5-fluouracil + folinic acid
FU	follow-up
GEJ	gastro-esophageal junction
Gem	gemcitabine
GGT	gamma-glutamyltransferase
GI	gastrointestinal
Gy	Gray
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HR	hazard ratio
HRQoL	health-related quality of life
ID	identification
IP	irinotecan + cisplatin
ITT	intent-to-treat
KRAS	Ki-ras2 Kirsten rat sarcoma viral oncogene homolog
LDH	lactate dehydrogenase
Nimo	nimotuzumab
mAb	monoclonal antibody
MAPK	mitogen-activated protein kinase
mCRC	metastatic colorectal cancer
mo	months
MRD	molecular residual disease
MRI	magnetic resonance imaging
MSI(-H)	(high) microsatellite instability
MSS	microsatellite stable
NA	not available
Nal-IRI	liposomal irinotecan
NE	not evaluable/estimable
Neg	negative
Neo	neoadjuvant
NGS	next generation sequencing
NR	not reached
ORR	overall/objective response rate
OR	odds ratio
(m)OS	(median) overall survival
PBO	placebo
pCR	pathological complete response
PCR	polymerase chain reaction
PD	progressive disease
PDAC	pancreatic ductal adenocarcinoma
PD-(L)1	programmed death (-ligand) 1
Pembro	pembrolizumab
(m)PFS	(median) progression-free survival
Pos	positive
PR	partial response
PS	performance status
PTR	primary tumor resection
PVE	portal vein embolization
q(2/3/4)w	every (2/3/4) week(s)
QoL	quality of life
R	randomized
R0/1/x	resection 0, 1 x
RAS	rat sarcoma virus
RECIST	Response Evaluation Criteria In Solid Tumors
Ref	reference
RFS	recurrence-free survival
RP2D	recommended phase 2 dose
RR	response rate
RT	radiotherapy
SAE	serious adverse event
SD	stable disease
SoC	standard of care
TACE	transarterial chemoembolization
TEAE	treatment-emergent adverse event
TFS	treatment-free survival
TRAE	treatment-related adverse event
TRG	tumor regression grade
(m)TTP	(median) time to progression
(m)TTR	(median) time to response
WBC	white blood cell
WHO	World Health Organization
WT	wild-type
yr	year

Mechanism of action for new molecules

Molecule		Mechanism of action
Eryaspase	Asparaginase encapsulated in red blood cells	Induces the degradation of asparagine and glutamine involved in cancer cell growth and survival
Adagrasib	KRAS G12C inhibitor	Irreversibly and selectively binds KRAS G12C locking it in its inactive state with KRAS being a key mediator of the RAS/MAPK signaling
Sintilimab	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
Nimotuzumab	Human anti-EGFR monoclonal antibody	Disrupts the interaction of EGFR with its ligand to block the EGFR signalling pathway, mediates antibody-dependent cell cytotoxicity, complement dependent-cytotoxicity and other immune effects, induce EGFR endocytosis and degradation
Dostarlimab	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

Contents

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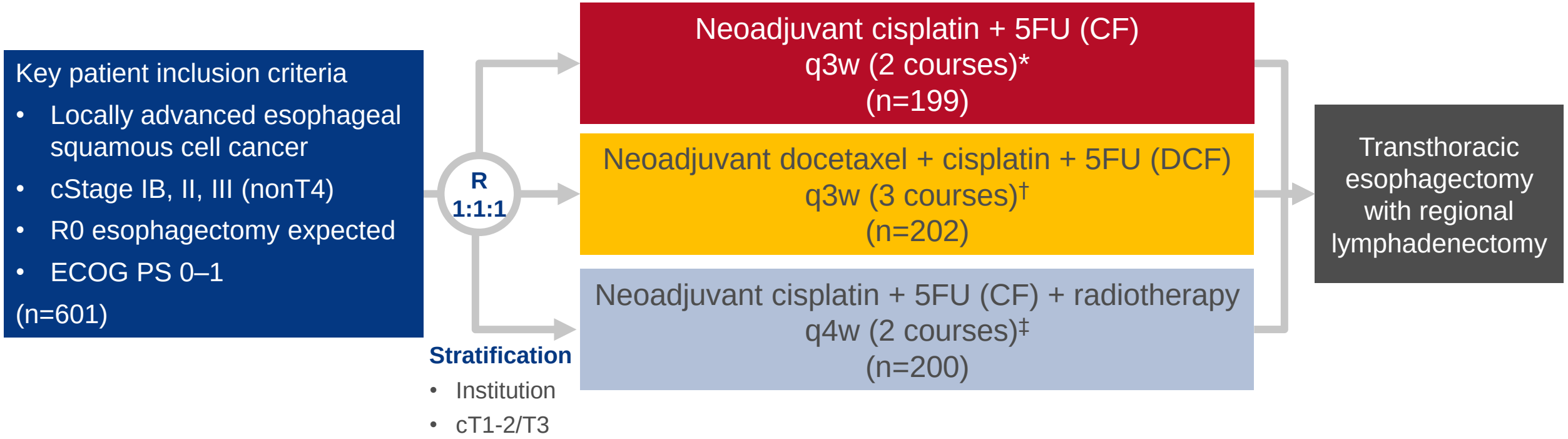
CANCERS OF THE OESOPHAGUS AND STOMACH

238: A randomized controlled phase III trial comparing two chemotherapy regimen and chemoradiotherapy regimen as neoadjuvant treatment for locally advanced esophageal cancer, JCOG1109 NExT study – Kato K, et al

Study objective

- To evaluate the efficacy and safety of neoadjuvant chemotherapy or chemoradiotherapy regimens in patients with locally advanced esophageal squamous cell carcinoma in Japanese centers in the JCOG1109 NExT study



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, R0 resection rate, RR, pCR, safety

*Cisplatin 80 mg/m^2 D1 + 5FU 800 mg/m^2 D1–5; †docetaxel 70 mg/m^2 D1 + cisplatin 70 mg/m^2 D1 + 5FU 750 mg/m^2 D1–5; ‡cisplatin 75 mg/m^2 D1 + 5FU 1000 mg/m^2 D1–4 + radiotherapy 41.4 Gy

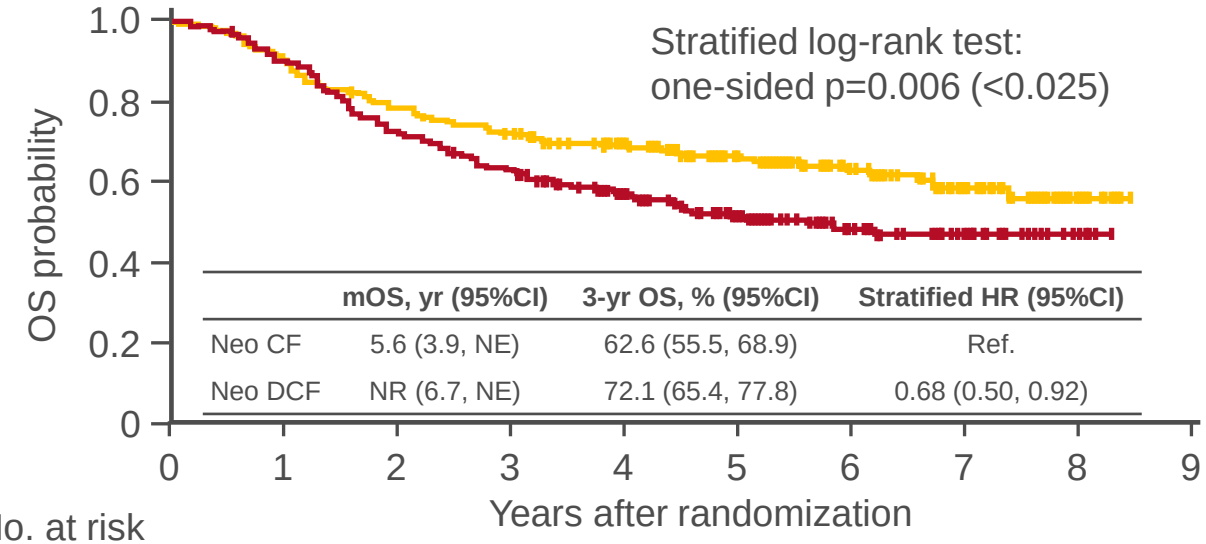
Kato K, et al. J Clin Oncol 2022;40(suppl):abstr 238

238: A randomized controlled phase III trial comparing two chemotherapy regimen and chemoradiotherapy regimen as neoadjuvant treatment for locally advanced esophageal cancer, JCOG1109 NExT study – Kato K, et al

Key results

Overall survival

Neoadjuvant CF vs. neoadjuvant DCF

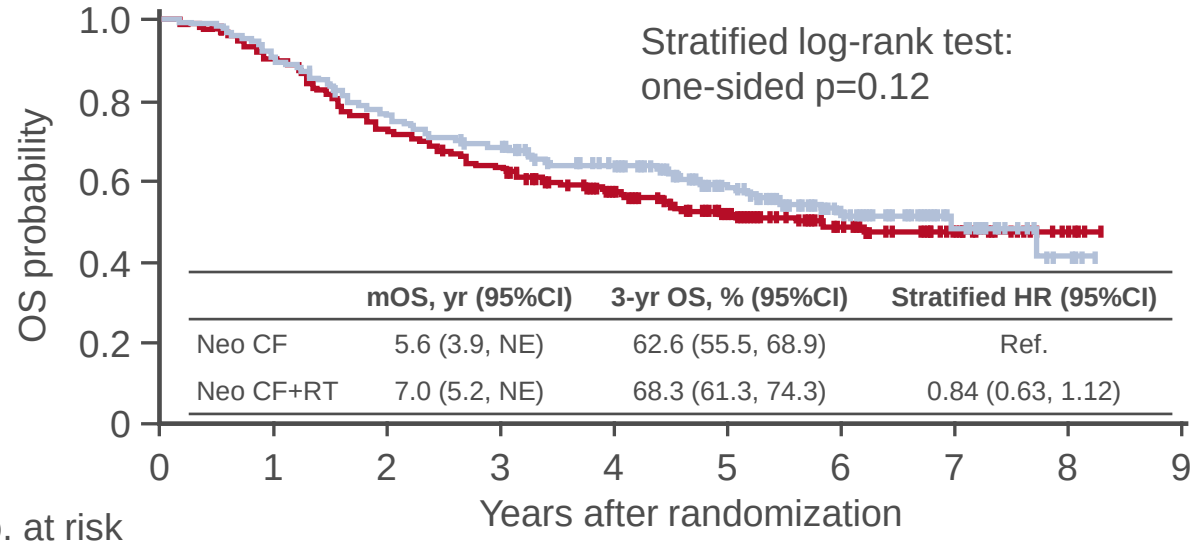


	mOS, yr (95%CI)	3-yr OS, % (95%CI)	Stratified HR (95%CI)
Neo CF	5.6 (3.9, NE)	62.6 (55.5, 68.9)	Ref.
Neo DCF	NR (6.7, NE)	72.1 (65.4, 77.8)	0.68 (0.50, 0.92)

No. at risk

Neo CF	199	178	143	123	98	66	38	19	4	0
Neo DCF	202	182	156	143	113	82	56	26	8	0

Neoadjuvant CF vs. neoadjuvant CF + radiotherapy



	mOS, yr (95%CI)	3-yr OS, % (95%CI)	Stratified HR (95%CI)
Neo CF	5.6 (3.9, NE)	62.6 (55.5, 68.9)	Ref.
Neo CF+RT	7.0 (5.2, NE)	68.3 (61.3, 74.3)	0.84 (0.63, 1.12)

No. at risk

Neo CF	199	178	143	123	98	66	38	19	4	0
Neo CF+RT	200	182	151	133	111	79	47	19	4	0

Kato K, et al. J Clin Oncol 2022;40(suppl):abstr 238

238: A randomized controlled phase III trial comparing two chemotherapy regimen and chemoradiotherapy regimen as neoadjuvant treatment for locally advanced esophageal cancer, JCOG1109 NExT study – Kato K, et al

Key results (cont.)

	Neo CF (n=199)	Neo DCF (n=202)	Neo CF + RT (n=200)
mPFS, yr (95%CI)	2.7 (1.8, 4.8)	NR (5.2, NE)	5.3 (3.4, NE)
HR (95%CI)	Ref	0.67 (0.51, 0.88)	0.77 (0.59, 1.01)
Surgical outcomes, n	188	185	178
R0, n (%)	168 (90.3)	173 (94.5)	175 (98.9)
Underwent surgery, n	186	183	177
pCR, n (%)	4 (2.2)	34 (18.6)	65 (36.7)
No residual tumor, n (%)	4 (2.2)	40 (21.9)	77 (43.5)

Grade 3–4 AEs during neoadjuvant treatment occurring in ≥10%, %	Neo CF (n=193)	Neo DCF (n=196)	Neo CF + RT (n=191)
Leukocytopenia	6.7	63.8	53.9
Neutropenia	23.4	85.2	44.5
Hyponatremia	6.2	26.0	11.0
Febrile neutropenia	1.0	16.3	4.7
Appetite loss	8.3	21.4	14.7

Conclusions

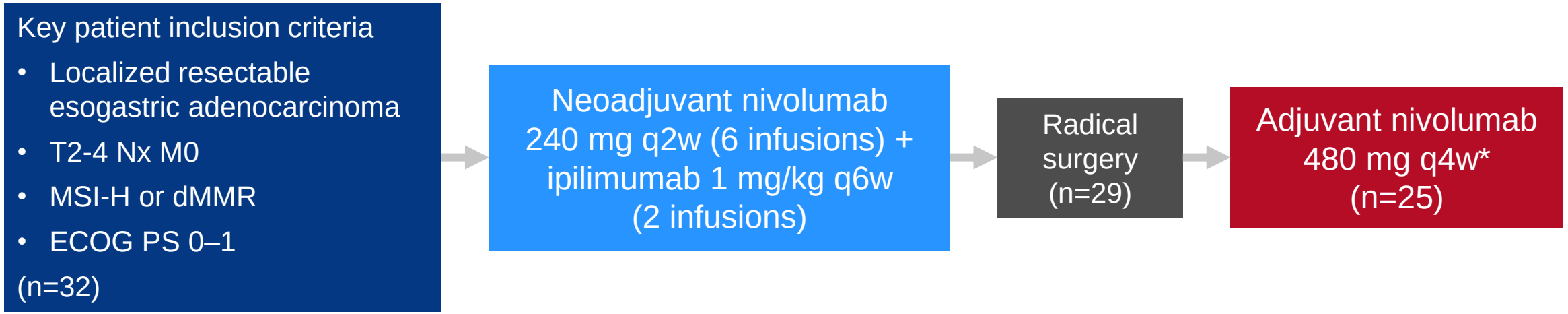
- **In patients with locally advanced esophageal squamous cell carcinoma, neoadjuvant DCF, but not neoadjuvant CF + radiotherapy, significantly improved OS compared with neoadjuvant CF and had a manageable safety profile**

Kato K, et al. J Clin Oncol 2022;40(suppl):abstr 238

244: Neoadjuvant nivolumab plus ipilimumab and adjuvant nivolumab in patients (pts) with localized microsatellite instability-high (MSI)/mismatch repair deficient (dMMR) oeso-gastric adenocarcinoma (OGA): The GERCOR NEONIPIGA phase II study – André T, et al

Study objective

- To evaluate the efficacy and safety of neoadjuvant nivolumab + ipilimumab and adjuvant nivolumab in patients with localized MSI-H or dMMR esogastric adenocarcinoma in French centers in the phase 2 GERCOR NEONIPIGA study



PRIMARY ENDPOINT

- pCR

SECONDARY ENDPOINTS

- EFS, OS, safety

*Only patients with Becker tumor regression grade <3 received adjuvant nivolumab

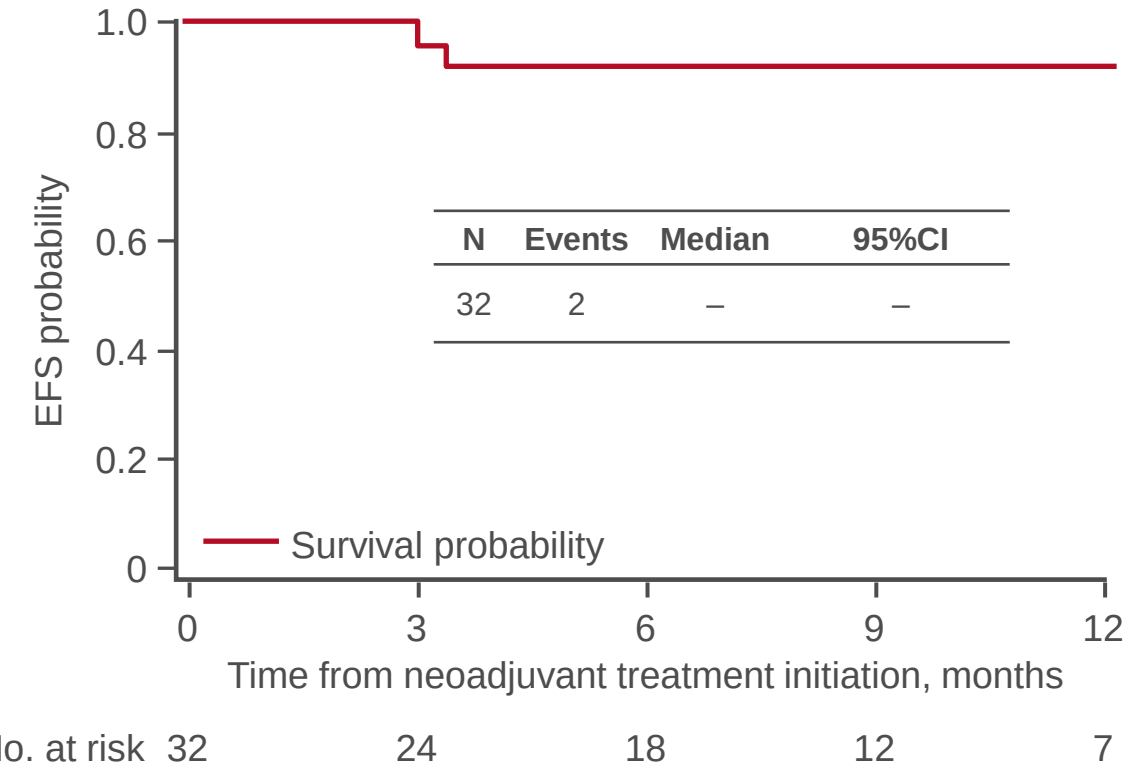
André T, et al. J Clin Oncol 2022;40(suppl):abstr 244

244: Neoadjuvant nivolumab plus ipilimumab and adjuvant nivolumab in patients (pts) with localized microsatellite instability-high (MSI)/mismatch repair deficient (dMMR) oeso-gastric adenocarcinoma (OGA): The GERCOR NEONIPIGA phase II study – André T, et al

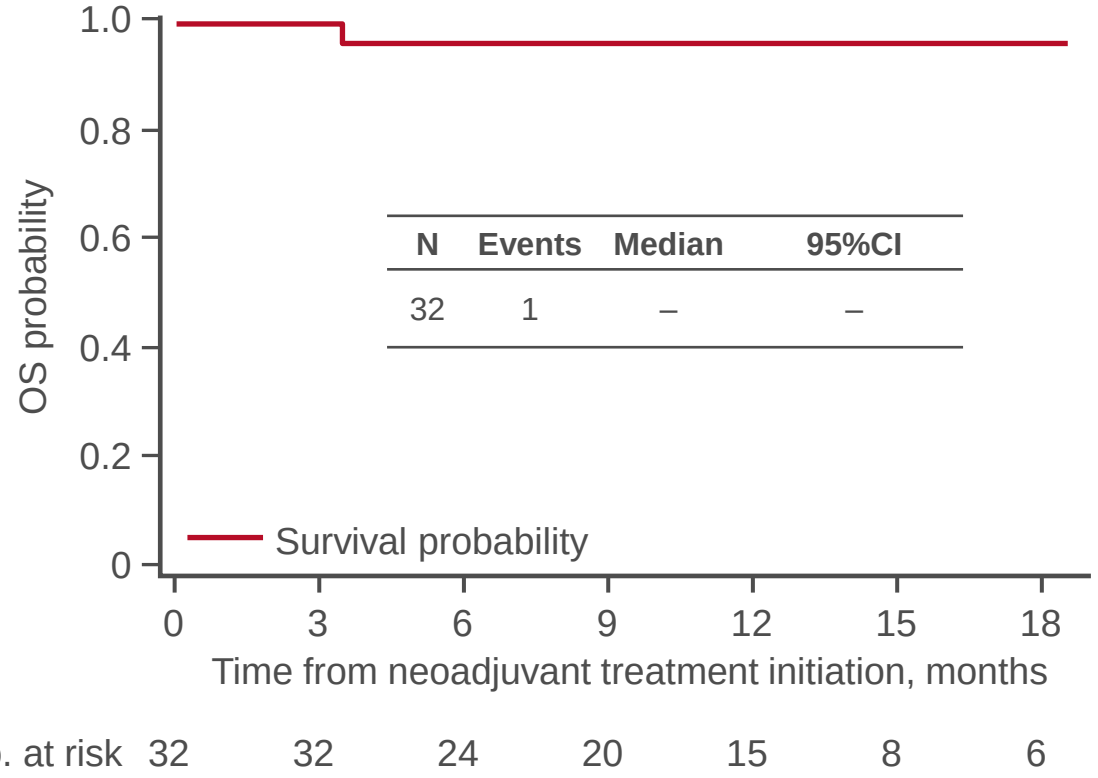
Key results

- pCR was achieved by 17 of 29 (58.6%) patients

Event-free survival



Overall survival



André T, et al. J Clin Oncol 2022;40(suppl):abstr 244

244: Neoadjuvant nivolumab plus ipilimumab and adjuvant nivolumab in patients (pts) with localized microsatellite instability-high (MSI)/mismatch repair deficient (dMMR) oeso-gastric adenocarcinoma (OGA): The GERCOR NEONIPIGA phase II study – André T, et al

Key results (cont.)

Grade 3–4 AEs during neoadjuvant therapy, n (%)	n=32
Any TRAE	8 (25)
Led to discontinuation	5 (16)
Colitis/ileitis	2 (6)
Hepatitis	2 (6)
Decreased appetite	2 (6)
Other	2 (6)
Diarrhea	1 (3)
Adrenal insufficiency/hypophysitis	1 (3)
Vomiting	1 (3)

Per and/or post-op complications, n (%)	n=29
Yes	17 (58.5)
Fistula	6 (27)
Pancreatitis	3 (14)
Ileus	2 (9)
Pneumonia	2 (9)
Atrial fibrillation	2 (9)
Death	1 (4.5)
Other	6 (27)

Conclusions

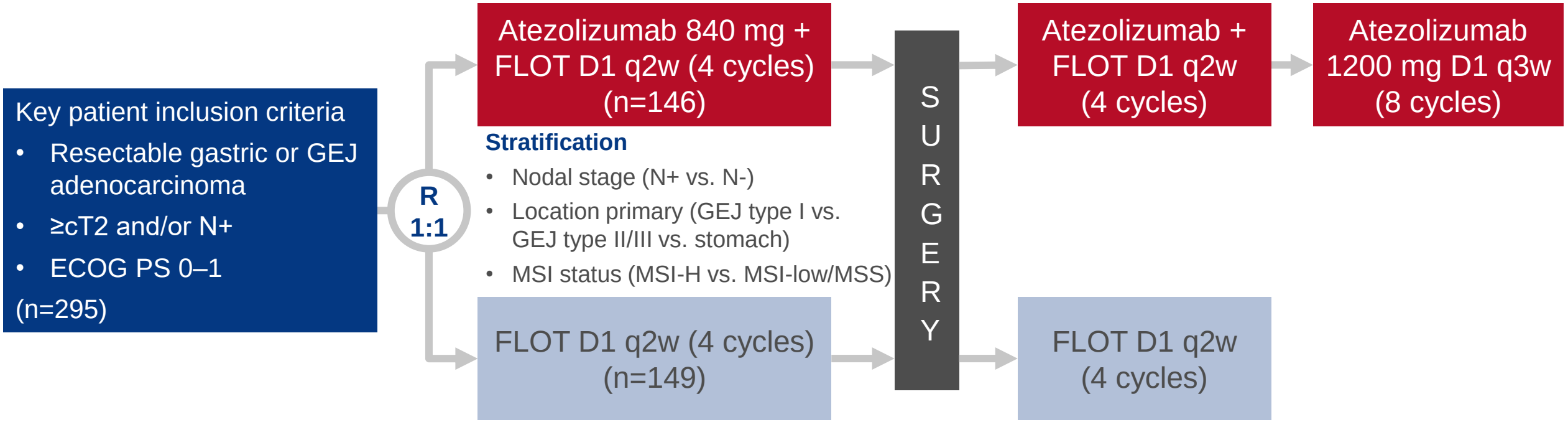
- **In patients with MSI-H or dMMR esogastric adenocarcinoma, neoadjuvant nivolumab + ipilimumab followed by adjuvant nivolumab was associated with high pCR rates (58.6%) and there were no new safety concerns**

André T, et al. J Clin Oncol 2022;40(suppl):abstr 244

4003: Surgical and pathological outcome, and pathological regression, in patients receiving perioperative atezolizumab in combination with FLOT chemotherapy versus FLOT alone for resectable esophagogastric adenocarcinoma: Interim results from DANTE, a randomized, multicenter, phase IIb trial of the FLOT-AIO German Gastric Cancer Group and Swiss SAKK – Al-Batran S-E, et al

Study objective

- To evaluate the efficacy and safety of atezolizumab + FLOT in patients with resectable esophagogastric adenocarcinoma in German and Swiss centers in the phase 2b DANTE study (interim analysis)



PRIMARY ENDPOINTS

- PFS, DFS

SECONDARY ENDPOINTS

- Surgical outcomes, OS, safety

FLOT, docetaxel 50 mg/m^2 + oxaliplatin 85 mg/m^2 + leucovorin 200 mg/m^2 + 5FU 2600 mg/m^2 D1 IV

Al-Batran S-E, et al. J Clin Oncol 2022;40(suppl):abstr 4003

4003: Surgical and pathological outcome, and pathological regression, in patients receiving perioperative atezolizumab in combination with FLOT chemotherapy versus FLOT alone for resectable esophagogastric adenocarcinoma: Interim results from DANTE, a randomized, multicenter, phase IIb trial of the FLOT-AIO German Gastric Cancer Group and Swiss SAKK – Al-Batran S-E, et al

Key results

AEs, n (%)	Atezolizumab + FLOT (n=144)	FLOT (n=148)
Any grade 3–4	130 (90)	125 (85)
Any grade 5	7 (5)	8 (5)
SAE	99 (69)	98 (66)
Treatment-related SAE	60 (42)	46 (31)
Treatment-related grade 3–4	51 (35)	31 (21)
Treatment-related led to death	1 (<1)	2 (1)

Surgical and margin-free resection, n (%)	Atezolizumab + FLOT (n=146)	FLOT (n=149)
Resectional tumor surgery	141 (97)	143 (96)
Margin-free (R0) resection		
Among those having surgery	135 (96)	136 (95)
ITT	135 (93)	136 (91)
Lymph nodes removed, median (25%, 75% quartile)	30 (5–139)	29 (11–81)

Surgical morbidity/ mortality, n (%)	Atezolizumab + FLOT (n=141)	FLOT (n=143)
Median hospitalization, days	16	15
Complications	64 (45)	60 (42)
Surgical	25 (18)	26 (18)
Medical	35 (25)	27 (19)
Both	4 (3)	7 (5)
Re-operation	14 (10)	16 (11)
Death in hospital	4 (3)	3 (2)
Death 60 days	4 (3)	3 (2)

Al-Batran S-E, et al. J Clin Oncol 2022;40(suppl):abstr 4003

4003: Surgical and pathological outcome, and pathological regression, in patients receiving perioperative atezolizumab in combination with FLOT chemotherapy versus FLOT alone for resectable esophagogastric adenocarcinoma: Interim results from DANTE, a randomized, multicenter, phase IIb trial of the FLOT-AIO German Gastric Cancer Group and Swiss SAKK – Al-Batran S-E, et al

Key results

Pathological regression*, n (%)	Local assessment				Central assessment			
	TRG1a		TRG1a/b		TRG1a		TRG1a/b	
	Atezo + FLOT	FLOT	Atezo + FLOT	FLOT	Atezo + FLOT	FLOT	Atezo + FLOT	FLOT
All patients (n=295; 146/149)	35 (24)	23 (15)	71 (49)	58 (39)	37 (25)	36 (24)	72 (49)	66 (44)
PD-L1 CPS ≥1 (n=170; 82/88)	20 (24)	13 (15)	42 (51)	40 (46)	21 (26)	20 (23)	43 (52)	41 (47)
PD-L1 CPS ≥5 (n=81; 40/41)	11 (28)	8 (20)	22 (55)	18 (44)	13 (33)	9 (22)	21 (53)	19 (46)
PD-L1 CPS ≥10 (n=53; 27/26)	9 (33)	3 (12)	18 (67)	10 (39)	11 (41)	5 (19)	19 (70)	13 (50)
MSI-H (n=23; 8/15)	5 (63)	4 (27)	6 (75)	7 (47)	5 (63)	4 (27)	6 (75)	7 (47)

Conclusions

- **In patients with resectable esophagogastric adenocarcinoma, perioperative atezolizumab + FLOT improved downstaging and pathological regression, particularly in those with higher PD-L1 expression or MSI-H tumors and was generally well-tolerated**

*Pathological complete and subtotal regression according to Becker criteria

Al-Batran S-E, et al. J Clin Oncol 2022;40(suppl):abstr 4003

CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

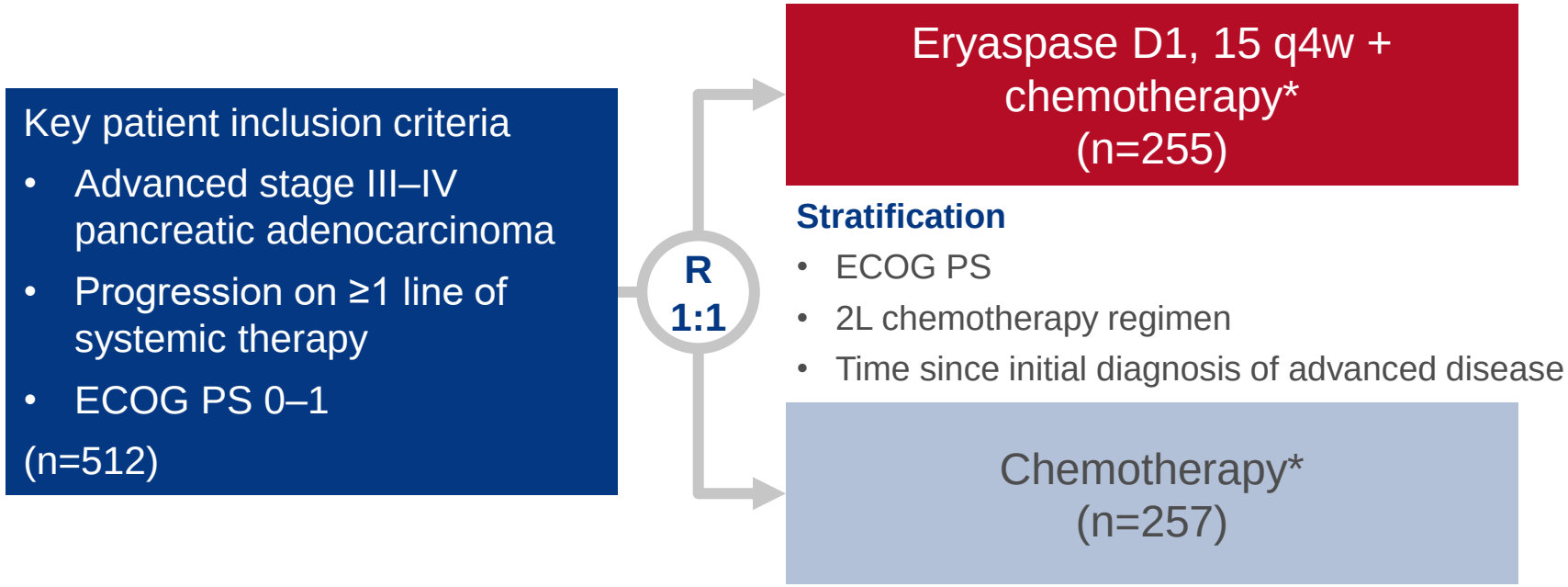
Cancers of the pancreas, small bowel and hepatobiliary tract

PANCREATIC CANCER

518: Trybeca-1: A randomized, phase 3 study of eryaspase in combination with chemotherapy versus chemotherapy alone as second-line treatment in patients with advanced pancreatic adenocarcinoma (NCT03665441) – Hammel P, et al

Study objective

- To evaluate the efficacy and safety of eryaspase combined with chemotherapy in previously treated patients with advanced pancreatic adenocarcinoma



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR, DoR, DCR, QoL, safety

*Gemcitabine/nab-paclitaxel or irinotecan/5FU depending on first-line of therapy

Hammel P, et al. J Clin Oncol 2022;40(suppl):abstr 518

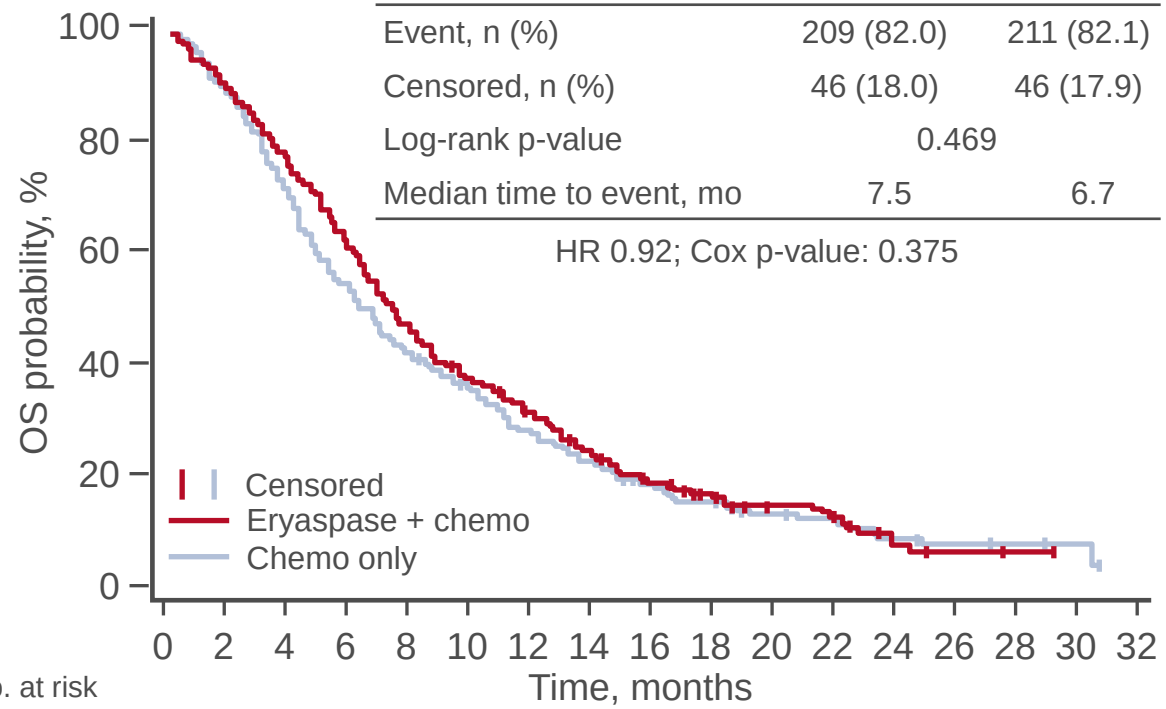
518: Trybeca-1: A randomized, phase 3 study of eryaspase in combination with chemotherapy versus chemotherapy alone as second-line treatment in patients with advanced pancreatic adenocarcinoma (NCT03665441) – Hammel P, et al

Key results

Overall survival

	Eryaspase + chemo (n=255)	Chemo (n=257)
Event, n (%)	209 (82.0)	211 (82.1)
Censored, n (%)	46 (18.0)	46 (17.9)
Log-rank p-value	0.469	
Median time to event, mo	7.5	6.7

HR 0.92; Cox p-value: 0.375

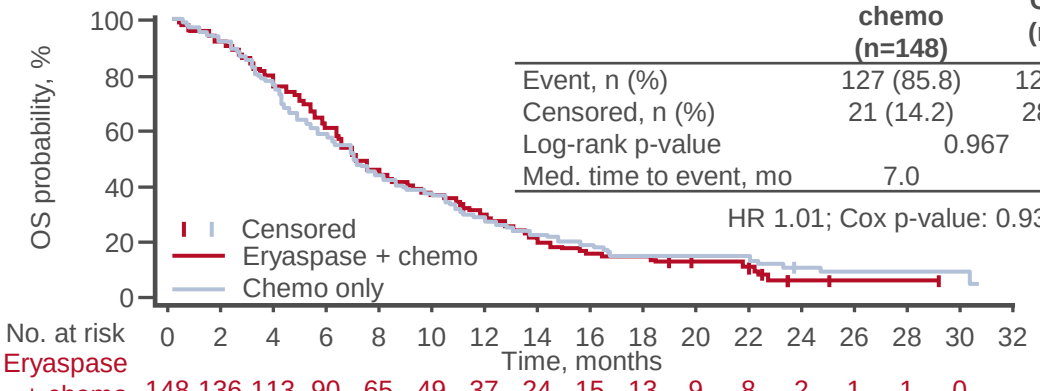


No. at risk																
Eryaspase + chemo	255	227	189	151	115	84	67	46	33	24	17	14	5	3	1	0
Chemo alone	257	224	177	132	101	82	58	42	28	22	15	13	8	5	3	2	0

Gemcitabine/nab-paclitaxel

	Eryaspase + chemo (n=148)	Chemo (n=148)
Event, n (%)	127 (85.8)	120 (81.1)
Censored, n (%)	21 (14.2)	28 (18.9)
Log-rank p-value	0.967	
Med. time to event, mo	7.0	6.9

HR 1.01; Cox p-value: 0.934

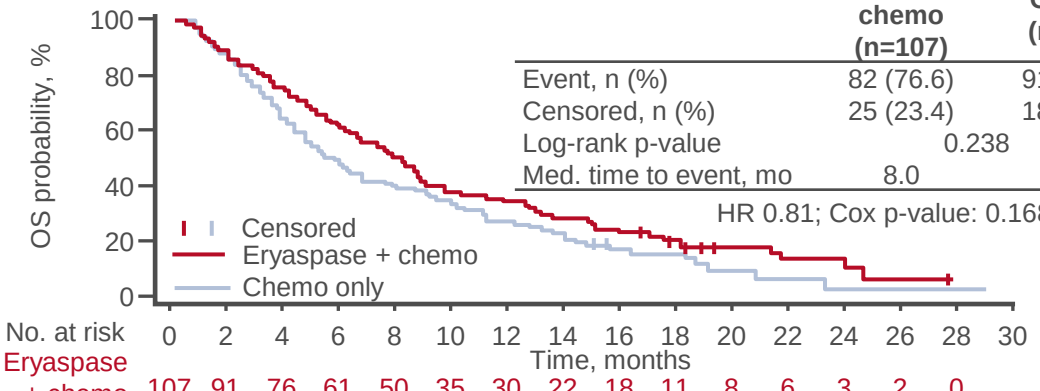


No. at risk																
Eryaspase + chemo	148	136	113	90	65	49	37	24	15	13	9	8	2	1	1	0
Chemo alone	148	132	108	81	59	47	34	25	17	13	11	11	7	4	2	2	0

Fluoropyrimidine/irinotecan

	Eryaspase + chemo (n=107)	Chemo (n=109)
Event, n (%)	82 (76.6)	91 (83.5)
Censored, n (%)	25 (23.4)	18 (16.5)
Log-rank p-value	0.238	
Med. time to event, mo	8.0	5.7

HR 0.81; Cox p-value: 0.168



No. at risk															
Eryaspase + chemo	107	91	76	61	50	35	30	22	18	11	8	6	3	2	0
Chemo alone	109	92	69	51	42	35	24	17	11	9	4	2	1	1	1	0

Hammel P, et al. J Clin Oncol 2022;40(suppl):abstr 518

518: Trybeca-1: A randomized, phase 3 study of eryaspase in combination with chemotherapy versus chemotherapy alone as second-line treatment in patients with advanced pancreatic adenocarcinoma (NCT03665441) – Hammel P, et al

Key results (cont.)

	Eryaspase + chemo (n=255)	Chemotherapy (n=257)
BOR, n (%)		
CR	4 (1.6)	1 (0.4)
PR	37 (14.5)	31 (12.1)
SD	106 (41.6)	94 (36.6)
PD	77 (30.2)	89 (34.6)
NE	31 (12.2)	42 (16.3)
DCR, n (%)	147 (57.6)	126 (49.0)

Grade 3–4 AEs, n (%)	Eryaspase + chemo (n=248)	Chemotherapy (n=246)
Neutropenia	63 (25.4)	50 (20.3)
Anemia	43 (17.3)	30 (12.2)
Asthenia	42 (16.9)	34 (13.8)
Thrombocytopenia	28 (11.3)	24 (9.8)
Diarrhea	19 (7.7)	17 (6.9)
Leukopenia	16 (6.5)	8 (3.3)
Peripheral neutopathy	14 (5.6)	10 (4.1)
Abdominal pain	14 (5.6)	9 (3.7)
GGT increased	12 (4.8)	8 (3.3)

Conclusions

- **In previously treated patients with advanced pancreatic adenocarcinoma, eryaspase + chemotherapy did not significantly improve OS compared with chemotherapy alone, although there was a trend for improvement in those who received eryaspase + fluoropyrimidine/irinotecan, and was generally well-tolerated**

Hammel P, et al. J Clin Oncol 2022;40(suppl):abstr 518

519: KRYSTAL-1: Updated activity and safety of adagrasib (MRTX849) in patients (Pts) with unresectable or metastatic pancreatic cancer (PDAC) and other gastrointestinal (GI) tumors harboring a KRASG12C mutation – Bekaii-Saab TS, et al

Study objective

- To evaluate the efficacy and safety of adagrasib in the cohort of previously treated patients with unresectable or metastatic solid tumors including pancreatic and other GI cancers (excluding CRC) and harboring a KRAS G12C mutation* in US centers in the phase 2 portion of the KRYSTAL-1 study

Key patient inclusion criteria

- Unresectable or metastatic pancreatic or other GI cancers (excluding CRC)
- KRAS G12C mutation
- No available treatment with curative intent or SoC

(n=565)

Phase 1
Dose escalation

Adagrasib
150, 300,
600, 1200 mg/day

Phase 1b
Dose expansion + combination

Adagrasib 600 mg/day
(n=2)

Adagrasib 600 mg/day + cetuximab
(n=32)

Phase 2

Adagrasib
600 mg/day
(n=42†)

PRIMARY ENDPOINT

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

SECONDARY ENDPOINTS

- Phase 2: DoR, PFS, OS, safety

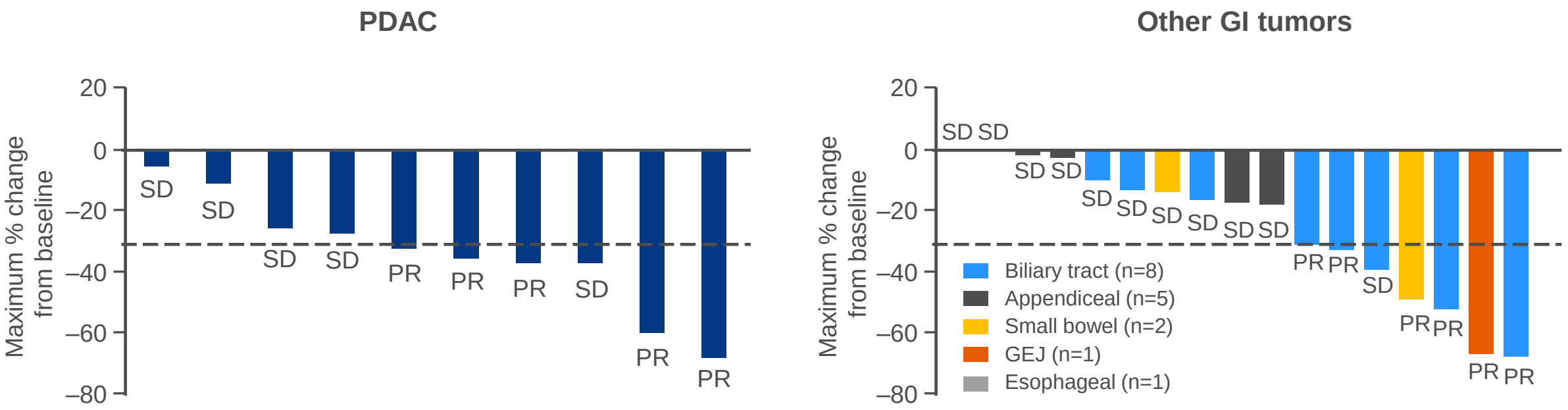
*KRAS mutations occur in ~90% of pancreatic cancer with ~2% being KRAS G12C mutations;
†PDAC, n=12 and other GI cancers, n=18

Bekaii-Saab TS, et al. J Clin Oncol 2022;40(suppl):abstr 519

519: KRYSTAL-1: Updated activity and safety of adagrasib (MRTX849) in patients (Pts) with unresectable or metastatic pancreatic cancer (PDAC) and other gastrointestinal (GI) tumors harboring a KRASG12C mutation – Bekaii-Saab TS, et al

Key results

Best tumor change from baseline (evaluable patients)



Bekaii-Saab TS, et al. J Clin Oncol 2022;40(suppl):abstr 519

519: KRYSTAL-1: Updated activity and safety of adagrasib (MRTX849) in patients (Pts) with unresectable or metastatic pancreatic cancer (PDAC) and other gastrointestinal (GI) tumors harboring a KRASG12C mutation – Bekaii-Saab TS, et al

Key results (cont.)

	PDAC (n=10)	Other GI cancers (n=17)
ORR, n (%)	5 (50)	6 (35)
BOR, n (%)		
PR	5 (50)	6 (35)
SD	5 (50)	11 (65)
DCR, n (%)	10 (100)	17 (100)
mTTR, mo	2.8	1.3
mDoR, mo	6.97	7.85
mPFS, mo (95%CI)	6.6 (1.0, 9.7)	7.9 (6.9, 11.3)
Treatment ongoing, %	50	65

Grade 3 TRAEs, %	Overall (n=42)	Overall GI cancers (n=30)
Any	21	27
Fatigue	7	10
QT prolongation	5	7
Nausea	2	3
AST increased	2	3
Anemia	2	3
ALT increased	2	3

Conclusions

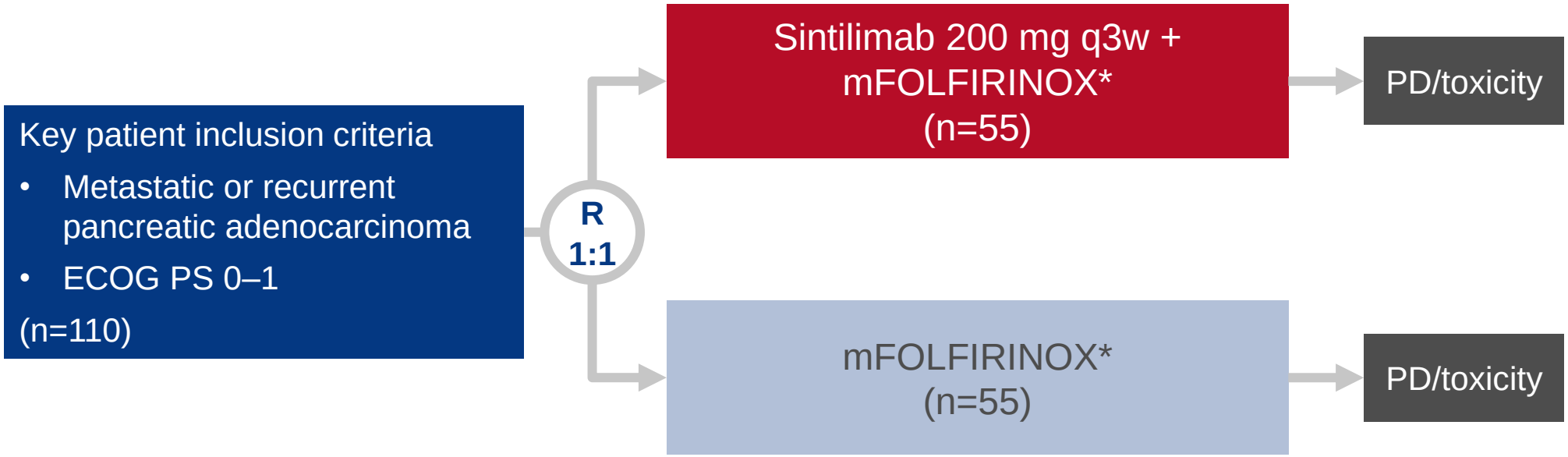
- **In previously treated patients with PDAC or other GI cancers harboring KRAS G12C mutation, adagrasib showed promising clinical activity and was generally well-tolerated**

Bekaii-Saab TS, et al. J Clin Oncol 2022;40(suppl):abstr 519

560: Randomized phase III study of sintilimab in combination with modified FOLFIRINOX versus FOLFRINOX alone in patients with metastatic and recurrent pancreatic cancer in China: The CSIPD3 trial – Fu Q, et al

Study objective

- To evaluate the efficacy and safety of sintilimab combined mFOLFIRINOX in patients with metastatic and recurrent pancreatic cancer in Chinese centers in the CSIPD3 study



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR, DCR, safety

*Irinotecan 85 mg/m^2 + oxaliplatin 68 mg/m^2 followed by 5FU 2400 mg/m^2 q2w

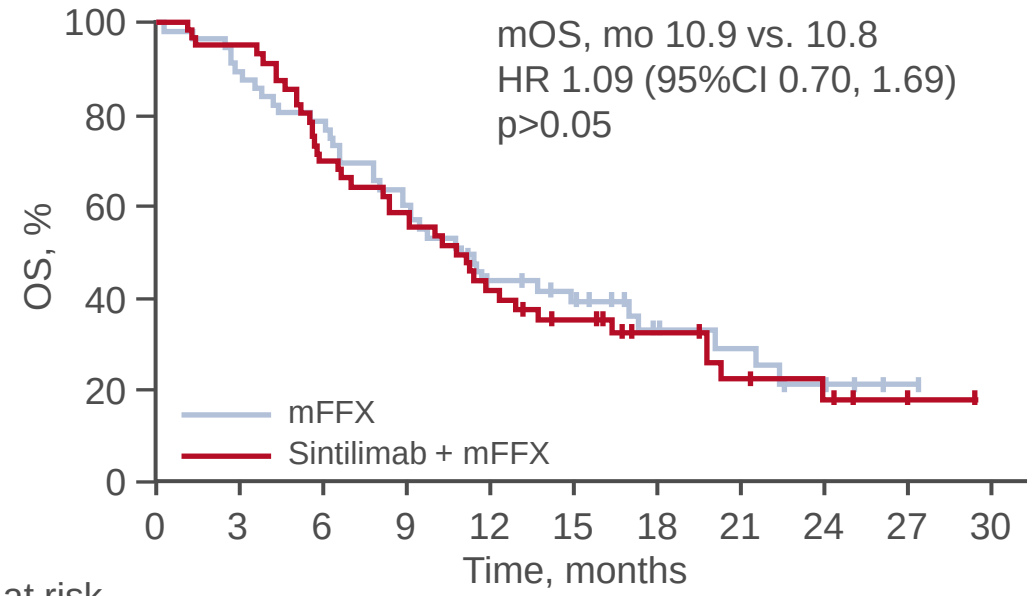
Presented by Tingbo Liang

Fu Q, et al. J Clin Oncol 2022;40(suppl):abstr 560

560: Randomized phase III study of sintilimab in combination with modified FOLFIRINOX versus FOLFRINOX alone in patients with metastatic and recurrent pancreatic cancer in China: The CSIPD3 trial – Fu Q, et al

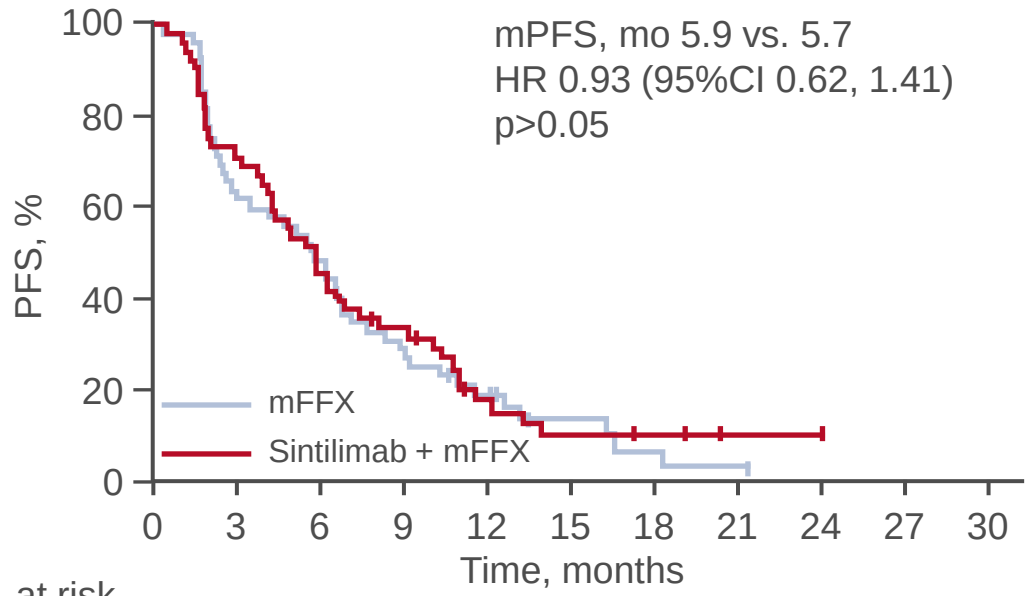
Key results

Overall survival



No. at risk											
Sintilimab + mFFX	55	53	39	32	22	16	11	7	5	2	0
mFFX	55	50	44	35	22	18	11	8	4	2	0

Progression-free survival



No. at risk											
Sintilimab + mFFX	52	38	26	17	8	5	4	2	2	0	0
mFFX	53	33	26	16	10	5	3	2	1	0	0

Fu Q, et al. J Clin Oncol 2022;40(suppl):abstr 560

560: Randomized phase III study of sintilimab in combination with modified FOLFIRINOX versus FOLFRINOX alone in patients with metastatic and recurrent pancreatic cancer in China: The CSIPD3 trial – Fu Q, et al

Key results (cont.)

	Sintilimab + mFOLFIRINOX (n=55)	mFOLFIRINOX (n=55)	p-value
ORR, %	50	23.9	<0.05
BOR, %			
CR	1	0	
PR	21	11	
SD	15	22	
PD	7	13	
NE	11	9	
DCR, %	84.0	71.7	>0.05
mDoR, mo	7.85	4.63	>0.05

AEs, n (%)	Sintilimab + mFOLFIRINOX (n=53)	mFOLFIRINOX (n=54)
TEAE		
Grade ≥3	45 (84.9)	40 (74.1)
Neutropenia	31 (58.5)	24 (44.4)
Thrombocytopenia	9 (17.0)	6 (11.1)
Anemia	7 (13.2)	7 (13.0)
Vomiting	7 (13.2)	6 (11.1)
Aminotransferase increased	6 (11.3)	3 (5.6)
Immune-mediated		
Grade ≥3	3 (5.7)	-
Pulmonary	3 (5.7)	-

Conclusions

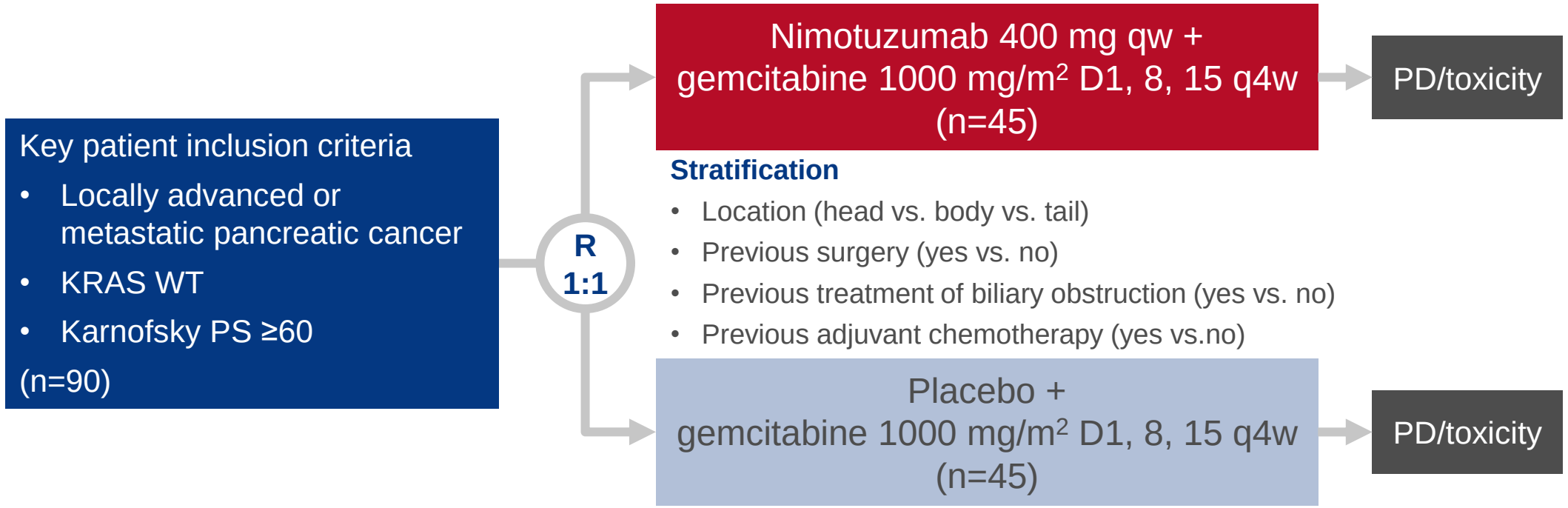
- **In patients with metastatic and recurrent pancreatic cancer, sintilimab combined with mFOLFIRINOX demonstrated significant improvement in ORR, but not OS or PFS, and had a manageable safety profile**

Fu Q, et al. J Clin Oncol 2022;40(suppl):abstr 560

LBA4011: Nimotuzumab combined with gemcitabine versus gemcitabine in K-RAS wild-type locally advanced or metastatic pancreatic cancer: A prospective, randomized-controlled, double-blinded, multicenter, and phase III clinical trial – Qin S, et al

Study objective

- To evaluate the efficacy and safety of nimotuzumab + gemcitabine in patients with KRAS WT locally advanced or metastatic pancreatic cancer in Chinese centers in the phase 3 NOTABLE study



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, TTP, ORR, DCR, CBR, safety

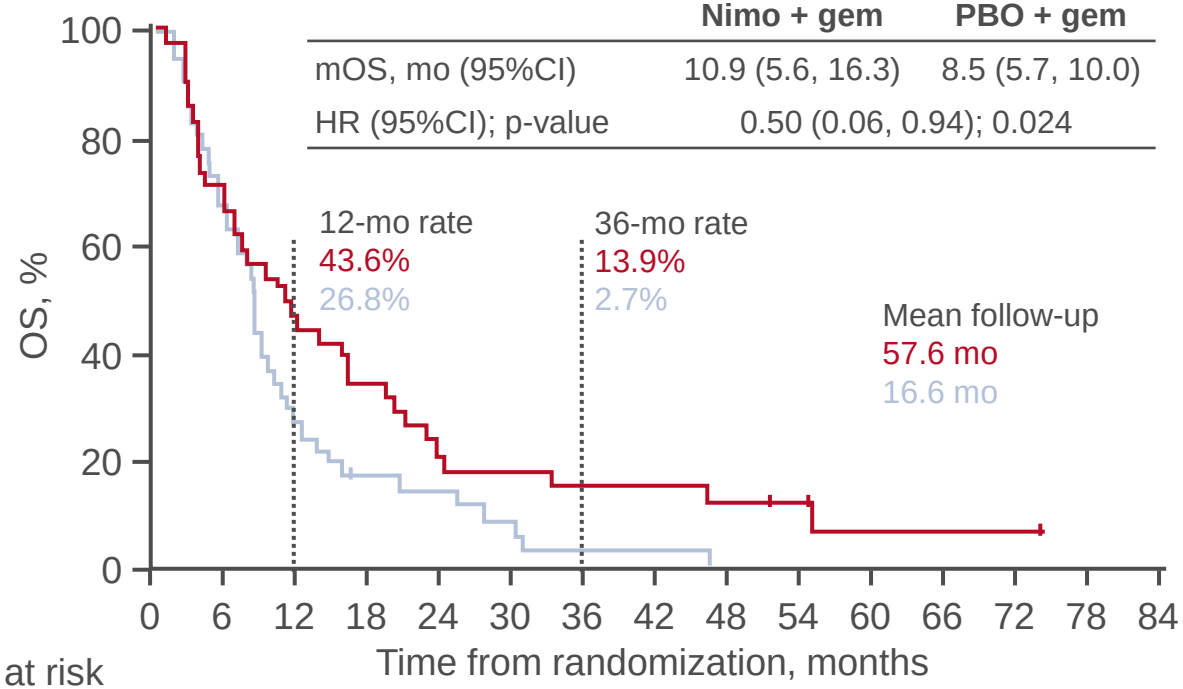
Qin S, et al. J Clin Oncol 2022;40(suppl):abstr LBA4011

LBA4011: Nimotuzumab combined with gemcitabine versus gemcitabine in K-RAS wild-type locally advanced or metastatic pancreatic cancer: A prospective, randomized-controlled, double-blinded, multicenter, and phase III clinical trial – Qin S, et al

Key results

Overall survival

	Nimo + gem	PBO + gem
mOS, mo (95%CI)	10.9 (5.6, 16.3)	8.5 (5.7, 10.0)
HR (95%CI); p-value	0.50 (0.06, 0.94); 0.024	

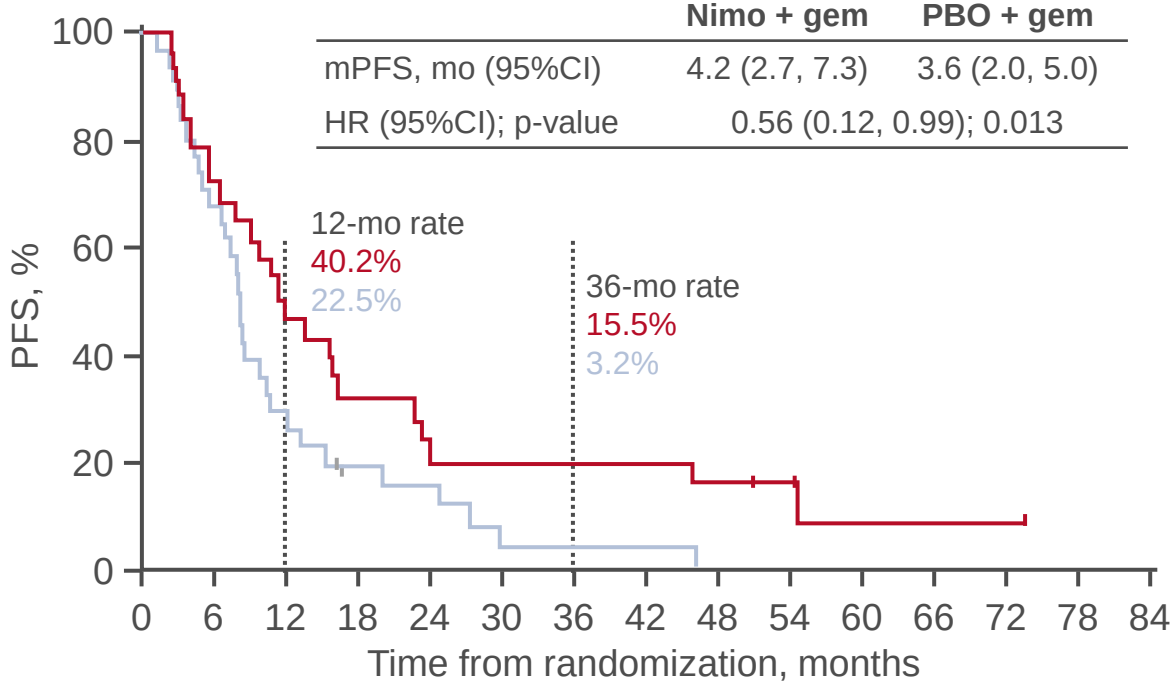


No. at risk

Nimo + gem	41	27	17	13	7	6	5	5	4	3	1	1	1	0
PBO + gem	41	27	11	6	5	3	1	1	0					

Progression-free survival

	Nimo + gem	PBO + gem
mPFS, mo (95%CI)	4.2 (2.7, 7.3)	3.6 (2.0, 5.0)
HR (95%CI); p-value	0.56 (0.12, 0.99); 0.013	



Nimo + gem	28	20	12	8	6	5	5	5	4	3	1	1	1	0
PBO + gem	31	21	9	5	4	2	1	1	0					

Qin S, et al. J Clin Oncol 2022;40(suppl):abstr LBA4011

LBA4011: Nimotuzumab combined with gemcitabine versus gemcitabine in K-RAS wild-type locally advanced or metastatic pancreatic cancer: A prospective, randomized-controlled, double-blinded, multicenter, and phase III clinical trial – Qin S, et al

Key results

	Nimotuzumab + gemcitabine	Placebo + gemcitabine	p-value
ORR, %	7.3	9.8	>0.05
BOR, %			
CR	0	0	
PR	3	4	
SD	26	22	
PD	9	14	
NE	3	1	
DCR, %	68.3	63.4	0.641
CBR, %	39.3	32.3	0.573
mTTP, mo (95%CI)	4.7 (2.7, 9.0)	3.7 (2.0, 5.4)	>0.05
HR (95%CI); p-value	0.67 (0.39, 1.15); 0.137		

AEs, n (%)	Nimotuzumab + gemcitabine (n=45)	Placebo + gemcitabine (n=45)	p-value
Any	31 (68.9)	29 (64.4)	0.655
Serious	1 (2.2)	2 (4.4)	>0.999
Led to dose reduction or discontinuation	4 (8.9)	6 (13.3)	0.502
Led to discontinuation	2 (4.4)	2 (4.4)	>0.999
Led to death	0	1 (2.2)	>0.999
Led to withdrawal	2 (4.4)	1 (2.2)	>0.999

Conclusions

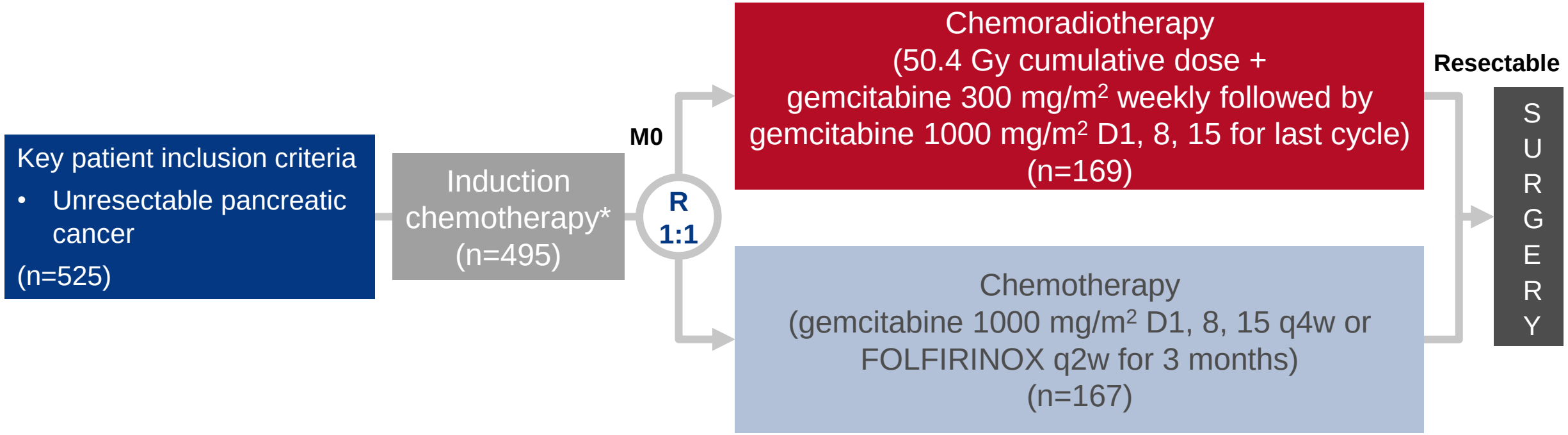
- **In patients with locally advanced or metastatic KRAS WT pancreatic cancer, nimotuzumab + gemcitabine significantly improved survival compared with gemcitabine alone and was generally well-tolerated**

Qin S, et al. J Clin Oncol 2022;40(suppl):abstr LBA4011

4008: Randomized phase III trial of induction chemotherapy followed by chemoradiotherapy or chemotherapy alone for nonresectable locally advanced pancreatic cancer: First results of the CONKO-007 trial – Fietkau R, et al

Study objective

- To evaluate the efficacy and safety of induction chemotherapy followed by chemoradiotherapy in patients with unresectable locally advanced pancreatic cancer in German centers in the CONKO-007 study



PRIMARY ENDPOINT

- R0 resection rate

SECONDARY ENDPOINTS

- OS, DFS, safety

*Gemcitabine 1000 mg/m² D1, 8, 15 q4w (3 cycles) or FOLFIRINOX q2w (6 cycles)

Fietkau R, et al. J Clin Oncol 2022;40(suppl):abstr 4008

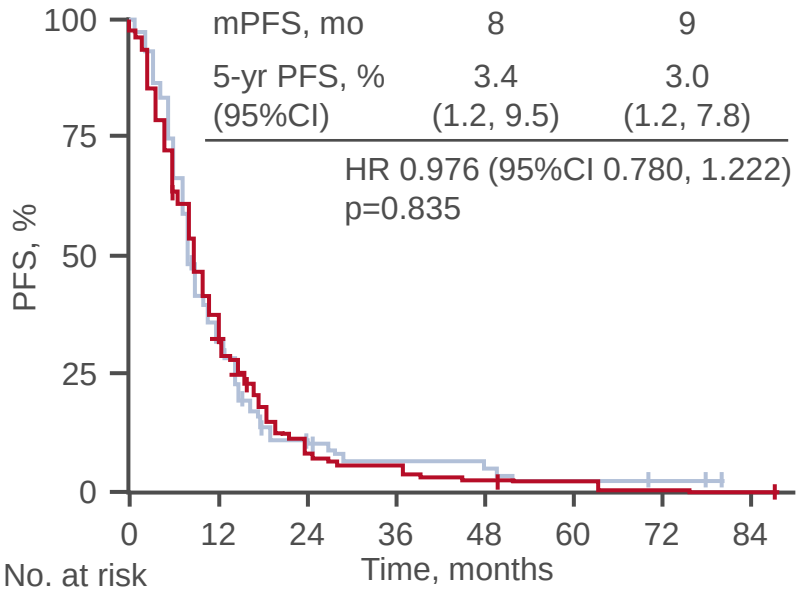
4008: Randomized phase III trial of induction chemotherapy followed by chemoradiotherapy or chemotherapy alone for nonresectable locally advanced pancreatic cancer: First results of the CONKO-007 trial – Fietkau R, et al

Key results

Progression-free survival

	CT (n=167)	CT + CRT (n=169)
mPFS, mo	8	9
5-yr PFS, % (95%CI)	3.4 (1.2, 9.5)	3.0 (1.2, 7.8)

HR 0.976 (95%CI 0.780, 1.222)
p=0.835



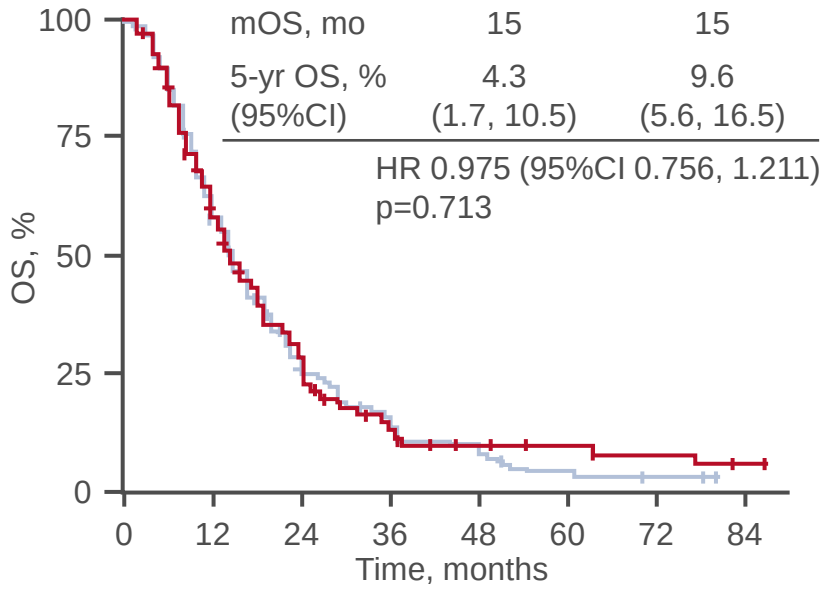
No. at risk (no. censored)

CT	167	57	16	6	6	3	2	0
	(2)	(7)	(11)	(14)	(14)	(14)	(15)	(17)
CT + CRT	169	63	15	9	5	3	2	1
	(0)	(4)	(10)	(10)	(10)	(11)	(11)	(11)

Overall survival

	CT (n=167)	CT + CRT (n=169)
mOS, mo	15	15
5-yr OS, % (95%CI)	4.3 (1.7, 10.5)	9.6 (5.6, 16.5)

HR 0.975 (95%CI 0.756, 1.211)
p=0.713

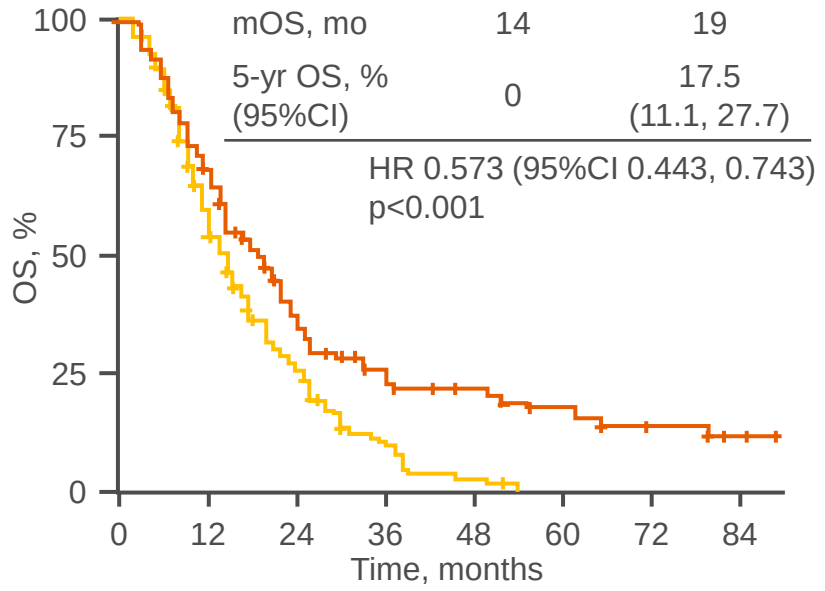


	167	96	38	17	11	4	2	0
	(2)	(11)	(20)	(24)	(24)	(25)	(26)	(28)
	169	105	42	18	8	6	4	2
	(0)	(7)	(18)	(22)	(25)	(27)	(28)	(29)

Overall survival according to surgery

	No surgery (n=214)	Surgery (n=122)
mOS, mo	14	19
5-yr OS, % (95%CI)	0	17.5 (11.1, 27.7)

HR 0.573 (95%CI 0.443, 0.743)
p<0.001



No surgery	214	117	44	14	4	0	0	0
	(2)	(16)	(24)	(28)	(28)	(29)	(29)	(29)
Surgery	122	86	36	21	15	10	6	2
	(0)	(2)	(14)	(18)	(21)	(23)	(25)	(28)

Fietkau R, et al. J Clin Oncol 2022;40(suppl):abstr 4008

4008: Randomized phase III trial of induction chemotherapy followed by chemoradiotherapy or chemotherapy alone for nonresectable locally advanced pancreatic cancer: First results of the CONKO-007 trial – Fietkau R, et al

Key results

	CRM- (n=44)	CRM+ (n=38)	R0 (n=73)	R1 (n=21)	Rx (n=242)	Not randomized (n=159)
mOS, mo	36	18	26	17	16	9
5-yr OS, % (95%CI)	35.9 (22.6, 57.0)	9.0 (2.6, 31.7)	27.3 (17.4, 42.8)	8.0 (1.4, 45.0)	0	0
HR (95%CI); p-value						
vs CRM+ or R1	2.29 (1.36, 3.88); 0.002		2.16 (1.25, 3.72); 0.006			
vs Rx	3.12 (2.03, 4.77); <0.001	1.36 (0.93, 1.99); 0.117	2.49 (1.79, 3.46); <0.001	1.15 (0.71, 1.87); 0.563		
vs not randomized	5.20 (3.35, 8.06); <0.001		4.16 (2.94, 5.89); <0.001			

Conclusions

- **In patients with unresectable locally advanced pancreatic cancer, chemoradiotherapy after induction chemotherapy demonstrated significant improvement in R0 resection rate in the surgically treated group, but not in all randomized patients, compared with chemotherapy**

Fietkau R, et al. J Clin Oncol 2022;40(suppl):abstr 4008

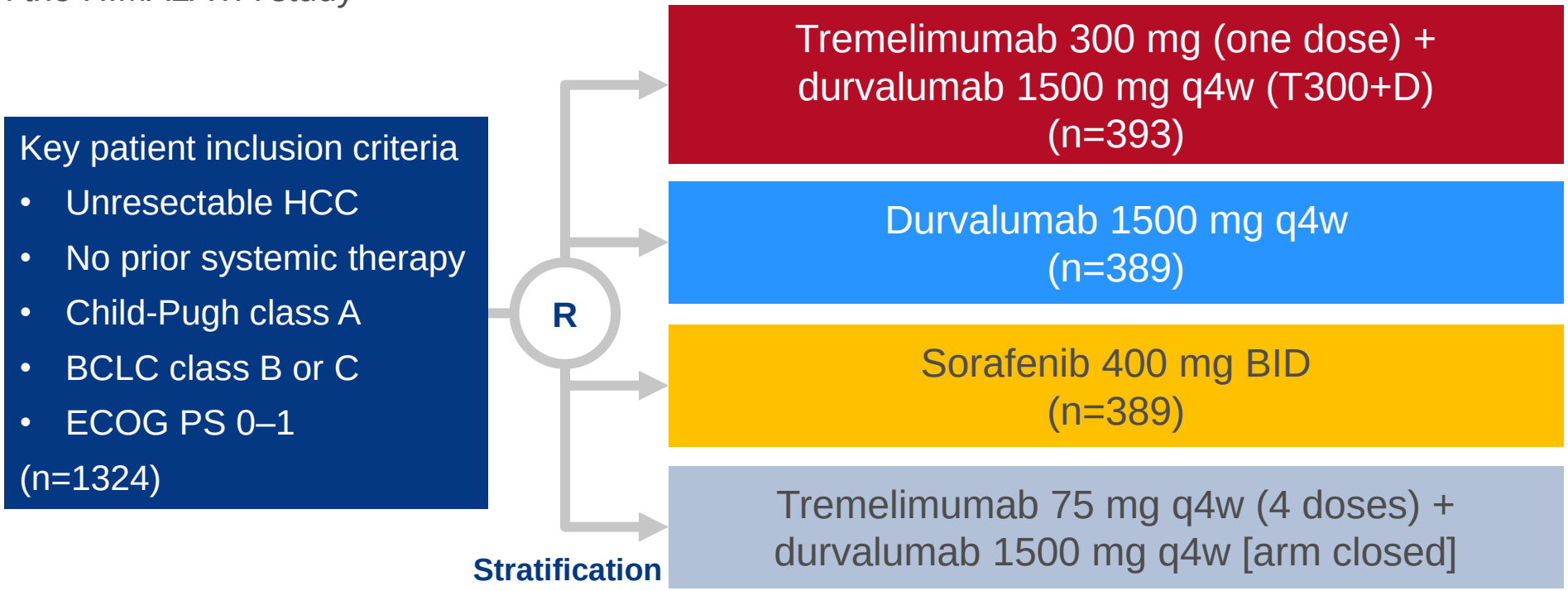
Cancers of the pancreas, small bowel and hepatobiliary tract

HEPATOCELLULAR CARCINOMA

379: Phase 3 randomized, open-label, multicenter study of tremelimumab (T) and durvalumab (D) as first-line therapy in patients (pts) with unresectable hepatocellular carcinoma (uHCC): HIMALAYA – Abou-Alfa GK, et al

Study objective

- To evaluate the efficacy and safety of 1L tremelimumab + durvalumab or durvalumab alone in patients with unresectable HCC in the HIMALAYA study



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR, DoR, safety

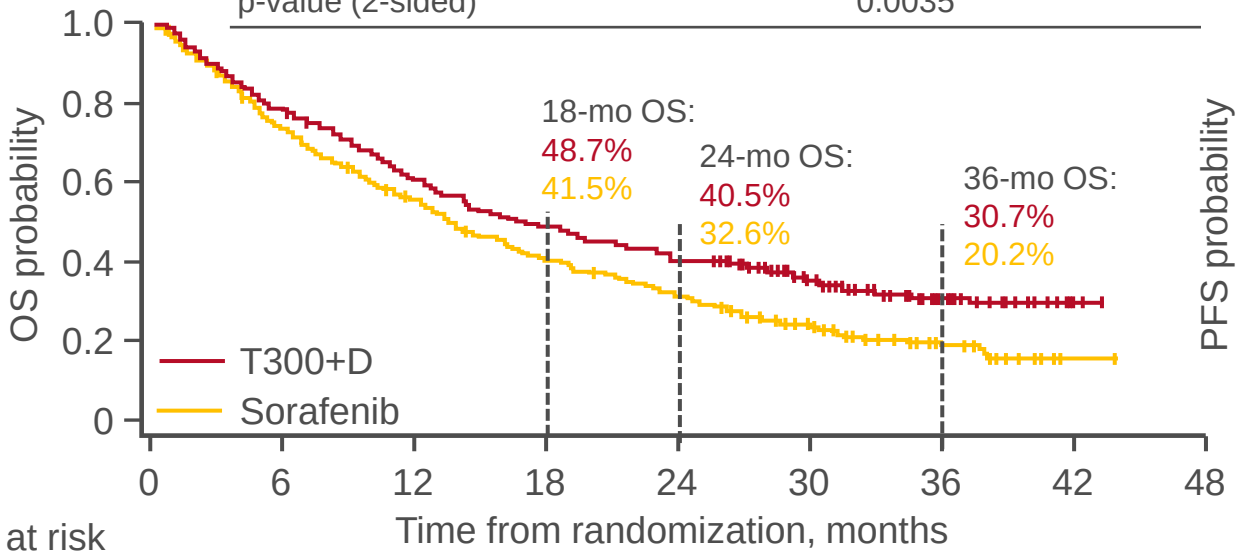
Abou-Alfa GK, et al. J Clin Oncol 2022;40(suppl):abstr 379

379: Phase 3 randomized, open-label, multicenter study of tremelimumab (T) and durvalumab (D) as first-line therapy in patients (pts) with unresectable hepatocellular carcinoma (uHCC): HIMALAYA – Abou-Alfa GK, et al

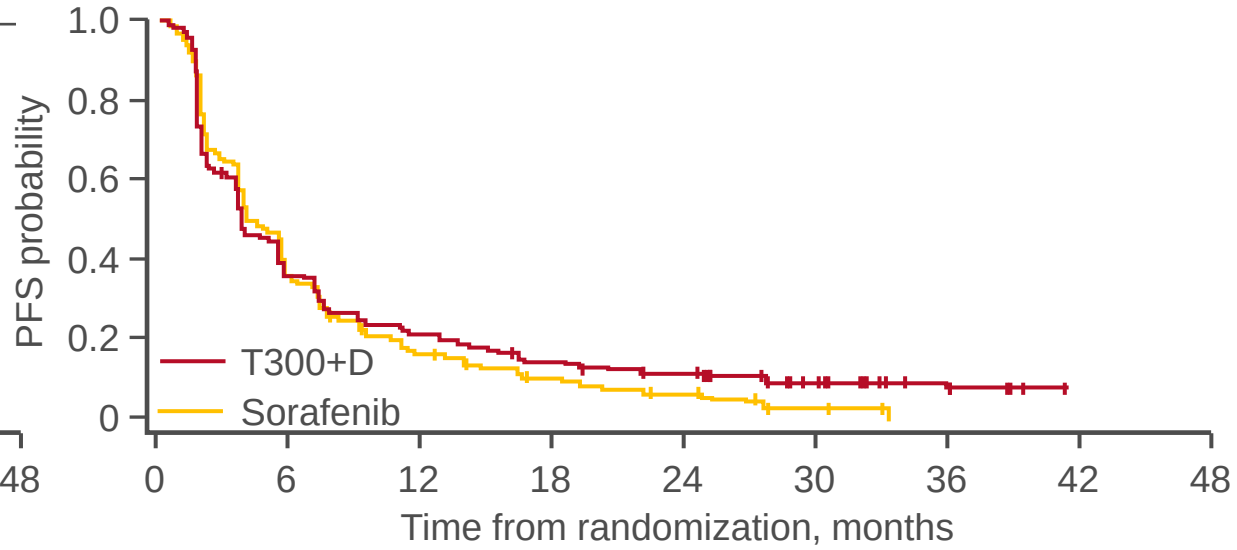
Key results

OS for T300+D vs. sorafenib

	T300+D (n=393)	Sorafenib (n=389)
OS events, n (%)	262 (66.7)	293 (75.3)
mOS, mo (95%CI)	16.4 (14.2, 19.6)	13.8 (12.3, 16.1)
HR (96.02%CI)	0.78 (0.65, 0.92)	
p-value (2-sided)	0.0035	



PFS for T300+D vs. sorafenib



No. at risk

T300+D	393	308	235	190	158	98	32	1	0	393	135	81	55	43	26	7	0	0
Sorafenib	389	283	211	155	121	62	21	1	0	389	118	53	31	18	6	0	0	0

Abou-Alfa GK, et al. J Clin Oncol 2022;40(suppl):abstr 379

379: Phase 3 randomized, open-label, multicenter study of tremelimumab (T) and durvalumab (D) as first-line therapy in patients (pts) with unresectable hepatocellular carcinoma (uHCC): HIMALAYA – Abou-Alfa GK, et al

Key results (cont.)

	T300+D (n=393)	Durvalumab (n=389)	Sorafenib (n=389)
ORR, n (%)	79 (20.1)	66 (17.0)	20 (5.1)
BOR, n (%)			
CR	12 (3.1)	6 (1.5)	0
PR	67 (17.0)	60 (15.4)	20 (5.1)
SD	157 (39.9)	147 (37.8)	216 (55.5)
PD	157 (39.9)	176 (45.2)	153 (39.3)
DCR, %	60.1	54.8	60.7
mDoR, mo (25th, 75th percentile)	22.34 (8.54, NR)	16.82 (7.43, NR)	18.43 (6.51, 25.99)
mTTR, mo (95%CI)	2.17 (1.84, 3.98)	2.09 (1.87, 3.98)	3.78 (1.89, 8.44)
mOS, mo (95%CI)		16.6 (14.1, 19.1)	13.8 (12.3, 16.1)
HR (95.67%CI)		0.86 (0.73, 1.03)	

TRAEs, n (%)	T300+D (n=388)	Durvalumab (n=388)	Sorafenib (n=374)
Any	294 (75.8)	202 (52.1)	317 (84.8)
Grade 3–4	100 (25.8)	50 (12.9)	138 (36.9)
Serious	68 (17.5)	32 (8.2)	35 (9.4)
Led to discontinuation	32 (8.2)	16 (4.1)	41 (11.0)
Led to death	9 (2.3)	0	3 (0.8)

Conclusions

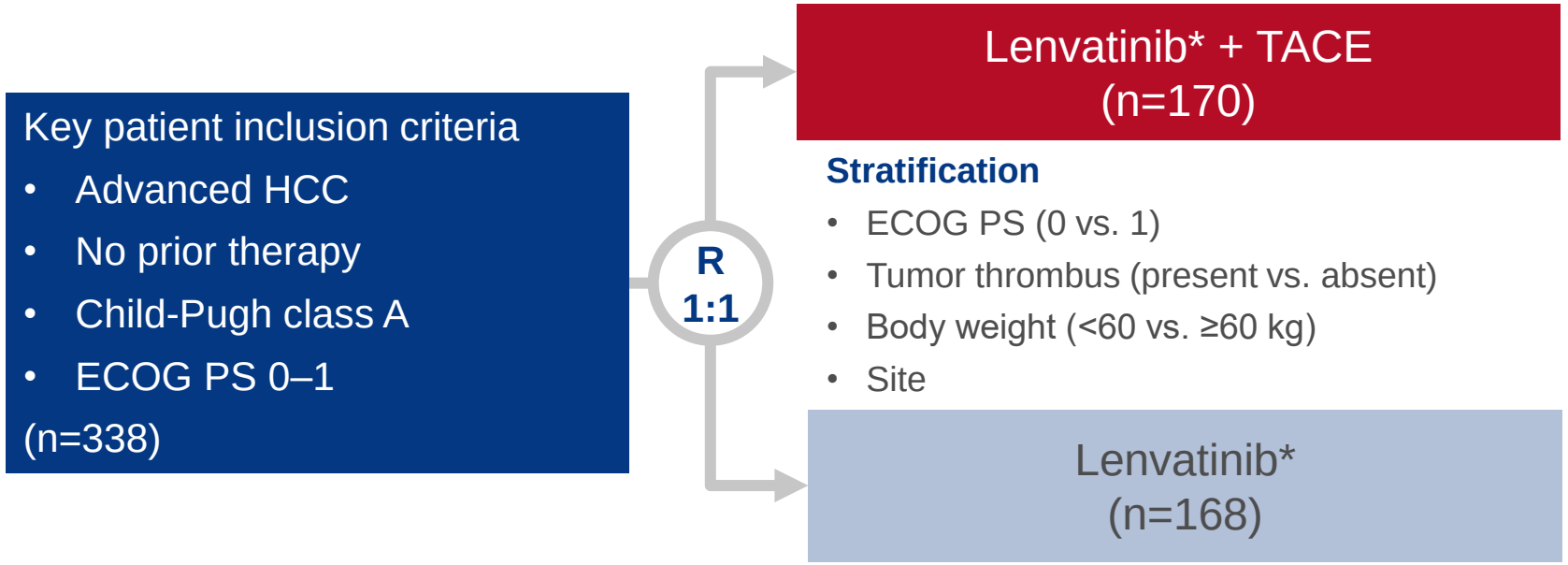
- **In treatment-naïve patients with unresectable HCC, tremelimumab (priming dose) + durvalumab demonstrated a significant improvement in OS compared with sorafenib and had a manageable safety profile**

Abou-Alfa GK, et al. J Clin Oncol 2022;40(suppl):abstr 379

380: Lenvatinib combined with transarterial chemoembolization as first-line treatment of advanced hepatocellular carcinoma: A phase 3, multicenter, randomized controlled trial – Peng Z, et al

Study objective

- To evaluate the efficacy and safety of 1L lenvatinib combined with TACE in patients with advanced HCC in the LAUNCH study



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, TTP, ORR, QoL, safety

*Initial dose 12 mg/day for patients weighing ≥60 kg and 8 mg/day for patients weighing <60 kg

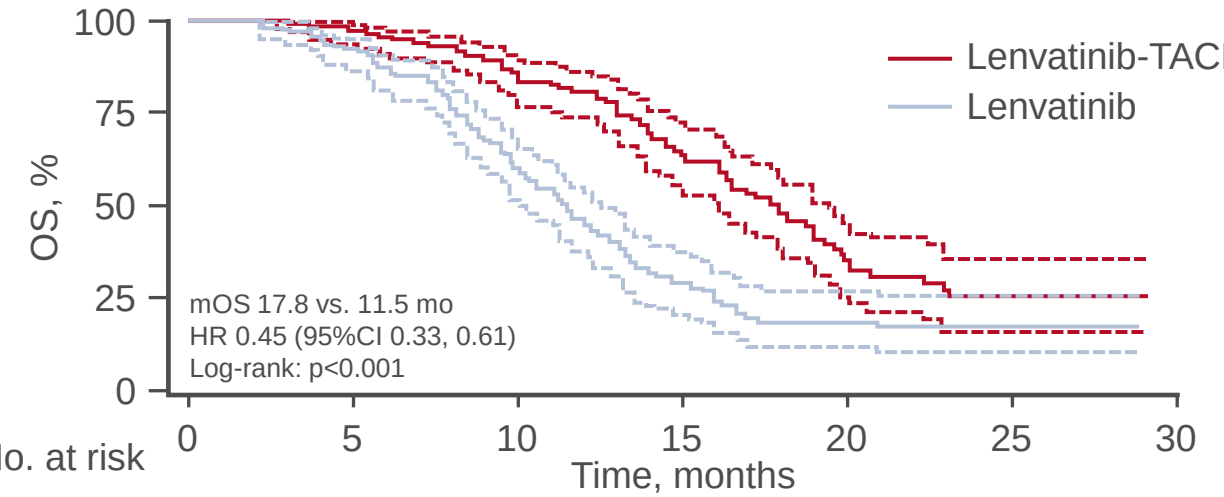
Presented by Ming Kuang

Peng Z, et al. J Clin Oncol 2022;40(suppl):abstr 380

380: Lenvatinib combined with transarterial chemoembolization as first-line treatment of advanced hepatocellular carcinoma: A phase 3, multicenter, randomized controlled trial – Peng Z, et al

Key results

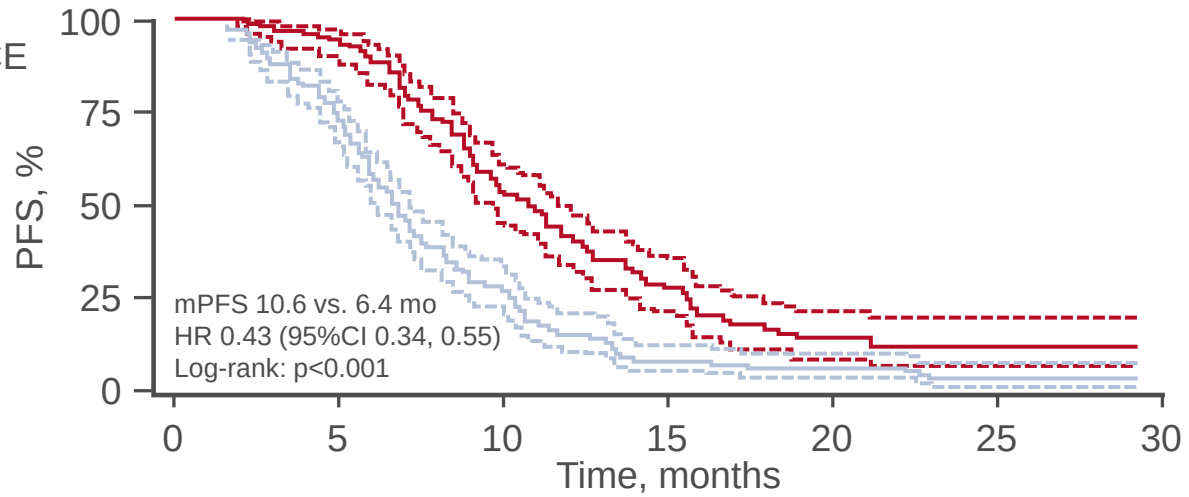
Overall survival



No. at risk

LEN-TACE	170	166	112	65	25	8	0
LEN	168	153	78	28	15	3	0

Progression-free survival



LEN-TACE	170	160	73	32	7	3	0
LEN	168	117	33	8	6	3	0

	No. of events/ No. of pts (%)	mOS, mo (95%CI)	6-mo OS, % (95%CI)	12-mo OS, % (95%CI)	24-mo OS, % (95%CI)
LEN-TACE	75/170 (44.1)	17.8 (16.1, 19.5)	95.9 (91.5, 98.0)	81.5 (74.0, 87.0)	26.1 (16.8, 36.4)
LEN	104/168 (61.9)	11.5 (10.3, 12.7)	87.4 (81.3, 91.6)	46.9 (38.2, 55.0)	17.8 (11.0, 26.0)

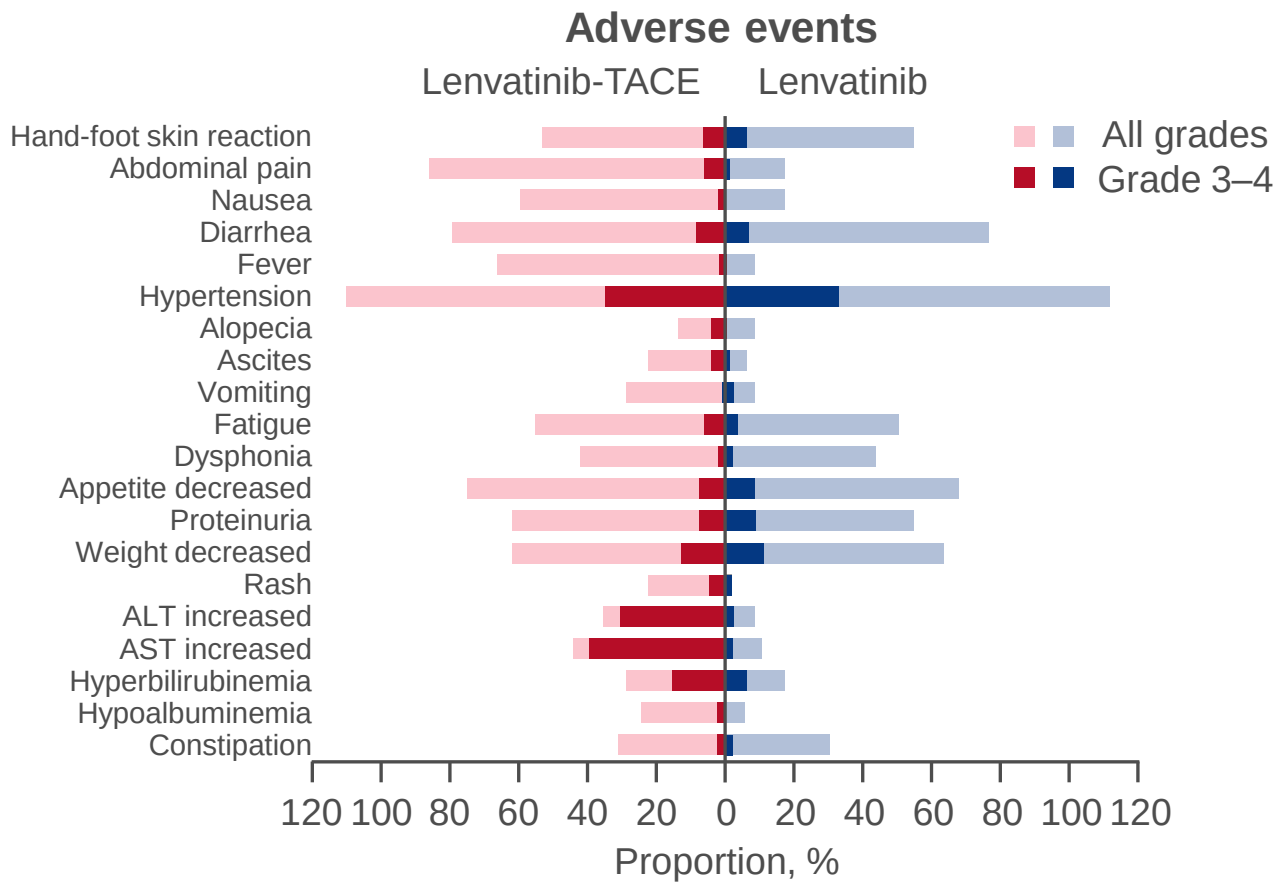
	No. of events/ No. of pts (%)	mPFS, mo (95%CI)	6-mo PFS, % (95%CI)	12-mo PFS, % (95%CI)
LEN-TACE	122/170 (71.8)	10.6 (9.5, 11.7)	88.2 (82.3, 92.2)	39.2 (31.2, 47.0)
LEN	149/168 (88.7)	6.4 (5.8, 7.0)	54.8 (46.9, 61.9)	14.3 (9.1, 20.6)

Peng Z, et al. J Clin Oncol 2022;40(suppl):abstr 380

380: Lenvatinib combined with transarterial chemoembolization as first-line treatment of advanced hepatocellular carcinoma: A phase 3, multicenter, randomized controlled trial – Peng Z, et al

Key results (cont.)

	Lenvatinib + TACE (n=170)	Lenvatinib (n=168)	p-value
ORR, n (%)	78 (45.9)	35 (20.8)	<0.001
BOR, n (%)			
CR	1 (0.6)	1 (0.6)	0.993
PR	77 (45.3)	34 (20.2)	<0.001
SD	79 (46.5)	87 (51.8)	0.328
PD	13 (7.6)	46 (27.4)	<0.001
DCR, n (%)	157 (92.4)	122 (72.6)	<0.001



Conclusions

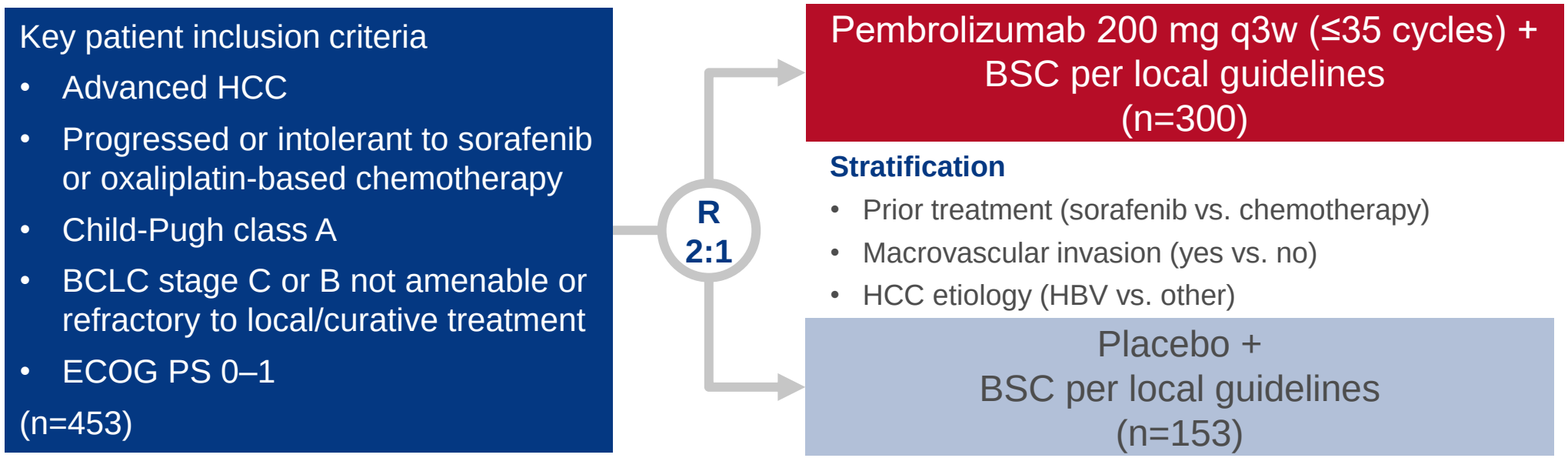
- **In treatment naïve patients with advanced HCC, lenvatinib + TACE was feasible and demonstrated improvements in outcomes as well as an acceptable safety profile**

Peng Z, et al. J Clin Oncol 2022;40(suppl):abstr 380

383: Pembrolizumab plus best supportive care versus placebo plus best supportive care as second-line therapy in patients in Asia with advanced hepatocellular carcinoma (HCC): Phase 3 KEYNOTE-394 study – Qin S, et al

Study objective

- To evaluate the efficacy and safety of pembrolizumab + BSC in patients with advanced HCC in Asian centers in the KEYNOTE-394 study



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR, DoR, DCR, TTP, safety

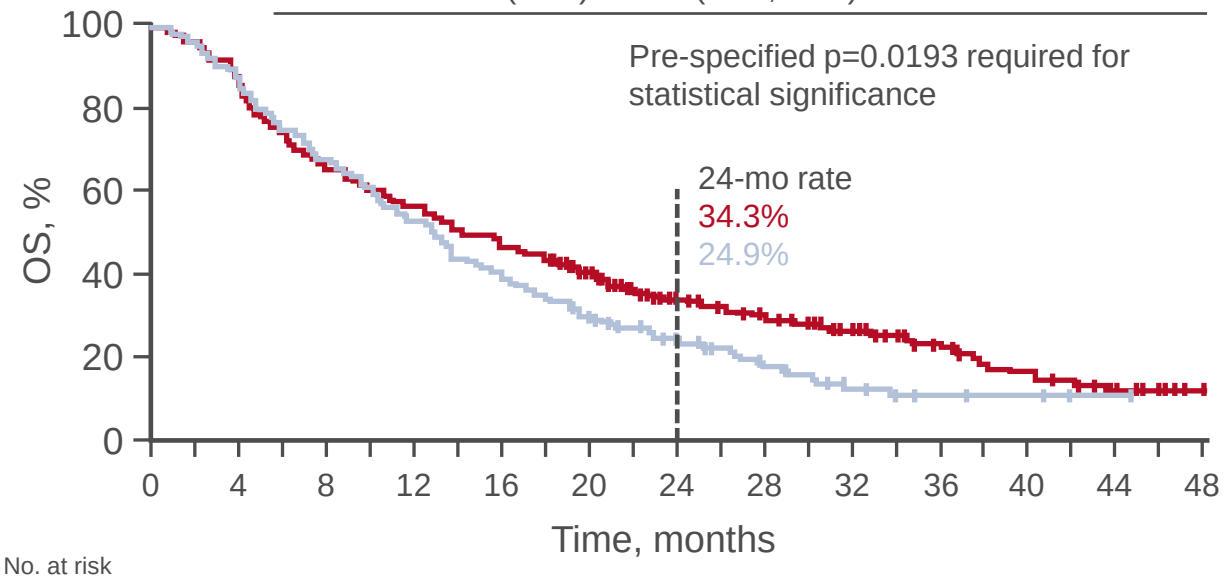
Qin S, et al. J Clin Oncol 2022;40(suppl):abstr 383

383: Pembrolizumab plus best supportive care versus placebo plus best supportive care as second-line therapy in patients in Asia with advanced hepatocellular carcinoma (HCC): Phase 3 KEYNOTE-394 study – Qin S, et al

Key results

Overall survival

	Events, n (%)	mOS, mo (95%CI)	HR (95%CI)	p-value
Pembro	222 (74.0)	14.6 (12.6, 18.0)	0.79 (0.63, 0.99)	0.0180
Placebo	128 (83.7)	13.0 (10.5, 15.1)		

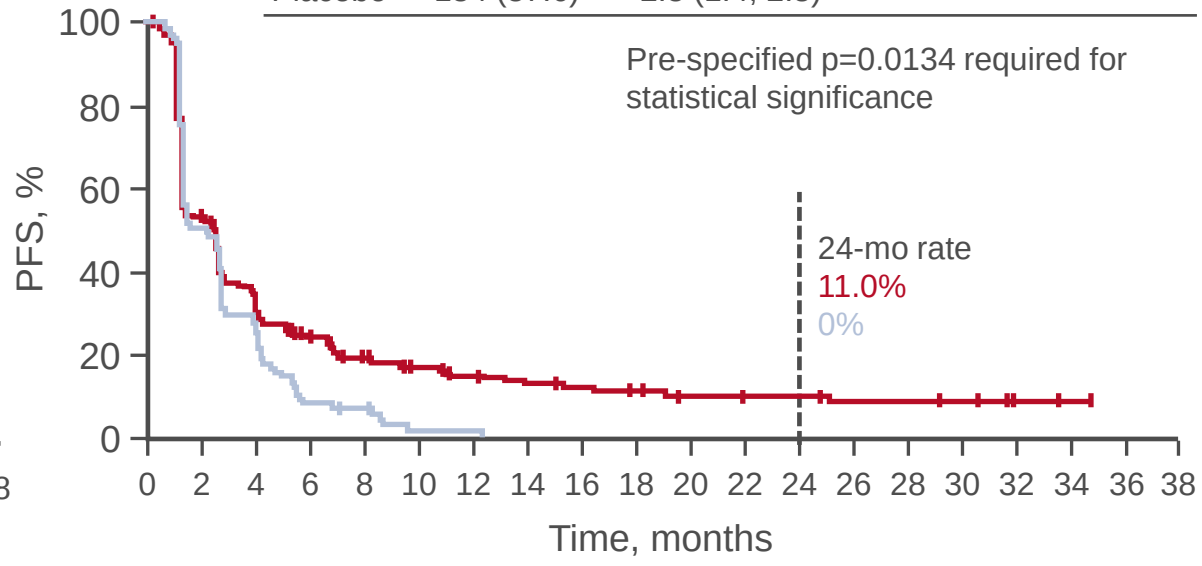


No. at risk

Pembro	300	290	260	225	199	185	171	154	143	134	115	90	78	69	61	53	39	32	24	16	14	11	7	4	0
Placebo	153	148	135	116	104	94	81	67	62	54	44	37	31	25	19	16	9	6	5	3	3	1	1	0	0

Progression-free survival

	Events, n (%)	mPFS, mo (95%CI)	HR (95%CI)	p-value
Pembro	237 (79.0)	2.6 (1.5, 2.8)	0.74 (0.60, 0.92)	0.0032
Placebo	134 (87.6)	2.3 (1.4, 2.8)		



Pembro	300	149	97	62	44	31	26	21	19	16	12	11	11	7	7	6	3	1	0	0
Placebo	153	72	35	8	6	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0

Qin S, et al. J Clin Oncol 2022;40(suppl):abstr 383

383: Pembrolizumab plus best supportive care versus placebo plus best supportive care as second-line therapy in patients in Asia with advanced hepatocellular carcinoma (HCC): Phase 3 KEYNOTE-394 study – Qin S, et al

Key results (cont.)

	Pembrolizumab (n=300)	Placebo (n=153)
ORR, % (95%CI)	12.7 (9.1, 17.0)	1.3 (0.2, 4.6)
BOR, n (%)		
CR	6 (2.0)	1 (0.7)
PR	32 (10.7)	1 (0.7)
SD	115 (38.3)	70 (45.8)
Sustained SD	26 (8.7)	8 (5.2)
PD	129 (43.0)	72 (47.1)
NE	10 (3.3)	1 (0.7)
NA	8 (2.7)	8 (5.2)
mDoR, mo (range)	23.9 (2.8–32.0+)	5.6 (3.0+–5.6)

AEs, n (%)	Pembrolizumab (n=299)	Placebo (n=153)
TRAE	200 (66.9)	76 (49.7)
Grade 3–5	43 (14.4)	9 (5.9)
Led to discontinuation	12 (4.0)	1 (0.7)
Led to death	3 (1.0)	0
Immune-mediated	54 (18.1)	16 (10.5)
Grade 3–5	9 (3.0)	0
Led to discontinuation	5 (1.7)	0
Led to death	1 (0.3)	0
Hepatitis	5 (1.7)	0

Conclusions

- **In previously treated patients with advanced HCC, pembrolizumab + BSC demonstrated significant improvement in outcomes and had a manageable safety profile**

Qin S, et al. J Clin Oncol 2022;40(suppl):abstr 383

Cancers of the pancreas, small bowel and hepatobiliary tract

BILIARY TRACT CANCER

378: A phase 3 randomized, double-blind, placebo-controlled study of durvalumab in combination with gemcitabine plus cisplatin (GemCis) in patients (pts) with advanced biliary tract cancer (BTC): TOPAZ-1 – Oh D-Y, et al

Study objective

- To evaluate the efficacy and safety of durvalumab + gemcitabine + cisplatin in patients with advanced biliary tract cancer in the TOPAZ-1 study

Key patient inclusion criteria

- Locally advanced or metastatic biliary tract cancer
- Treatment naïve if unresectable or metastatic at initial diagnosis
- ECOG PS 0–1

(n=685)

R 1:1

Durvalumab 1500 mg q3w + gemcitabine + cisplatin* (8 cycles) (n=341) → Durvalumab 1500 mg q4w → PD/ toxicity

Placebo + gemcitabine + cisplatin* (8 cycles) (n=344) → Placebo → PD/ toxicity

Stratification

- Disease status (initially unresectable vs. recurrent)
- Primary tumor location (intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, gallbladder cancer)

PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR, DoR, safety

*Gemcitabine 1000 mg/m^2 + cisplatin 25 mg/m^2 D1, 8 q3w

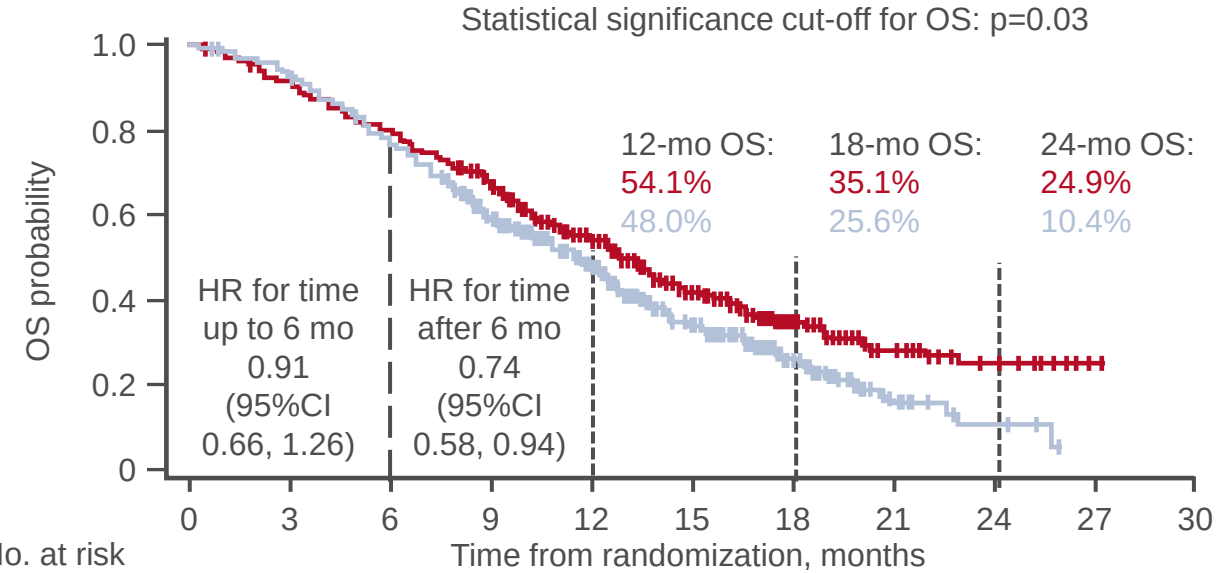
Oh D-Y, et al. J Clin Oncol 2022;40(suppl):abstr 378

378: A phase 3 randomized, double-blind, placebo-controlled study of durvalumab in combination with gemcitabine plus cisplatin (GemCis) in patients (pts) with advanced biliary tract cancer (BTC): TOPAZ-1 – Oh D-Y, et al

Key results

Overall survival

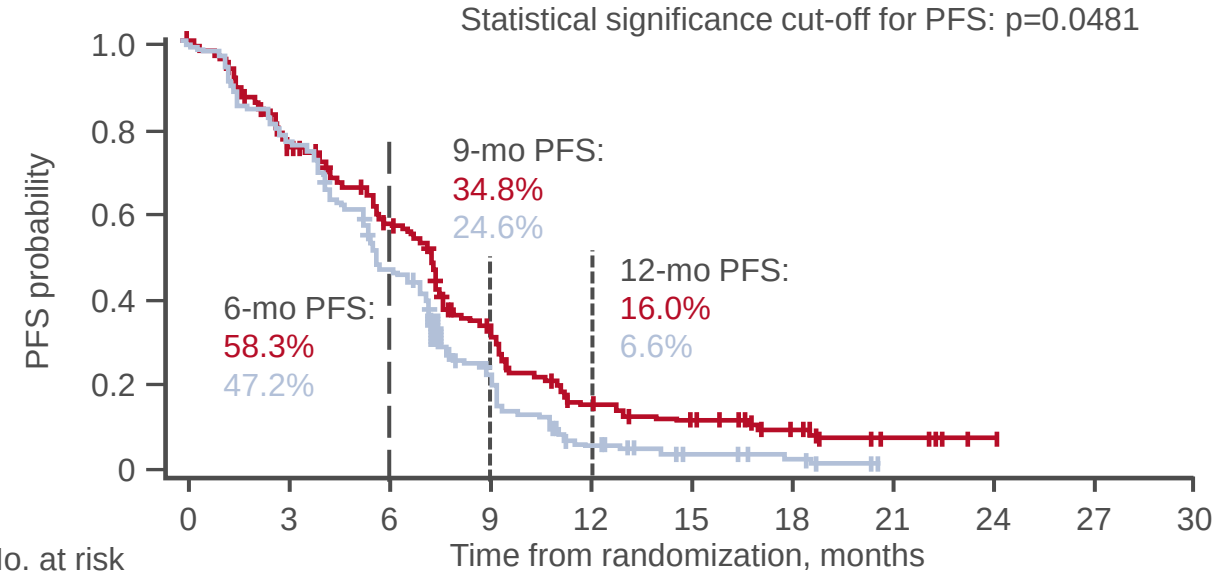
	mOS, mo (95%CI)	HR (95%CI)	p-value
Durvalumab + GemCis (n=341)	12.8 (11.1, 14.0)	0.80 (0.66, 0.97)	0.021
Placebo + GemCis (n=344)	11.5 (10.1, 12.5)		



No. at risk										
Durv + GemCis	341	309	268	208	135	79	49	24	9	1
Placebo + GemCis	344	317	261	183	125	65	29	10	4	0

Progression-free survival

	mPFS, mo (95%CI)	HR (95%CI)	p-value
Durvalumab + GemCis (n=341)	7.2 (6.7, 7.4)	0.75 (0.63, 0.89)	0.001
Placebo + GemCis (n=344)	5.7 (5.6, 6.7)		



No. at risk										
Durv + GemCis	341	258	189	100	38	25	15	5	0	
Placebo + GemCis	344	255	149	71	17	7	4	0	0	

Oh D-Y, et al. J Clin Oncol 2022;40(suppl):abstr 378

378: A phase 3 randomized, double-blind, placebo-controlled study of durvalumab in combination with gemcitabine plus cisplatin (GemCis) in patients (pts) with advanced biliary tract cancer (BTC): TOPAZ-1 – Oh D-Y, et al

Key results (cont.)

	Durvalumab + GemCis (n=341)	Placebo + GemCis (n=343)
ORR, n (%)	91 (26.7)	64 (18.7)
OR (95%CI); p-value	1.60 (1.11, 2.31); 0.011	
BOR, n (%)		
CR	7 (2.1)	2 (0.6)
PR	84 (24.6)	62 (18.1)
DCR, n (%)	291 (85.3)	274 (82.6)
	n=91	n=64
mDoR, mo (1, 3 quartile)	6.4 (4.6, 17.2)	6.2 (3.8, 9.0)
mTTR, mo (1, 3 quartile)	1.6 (1.3, 3.0)	2.7 (1.4, 4.1)

TRAEs, n (%)	Durvalumab + GemCis (n=338)	Placebo + GemCis (n=342)
Any	314 (92.9)	308 (90.1)
Grade 3–4	212 (62.7)	222 (64.9)
Serious	53 (15.7)	59 (17.3)
Led to discontinuation	30 (8.9)	39 (11.4)
Led to death	2 (0.6)	1 (0.3)

Conclusions

- **In patients with advanced biliary tract cancer, 1L durvalumab + gemcitabine + cisplatin demonstrated a significant improvement in survival compared with gemcitabine + cisplatin with an acceptable safety profile**

Oh D-Y, et al. J Clin Oncol 2022;40(suppl):abstr 378

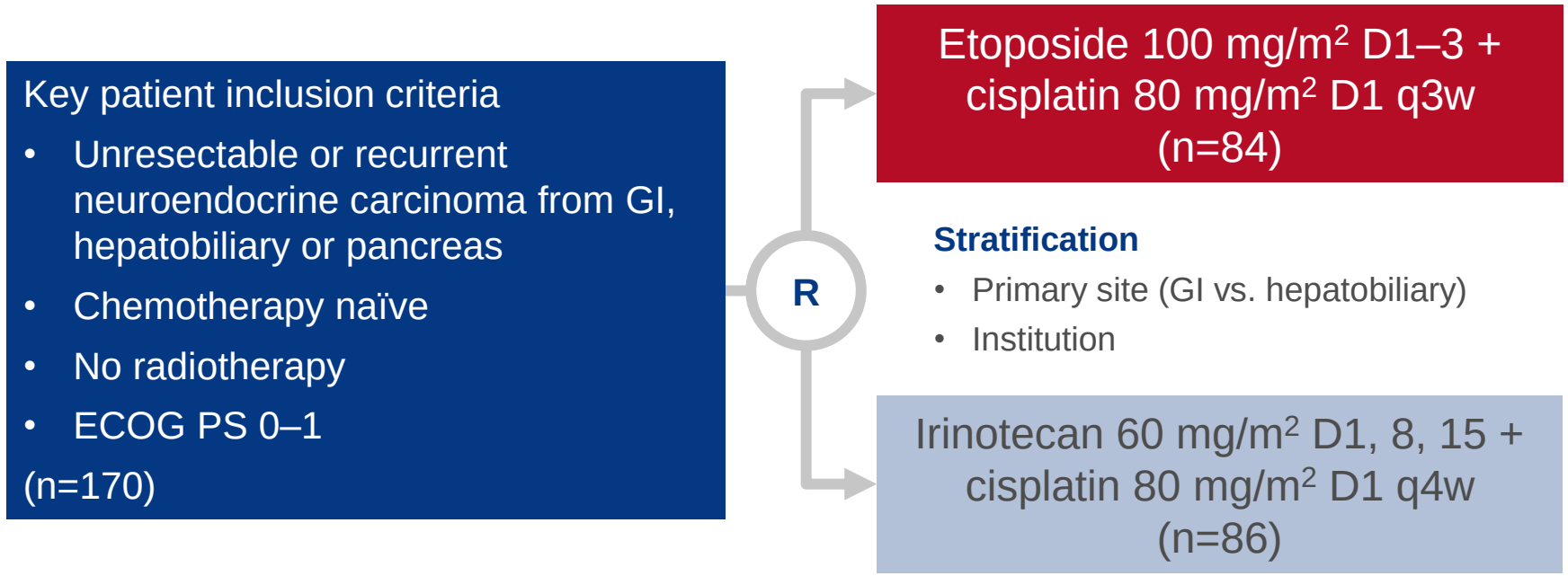
Cancers of the pancreas, small bowel and hepatobiliary tract

NEUROENDOCRINE TUMOUR

501: Randomized phase III study of etoposide plus cisplatin versus irinotecan plus cisplatin in advanced neuroendocrine carcinoma of the digestive system: A Japan Clinical Oncology Group study (JCOG1213) – Morizane C, et al

Study objective

- To evaluate the efficacy and safety of etoposide + cisplatin vs. irinotecan + cisplatin in patients with neuroendocrine carcinoma of the digestive system in Japanese centers in the JCOG1213 study



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, RR, safety

Morizane C, et al. J Clin Oncol 2022;40(suppl):abstr 501

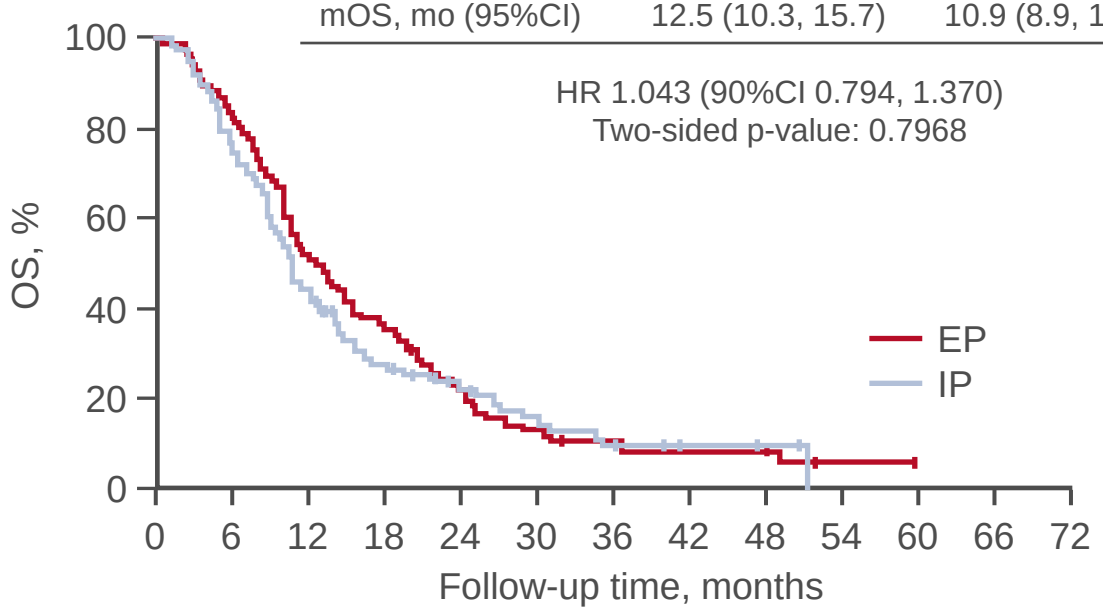
501: Randomized phase III study of etoposide plus cisplatin versus irinotecan plus cisplatin in advanced neuroendocrine carcinoma of the digestive system: A Japan Clinical Oncology Group study (JCOG1213) – Morizane C, et al

Key results

Overall survival

	EP (n=84)	IP (n=86)
1-yr OS, % (95%CI)	52.1 (40.1, 62.8)	41.8 (30.8, 52.3)
mOS, mo (95%CI)	12.5 (10.3, 15.7)	10.9 (8.9, 13.1)

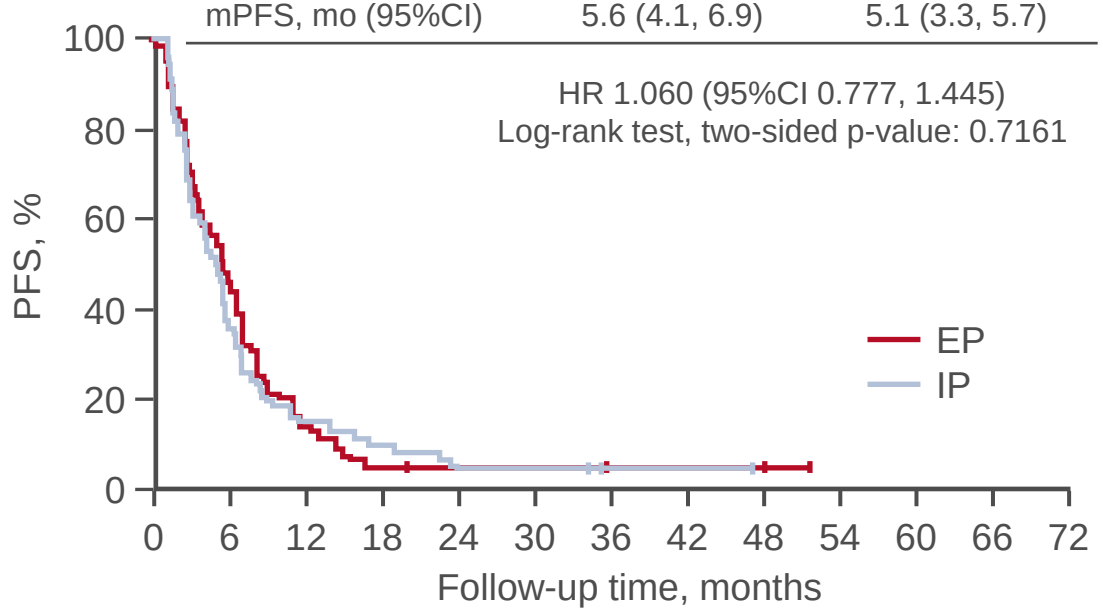
HR 1.043 (90%CI 0.794, 1.370)
Two-sided p-value: 0.7968



Progression-free survival

	EP (n=84)	IP (n=86)
1-yr PFS, % (95%CI)	14.3 (7.8, 22.6)	15.1 (8.5, 23.5)
mPFS, mo (95%CI)	5.6 (4.1, 6.9)	5.1 (3.3, 5.7)

HR 1.060 (95%CI 0.777, 1.445)
Log-rank test, two-sided p-value: 0.7161



Morizane C, et al. J Clin Oncol 2022;40(suppl):abstr 501

501: Randomized phase III study of etoposide plus cisplatin versus irinotecan plus cisplatin in advanced neuroendocrine carcinoma of the digestive system: A Japan Clinical Oncology Group study (JCOG1213) – Morizane C, et al

Key results (cont.)

	Etoposide + cisplatin (n=77)	Irinotecan + cisplatin (n=80)
ORR, % (95%CI)	54.5 (42.8, 65.9)	52.5 (41.0, 63.8)
BOR, n (%)		
CR	0	1 (1.3)
PR	42 (54.5)	41 (51.3)
SD	24 (31.2)	25 (31.3)
PD	10 (13.0)	12 (15.0)
NE	1 (1.3)	1 (1.3)

Grade 3–4 AEs occurring in ≥10%, %	Etoposide + cisplatin (n=82)	Irinotecan + cisplatin (n=82)
Neutrophil count decreased	91.5	53.7
WBC count decreased	61.0	30.5
Febrile neutropenia	26.8	12.2
Anemia	25.6	17.1
Anorexia	13.4	15.9
ALT increased	13.4	9.8
Hyponatremia	13.4	8.5
Platelet count decreased	12.2	3.7
Fatigue	11.0	8.5

Conclusions

- **In patients with advanced neuroendocrine carcinoma of the digestive system, neither of the regimens could prove superiority. Both cisplatin-etoposide or cisplatin-irinotecan combinations remain the standard 1L chemotherapy options**

Morizane C, et al. J Clin Oncol 2022;40(suppl):abstr 501

4005: NET-02: A multicenter, randomized, phase II trial of liposomal irinotecan (nal-IRI) and 5-fluorouracil (5-FU)/folinic acid or docetaxel as second-line therapy in patients (pts) with progressive poorly differentiated extra-pulmonary neuroendocrine carcinoma (PD-EP-NEC) – McNamara MG, et al

Study objective

- To evaluate the efficacy and safety of 2L liposomal irinotecan (nal-IRI) + 5FU or docetaxel in patients with progressive poorly differentiated extra-pulmonary neuroendocrine carcinoma in UK centers in the phase 2 NET-02 study

Key patient inclusion criteria

- Poorly differentiated extra-pulmonary neuroendocrine carcinoma
- Disease progression or discontinuation due to intolerance of prior 1L platinum-based chemotherapy
- Ki67 >20%
- ECOG PS 0–2

(n=58)

R 1:1

Arm A
nal-IRI 70 mg/m^2 + 5FU 2400 mg/m^2 + folinic acid q2w
(n=29)

→ PD/ toxicity

Stratification

- Site
- Ki67 (<55% vs. ≥55%)
- ECOG PS (0/1 vs. 2)
- Presence of liver metastases (yes vs. no)
- Response to prior platinum-based therapy

Arm B
Docetaxel 75 mg/m^2 q3w
(n=29)

→ PD/ toxicity

PRIMARY ENDPOINT

- 6-month PFS rate

SECONDARY ENDPOINTS

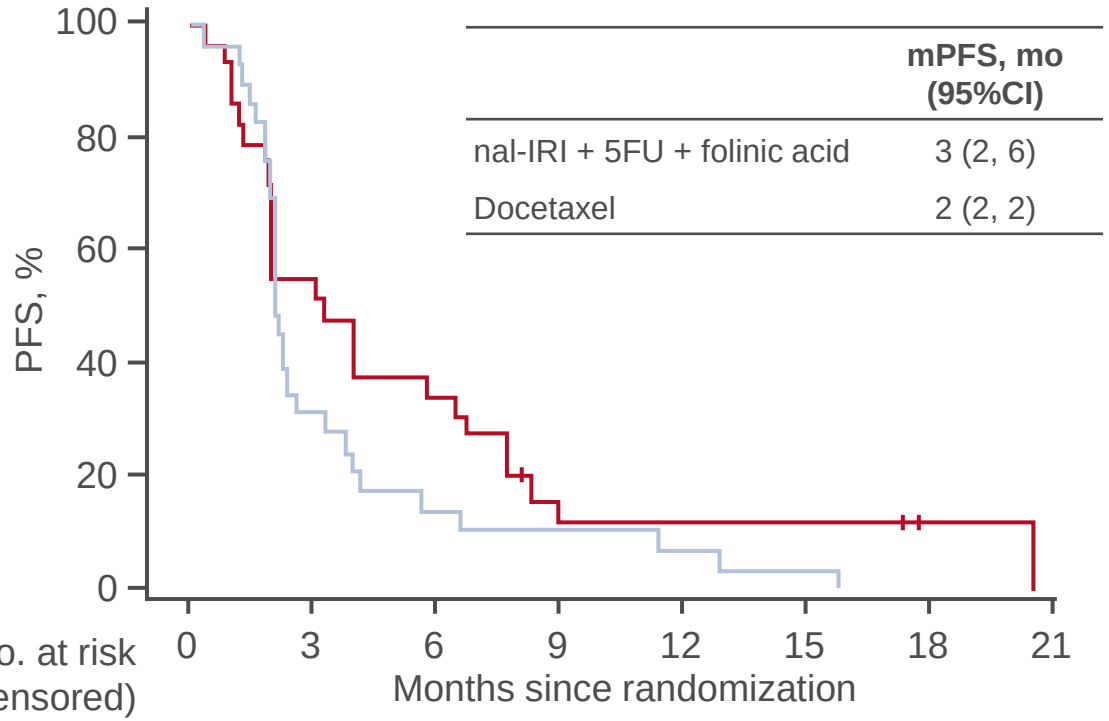
- ORR, PFS, OS, QoL, safety

McNamara MG, et al. J Clin Oncol 2022;40(suppl):abstr 4005

4005: NET-02: A multicenter, randomized, phase II trial of liposomal irinotecan (nal-IRI) and 5-fluorouracil (5-FU)/folinic acid or docetaxel as second-line therapy in patients (pts) with progressive poorly differentiated extra-pulmonary neuroendocrine carcinoma (PD-EP-NEC) – McNamara MG, et al

Key results

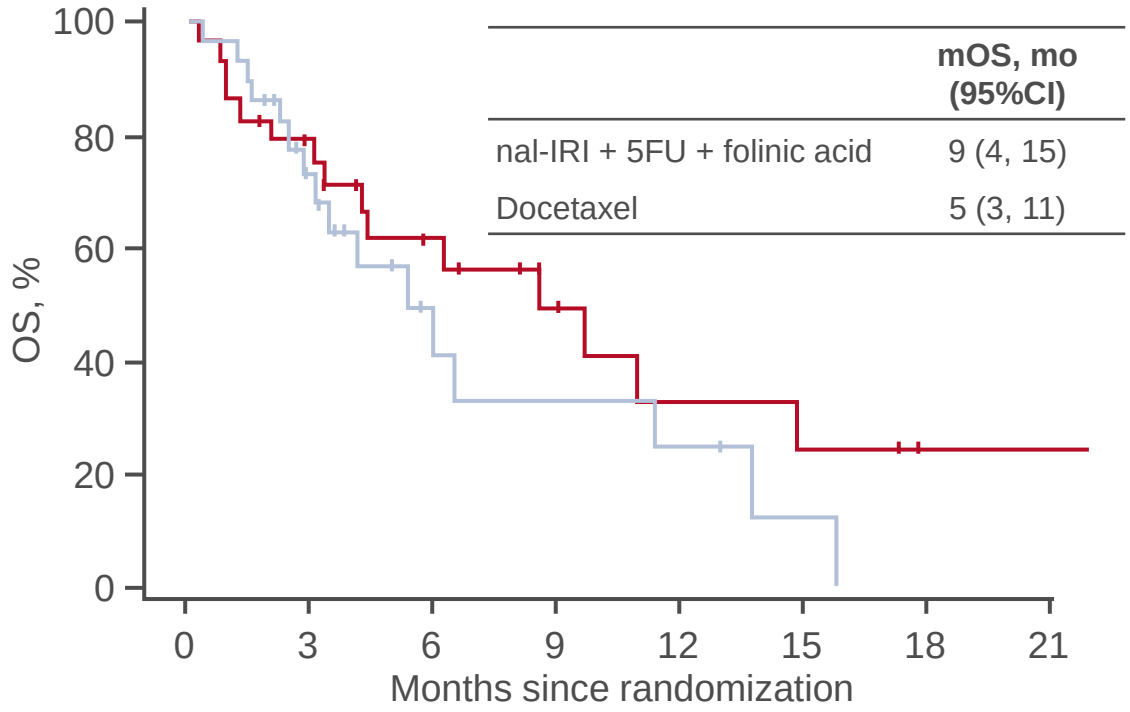
Progression-free survival



	mPFS, mo (95%CI)
nal-IRI + 5FU + folinic acid	3 (2, 6)
Docetaxel	2 (2, 2)

No. at risk (censored)	0	3	6	9	12	15	18	21
nal-IRI + 5FU + folinic acid	29 (0)	16 (0)	10 (0)	3 (1)	3 (1)	3 (1)	1 (3)	0 (3)
Docetaxel	29 (0)	9 (0)	4 (0)	3 (0)	2 (0)	1 (0)	0 (0)	

Overall survival



	mOS, mo (95%CI)
nal-IRI + 5FU + folinic acid	9 (4, 15)
Docetaxel	5 (3, 11)

	0	3	6	9	12	15	18	21
nal-IRI + 5FU + folinic acid	29 (0)	20 (3)	12 (7)	7 (10)	4 (11)	3 (11)	1 (13)	1 (13)
Docetaxel	29 (0)	15 (7)	5 (12)	4 (12)	3 (12)	1 (13)	0 (13)	

McNamara MG, et al. J Clin Oncol 2022;40(suppl):abstr 4005

4005: NET-02: A multicenter, randomized, phase II trial of liposomal irinotecan (nal-IRI) and 5-fluorouracil (5-FU)/folinic acid or docetaxel as second-line therapy in patients (pts) with progressive poorly differentiated extra-pulmonary neuroendocrine carcinoma (PD-EP-NEC) – McNamara MG, et al

Key results (cont.)

Outcome	nal-IRI + 5FU + folinic acid	Docetaxel
6-mo PFS rate, %	31	13.8
ORR, % (95%CI)	10.3 (2.2, 27.4)	10.3 (2.2, 27.4)

AEs, n (%)	nal-IRI + 5FU + folinic acid (n=29)	Docetaxel (n=29)
Any	27 (93.1)	28 (96.6)
Grade ≥3	16 (55.2)	17 (58.6)
Serious	10 (34.5)	7 (24.1)
Led to dose reduction	8 (28)	8 (28)

Conclusions

- **In patients with progressive poorly differentiated extra-pulmonary neuroendocrine carcinoma, liposomal irinotecan + 5FU + folinic acid met the primary endpoint of improving 6-month PFS rate and there were no new safety signals reported**

McNamara MG, et al. J Clin Oncol 2022;40(suppl):abstr 4005

CANCERS OF THE COLON, RECTUM AND ANUS

9: Association of circulating tumor DNA dynamics with clinical outcomes in the adjuvant setting for patients with colorectal cancer from an observational GALAXY study in CIRCULATE-Japan – Kotaka M, et al

Study objective

- To evaluate whether ctDNA-based molecular residual disease (MRD) can be used for selecting patients with CRC who will benefit from SoC adjuvant chemotherapy (ACT) – an analysis of the GALAXY study conducted in Japanese centers

Methods

- Patients with CRC (n=1040) had post-surgical MRD measured using a personalized tumor-informed assay (Signatera bespoke multiplex PCR NGS)
- Blood samples were collected before surgery and 4, 12, 24, 36, 48, 72 and 96 weeks after surgery
- Associations with MRD and 6-month DFS were assessed
- The following cohorts were examined: dynamics analysis, n=838; clearance analysis (all outcomes), n=183 (post-op-4w ctDNA positive) and ctDNA negative, n=521 (post-op-4w ctDNA negative)

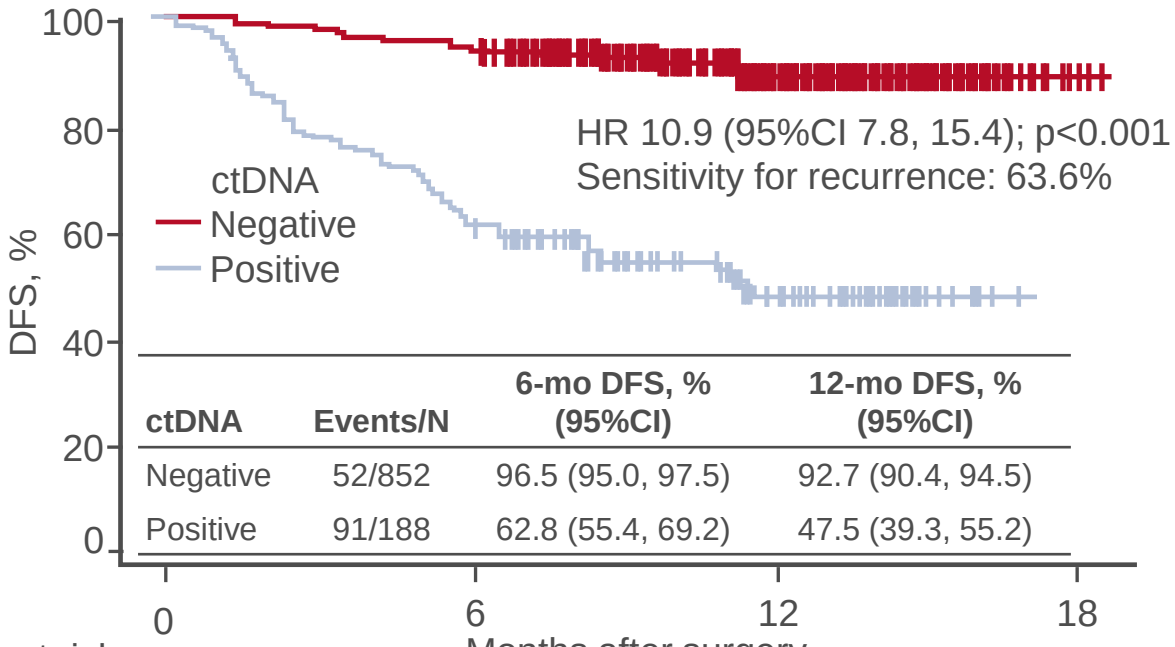
Kotaka M, et al. J Clin Oncol 2022;40(suppl):abstr 9

9: Association of circulating tumor DNA dynamics with clinical outcomes in the adjuvant setting for patients with colorectal cancer from an observational GALAXY study in CIRCULATE-Japan – Kotaka M, et al

Key results

Disease-free survival by post-op-4w ctDNA status

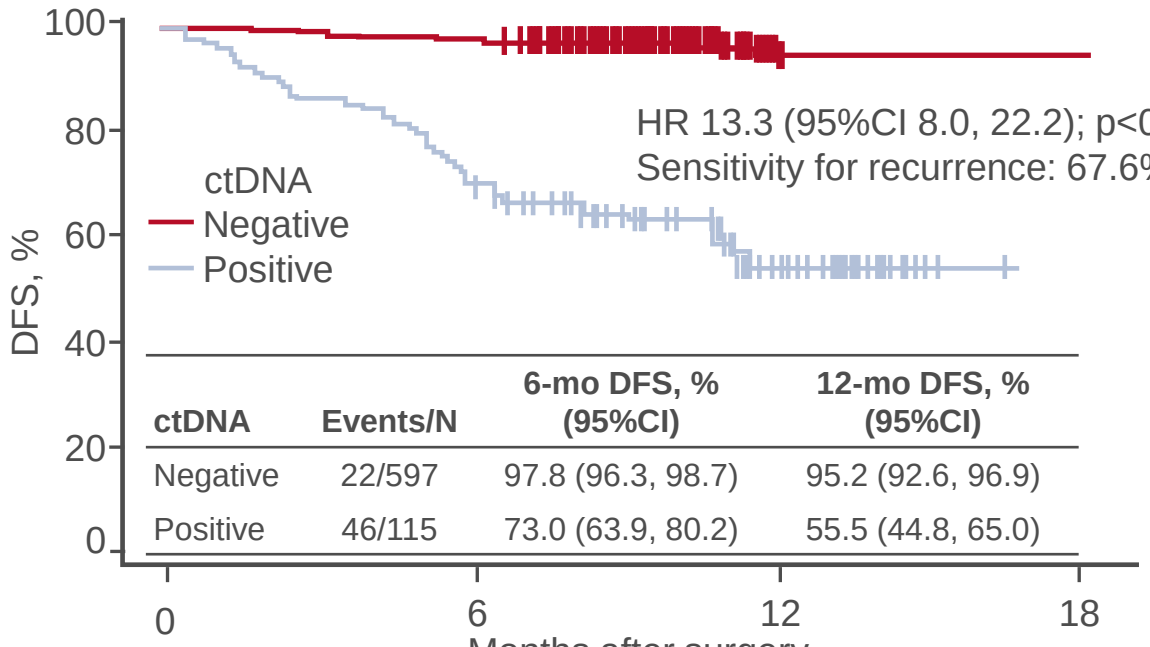
pStage I–IV



ctDNA	Events/N	6-mo DFS, % (95%CI)	12-mo DFS, % (95%CI)
Negative	52/852	96.5 (95.0, 97.5)	92.7 (90.4, 94.5)
Positive	91/188	62.8 (55.4, 69.2)	47.5 (39.3, 55.2)

No. at risk				
Negative	852	822	310	1
Positive	188	118	38	0

pStage II–III



ctDNA	Events/N	6-mo DFS, % (95%CI)	12-mo DFS, % (95%CI)
Negative	22/597	97.8 (96.3, 98.7)	95.2 (92.6, 96.9)
Positive	46/115	73.0 (63.9, 80.2)	55.5 (44.8, 65.0)

No. at risk				
Negative	597	584	223	0
Positive	115	84	31	0

Kotaka M, et al. J Clin Oncol 2022;40(suppl):abstr 9

9: Association of circulating tumor DNA dynamics with clinical outcomes in the adjuvant setting for patients with colorectal cancer from an observational GALAXY study in CIRCULATE-Japan – Kotaka M, et al

Key results (cont.)

ctDNA dynamics from 4w to 12w postoperative timepoint	Neg > Neg	Neg > Pos	Pos > Neg	Pos > Pos
Events/N	31/660	13/32	4/62	50/84
6-mo DFS rate, %	98.0	62.5	100	58.3
HR (95%CI); p-value	0.8 (0.27, 2.15); 0.60	9.2 (3.0, 28.4); <0.001	Ref.	15.8 (5.7, 44.2); <0.001

DFS	ctDNA positive population						ctDNA negative population	
	High-risk pStage II		pStage III		pStage IV		High-risk pStage II–III	
	With ACT	Without ACT	With ACT	Without ACT	With ACT	Without ACT	With ACT	Without ACT
Events/N	1/9	7/13	17/65	19/25	9/22	35/46	7/214	12/317
12-mo DFS rate, %	88.9 (43.3, 98.4)	46.2 (19.2, 69.6)	68.3 (53.4, 79.2)	24.0 (9.8, 41.7)	53.7 (28.4, 73.6)	22.3 (11.2, 35.7)	96.2 (92.1, 98.2)	94.7 (90.5, 97.1)
HR (95%CI); p-value	9.4 (1.1, 79.1); 0.04		8.8 (3.9, 19.5); <0.001		2.4 (1.1, 5.2); 0.02		1.3 (0.5, 3.6); 0.63	

Conclusions

- **In patients with CRC, using the personalized tumor-informed assay to stratify post-surgical decisions was able to identify patients likely to benefit from adjuvant chemotherapy across all stages**

Kotaka M, et al. J Clin Oncol 2022;40(suppl):abstr 9

10: A randomized phase III trial of mFOLFOX7 or CapeOX plus bevacizumab versus 5-FU/l-LV or capecitabine plus bevacizumab as initial therapy in elderly patients with metastatic colorectal cancer: JCOG1018 study (RESPECT) – Hamaguchi T, et al

Study objective

- To evaluate the efficacy and safety of the addition of oxaliplatin to fluoropyrimidine + bevacizumab in elderly patients with mCRC in Japanese centers in the RESPECT study

Key patient inclusion criteria

- Unresectable mCRC
- ECOG PS 0–2 for patients aged ≥75 years
  or
  ECOG PS 2 for patients aged 70–74 years

(n=251*)

R 1:1

Oxaliplatin arm
mFOLFOX7 or CAPOX + bevacizumab
(n=126)

Stratification

- ECOG PS (0–1 or 2)
- Age (≥85, 80–84, 75–79 or 70–74 years)
- Number of metastatic sites (1 or ≥2)
- Institute

No oxaliplatin arm
5FU/levoleucovorin or capecitabine + bevacizumab
(n=125)

PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

- OS, ORR, QoL, safety

*Protocol was amended owing to poor accrual and delays to 250 patients rather than 380 patients

Hamaguchi T, et al. J Clin Oncol 2022;40(suppl):abstr 10

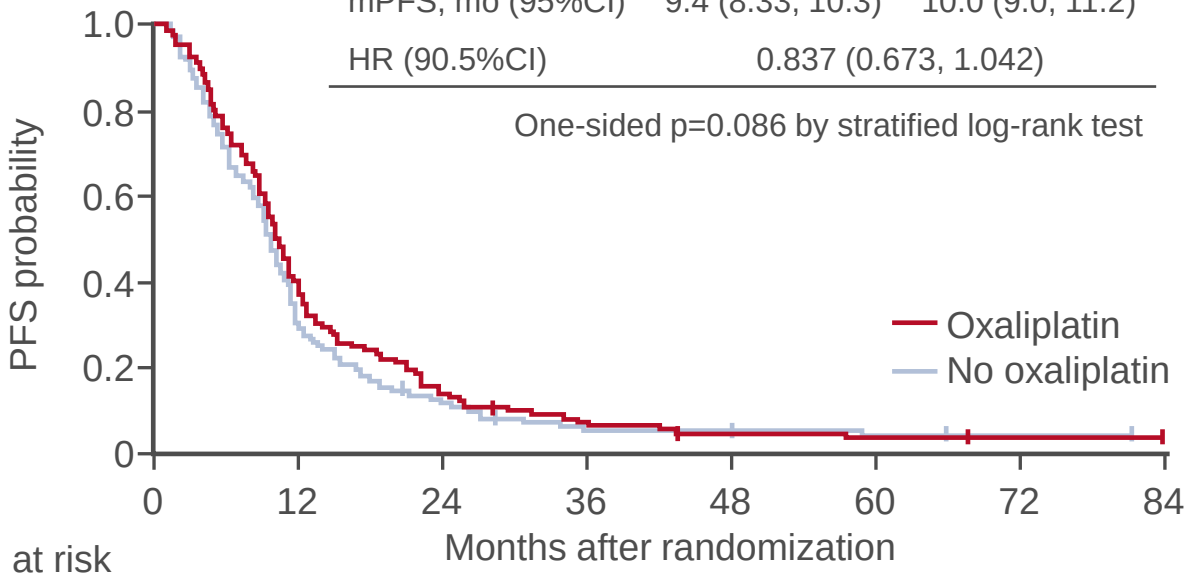
10: A randomized phase III trial of mFOLFOX7 or CapeOX plus bevacizumab versus 5-FU/l-LV or capecitabine plus bevacizumab as initial therapy in elderly patients with metastatic colorectal cancer: JCOG1018 study (RESPECT) – Hamaguchi T, et al

Key results

Progression-free survival

	No oxaliplatin (n=125)	Oxaliplatin (n=126)
Events, n	119	122
mPFS, mo (95%CI)	9.4 (8.33, 10.3)	10.0 (9.0, 11.2)
HR (90.5%CI)	0.837 (0.673, 1.042)	

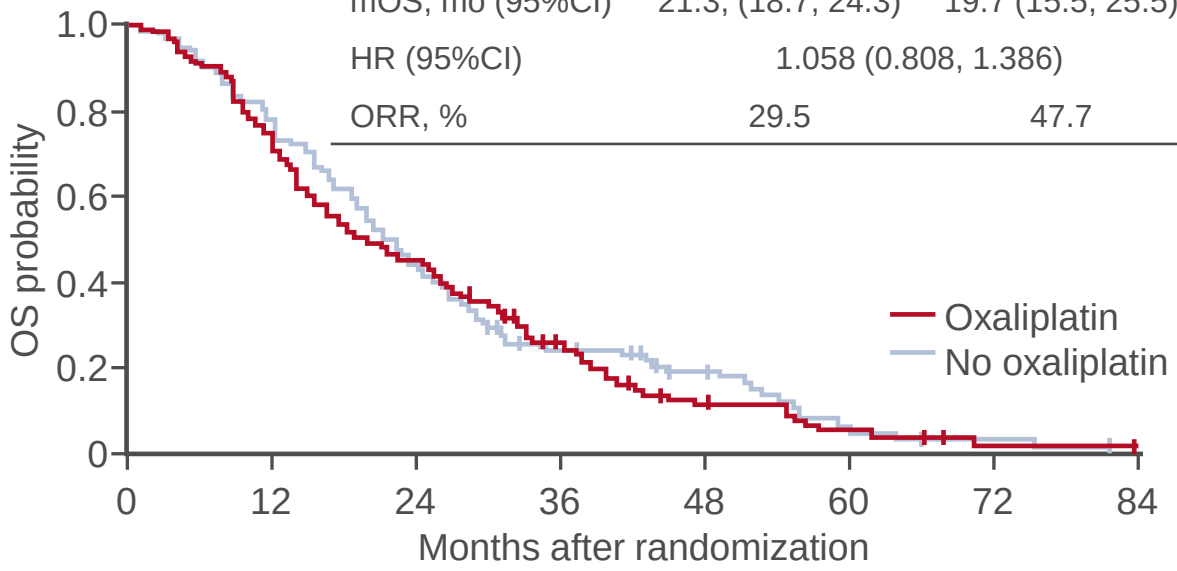
One-sided p=0.086 by stratified log-rank test



No. at risk							
No oxaliplatin 125	35	12	4	4	2	1	0
Oxaliplatin 126	46	16	7	3	2	1	0

Overall survival

	No oxaliplatin (n=125)	Oxaliplatin (n=126)
Events, n	109	114
mOS, mo (95%CI)	21.3, (18.7, 24.3)	19.7 (15.5, 25.5)
HR (95%CI)	1.058 (0.808, 1.386)	
ORR, %	29.5	47.7



No oxaliplatin 125	125	95	54	24	15	4	2	0
Oxaliplatin 126	126	91	57	28	11	5	1	0

Hamaguchi T, et al. J Clin Oncol 2022;40(suppl):abstr 10

10: A randomized phase III trial of mFOLFOX7 or CapeOX plus bevacizumab versus 5-FU/l-LV or capecitabine plus bevacizumab as initial therapy in elderly patients with metastatic colorectal cancer: JCOG1018 study (RESPECT) – Hamaguchi T, et al

Key results (cont.)

AEs, n (%)		Oxaliplatin arm (n=123)	No oxaliplatin arm (n=124)
Grade 3–4 hematological	Neutropenia	29 (24)	18 (15)
Grade 2–4 non-hematological	Sensory neuropathy	70 (57)	19 (15)
	Fatigue	39 (32)	26 (21)
	Nausea	27 (22)	12 (10)
	Diarrhea	20 (16)	9 (7)
	Stomatitis	14 (11)	14 (11)
Grade 3–4 bevacizumab-related	Hypertension	24 (20)	19 (15)
	Thromboembolism	3 (2)	3 (2)
	Bleeding	3 (2)	1 (0.8)
Treatment-related death		3 (2)	1 (0.8)

Conclusions

- **In elderly patients with mCRC, oxaliplatin combined with fluoropyrimidine + bevacizumab failed to provide any additional PFS benefit over fluoropyrimidine + bevacizumab alone and was associated with more frequent and severe AEs**

Hamaguchi T, et al. J Clin Oncol 2022;40(suppl):abstr 10

11: Prognostic impact of early treatment discontinuation and early oxaliplatin discontinuation in patients treated with 6 months of oxaliplatin-based adjuvant chemotherapy for stage III colon cancer: an ACCENT/IDEA pooled analysis of 11 trials – Gallois C, et al

Study objective

- To evaluate the prognostic impact of early discontinuation of treatment (ETD) or oxaliplatin (EOD) in patients with stage III colon cancer

Methods

- Data from 11 clinical trials in the ACCENT and IDEA databases were collected for patients with stage III colon cancer (n=10,444) who were due to receive 6 months of adjuvant fluoropyrimidine + oxaliplatin (FOLFOX, n=7033 or CAPOX, n=3411)
- ETD was defined as discontinuation of treatment before 75% of planned chemotherapy cycles and EOD was defined as discontinuation of oxaliplatin before 75% of planned cycles only (fluoropyrimidine continued)
- A Cox model adjusted for prognostic factors was used to assess the associations between ETD and EOD with OS and DFS

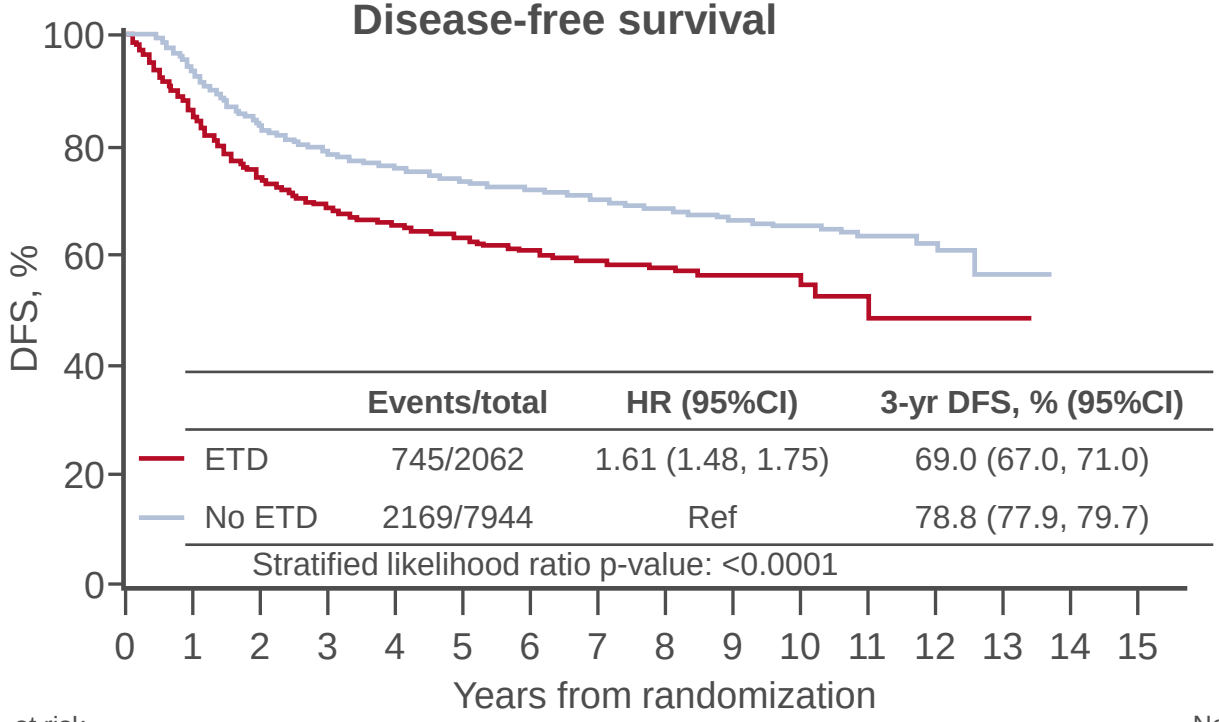
Gallois C, et al. J Clin Oncol 2022;40(suppl):abstr 11

11: Prognostic impact of early treatment discontinuation and early oxaliplatin discontinuation in patients treated with 6 months of oxaliplatin-based adjuvant chemotherapy for stage III colon cancer: an ACCENT/IDEA pooled analysis of 11 trials – Gallois C, et al

Key results

- ETD and EOD were associated with older age, female gender, ECOG PS ≥1 and CAPOX regimen along with malnutrition for ETD only

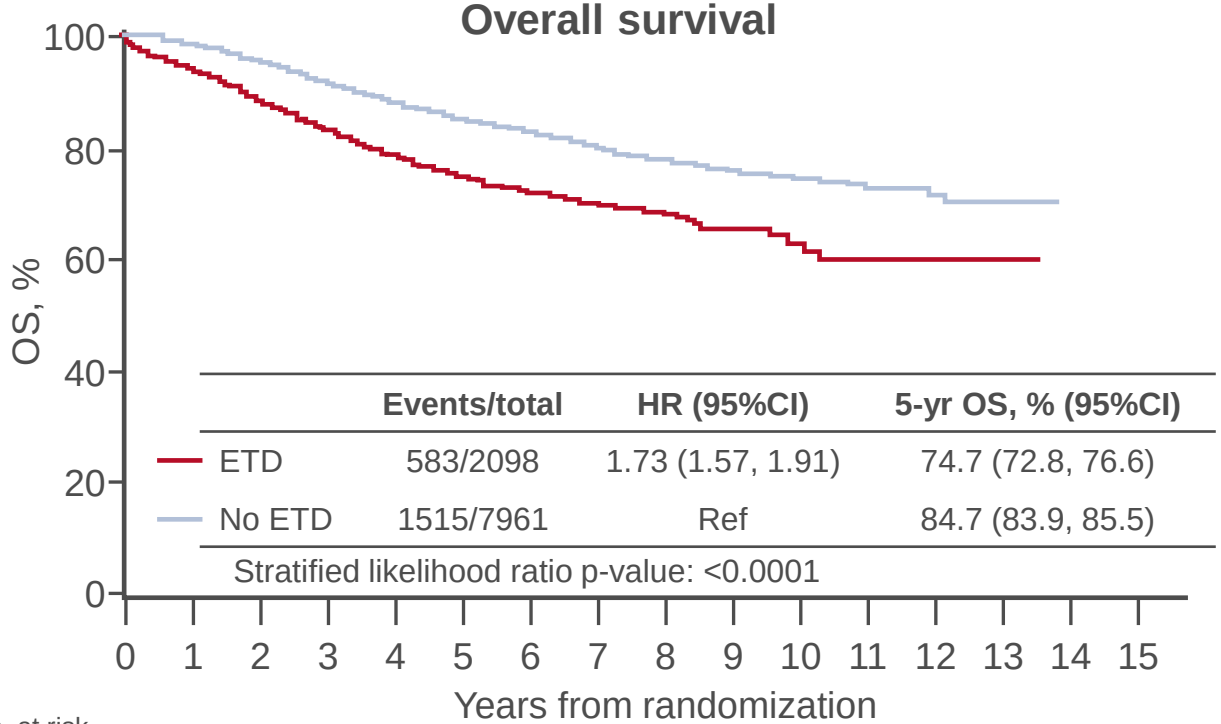
Disease-free survival



No. at risk

ETD	2062	1657	1405	1169	976	778	542	328	163	72	33	13	7	1	0
No ETD	7944	7359	6467	5652	4883	3867	2795	1742	896	407	182	87	28	4	0

Overall survival



No. at risk

ETD	2098	1871	1725	1564	1391	1201	862	465	226	94	40	16	7	1	0
No ETD	7961	7818	7481	6974	6420	5617	4265	2414	1181	559	247	103	33	5	0

Gallois C, et al. J Clin Oncol 2022;40(suppl):abstr 11

11: Prognostic impact of early treatment discontinuation and early oxaliplatin discontinuation in patients treated with 6 months of oxaliplatin-based adjuvant chemotherapy for stage III colon cancer: an ACCENT/IDEA pooled analysis of 11 trials – Gallois C, et al

Key results (cont.)

Multivariate analysis ETD vs. no ETD		DFS		OS	
		HR	p-value	HR	p-value
Overall population	Low-risk group	1.50	<0.001	1.72	<0.001
	High-risk group	1.34	<0.001	1.38	<0.001
FOLFOX	Low-risk group	1.63	<0.001	1.96	<0.001
	High-risk group	1.28	0.01	1.30	0.02
CAPOX	Low-risk group	1.03	0.9	1.02	0.9
	High-risk group	1.72	0.005	1.84	0.009

Multivariate analysis EOD vs. no EOD	DFS		OS	
	HR	p-value	HR	p-value
FOLFOX	0.91	0.3	0.95	0.7
CAPOX	1.10	0.6	0.97	0.9
Low-risk group	0.99	1.0	1.03	0.8
High-risk group	0.93	0.5	0.91	0.5

Conclusions

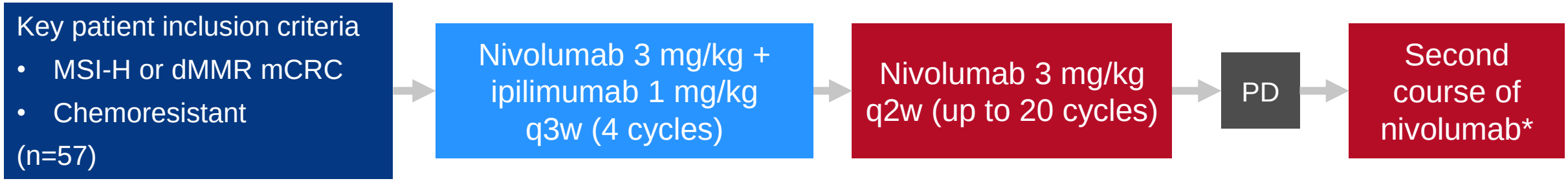
- **In patients with stage III colon cancer scheduled to receive a 6-month adjuvant regimen, maintaining the planned number of treatment cycles appears to be important. Oxaliplatin should be stopped if grade ≥2 neurotoxicity occurs at any time point. In patients with grade 1–2 neurotoxicity, stopping oxaliplatin after 3 months of treatment does not seem impair clinical outcomes and is a potential valid option**

Gallois C, et al. J Clin Oncol 2022;40(suppl):abstr 11

13: One-year duration of nivolumab plus ipilimumab in patients (pts) with microsatellite instability-high/mismatch repair-deficient (MSI/dMMR) metastatic colorectal cancer (mCRC): Long-term follow-up of the GERCOR NIPICOL phase II study – Cohen R, et al

Study objective

- To evaluate the long-term efficacy and safety of nivolumab + ipilimumab in patients with MSI-H or dMMR mCRC in French centers in the phase 2 GERCOR NIPICOL study



PRIMARY ENDPOINT

- 12-week DCR (RECIST v1.1)

SECONDARY ENDPOINTS

- DoR, PFS†, safety

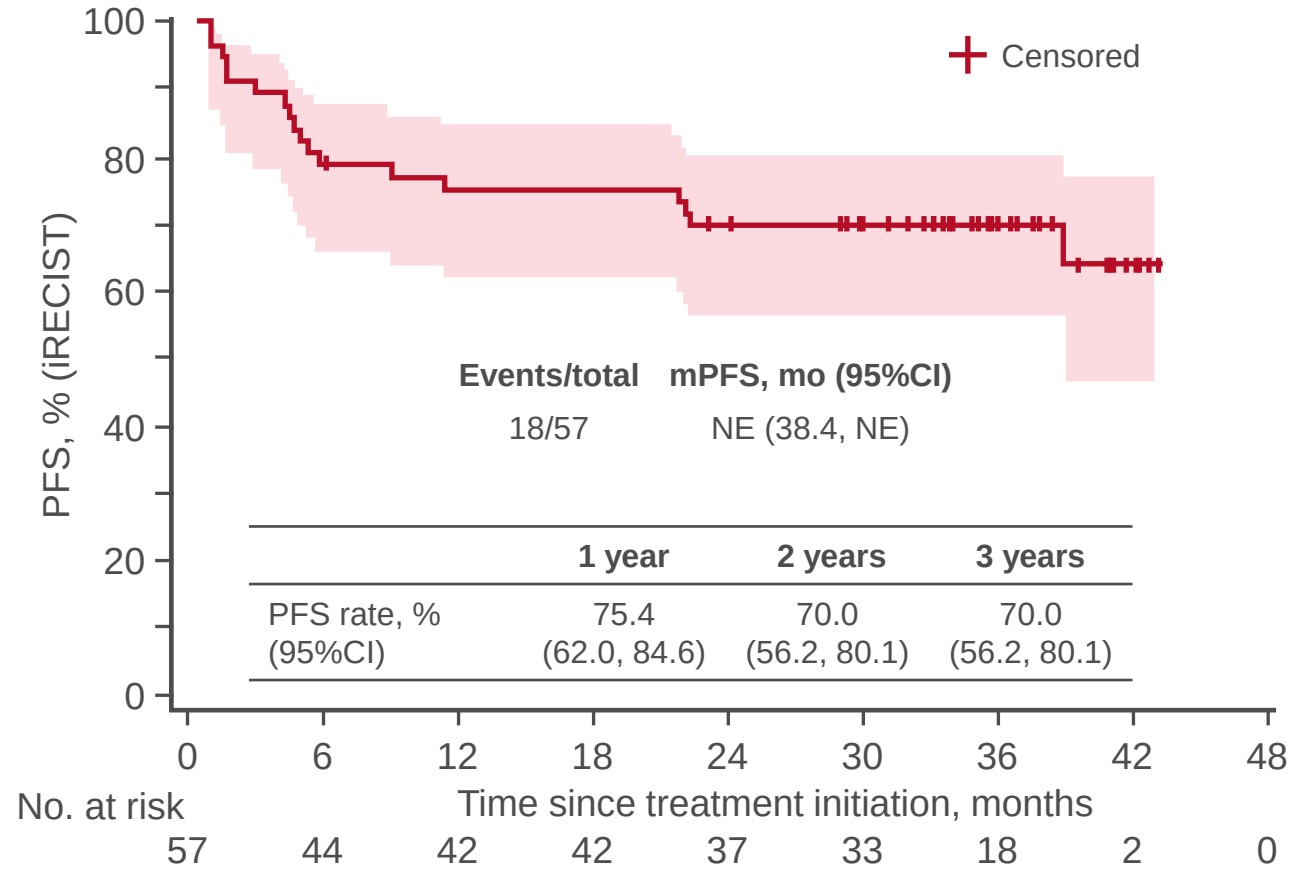
*For patients who completed 1 year of treatment and had later progressive disease;
†landmark analysis of patients free of progression and alive at 1 year (n=42)

Cohen R, et al. J Clin Oncol 2022;40(suppl):abstr 13

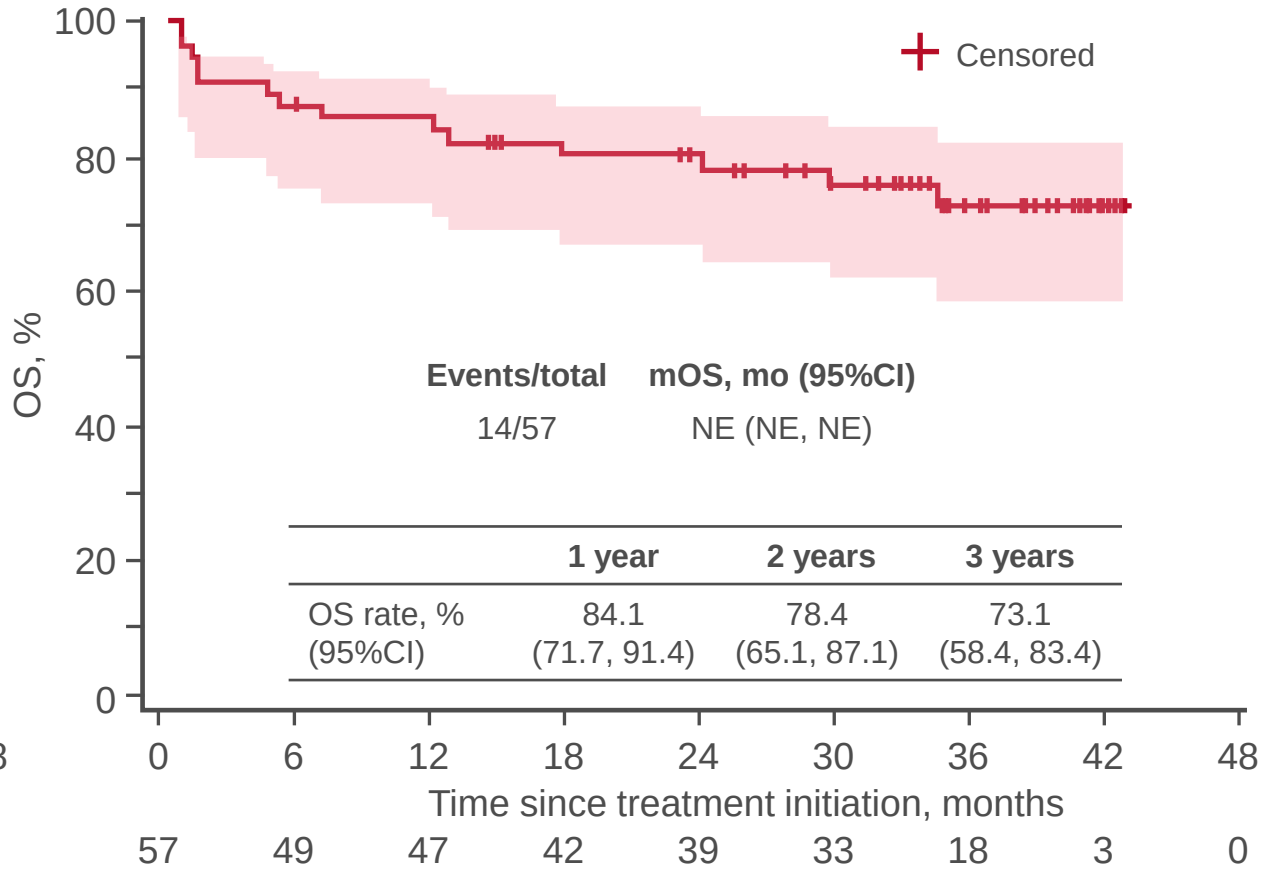
13: One-year duration of nivolumab plus ipilimumab in patients (pts) with microsatellite instability-high/mismatch repair-deficient (MSI/dMMR) metastatic colorectal cancer (mCRC): Long-term follow-up of the GERCOR NIPICOL phase II study – Cohen R, et al

Key results

Progression-free survival



Overall survival

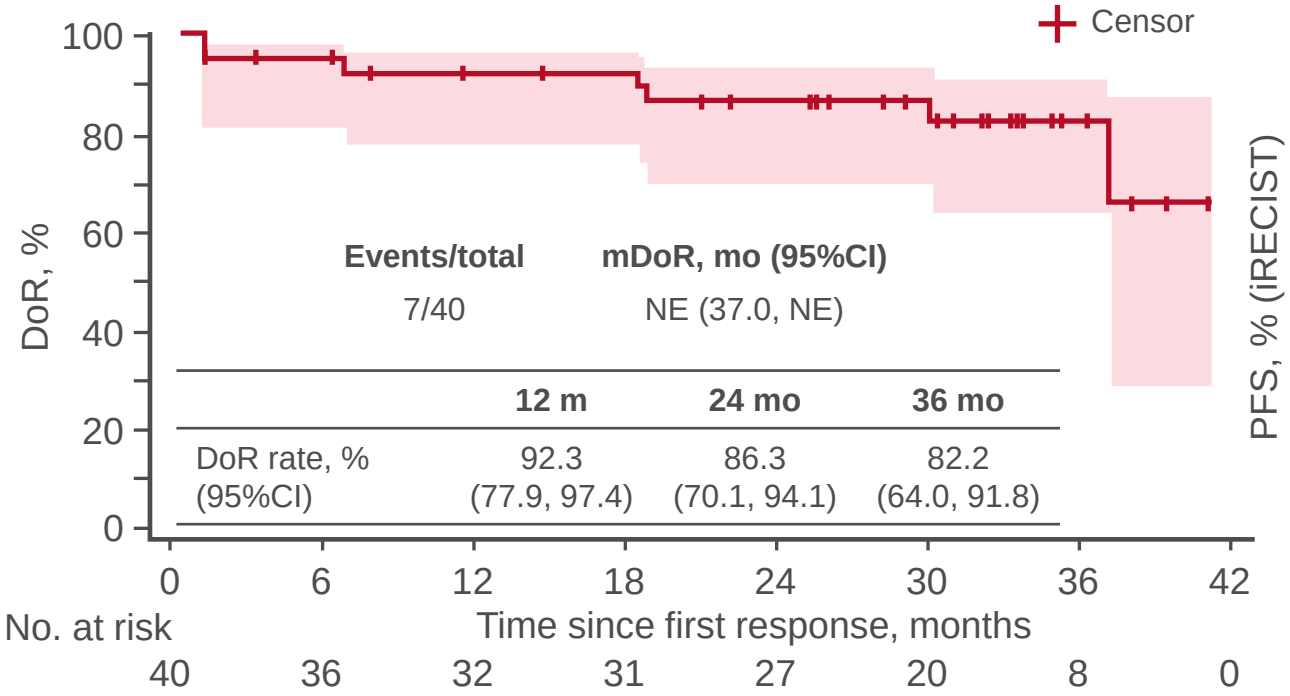


Cohen R, et al. J Clin Oncol 2022;40(suppl):abstr 13

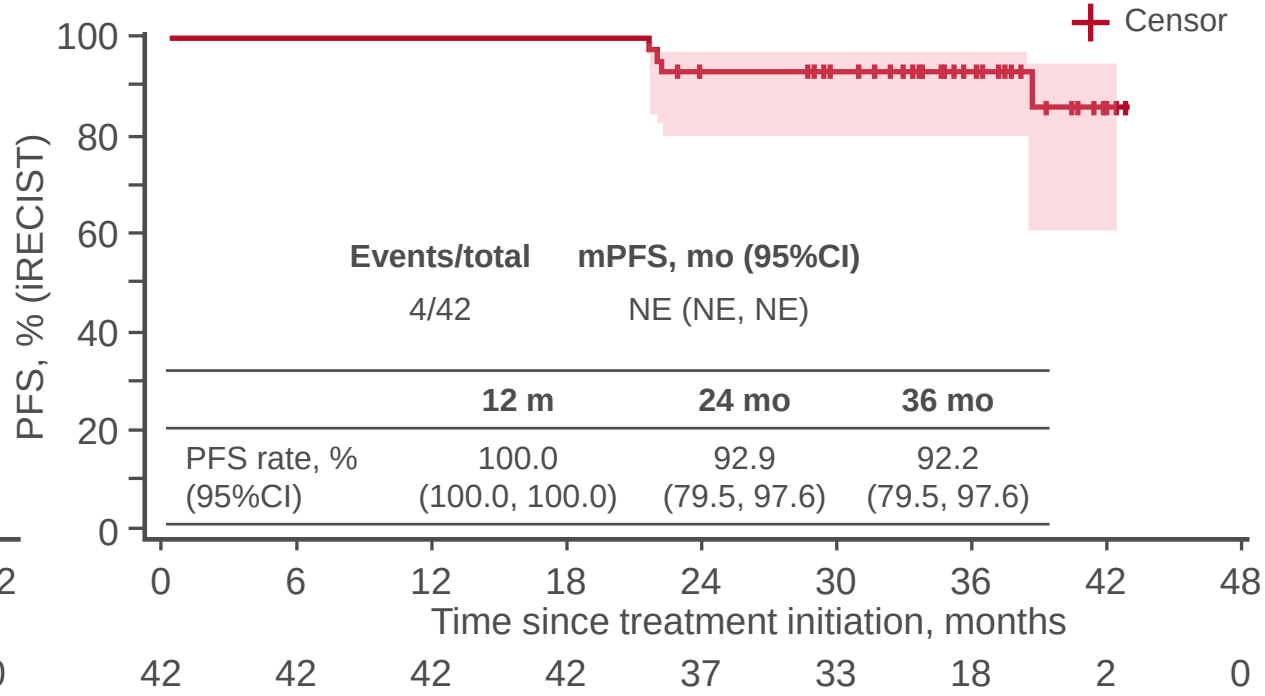
13: One-year duration of nivolumab plus ipilimumab in patients (pts) with microsatellite instability-high/mismatch repair-deficient (MSI/dMMR) metastatic colorectal cancer (mCRC): Long-term follow-up of the GERCOR NIPICOL phase II study – Cohen R, et al

Key results (cont.)

Duration of response



Landmark analysis*



Conclusions

- **In patients with MSI-H or dMMR mCRC, 1-year of nivolumab maintenance after induction with nivolumab + ipilimumab demonstrated comparable findings to other studies in this patient population and raises the question of whether 2 years of treatment is necessary in all patients**

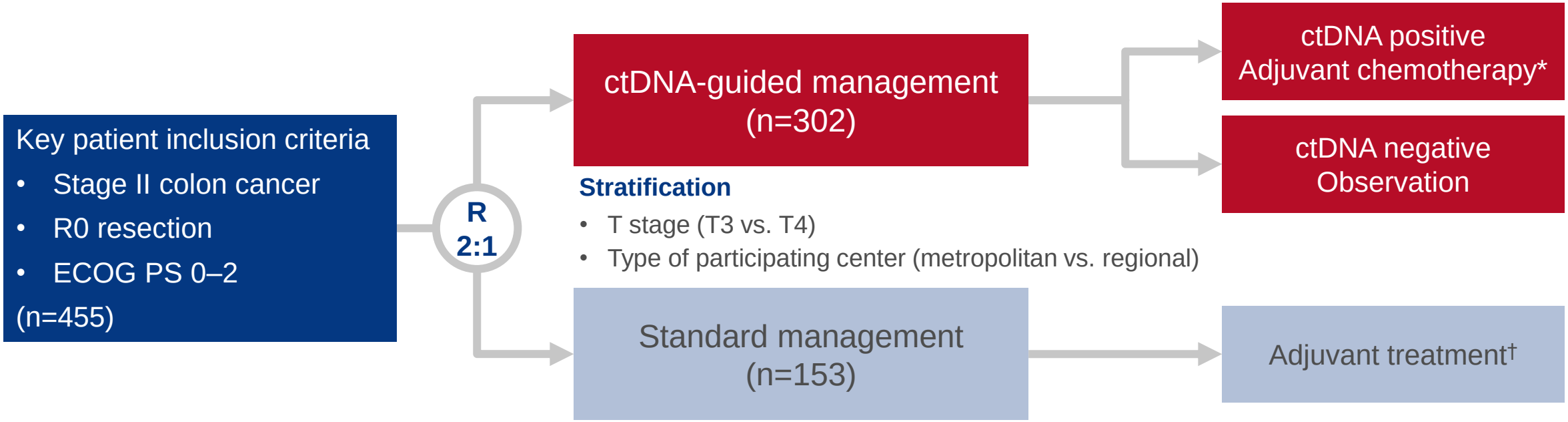
*Landmark analysis of patients free of progression and alive at 1 year (n=42)

Cohen R, et al. J Clin Oncol 2022;40(suppl):abstr 13

LBA100: Adjuvant chemotherapy guided by circulating tumor DNA analysis in stage II colon cancer: The randomized DYNAMIC trial – 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 centers 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

Tie J, et al. J Clin Oncol 2022;40(suppl):abstr LBA100

LBA100: Adjuvant chemotherapy guided by circulating tumor DNA analysis in stage II colon cancer: The randomized DYNAMIC trial – Tie J, et al

Key results

Treatment information	ctDNA-guided* (n=294)	Standard management (n=147)	p-value
Adjuvant chemotherapy, n (%)	45 (15)	41 (28)	0.0017
Chemotherapy regimen received, n (%) Oxaliplatin-based doublet Single agent fluoropyrimidine	 28/45 (62) 17/45 (38)	 4/41 (10) 37/41 (90)	<0.0001
Median time from surgery to commencing chemotherapy, days (range)	83 (76–89)	53 (49–61)	<0.0001
Median treatment duration, weeks (range)	24 (19–24)	24 (21–24)	0.9318
Completed planned treatment, n (%)	38 (85)	32 (78)	0.7036
Median full dose delivered, % (IQR)	78 (56–100)	84 (64–100)	0.6194

*Plasma samples were collected at Week 4 and 7 post-operatively and the Safe-SeqS tumor-informed personalized ctDNA assay was used

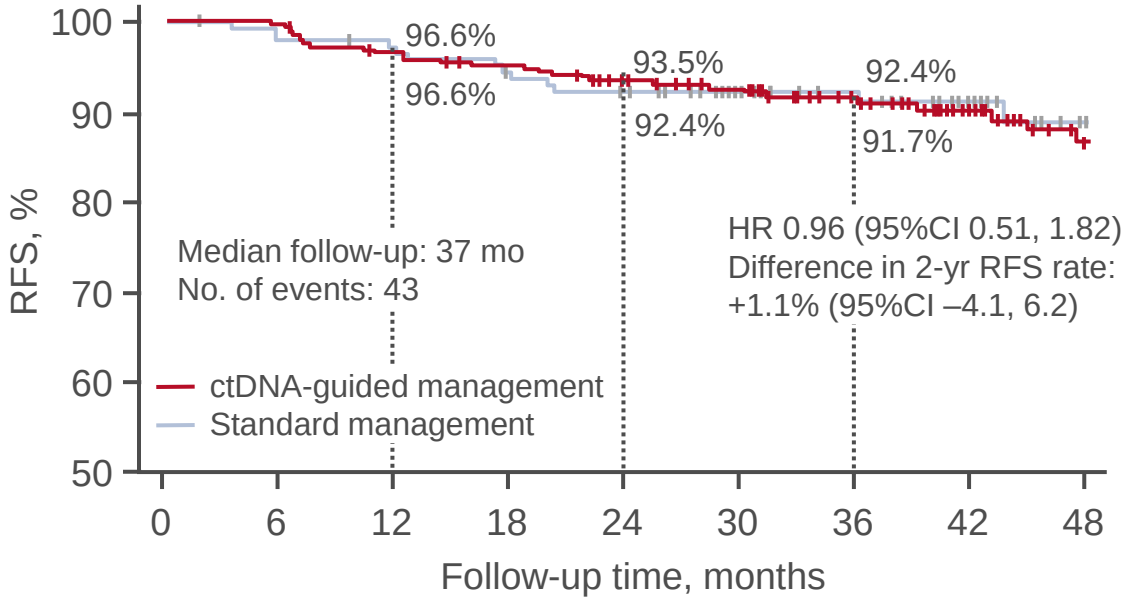
Tie J, et al. J Clin Oncol 2022;40(suppl):abstr LBA100

LBA100: Adjuvant chemotherapy guided by circulating tumor DNA analysis in stage II colon cancer: The randomized DYNAMIC trial – Tie J, et al

Key results

Recurrence-free survival

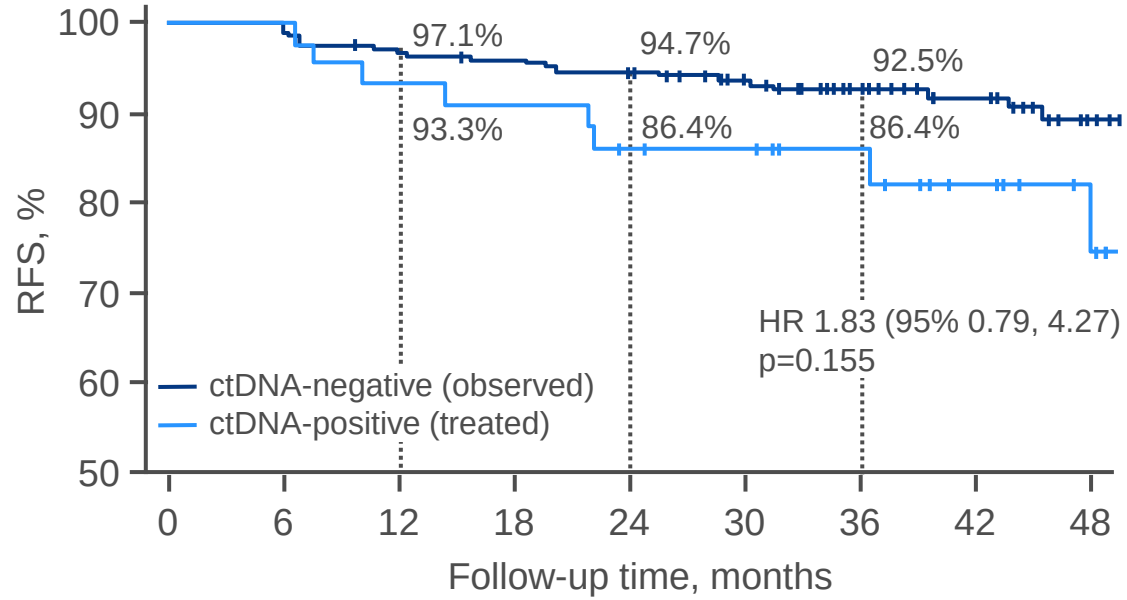
ctDNA-guided vs standard



No. at risk

ctDNA-guided	294	292	281	273	259	207	155	109	64
Standard	147	144	142	136	128	97	78	57	33

ctDNA negative vs positive



No. at risk

ctDNA-	246	244	236	231	220	160	131	93	55
ctDNA+	45	45	42	39	36	36	22	16	9

Tie J, et al. J Clin Oncol 2022;40(suppl):abstr LBA100

LBA100: Adjuvant chemotherapy guided by circulating tumor DNA analysis in stage II colon cancer: The randomized DYNAMIC trial – Tie J, et al

Key results

Group		RFS rate, %		HR (95%CI)
		24-mo	36-mo	
ctDNA-negative	Low-risk	97.4	96.7	1
	High-risk	89.7	86.4	3.04 (1.26, 7.34)
ctDNA-positive		86.4	85.1	3.69 (1.39, 9.87)
ctDNA-negative	T3	96.7	94.2	1
	T4	81.3	81.3	2.60 (1.91, 6.71)
ctDNA-positive		86.4	86.4	2.62 (1.11, 6.20)

Conclusions

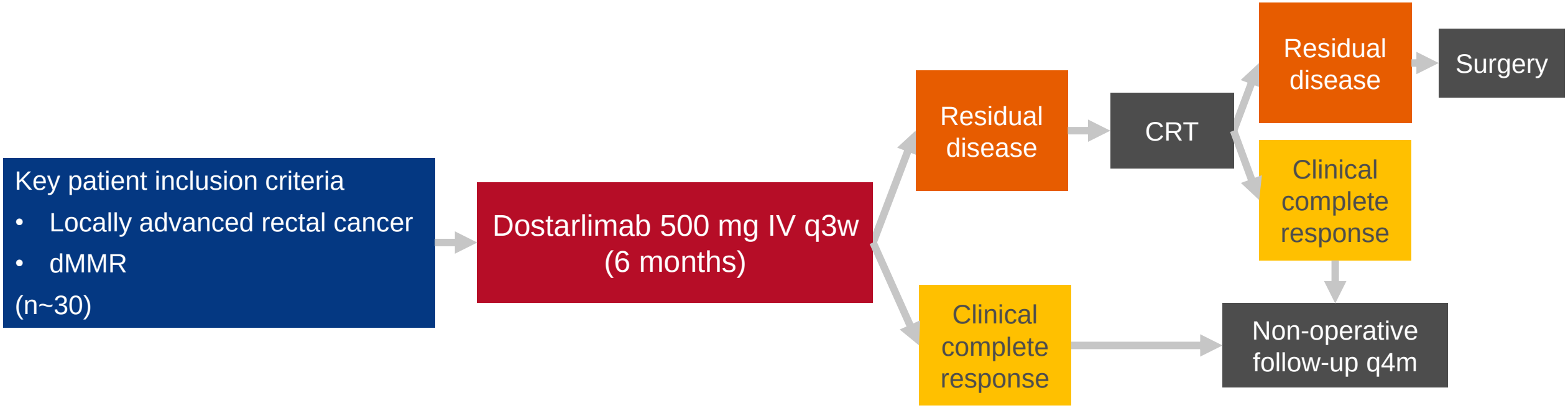
- **In patients with stage II colon cancer, ctDNA-guided management demonstrated a substantial reduction in the number of patients requiring adjuvant chemotherapy without compromising RFS compared with standard management although patients who were ctDNA-positive after surgery did drive benefit from adjuvant chemotherapy**

Tie J, et al. J Clin Oncol 2022;40(suppl):abstr LBA100

LBA5: Single agent PD-1 blockade as curative-intent treatment in mismatch repair deficient locally advanced rectal cancer – Cercek A, et al

Study objective

- To evaluate the efficacy and safety of dostarlimab, a PD-1 inhibitor, in patients with dMMR locally advanced rectal cancer



PRIMARY ENDPOINTS

- ORR, pCR

SECONDARY ENDPOINTS

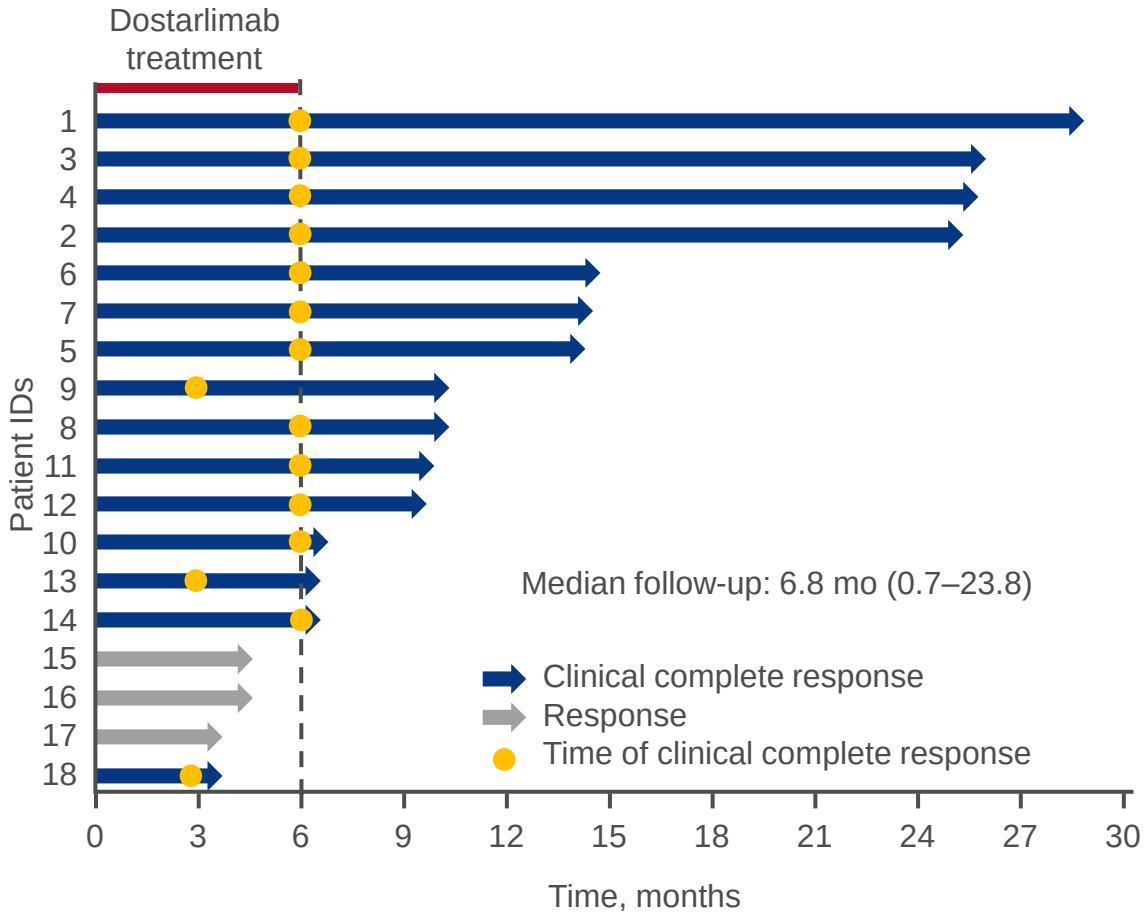
- Safety

Cercek A, et al. J Clin Oncol 2022;40(suppl):abstr LBA5

LBA5: Single agent PD-1 blockade as curative-intent treatment in mismatch repair deficient locally advanced rectal cancer – Cercek A, et al

Key results

ID	Age	T stage	N stage	FU, mo	Digital rectal exam response	Endoscopic best response	Rectal MRI best response	Overall response
1	38	T4	N+	23.8	CR	CR	CR	cCR
2	30	T3	N+	20.5	CR	CR	CR	cCR
3	61	T1/2	N+	20.6	CR	CR	CR	cCR
4	28	T4	N+	20.5	CR	CR	CR	cCR
5	53	T1/2	N+	9.1	CR	CR	CR	cCR
6	77	T1/2	N+	11.0	CR	CR	CR	cCR
7	77	T1/2	N+	8.7	CR	CR	CR	cCR
8	55	T3	N+	5.0	CR	CR	CR	cCR
9	68	T3	N+	4.9	CR	CR	CR	cCR
10	78	T3	N-	1.7	CR	CR	CR	cCR
11	55	T3	N+	4.7	CR	CR	CR	cCR
12	27	T3	N+	4.4	CR	CR	CR	cCR
13	26	T3	N+	0.8	CR	CR	CR	cCR
14	43	T3	N+	0.7	CR	CR	CR	cCR



Cercek A, et al. J Clin Oncol 2022;40(suppl):abstr LBA5

LBA5: Single agent PD-1 blockade as curative-intent treatment in mismatch repair deficient locally advanced rectal cancer – Cercek A, et al

Key results (cont.)

- No grade 3–4 AEs were reported
- No patients required chemotherapy, radiotherapy or surgery and there was no disease recurrence during the follow-up period

Conclusions

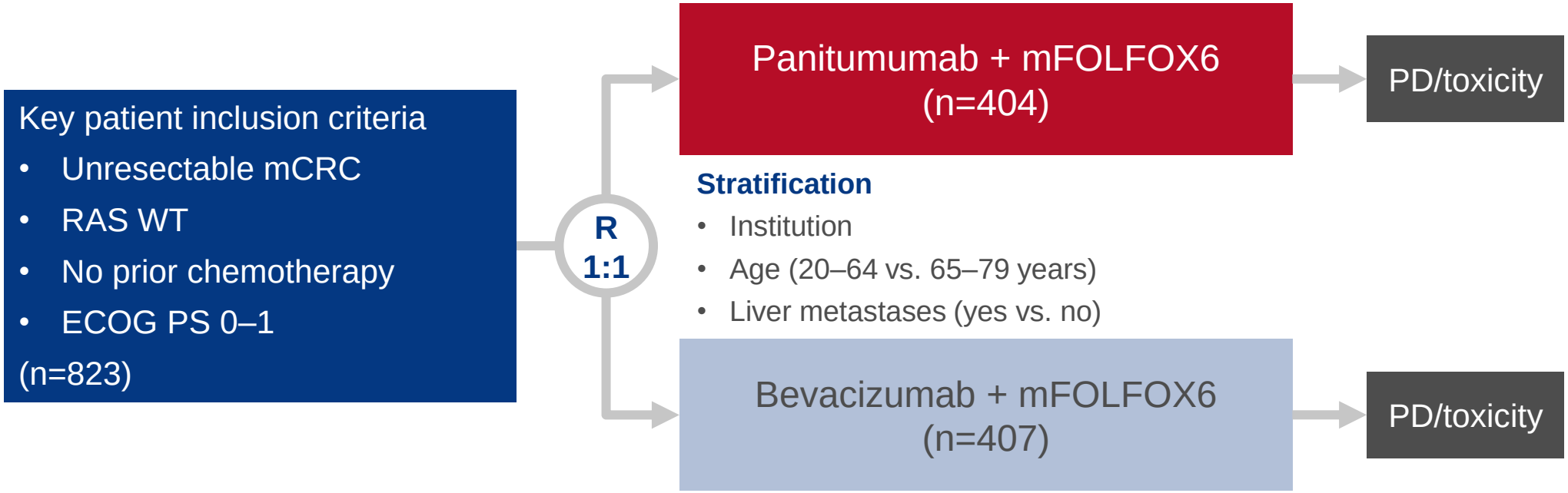
- **In patients with locally advanced rectal cancer, dostarlimab demonstrated clinical complete response in all of the first 14 consecutive patients treated and may enable chemotherapy, radiotherapy and surgery to be eliminated in the tumor agnostic dMMR population with early stage disease, although results from long-term follow-up are required**

Cercek A, et al. J Clin Oncol 2022;40(suppl):abstr LBA5

LBA1: Panitumumab (PAN) plus mFOLFOX6 versus bevacizumab (BEV) plus mFOLFOX6 as first-line treatment in patients with RAS wild-type (WT) metastatic colorectal cancer (mCRC): Results from the phase 3 PARADIGM trial – Yoshino T, 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 phase 3 PARADIGM study



PRIMARY ENDPOINT

- OS (left-sided population)

SECONDARY ENDPOINTS

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

Yoshino T, et al. J Clin Oncol 2022;40(suppl):abstr LBA1

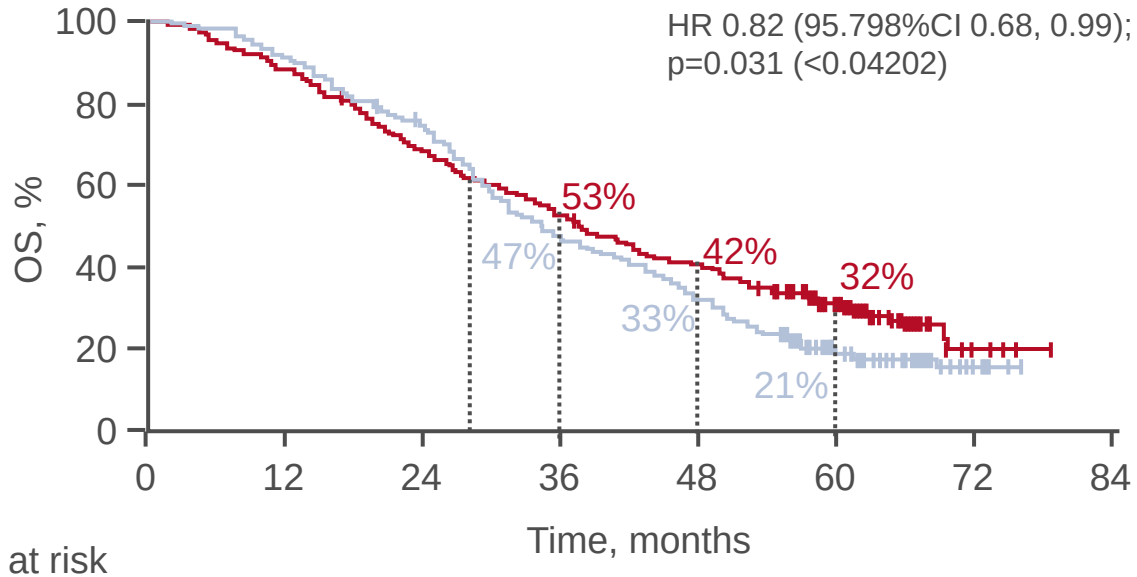
LBA1: Panitumumab (PAN) plus mFOLFOX6 versus bevacizumab (BEV) plus mFOLFOX6 as first-line treatment in patients with RAS wild-type (WT) metastatic colorectal cancer (mCRC): Results from the phase 3 PARADIGM trial – Yoshino T, et al

Key results

Overall survival

Left-sided population

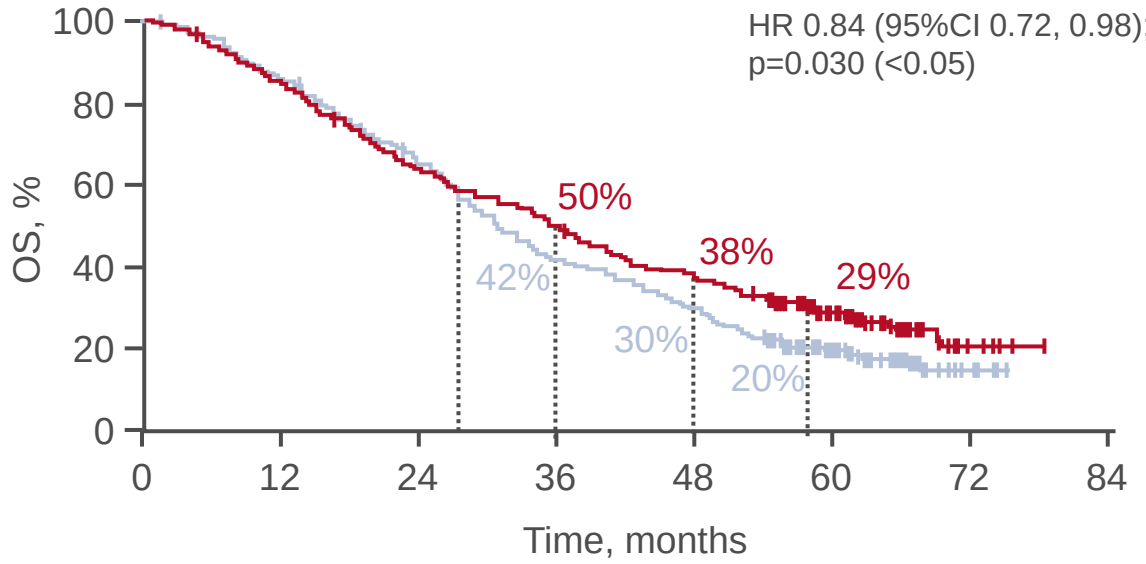
	Events, n (%)	mOS, mo (95.798%CI)
Panitumumab + mFOLFOX6 (n=312)	218 (69.9)	37.9 (34.1, 42.6)
Bevacizumab + mFOLFOX6 (n=292)	230 (78.7)	34.3 (30.9, 40.3)



No. at risk							
Panitumumab 312	276	213	166	129	68	5	0
Bevacizumab 292	266	212	136	96	40	5	0

Overall population

	Events, n (%)	mOS, mo (95%CI)
Panitumumab + mFOLFOX6 (n=400)	291 (72.8)	36.2 (32.0, 39.0)
Bevacizumab + mFOLFOX6 (n=402)	322 (80.1)	31.3 (29.3, 34.1)



No. at risk							
Panitumumab 400	338	253	199	150	80	6	0
Bevacizumab 402	348	265	166	119	54	5	0

Yoshino T, et al. J Clin Oncol 2022;40(suppl):abstr LBA1

LBA1: Panitumumab (PAN) plus mFOLFOX6 versus bevacizumab (BEV) plus mFOLFOX6 as first-line treatment in patients with RAS wild-type (WT) metastatic colorectal cancer (mCRC): Results from the phase 3 PARADIGM trial – Yoshino T, et al

Key results

Outcome	Left-sided population		Overall population	
	Panitumumab	Bevacizumab	Panitumumab	Bevacizumab
mPFS, mo (95%CI)	13.7 (12.7, 15.3)	13.2 (11.4, 14.5)	12.9 (11.3, 13.6)	12.0 (11.3, 13.5)
HR (95%CI)	0.98 (0.82, 1.17)		1.01 (0.87, 1.18)	
RR, % (95%CI)	80.2 (75.3, 84.5)	68.6 (62.9, 74.0)	74.9 (70.3, 79.1)	67.3 (62.4, 71.9)
Difference, % (95%CI)	11.2 (4.4, 17.9)		7.7 (1.5, 13.8)	
DCR, % (95%CI)	97.4 (94.9, 98.9)	96.5 (93.7, 98.3)	94.9 (92.3, 96.9)	95.5 (92.9, 97.3)
mDoR, mo (95%CI)	13.1 (11.1, 14.8)	11.2 (9.6, 13.1)	11.9 (10.5, 13.4)	10.7 (9.5, 12.2)
R0 rate, % (95%CI)	18.3 (14.1, 23.0)	11.6 (8.2, 15.9)	16.5 (13.0, 20.5)	10.9 (8.1, 17.1)

AEs, n (%)	Panitumumab (n=404)	Bevacizumab (n=407)
Any	402 (99.5)	399 (98.0)
Grade ≥3	290 (71.8)	264 (64.9)
Serious treatment-related	72 (17.8)	44 (10.8)
Led to discontinuation	96 (23.8)	75 (18.4)

Conclusions

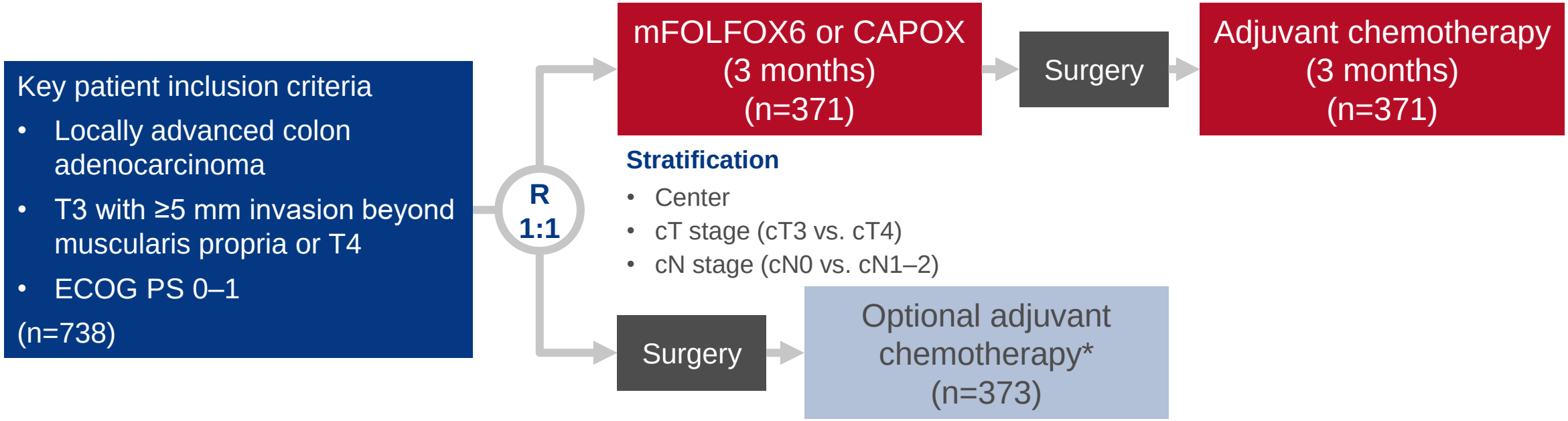
- **In patients with RAS WT mCRC, IL panitumumab + mFOLFOX6 was found to be superior to bevacizumab + mFOLFOX6 for the primary endpoint (OS in left-sided population) and had a manageable safety profile**

Yoshino T, et al. J Clin Oncol 2022;40(suppl):abstr LBA1

3500: Perioperative chemotherapy with mFOLFOX6 or CAPOX for patients with locally advanced colon cancer (OPTICAL): A multicenter, randomized, phase 3 trial – Hu H, et al

Study objective

- To evaluate the efficacy and safety of perioperative chemotherapy, mFOLFOX6 or CAPOX, in patients with locally advanced colon cancer in Chinese centers in the phase 3 OPTICAL study



PRIMARY ENDPOINT

- 3-year DFS

SECONDARY ENDPOINTS

- pCR, OS, safety

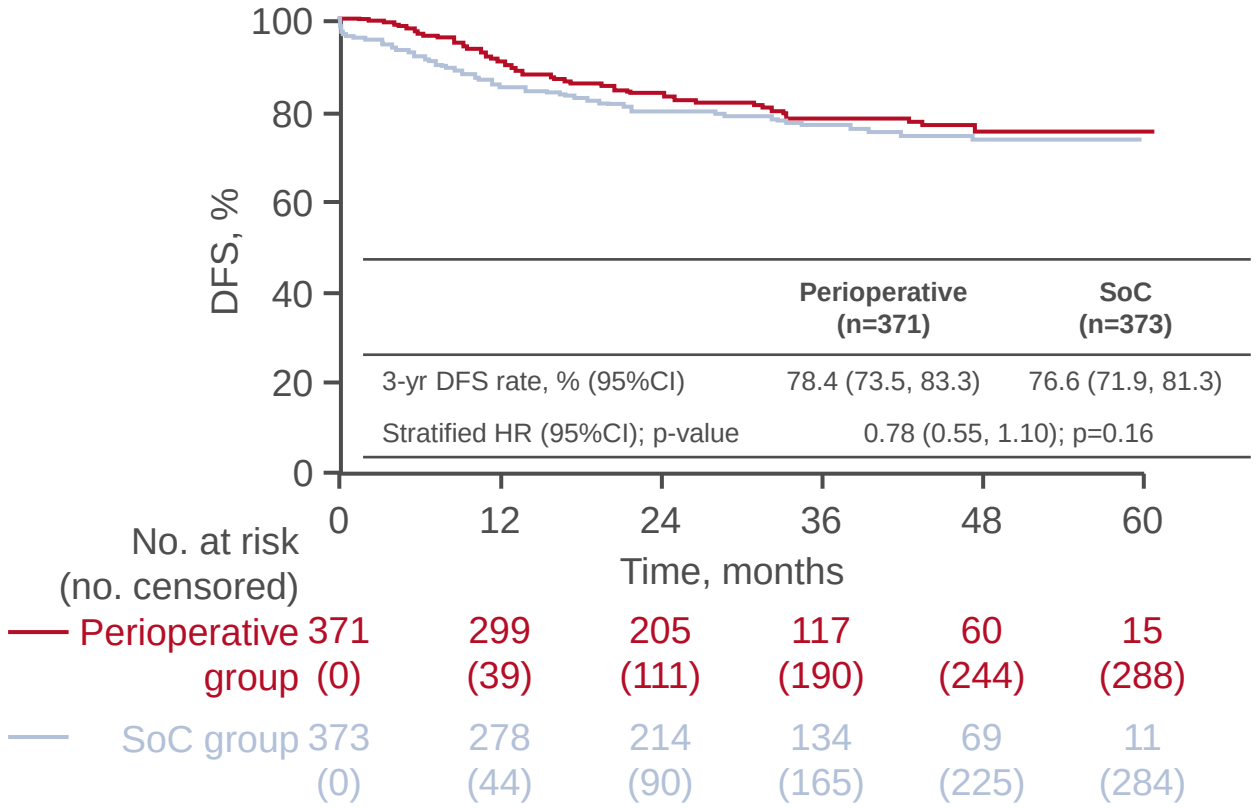
*Physician's discretion according to pathological stage

Hu H, et al. J Clin Oncol 2022;40(suppl):abstr 3500

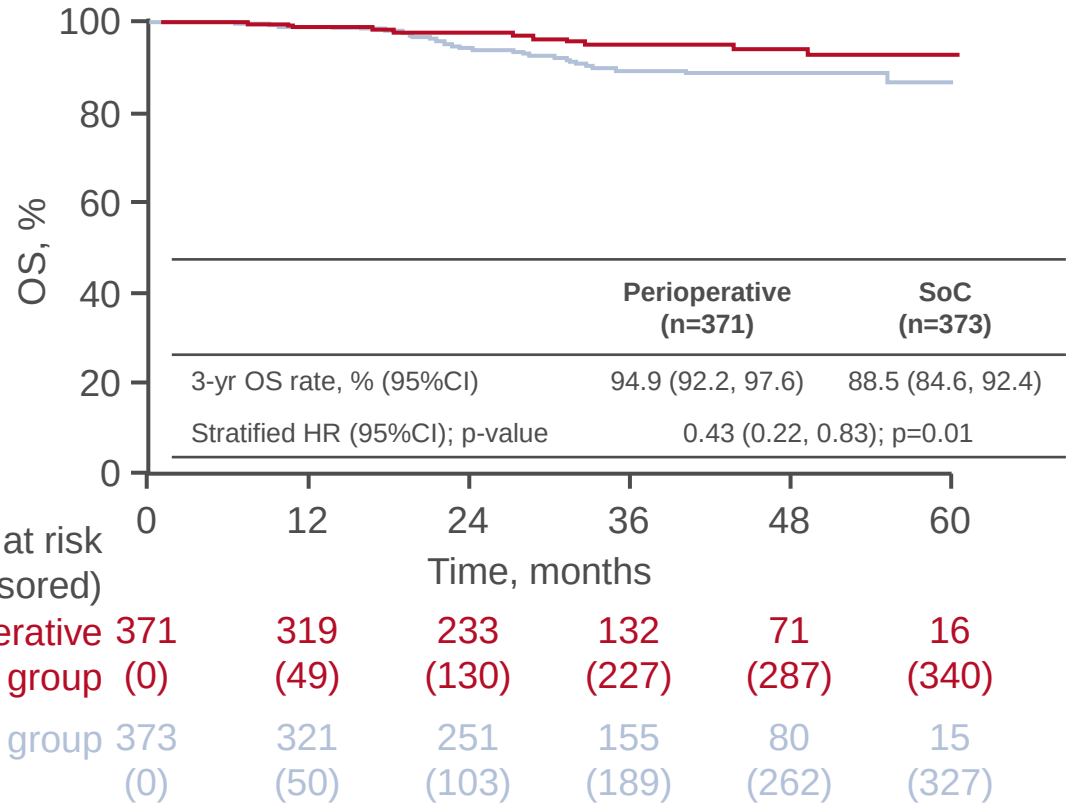
3500: Perioperative chemotherapy with mFOLFOX6 or CAPOX for patients with locally advanced colon cancer (OPTICAL): A multicenter, randomized, phase 3 trial – Hu H, et al

Key results

Disease-free survival



Overall survival



Hu H, et al. J Clin Oncol 2022;40(suppl):abstr 3500

3500: Perioperative chemotherapy with mFOLFOX6 or CAPOX for patients with locally advanced colon cancer (OPTICAL): A multicenter, randomized, phase 3 trial – Hu H, et al

Key results

Surgical outcomes, n (%)	Perioperative (n=366)	SoC (n=373)	p-value
Surgical approach			
Laparoscopic	295 (81)	308 (83)	0.610
Open	67 (18)	63 (17)	
Laparoscopic converted to open	4 (1)	2 (1)	
Resection limits			
R0	357 (97)	356 (95)	0.121
R1	2 (1)	2 (1)	
R2	2 (1)	6 (2)	
Rx	2 (1)	9 (2)	
Non-resectional surgery	3 (1)	0	

Surgical outcomes, n (%)		Perioperative (n=366)	SoC (n=373)	p-value
pT stage	pT0	29 (8)	0	<0.001
	pTis	1 (1)	0	
	pT1	7 (2)	0	
	pT2	45 (12)	22 (6)	
	pT3	243 (66)	276 (74)	
	pT4	38 (10)	75 (20)	
pN stage	pN0	249 (69)	200 (54)	<0.001
	pN1	88 (24)	129 (35)	
	pN2	26 (7)	44 (12)	
Disease stage	T0N0M0	27 (7)	0	<0.001
	TisN0M0	1 (1)	0	
	I	42 (12)	16 (4)	
	II	179 (48)	180 (48)	
	High-risk II	59 (16)	82 (22)	
	III	110 (30)	164 (44)	
	IV	4 (1)	13 (3)	

Conclusions

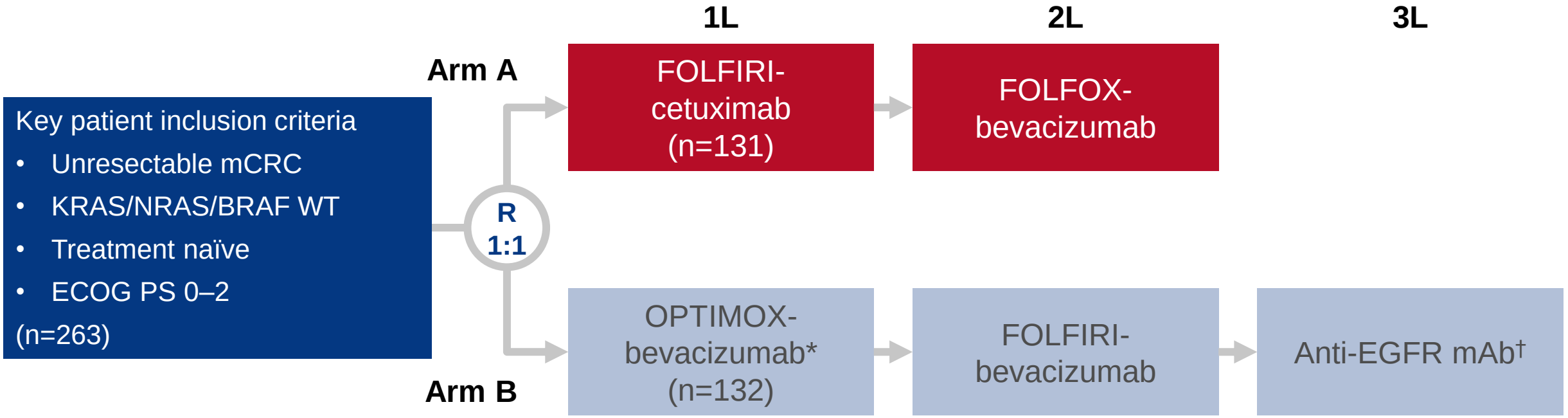
- **In patients with locally advanced colon cancer, perioperative chemotherapy administration was feasible without increasing surgical complications and perioperative mortality. Perioperative chemotherapy demonstrated a 7% pCR rate and 20% downstaging rate, but did not significantly improve 3-year DFS, the primary endpoint, compared with SoC**

Hu H, et al. J Clin Oncol 2022;40(suppl):abstr 3500

3504: STRATEGIC-1: Multi-line therapy trial in unresectable wild-type KRAS/NRAS/BRAF metastatic colorectal cancer—A GERCOR-PRODIGE randomized open-label phase III study – Chibaudel B, et al

Study objective

- To evaluate the efficacy and safety of multiple lines of therapy in patients with unresectable KRAS/NRAS/BRAF WT mCRC in French centers in the phase 3 STRATEGIC-1 study



PRIMARY ENDPOINT

- Duration of disease control (DDC)

SECONDARY ENDPOINTS

- OS, TFS, PFS, RR, HRQoL, safety

*Oxaliplatin stop-and-go; †cetuximab ± irinotecan or panitumumab

Chibaudel B, et al. J Clin Oncol 2022;40(suppl):abstr 3504

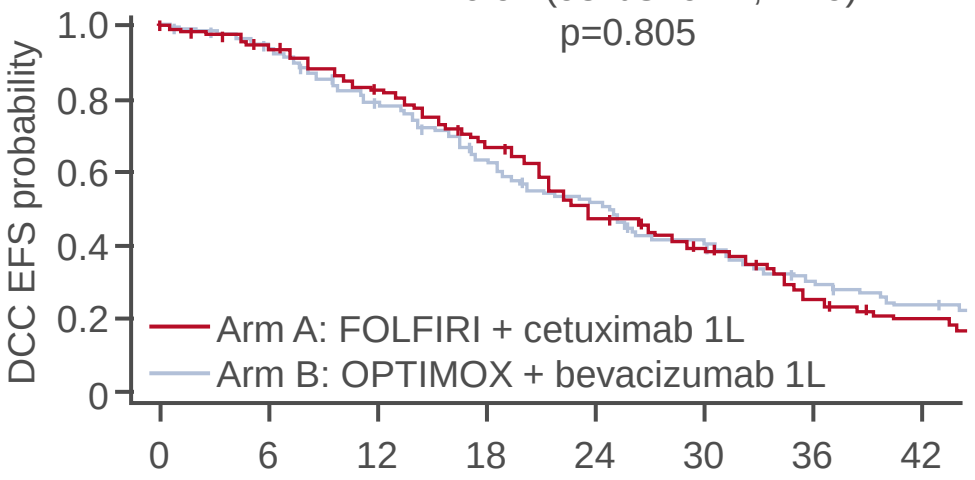
3504: STRATEGIC-1: Multi-line therapy trial in unresectable wild-type KRAS/NRAS/BRAF metastatic colorectal cancer—A GERCOR-PRODIGE randomized open-label phase III study – Chibaudel B, et al

Key results

Duration of disease control

	N	Event	mDCC, mo (95%CI)
Arm A	131	94	22.5 (20.1, 27.1)
Arm B	132	94	23.5 (17.9, 22.2)

HR 0.97 (95%CI 0.72, 1.29)
p=0.805

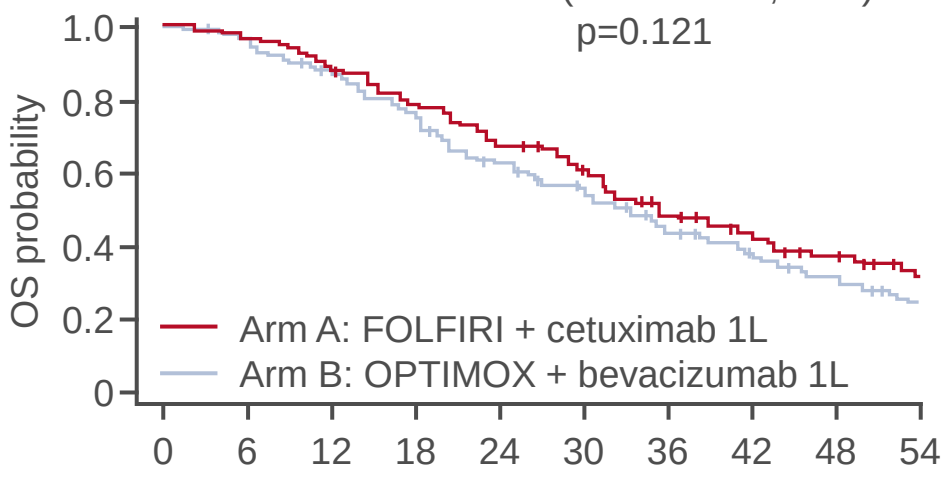


No. at risk								
Arm A	131	113	94	72	40	35	20	16
Arm B	132	115	89	63	50	38	24	19

Overall survival

	N	Event	mOS, mo (95%CI)
Arm A	131	82	37.8 (32.2, 47.7)
Arm B	132	95	34.4 (27.6, 42.2)

HR 1.26 (95%CI 0.94, 1.70)
p=0.121



No. at risk										
Arm A	131	126	116	102	90	79	59	47	36	26
Arm B	132	126	113	99	80	69	49	39	29	22

Chibaudel B, et al. J Clin Oncol 2022;40(suppl):abstr 3504

3504: STRATEGIC-1: Multi-line therapy trial in unresectable wild-type KRAS/NRAS/BRAF metastatic colorectal cancer—A GERCOR-PRODIGE randomized open-label phase III study – Chibaudel B, et al

Key results

Response, %	Arm A	Arm B	p-value
1L	FOLFOX-cetux	mFOLFOX7-bev	
Induction	82.4	69.7	<0.001
Re-introduction	59.1	32.8	0.046
2L	mFOLFOX6-bev	FOLFIRI-bev	
	21.2	18.3	0.734
3L		Cetux ± irinotecan or panitumumab	
		14.6	NA

AEs, %	Arm A	Arm B	p-value
Any	99.1	97.7	0.622
Grade 3–4	72.7	72.0	0.902
Serious	46.9	53.8	0.266

Conclusions

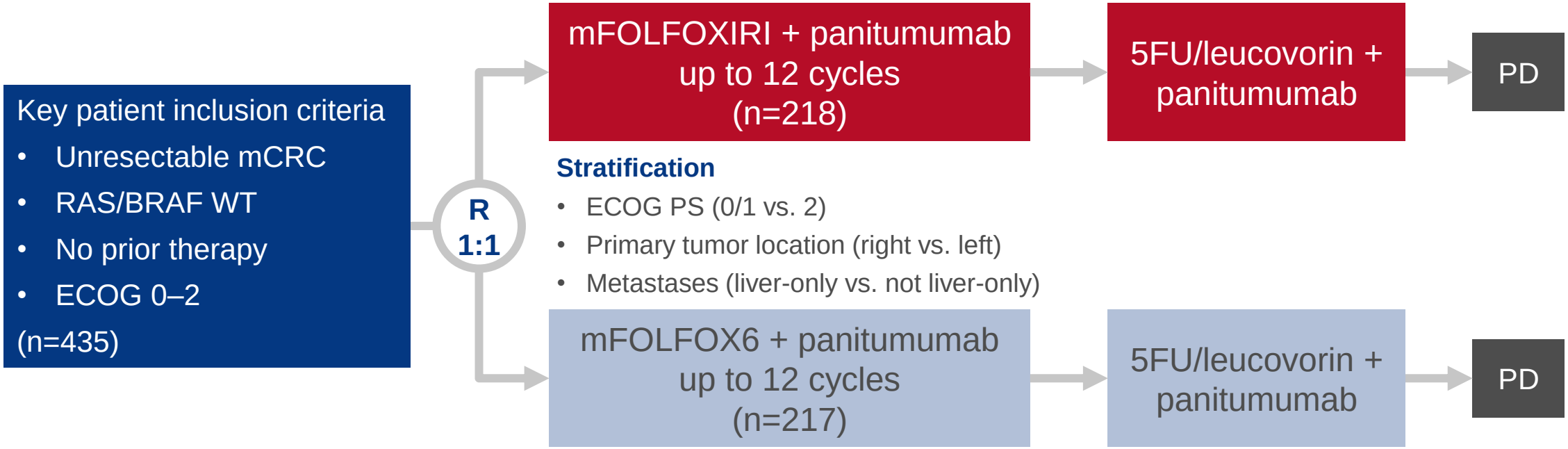
- **In patients with KRAS/NRAS/BRAF WT mCRC, there was no significant difference in duration of disease control between the two treatment arms although higher response rates and potentially better OS were observed in those who received FOLFIRI-cetuximab followed by mFOLFOX6-bevacizumab**

Chibaudel B, et al. J Clin Oncol 2022;40(suppl):abstr 3504

LBA3505: Modified FOLFOXIRI plus panitumumab (mFOLFOXIRI/PAN) versus mFOLFOX6/PAN as initial treatment of patients with unresectable RAS and BRAF wild-type metastatic colorectal cancer (mCRC): Results of the phase III randomized TRIPLETE study by GONO – Cremolini C, et al

Study objective

- To evaluate the efficacy and safety of 1L mFOLFOXIRI + panitumumab in patients with unresectable RAS/BRAF WT mCRC in Italian centers in the phase 3 TRIPLETE study



PRIMARY ENDPOINT

- ORR

SECONDARY ENDPOINTS

- Response, PFS, R0 rate, OS, safety

Cremolini C, et al. J Clin Oncol 2022;40(suppl):abstr LBA3505

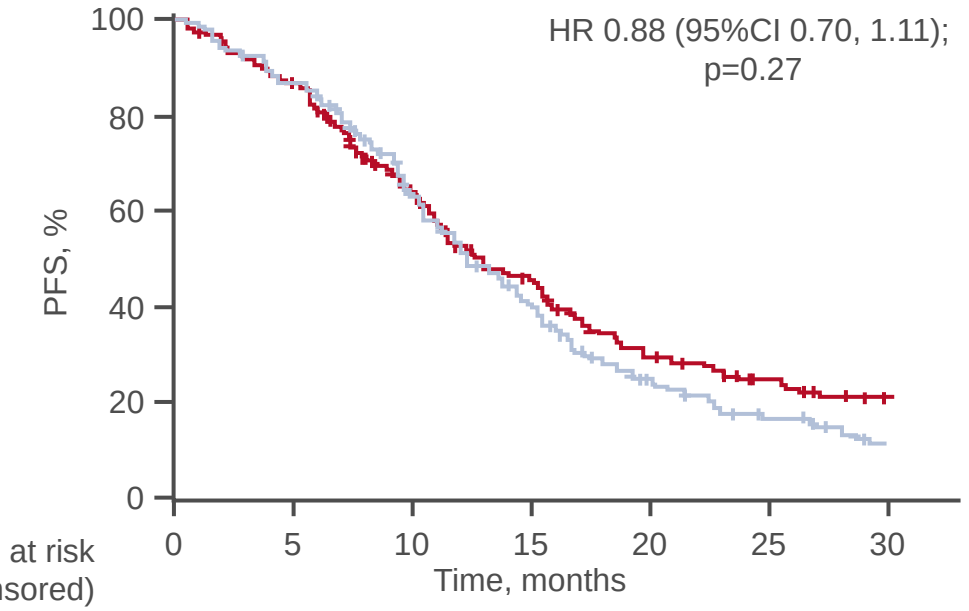
LBA3505: Modified FOLFOXIRI plus panitumumab (mFOLFOXIRI/PAN) versus mFOLFOX6/PAN as initial treatment of patients with unresectable RAS and BRAF wild-type metastatic colorectal cancer (mCRC): Results of the phase III randomized TRIPLETE study by GONO – Cremolini C, et al

Key results

Outcome, %	mFOLFOX6 + panitumumab (n=213)	mFOLFOXIRI + panitumumab (n=218)	OR (95%CI); p-value
CR	7	7	
PR	69	66	
SD	17	18	
PD	5	5	
NA	2	4	
ORR	76	73	0.87 (0.56,1.34); 0.526
R0 resection rate	29	25	0.81 (0.53, 1.23); 0.317

Progression-free survival

Median follow-up 26.5 mo	mFOLFOX6 + panitumumab (n=217)	mFOLFOXIRI + panitumumab (n=218)
Events, n (%)	157 (72)	148 (68)
mPFS, mos	12.3	12.7



Cremolini C, et al. J Clin Oncol 2022;40(suppl):abstr LBA3505

LBA3505: Modified FOLFOXIRI plus panitumumab (mFOLFOXIRI/PAN) versus mFOLFOX6/PAN as initial treatment of patients with unresectable RAS and BRAF wild-type metastatic colorectal cancer (mCRC): Results of the phase III randomized TRIPLETE study by GONO – Cremolini C, et al

Key results

Grade 3–4 AEs, %	FOLFOX + panitumumab (n=213)	mFOLFOXIRI + panitumumab (n=218)
Nausea	2	5
Vomiting	1	2
Diarrhea	7	23
Stomatitis	7	7
Neutropenia	20	32
Febrile neutropenia	3	5
Neurotoxicity	4	2
Fatigue	2	7
Skin rash	29	19
Hypomagnesemia	1	1

Conclusions

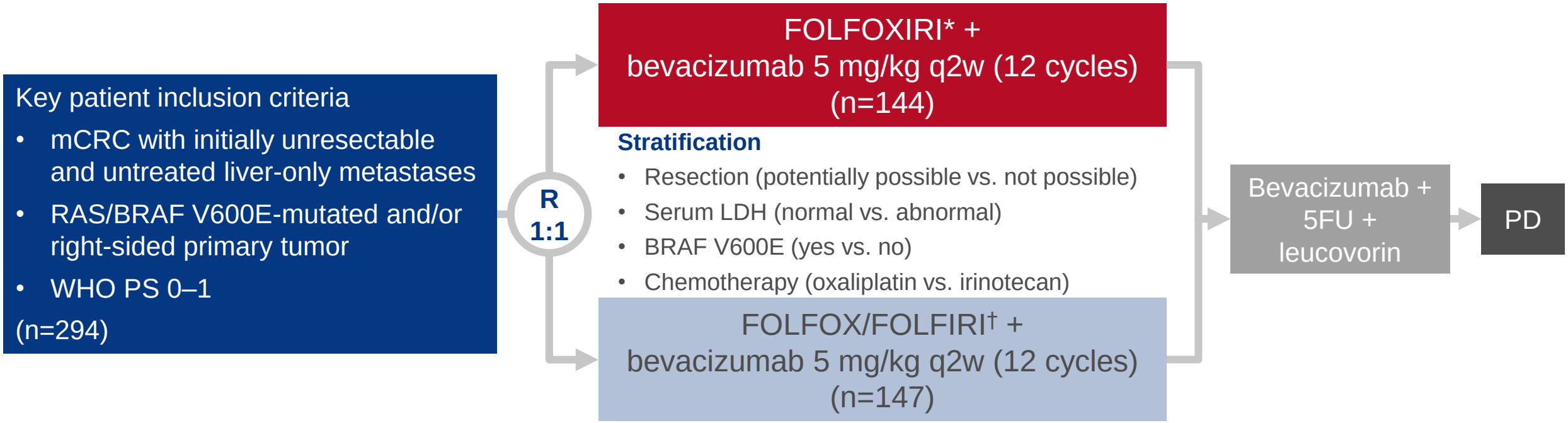
- **In patients with unresectable RAS/BRAK WT mCRC, mFOLFOXIRI + panitumumab did not significantly improve ORR compared with mFOLFOX6 + panitumumab**

Cremolini C, et al. J Clin Oncol 2022;40(suppl):abstr LBA3505

LBA3506: FOLFOXIRI + bevacizumab versus FOLFOX/FOLFIRI + bevacizumab in patients with initially unresectable colorectal liver metastases (CRLM) and right-sided and/or RAS/BRAFV600E-mutated primary tumor: Phase III CAIRO5 study of the Dutch Colorectal Cancer Group – Punt CJA, et al

Study objective

- To evaluate the efficacy and safety of FOLFOXIRI + bevacizumab in patients with initially unresectable colorectal liver metastases and/or RAS/BRAF V600E-mutated primary tumor in the phase 3 CAIRO5 study



PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

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

*Oxaliplatin 85 mg/m^2 + irinotecan 165 mg/m^2 + leucovorin 400 mg/m^2 + 5FU 3200 mg/m^2;
†oxaliplatin 85 mg/m^2 or irinotecan 180 mg/m^2 (patient preference) + leucovorin 400 mg/m^2 + 5FU 400 mg/m^2 bolus then 2400 mg/m^2

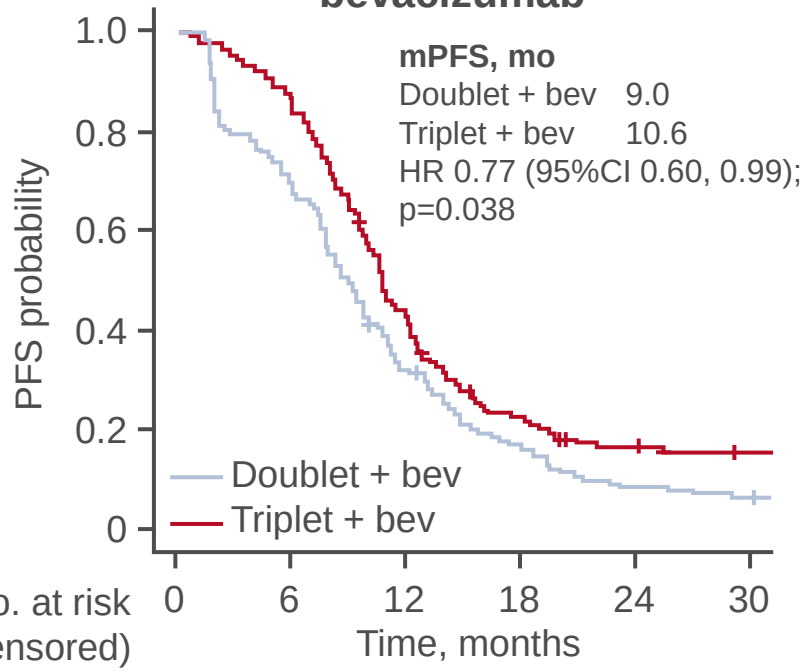
Punt CJA, et al. J Clin Oncol 2022;40(suppl):abstr LBA3506

LBA3506: FOLFOXIRI + bevacizumab versus FOLFOX/FOLFIRI + bevacizumab in patients with initially unresectable colorectal liver metastases (CRLM) and right-sided and/or RAS/BRAFV600E-mutated primary tumor: Phase III CAIRO5 study of the Dutch Colorectal Cancer Group – Punt CJA, et al

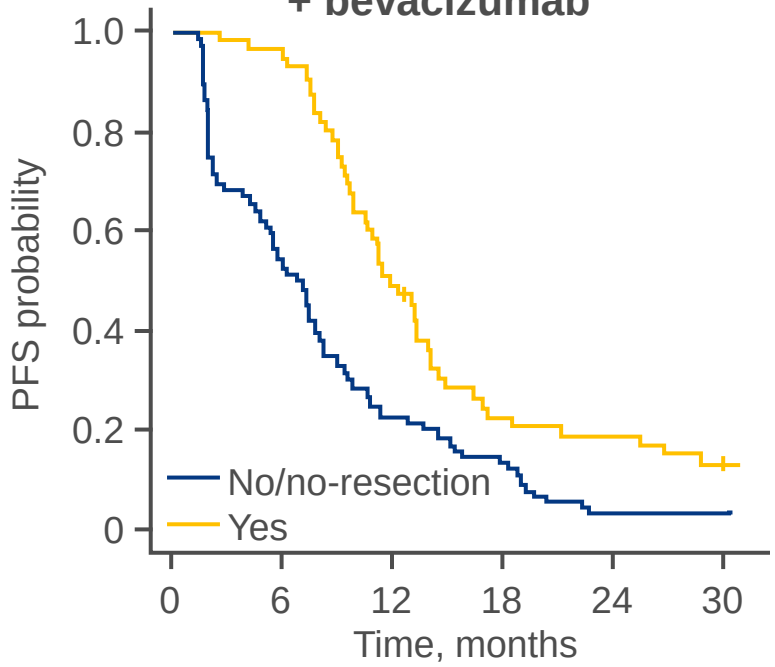
Key results

Progression-free survival

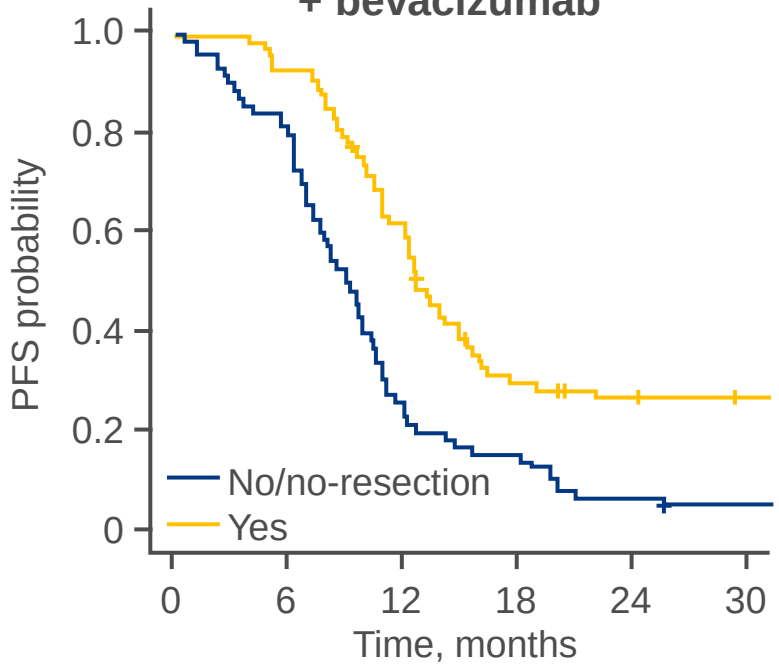
Triplet vs doublet + bevacizumab



FOLFOX/FOLFIRI + bevacizumab



FOLFOXIRI + bevacizumab



Punt CJA, et al. J Clin Oncol 2022;40(suppl):abstr LBA3506

LBA3506: FOLFOXIRI + bevacizumab versus FOLFOX/FOLFIRI + bevacizumab in patients with initially unresectable colorectal liver metastases (CRLM) and right-sided and/or RAS/BRAFV600E-mutated primary tumor: Phase III CAIRO5 study of the Dutch Colorectal Cancer Group – Punt CJA, et al

Key results

	FOLFOXIRI + bevacizumab	FOLFOX/ FOLFIRI + bevacizumab	p-value
Resectability, HR (95%CI)			0.98
Potentially resectable	0.74 (0.53, 1.05)		
Unresectable	0.67 (0.28, 1.58)		
Mutation status, HR (95%CI)			0.83
RAS mutation	0.76 (0.54, 1.07)		
BRAF V600E	0.72 (0.21, 2.48)		
WT + right-sided	0.54 (0.13, 2.26)		
mPFS, mo			
Without successful local therapy	9.0	7.0	<0.0001
With successful local therapy	12.7	11.9	<0.0001

	FOLFOXIRI + bevacizumab	FOLFOX/FOLFIRI + bevacizumab	p-value
Resection ± ablation rate, %	57	46	0.08
Postoperative complications	51	40	0.19
Clavien-Dindo			
Grade ≥3	27	15	0.08
Grade 5	2	0	
R0/1 resection ± ablation rate, %	51	37	0.02
2-stage surgery ± PVE	32	16	0.04
Grade ≥3 AEs, %			
Any	75.7	59.2	<0.001
Neutropenia	38.2	12.9	0.003
Diarrhea	19.4	3.4	<0.001
Death	1.4	0	<0.001

Conclusions

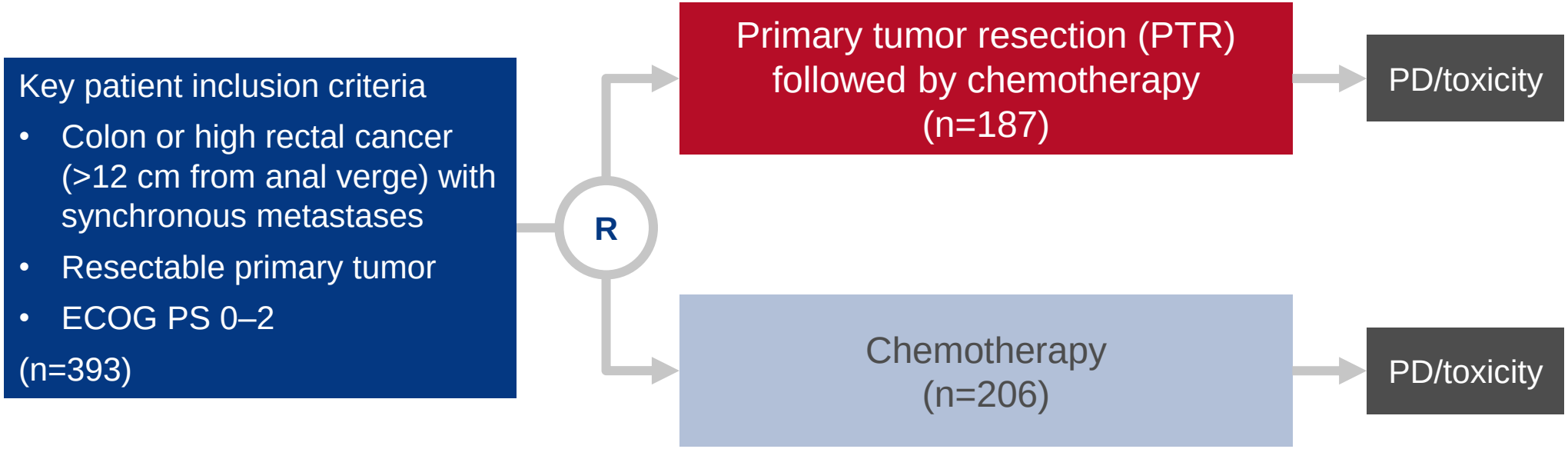
- **In patients with RAS/BRAF V600E-mutated or right-sided primary tumors and initially unresectable liver metastases, triplet chemotherapy demonstrated significant improvements in outcomes compared with doublet chemotherapy, but was associated with an increase in adverse events**

Punt CJA, et al. J Clin Oncol 2022;40(suppl):abstr LBA3506

LBA3507: Randomized clinical trial on resection of the primary tumor versus no resection prior to systemic therapy in patients with colon cancer and synchronous unresectable metastases – Rahbari NN, et al

Study objective

- To evaluate the efficacy and safety of resection prior to systemic therapy in patients with colon cancer and synchronous unresectable metastases in German and Spanish centers



PRIMARY ENDPOINT

- OS

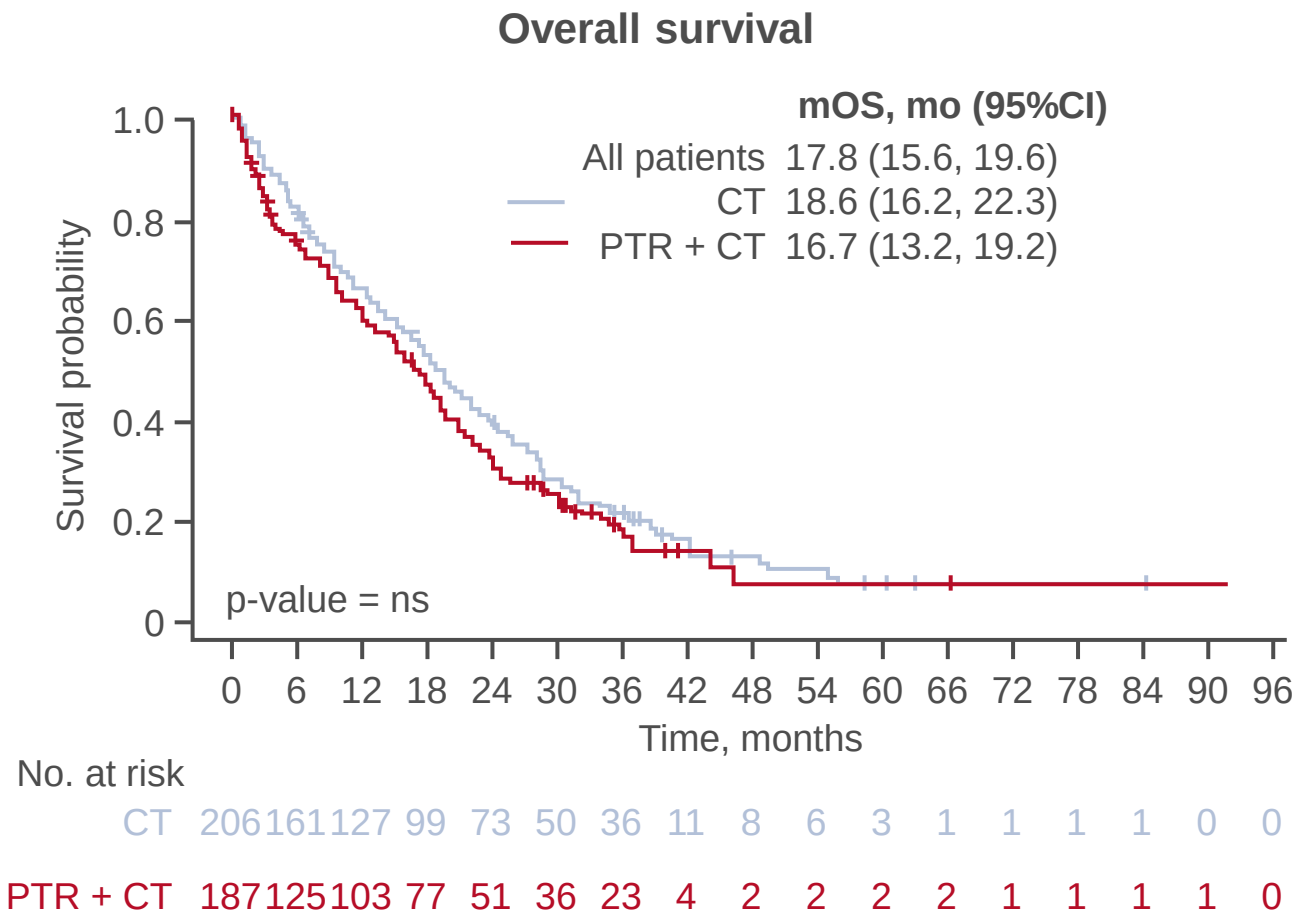
SECONDARY ENDPOINTS

- Perioperative morbidity/mortality, QoL, safety

Rahbari NN, et al. J Clin Oncol 2022;40(suppl):abstr LBA3507

LBA3507: Randomized clinical trial on resection of the primary tumor versus no resection prior to systemic therapy in patients with colon cancer and synchronous unresectable metastases – Rahbari NN, et al

Key results



Rahbari NN, et al. J Clin Oncol 2022;40(suppl):abstr LBA3507

LBA3507: Randomized clinical trial on resection of the primary tumor versus no resection prior to systemic therapy in patients with colon cancer and synchronous unresectable metastases – Rahbari NN, et al

Key results

SAEs, n (%)	CT (n=206)	PTR + CT (n=187)
Any	37 (18.0)	19 (10.2)
GI tract-related	22 (10.7)	8 (4.8)
SAEs, n	43	22
GI tract-related	24 (55.8)	8 (36.4)
Diarrhea	1 (2.3)	0
Vomiting	2 (4.7)	1 (4.5)
Ileus/bowel obstruction	18 (41.9)	2 (9.1)
Bowel perforation	3 (7.0)	3 (13.6)
Colonic fistula	0	2 (9.1)
Other	19 (44.2)	14 (4.8)

Conclusions

- **In patients with colon or high rectal cancer and synchronous unresectable metastases, resection of the primary tumor prior to chemotherapy did not improve OS compared with chemotherapy alone**

Rahbari NN, et al. J Clin Oncol 2022;40(suppl):abstr LBA3507