GI SLIDE DECK 2020

Selected abstracts from:

european society of digestive oncology
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Letter from ESDO

DEAR COLLEAGUES

It is our pleasure to present this ESDO slide set which has been designed to highlight and summarize key findings in digestive cancers from the major congresses in 2020. This slide set specifically focuses on the **2020 American Society of Clinical Oncology Virtual Scientific Program** and is available in English, French, Chinese and Japanese.

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

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

Yours sincerely,

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(ESDO Governing Board)

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european society of digestive oncology

ESDO Medical Oncology Slide Deck
Editors 2020

COLORECTAL CANCERS



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GASTRO-OESOPHAGEAL AND NEUROENDOCRINE TUMOURS


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Glossary

1L	first-line
2L	second-line
5FU	5-fluouracil
AE	adverse event
AFP	alpha-fetoprotein
ALT	alanine aminotransferase
ASCC	anal squamous cell carcinoma
AST	aspartate aminotransferase
AUC	area under the curve
BCLC	Barcelona clinic liver cancer
BICR	blinded-independent central review
bid	twice daily
BOR	best overall response
CA19-9	carbohydrate antigen 19-9
CAPOX	capecitabine + oxaliplatin
chemo	chemotherapy
CI	confidence interval
CPS	combined positive score
CR	complete response
CRC	colorectal cancer
CRT	chemoradiotherapy
D	day
DCR	disease control rate
(m)DFS	**(median)** disease-free survival
DLTs	dose-limiting toxicities
DMC	data monitoring committee
dMMR	deficient mismatch repair
DoR	duration of response
DoT	duration of treatment
DrTF	disease-related treatment failure
ECOG	Eastern Cooperative Oncology Group
EGFR	epidermal growth factor receptor
FGFR	fibroblast growth factor receptor
FISH	fluorescence in situ hybridization
FLOT	5-fluouracil + leucovorin + oxaliplatin + docetaxel
FOLFIRI	folinic acid + 5-fluouracil + irinotecan
(m)FOLFIRINOX	(modified) 5-fluouracil + leucovorin + oxaliplatin + irinotecan
(m)FOLFOX	(modified) leucovorin + 5-fluorouracil + oxaliplatin
FOLFOXIRI	5-fluouracil + leucovorin + oxaliplatin + irinotecan
GEJ	gastro-esophageal junction
gem	gemcitabine
GEMCAP	gemcitabine + capecitabine
GI	gastrointestinal
Gy	Gray
HCC	hepatocellular carcinoma
HER2	human epidermal growth factor receptor 2
HR	hazard ratio
iCCA	intrahepatic cholangiocarcinoma
ICR	independent central review
IHC	immunohistochemistry
ITT	intent-to-treat
iv	intravenous
LV	leucovorin
mCRC	metastatic colorectal cancer
MFS	metastasis-free survival
mo	months
MSI-H	high microsatellite instability
MSS	microsatellite stable
NA	not available
nab-P	nab-paclitaxel
NCCN	National Comprehensive Cancer Network
NE	not evaluable/estimable
NR	not reached
ORR	overall/objective response rate
OR	odds ratio
(m)OS	(median) overall survival
pani	panitumumab
pCR	pathological complete response
PD	progressive disease
PD-L1	programmed death-ligand 1
pembro	pembrolizumab
(m)PFS	(median) progression-free survival
pMMR	proficient mismatch repair
po	orally
PR	partial response
PS	performance status
pts	patients
q(2/3/4)w	every (2/3/4) week(s)
QoL	quality of life
R	randomized
R0	resection 0
RECIST	Response Evaluation Criteria In Solid Tumors
RFS	relapse-free survival
RR	relative risk
SAE	serious adverse events
SD	stable disease
TEAE	treatment-emergent adverse event
TRAE	treatment-related adverse event
TTP	time to progression
TTR	time to response
WHO	World Health Organization
WT	wild type
y	years

Contents

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

CANCERS OF THE OESOPHAGUS AND STOMACH

4500: Trastuzumab with trimodality treatment for esophageal adenocarcinoma with HER2 overexpression: NRG Oncology/RTOG 1010 – Safran H, et al

Study objective

- To evaluate the efficacy and safety of trastuzumab + trimodality treatment for patients with esophageal adenocarcinoma and HER2 overexpression

Key patient inclusion criteria

- Stage T1 N1-2, T2-3 N0-2 esophageal adenocarcinoma (mid, distal or GEJ and up to 5 cm of stomach)
- HER2 overexpression (IHC and FISH)
- Treatment naïve

(n=203)

R 1:1

Trastuzumab 4 mg/kg (1 week) then 2 mg/kg (q1w for 5 weeks) + chemoradiotherapy* then 6 mg/kg (1 dose) prior to surgery followed by 6 mg/kg q3w (13 courses) (n=102)

Stratification

- Presence of adenopathy (no vs. yes-celiac absent vs. yes-celiac present ≤2 cm)

Chemoradiotherapy* followed by surgery (n=101)

PRIMARY ENDPOINT

- DFS

SECONDARY ENDPOINTS

- OS, pCR rate, safety

*Paclitaxel 50 mg/m^2 + carboplatin AUC2 (6 weeks) with radiation (50.4 Gy in 28 fractions)

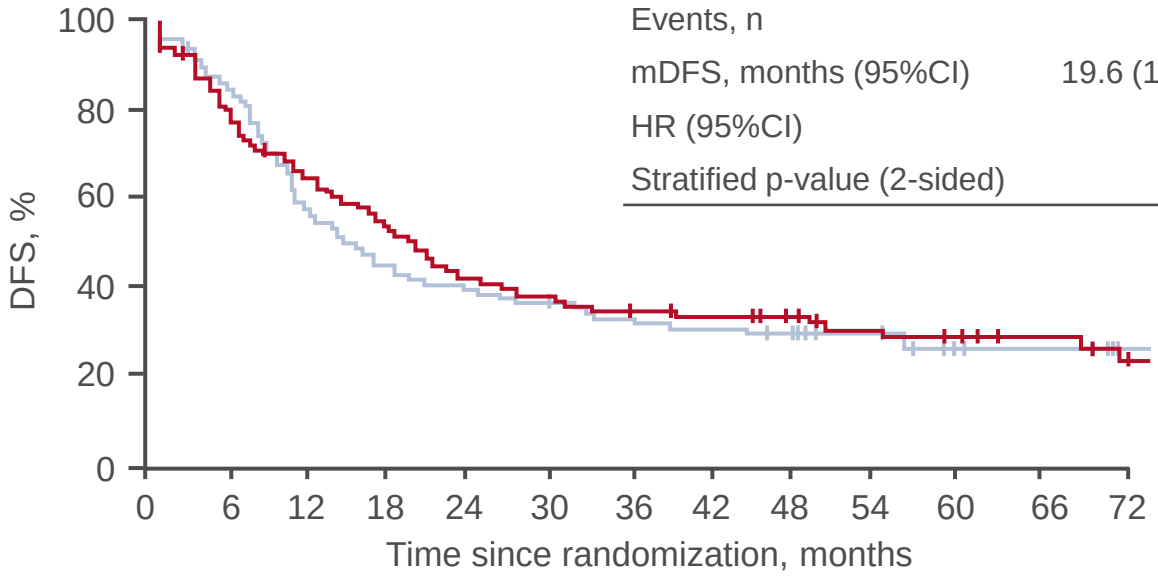
Safron H, et al. J Clin Oncol 2020;38(suppl);abstr 4500

4500: Trastuzumab with trimodality treatment for esophageal adenocarcinoma with HER2 overexpression: NRG Oncology/RTOG 1010 – Safran H, et al

Key results

DFS

	Trastuzumab + CRT (n=98)	CRT (n=96)
Events, n	68	67
mDFS, months (95%CI)	19.6 (13.5, 26.2)	14.2 (10.5, 23.0)
HR (95%CI)	0.97 (0.69, 1.36)	
Stratified p-value (2-sided)	0.85	



Trastuzumab + CRT	98	72	60	48	39	35	32	29	26	20	19	13	10
CRT	96	77	51	42	37	33	30	28	26	22	17	14	13

Safron H, et al. J Clin Oncol 2020;38(suppl);abstr 4500

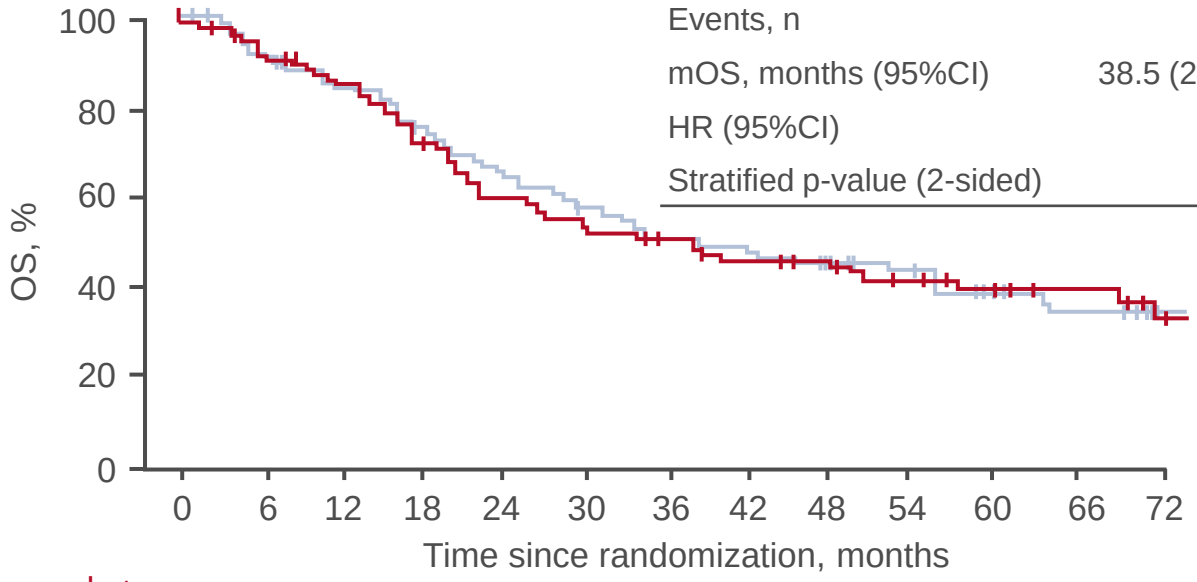
4500: Trastuzumab with trimodality treatment for esophageal adenocarcinoma with HER2 overexpression: NRG Oncology/RTOG 1010 – Safran H, et al

Key result

- No significant differences in pCR rate: 27% trastuzumab + CRT and 29% for CRT (p=0.71)

OS

	Trastuzumab + CRT (n=98)	CRT (n=96)
Events, n	54	55
mOS, months (95%CI)	38.5 (26.2, 70.4)	38.9 (29.0, 64.5)
HR (95%CI)	1.01 (0.69, 1.47)	
Stratified p-value (2-sided)	0.95	



Trastuzumab + CRT	98	87	79	67	55	51	46	40	37	26	23	16	12
CRT	96	87	78	69	61	52	46	44	39	31	24	17	15

Safron H, et al. J Clin Oncol 2020;38(suppl);abstr 4500

4500: Trastuzumab with trimodality treatment for esophageal adenocarcinoma with HER2 overexpression: NRG Oncology/RTOG 1010 – Safran H, et al

Key results (cont.)

Select grade ≥3 TRAEs, n (%)	Trastuzumab + CRT (n=95)	CRT (n=96)
Any	66 (69)	76 (79)
Hematologic	53 (56)	55 (57)
Cardiac disorders	5 (5)	3 (3)
GI disorders	28 (29)	20 (21)
Infections	11 (12)	7 (7)
Metabolism and nutrition	12 (13)	19 (20)

Conclusion

- **In patients with esophageal adenocarcinoma and HER2 overexpression, no improvements in DFS, OS or pCR or increased toxicity were observed with the addition of trastuzumab to trimodality treatment**

Safron H, et al. J Clin Oncol 2020;38(suppl);abstr 4500

4501: Perioperative ramucirumab in combination with FLOT versus FLOT alone for resectable esophagogastric adenocarcinoma (RAMSES/FLOT7): Results of the phase II-portion—A multicenter, randomized phase II/III trial of the German AIO and Italian GOIM – Al-Batran S-E, et al

Study objective

- To evaluate the efficacy and safety of perioperative ramucirumab + FLOT in patients with resectable esophagogastric adenocarcinoma

Key patient inclusion criteria

- Resectable gastric or GEJ adenocarcinoma (≥cT2 or cN+)
- No distant metastases
- HER2 negative
- ECOG PS ≤1

(n=180)

R 1:1

Ramucirumab 8 mg/kg q2w + FLOT* (4 cycles) then surgery then ramucirumab 8 mg/kg q2w + FLOT* (4 cycles) followed by ramucirumab (16 cycles) (n=89)

Stratification

- Tumor site (GEJ vs. gastric)
- Stage (T1/2 vs. T3/4 and/or N+)
- Histology (intestinal vs. diffuse/mixed or unknown)

FLOT* (4 cycles) then surgery followed by FLOT* (4 cycles) (n=91)

PRIMARY ENDPOINT

- Response (near or pCR)

SECONDARY ENDPOINTS

- R0 rate, PFS, OS, safety

*Four pre- and postoperative cycles of docetaxel 50 mg/m^2 + oxaliplatin 85 mg/m^2 + leucovorin 200 mg/m^2 + 5FU 2600 mg/m^2 q2w

Al-Batran S-E, et al. J Clin Oncol 2020;38(suppl);abstr 4501

4501: Perioperative ramucirumab in combination with FLOT versus FLOT alone for resectable esophagogastric adenocarcinoma (RAMSES/FLOT7): Results of the phase II-portion—A multicenter, randomized phase II/III trial of the German AIO and Italian GOIM – Al-Batran S-E, et al

Key results

Outcome, n (%)	Ramucirumab + FLOT (n=86)	FLOT (n=87)
≤T1	17 (20)	22 (25)
T2	12 (14)	10 (12)
T3	49 (57)	33 (38)
T4	6 (7)	12 (14)
N0	43 (50)	34 (39)
Pathological response	23 (27)	26 (30)
p-value	0.7363	
R0 rate	83 (97)	72 (83)
p-value	0.0049	

Al-Batran S-E, et al. J Clin Oncol 2020;38(suppl);abstr 4501

4501: Perioperative ramucirumab in combination with FLOT versus FLOT alone for resectable esophagogastric adenocarcinoma (RAMSES/FLOT7): Results of the phase II-portion—A multicenter, randomized phase II/III trial of the German AIO and Italian GOIM – Al-Batran S-E, et al

Key results (cont.)

Grade ≥3 AEs, n (%)	Ramucirumab + FLOT (n=88)	FLOT (n=90)
Any	78 (89)	69 (77)
SAEs	65 (74)	44 (49)
Neutropenia	35 (40)	33 (37)
Febrile	4 (5)	1 (1)
Diarrhea	12 (14)	9 (10)
Vomiting	7 (8)	2 (2)
Nausea	8 (9)	8 (9)
Hypertension	9 (10)	2 (2)
Peripheral sensory neuropathy	3 (3)	1 (1)
Thromboembolic	1 (1)	2 (2)

Conclusion

- **In patients with resectable esophagogastric adenocarcinoma, adding ramucirumab to FLOT was well tolerated and significantly improved R0 rate, but did not improve pathological response**

Al-Batran S-E, et al. J Clin Oncol 2020;38(suppl);abstr 4501

4502: Perioperative trastuzumab and pertuzumab in combination with FLOT versus FLOT alone for HER2-positive resectable esophagogastric adenocarcinoma: Final results of the PETRARCA multicenter randomized phase II trial of the AIO – Hofheinz RD, et al

Study objective

- To evaluate the efficacy and safety of trastuzumab + pertuzumab + FLOT in patients with resectable HER2-positive esophagogastric adenocarcinoma

Key patient inclusion criteria

- Resectable esophagogastric adenocarcinoma (cT2–4, cN any, cM0 or T any, cN+, cM0)
- HER2-positive
- ECOG PS ≤2

(n=81)

R 1:1

Trastuzumab* + pertuzumab† + FLOT‡ x4 then resection then trastuzumab* + pertuzumab† + FLOT‡ x4 followed by trastuzumab* + pertuzumab† (9 cycles q3w) (n=40)

FLOT‡ x4 then resection then FLOT‡ x4 (n=41)

Stratification

- ECOG PS (0–1 vs. 2), location of primary tumor (GEJ vs. stomach), age (<60 vs. 60–69 vs. ≥70 years)

PRIMARY ENDPOINT

- pCR

SECONDARY ENDPOINTS

- DFS, OS, R0 rate, safety

*Trastuzumab 8 (loading)/6 mg/kg D1, 22, 43; †pertuzumab 840 mg D1, 22, 43; ‡docetaxel 50 mg/m^2 + oxaliplatin 85 mg/m^2 + leucovorin 200 mg/m^2 + 5FU 2600 mg/m^2 D1, 15, 29, 43

Hofheinz RD, et al. J Clin Oncol 2020;38(suppl);abstr 4502

4502: Perioperative trastuzumab and pertuzumab in combination with FLOT versus FLOT alone for HER2-positive resectable esophagogastric adenocarcinoma: Final results of the PETRARCA multicenter randomized phase II trial of the AIO – Hofheinz RD, et al

Key result

	Trastuzumab + pertuzumab + FLOT (n=40)	FLOT (n=41)
pCR, n (%)	14 (35)	5 (12)
p-value	0.02	

ypT-stage, n (%)	Trastuzumab + pertuzumab + FLOT (n=40)	FLOT (n=41)
≤T1	17 (43)	11 (27)
T2	8 (20)	9 (22)
T3	14 (35)	17 (41)
T4	0 (0)	3 (7)
N0	27 (68)	16 (39)

Median follow-up: 22 months

Hofheinz RD, et al. J Clin Oncol 2020;38(suppl);abstr 4502

4502: Perioperative trastuzumab and pertuzumab in combination with FLOT versus FLOT alone for HER2-positive resectable esophagogastric adenocarcinoma: Final results of the PETRARCA multicenter randomized phase II trial of the AIO – Hofheinz RD, et al

Key results (cont.)

AEs, %	Trastuzumab + pertuzumab + FLOT (n=39)	FLOT (n=40)
Any grade 3–4 AEs	85	75
Any SAEs	67	58
AEs occurring in ≥5%		
Leukopenia	23	13
Neutropenia	28	30
Diarrhea	41	5
Vomiting	5	3
Nausea	8	10
Fatigue (grade 2–3)	23	15

Conclusions

- **In patients with HER2+ esophagogastric adenocarcinoma, pCR was significantly improved with the addition of trastuzumab + pertuzumab to FLOT**
- **There was a higher rate of AEs in the trastuzumab + pertuzumab + FLOT arm**

Hofheinz RD, et al. J Clin Oncol 2020;38(suppl);abstr 4502

4503: Pembrolizumab versus paclitaxel for previously treated patients with PD-L1–positive advanced gastric or gastroesophageal junction cancer (GC): Update from the phase III KEYNOTE-061 trial – Fuchs CS, et al

Study objective

- To evaluate the long-term efficacy and safety of pembrolizumab vs. paclitaxel in previously treated patients with advanced gastric/GEJ cancer in the KEYNOTE-061 study

Key patient inclusion criteria

- Adenocarcinoma of the stomach/GEJ
- Metastatic or locally advanced
- Unresectable
- PD after 1L chemotherapy containing platinum and fluoropyrimidine
- ECOG PS 0–1

(n=592)

R 1:1

Pembrolizumab 200 mg q3w (n*=196/296) → For 35 cycles or until PD/toxicity/ withdrawal/ investigator decision

Paclitaxel† (n*=199/296) → PD/toxicity/ withdrawal/ investigator decision

Stratification

- Geographic region
- ECOG PS (0 vs. 1)
- TTP on 1L therapy (<6 vs. ≥6 months)
- PD-L1 combined positive score (CPS <1 vs. ≥1)

PRIMARY ENDPOINTS

- OS‡, PFS in CPS ≥1 population

SECONDARY ENDPOINTS

- ORR, DoR in CPS ≥1 population
- Safety in all patients

*n for CPS ≥1 population/all patients; †80 mg/m^2 D1, 8, 15 of 4-week cycle; ‡pre-specified significance threshold for OS: p≤0.0135

Fuchs CS, et al. J Clin Oncol 2020;38(suppl);abstr 4503

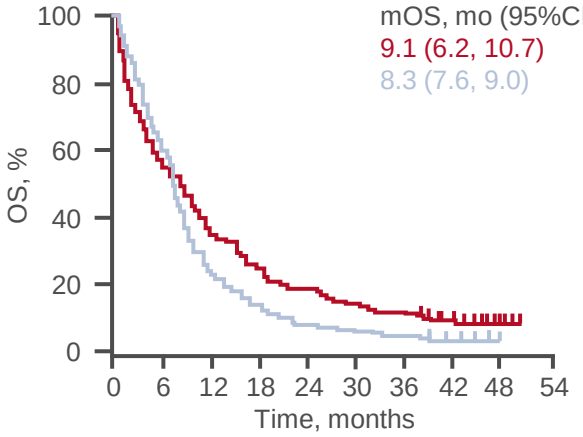
4503: Pembrolizumab versus paclitaxel for previously treated patients with PD-L1–positive advanced gastric or gastroesophageal junction cancer (GC): Update from the phase III KEYNOTE-061 trial – Fuchs CS, et al

Key results

OS

CPS ≥1

	Events/Pts	HR (95%CI)
Pembrolizumab	176/196	0.81 (0.66, 1.00)
Paclitaxel	190/199	

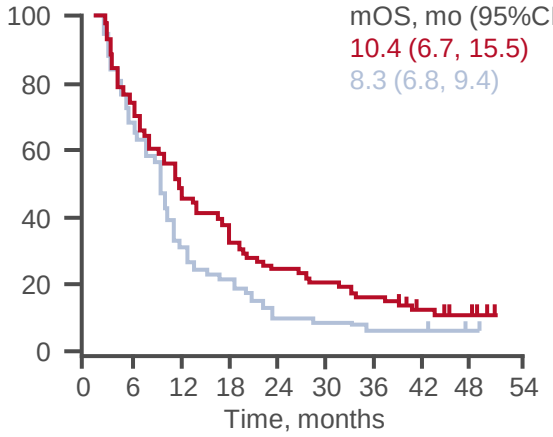


No. at risk

196	114	78	52	39	30	25	16	9	0
199	130	54	30	17	15	11	7	2	0

CPS ≥5

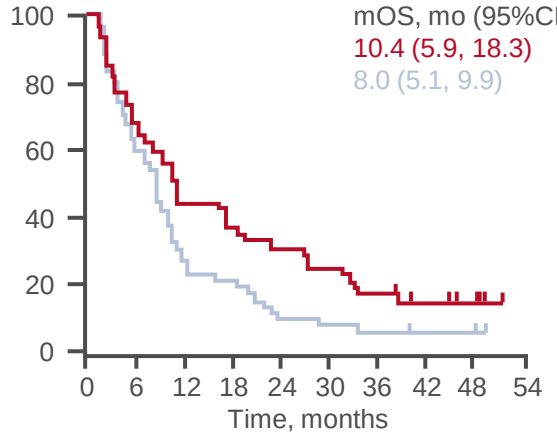
	Events/Pts	HR (95%CI)
Pembrolizumab	84/95	0.72 (0.53, 0.99)
Paclitaxel	86/91	



95	61	43	30	23	19	15	9	6	0
91	57	23	16	8	7	5	4	2	0

CPS ≥10

	Events/Pts	HR (95%CI)
Pembrolizumab	44/53	0.69 (0.46, 1.05)
Paclitaxel	51/55	



53	34	24	20	17	14	10	7	5	0
55	33	13	11	6	5	4	3	2	0

Fuchs CS, et al. J Clin Oncol 2020;38(suppl);abstr 4503

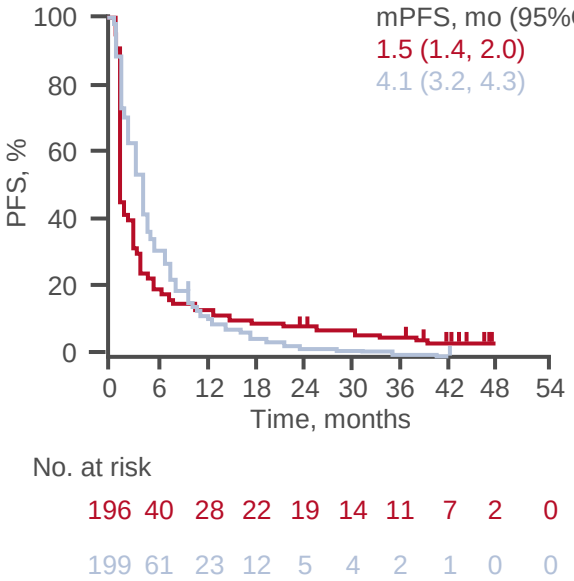
4503: Pembrolizumab versus paclitaxel for previously treated patients with PD-L1–positive advanced gastric or gastroesophageal junction cancer (GC): Update from the phase III KEYNOTE-061 trial – Fuchs CS, et al

Key results (cont.)

PFS

CPS ≥1

	Events/Pts	HR (95%CI)
Pembrolizumab	185/196	1.25 (1.02, 1.54)
Paclitaxel	192/199	

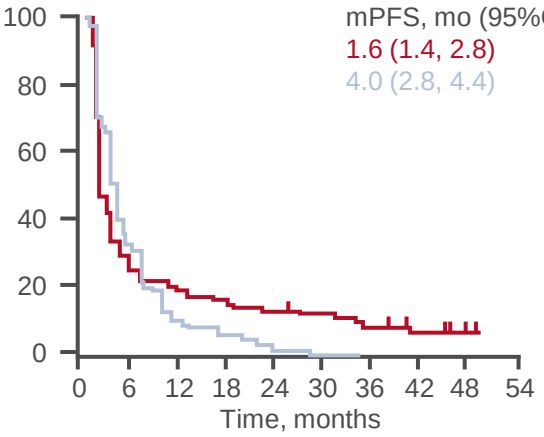


No. at risk

196	40	28	22	19	14	11	7	2	0
199	61	23	12	5	4	2	1	0	0

CPS ≥5

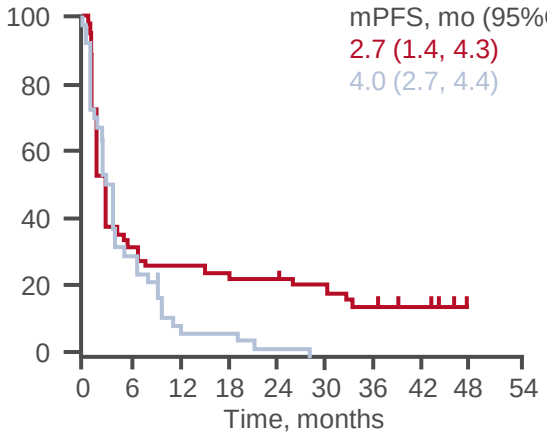
	Events/Pts	HR (95%CI)
Pembrolizumab	87/95	0.98 (0.71, 1.34)
Paclitaxel	87/91	



95	24	19	15	13	11	8	5	2	0
91	27	8	6	2	1	0	0	0	0

CPS ≥10

	Events/Pts	HR (95%CI)
Pembrolizumab	45/53	0.79 (0.51, 1.21)
Paclitaxel	52/55	



53	17	14	13	12	10	7	5	2	0
55	15	4	3	1	0	0	0	0	0

Fuchs CS, et al. J Clin Oncol 2020;38(suppl);abstr 4503

4503: Pembrolizumab versus paclitaxel for previously treated patients with PD-L1–positive advanced gastric or gastroesophageal junction cancer (GC): Update from the phase III KEYNOTE-061 trial – Fuchs CS, et al

Key results (cont.)

Outcome	CPS ≥1		CPS ≥5		CPS ≥10	
	Pembro (n=196)	Paclitaxel (n=199)	Pembro (n=95)	Paclitaxel (n=91)	Pembro (n=53)	Paclitaxel (n=55)
ORR, n (%)	32 (16.3)	27 (13.6)	19 (20.0)	13 (14.3)	13 (24.5)	5 (9.1)
BOR, n (%)						
CR	9 (4.6)	5 (2.5)	7 (7.4)	2 (2.2)	7 (13.2)	1 (1.8)
PR	23 (11.7)	22 (11.1)	12 (12.6)	11 (12.1)	6 (11.3)	4 (7.3)
SD	44 (22.4)	90 (45.2)	23 (24.2)	42 (46.2)	12 (22.6)	28 (50.9)
PD	95 (48.5)	46 (23.1)	45 (47.4)	20 (22.0)	23 (43.4)	11 (20.0)
Median DoR, months (range)	19.1 (1.4+ to 47.1+)	5.2 (1.3+ to 16.8)	32.7 (4.1 to 47.1+)	4.8 (1.3+ to 15.3)	NR (4.1 to 47.1+)	6.9 (2.6 to 6.9)

+ denotes ongoing

Fuchs CS, et al. J Clin Oncol 2020;38(suppl);abstr 4503

4503: Pembrolizumab versus paclitaxel for previously treated patients with PD-L1–positive advanced gastric or gastroesophageal junction cancer (GC): Update from the phase III KEYNOTE-061 trial – Fuchs CS, et al

Key results (cont.)

AEs, n (%)	Pembro (n=294)	Paclitaxel (n=276)
AEs	-	-
Grade 3–5	157 (53.4)	154 (55.8)
Serious AE	108 (36.7)	68 (24.6)
Led to treatment discontinuation	14 (4.8)	25 (9.1)
Death	10 (3.4)	8 (2.9)
Any TRAE	157 (53.4)	233 (84.4)
Grade 3–5	44 (15.0)	97 (35.1)
Serious TRAE	25 (8.5)	14 (5.1)
Led to treatment discontinuation	10 (3.4)	15 (5.4)
Death	3 (1.0)	1 (0.4)

Conclusions

- **In patients with PD-L1–positive advanced gastric or GEJ cancer, no significant differences in OS or PFS were observed with pembrolizumab and paclitaxel**
- **Pembrolizumab showed increased clinical benefit with increasing PD-L1 enrichment**

Fuchs CS, et al. J Clin Oncol 2020;38(suppl);abstr 4503

4514: FOLFIRI plus ramucirumab versus paclitaxel plus ramucirumab as second-line therapy for patients with advanced or metastatic gastroesophageal adenocarcinoma with or without prior docetaxel: Results from the phase II RAMIRIS Study of the AIO – Lorenzen S, et al

Study objective

- To evaluate the efficacy and safety of ramucirumab + FOLFIRI vs. ramucirumab + paclitaxel as a 2L treatment for patients with advanced gastroesophageal adenocarcinoma

Key patient inclusion criteria

- Metastatic or locally advanced adenocarcinoma of the stomach or GEJ
- PD after platinum and fluoropyrimidine containing regimen
- ECOG PS ≤1

(n=111)

R 2:1

Ramucirumab 8 mg/kg iv D1, 15 q4w + FOLFIRI* D1, 15 q4w (n=72)

Ramucirumab 8 mg/kg iv D1, 15 q4w + paclitaxel 80 mg/m^2 D1, 8, 15 q4w (n=38)

Stratification

- Previous docetaxel-containing therapy (yes vs. no)
- TTP during or after end of 1L therapy (≤3 vs. >3 months)

ENDPOINTS

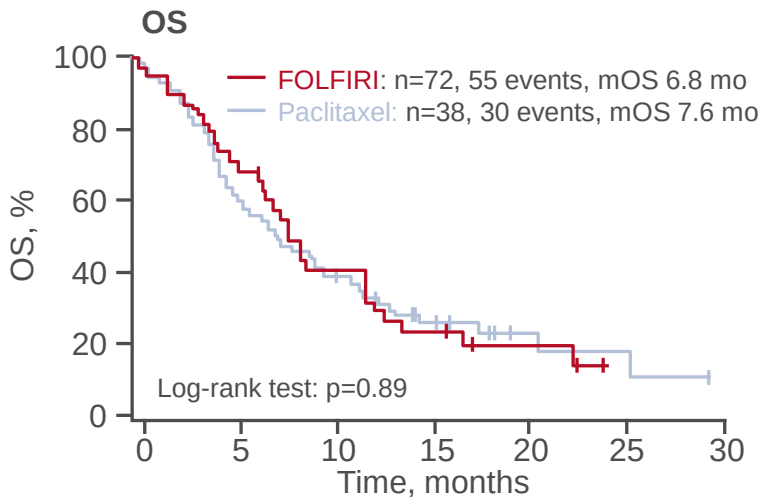
- OS, ORR, DCR, PFS, other response rates

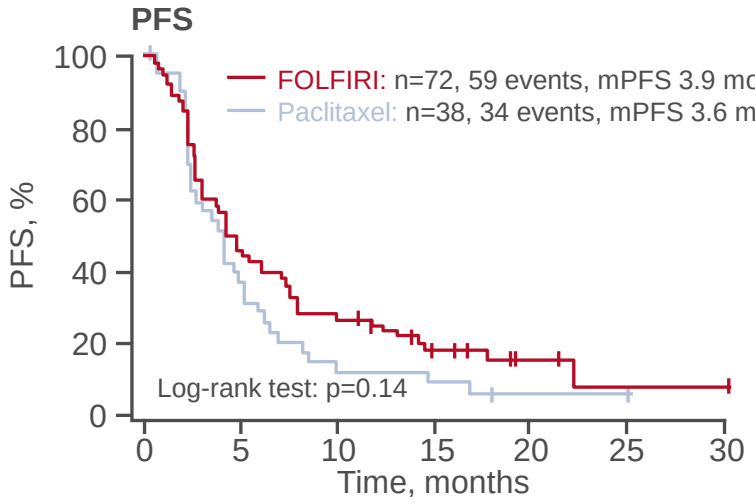
*Irinotecan 180 mg/m^2 + leucovorin 400 mg/m^2 + 5FU 400 mg/m^2 bolus then 2400 mg/m^2 continuous

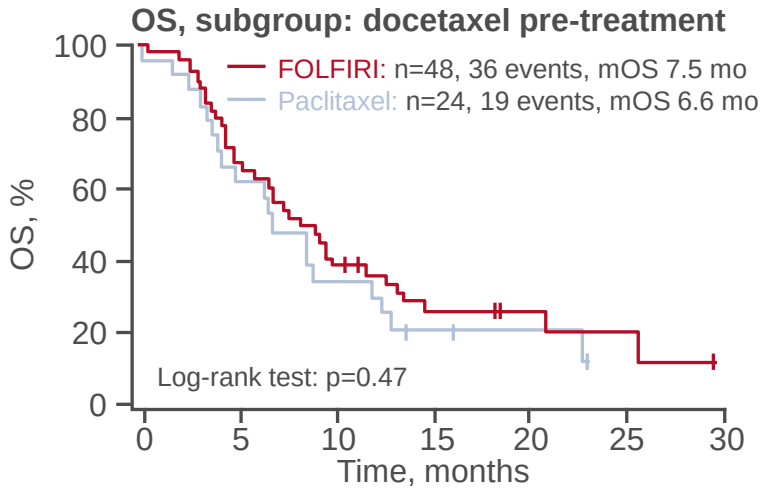
Lorenzen S, et al. J Clin Oncol 2020;38(suppl);abstr 4514

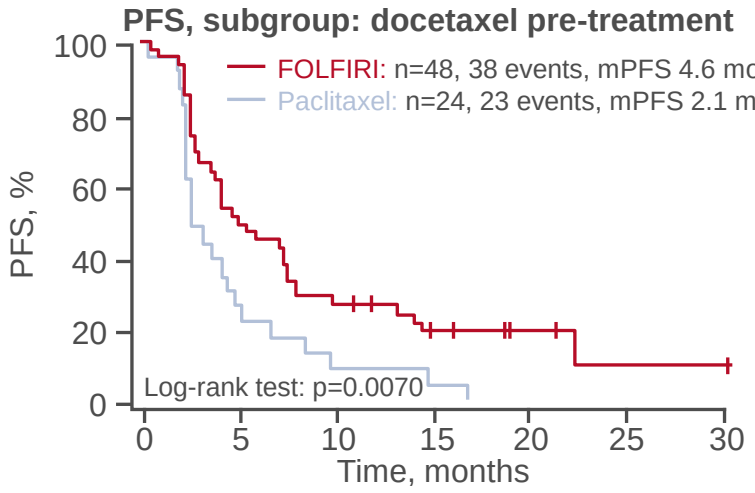
4514: FOLFIRI plus ramucirumab versus paclitaxel plus ramucirumab as second-line therapy for patients with advanced or metastatic gastroesophageal adenocarcinoma with or without prior docetaxel: Results from the phase II RAMIRIS Study of the AIO – Lorenzen S, et al

Key results









Lorenzen S, et al. J Clin Oncol 2020;38(suppl);abstr 4514

4514: FOLFIRI plus ramucirumab versus paclitaxel plus ramucirumab as second-line therapy for patients with advanced or metastatic gastroesophageal adenocarcinoma with or without prior docetaxel: Results from the phase II RAMIRIS Study of the AIO – Lorenzen S, et al

Key results (cont.)

Event, n (%)	FOLFIRI + ramucirumab (n=72)	Paclitaxel + ramucirumab (n=38)
CR	2 (3)	1 (3)
PR	14 (19)	3 (8)
SD	28 (39)	16 (42)
PD	18 (25)	10 (26)
No formal RECIST restaging	10 (14)	8 (21)
ORR	16 (22)	4 (11)
ORR in docetaxel pre-treated patients, n/N (%)	12/48 (25)	2/24 (8)
DCR	44 (61)	21 (58)
DCR in docetaxel pre-treated patients, n/N (%)	31/48 (65)	9/24 (37)

Conclusions

- **In patients with advanced or metastatic gastroesophageal adenocarcinoma, combining FOLFIRI with ramucirumab is feasible and demonstrated greater benefit in patients pre-treated with docetaxel**

Lorenzen S, et al. J Clin Oncol 2020;38(suppl);abstr 4514

CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

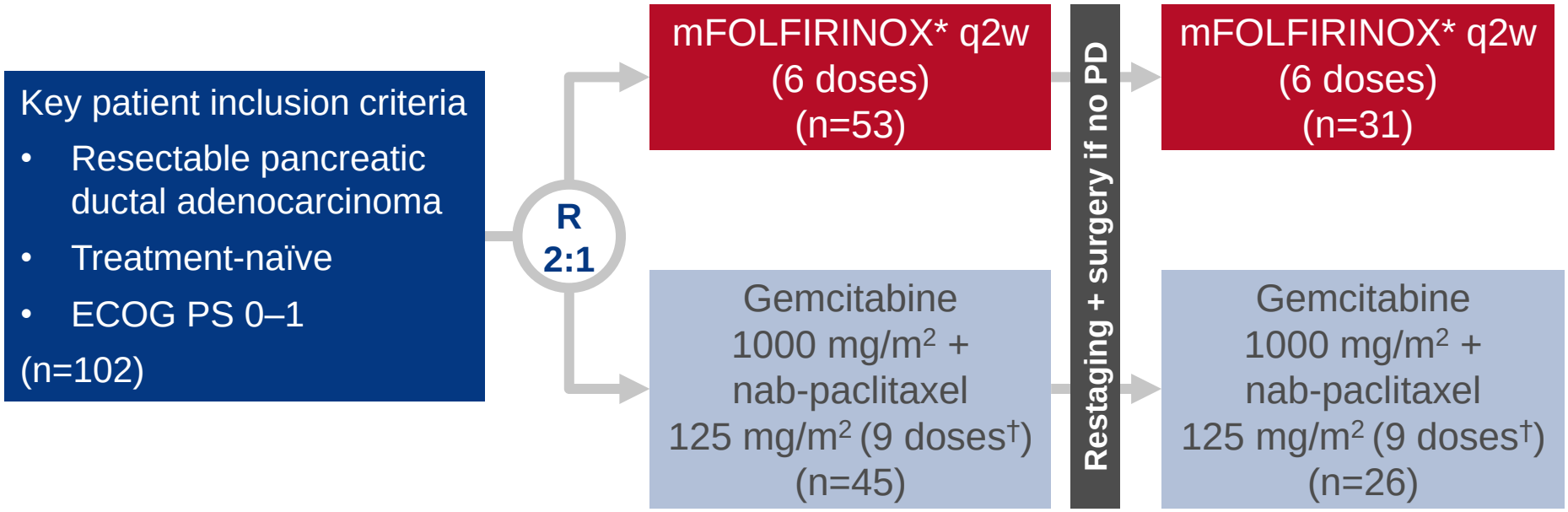
Cancers of the pancreas, small bowel and hepatobiliary tract

PANCREATIC CANCER

4504: SWOG S1505: Results of perioperative chemotherapy (peri-op CTx) with mFOLFIRINOX versus gemcitabine/nab-paclitaxel (Gem/nabP) for resectable pancreatic ductal adenocarcinoma (PDA) – Sohal D, et al

Study objective

- To evaluate the efficacy and safety of multi-agent perioperative chemotherapy in patients with resectable pancreatic ductal adenocarcinoma



PRIMARY ENDPOINT

- 2-year OS

SECONDARY ENDPOINTS

- DFS, safety

*Oxaliplatin 85 mg/m^2 + irinotecan 180 mg/m^2 + 5FU 2.4 g/m^2 over 46 h q2w; †D1, 8, 15 q4w

Sohal D, et al. J Clin Oncol 2020;38(suppl);abstr 4504

4504: SWOG S1505: Results of perioperative chemotherapy (peri-op CTx) with mFOLFIRINOX versus gemcitabine/nab-paclitaxel (Gem/nabP) for resectable pancreatic ductal adenocarcinoma (PDA) – Sohal D, et al

Key results

Baseline characteristics		mFOLFIRINOX (n=40)	Gemcitabine/nab-paclitaxel (n=33)
Median age, years (range)		66 (44–76)	64 (46–75)
Sex, n (%)	Female Male	19 (35) 36 (65)	23 (49) 24 (51)
Race, n (%)	White Black Unknown	52 (94) 2 (4) 1 (2)	39 (83) 5 (11) 3 (6)
ECOG PS, n (%)	0 1	34 (62) 21 (38)	31 (66) 16 (34)

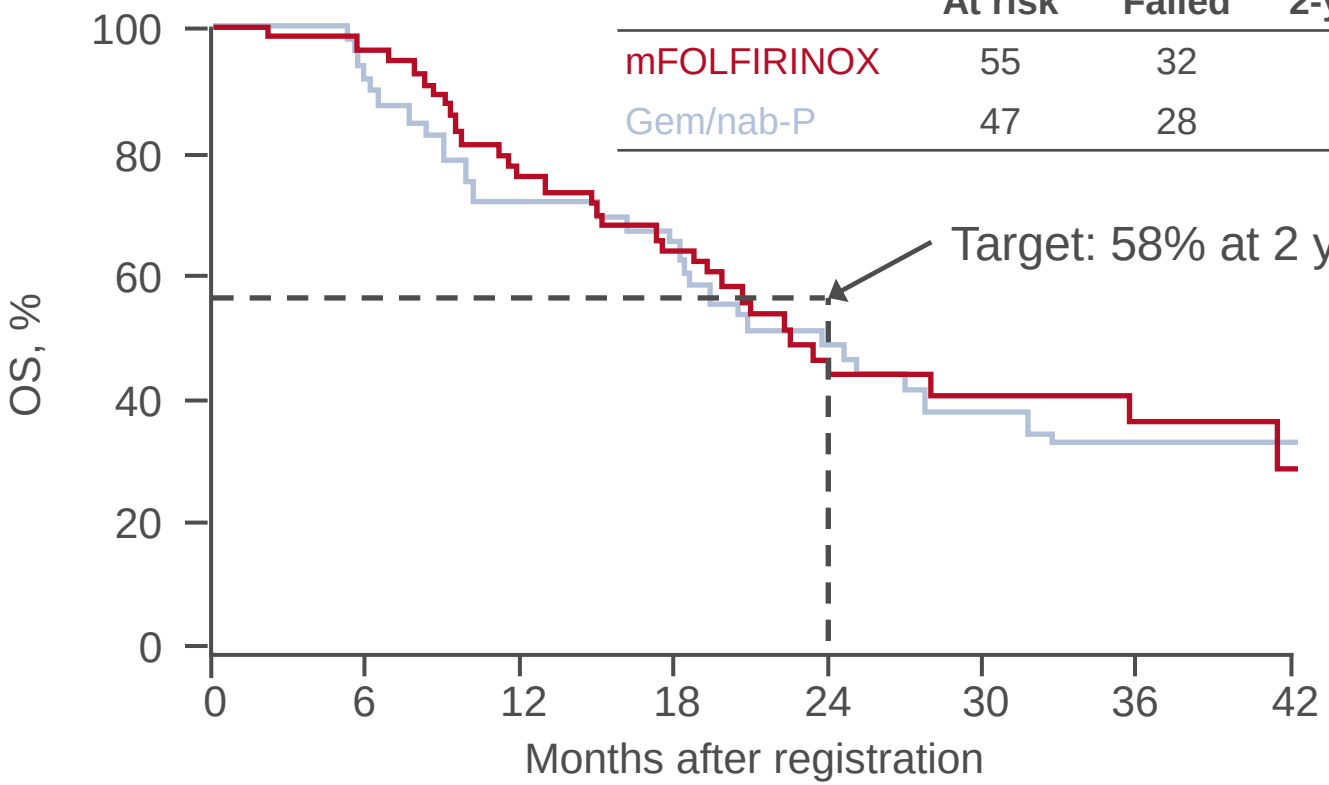
Sohal D, et al. J Clin Oncol 2020;38(suppl);abstr 4504

4504: SWOG S1505: Results of perioperative chemotherapy (peri-op CTx) with mFOLFIRINOX versus gemcitabine/nab-paclitaxel (Gem/nabP) for resectable pancreatic ductal adenocarcinoma (PDA) – Sohal D, et al

Key results (cont.)

OS

	At risk	Failed	2-y OS, %	mOS, mo
mFOLFIRINOX	55	32	43.1	22.4
Gem/nab-P	47	28	46.9	23.6



Sohal D, et al. J Clin Oncol 2020;38(suppl);abstr 4504

4504: SWOG S1505: Results of perioperative chemotherapy (peri-op CTx) with mFOLFIRINOX versus gemcitabine/nab-paclitaxel (Gem/nabP) for resectable pancreatic ductal adenocarcinoma (PDA) – Sohal D, et al

Key results (cont.)

Surgery results	mFOLFIRINOX (n=40)	Gemcitabine/nab-paclitaxel (n=33)
R0 resection, n (%)	34 (85)	28 (85)
Complete or major pathologic response, n (%)	10 (25)	14 (42)
Total nodes resected, median (range)	19 (1–56)	18 (3–45)
Node negative resection, n (%)	16 (40)	15 (45)
mDFS after resection, mo	10.9	14.2

Sohal D, et al. J Clin Oncol 2020;38(suppl);abstr 4504

4504: SWOG S1505: Results of perioperative chemotherapy (peri-op CTx) with mFOLFIRINOX versus gemcitabine/nab-paclitaxel (Gem/nabP) for resectable pancreatic ductal adenocarcinoma (PDA) – Sohal D, et al

Key results (cont.)

Grade 3/4 AEs, n (%)	Preoperative		Postoperative	
	mFOLFIRINOX (n=53)	Gem/nab-P (n=45)	mFOLFIRINOX (n=31)	Gem/nab-P (n=26)
Neutropenia	10 (19)	17 (38)	0	7 (27)
Febrile neutropenia	0	2 (4)	0	0
Diarrhea	9 (17)	4 (9)	2 (6)	1 (4)
Anemia	7 (13)	5 (11)	4 (13)	1 (4)
Neuropathy	5 (9)	3 (7)	5 (16)	1 (4)
Fatigue	5 (9)	3 (7)	1 (3)	0
Nausea	4 (8)	1 (2)	0	0

Conclusions

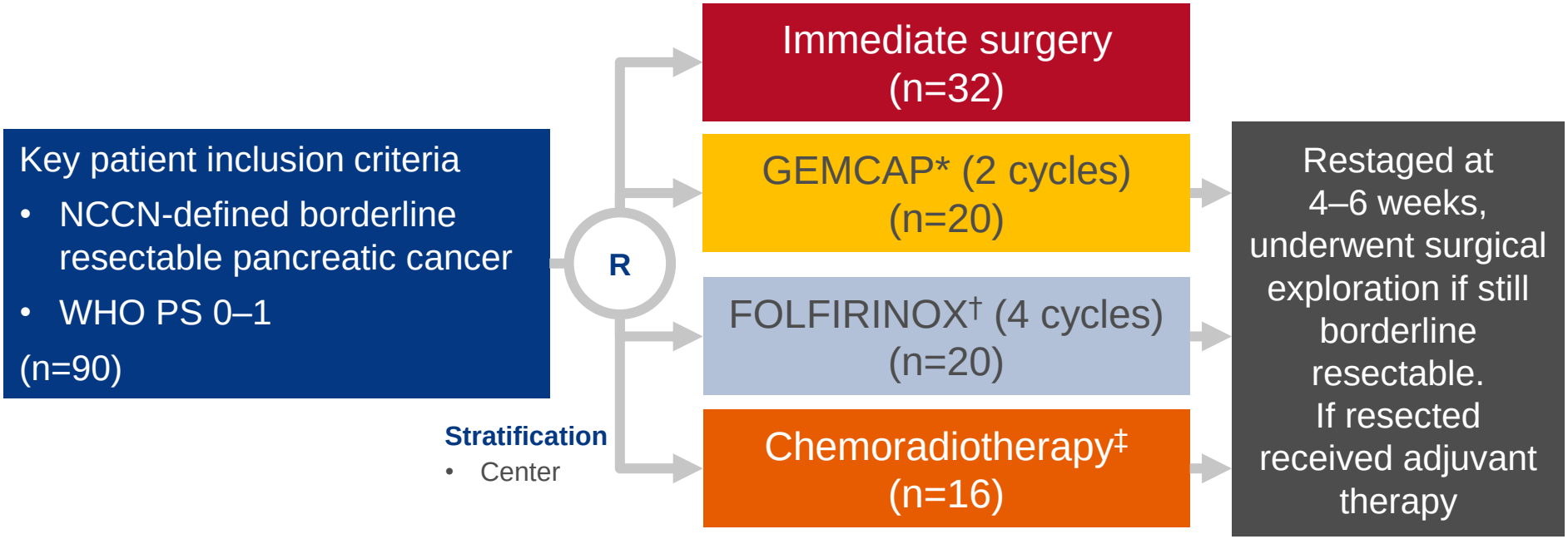
- **In patients with resectable pancreatic ductal adenocarcinoma, perioperative mFOLFIRINOX and gemcitabine + nab-paclitaxel seem to have similar activity; however, the primary endpoint (≥58% OS at 2 years) was not met in either treatment arm**

Sohal D, et al. J Clin Oncol 2020;38(suppl);abstr 4504

4505: ESPAC-5F: Four-arm, prospective, multicenter, international randomized phase II trial of immediate surgery compared with neoadjuvant gemcitabine plus capecitabine (GEMCAP) or FOLFIRINOX or chemoradiotherapy (CRT) in patients with borderline resectable pancreatic cancer – Ghaneh P, et al

Study objective

- To evaluate the efficacy and safety of immediate surgery compared with neoadjuvant gemcitabine + capecitabine (GEMCAP), FOLFIRINOX or chemoradiotherapy



PRIMARY ENDPOINT

- Resection rate (R1/R0); recruitment rate

SECONDARY ENDPOINTS

- R0 resection margin rate, OS, safety

*Gemcitabine 1000 mg/m^2 3 of 4 weeks; capecitabine 830 mg/m^2 21/28 days q4w; †oxaliplatin 85 mg/m^2, irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5FU 2400 mg/m^2 q2w; ‡capecitabine-based 50.4 Gy in 28 fractions over 5.5 weeks

Ghaneh P, et al. J Clin Oncol 2020;38(suppl);abstr 4505

4505: ESPAC-5F: Four-arm, prospective, multicenter, international randomized phase II trial of immediate surgery compared with neoadjuvant gemcitabine plus capecitabine (GEMCAP) or FOLFIRINOX or chemoradiotherapy (CRT) in patients with borderline resectable pancreatic cancer – Ghaneh P, et al

Key results

- Recruitment rate* was 20.74 (95%CI 16.68, 25.49)

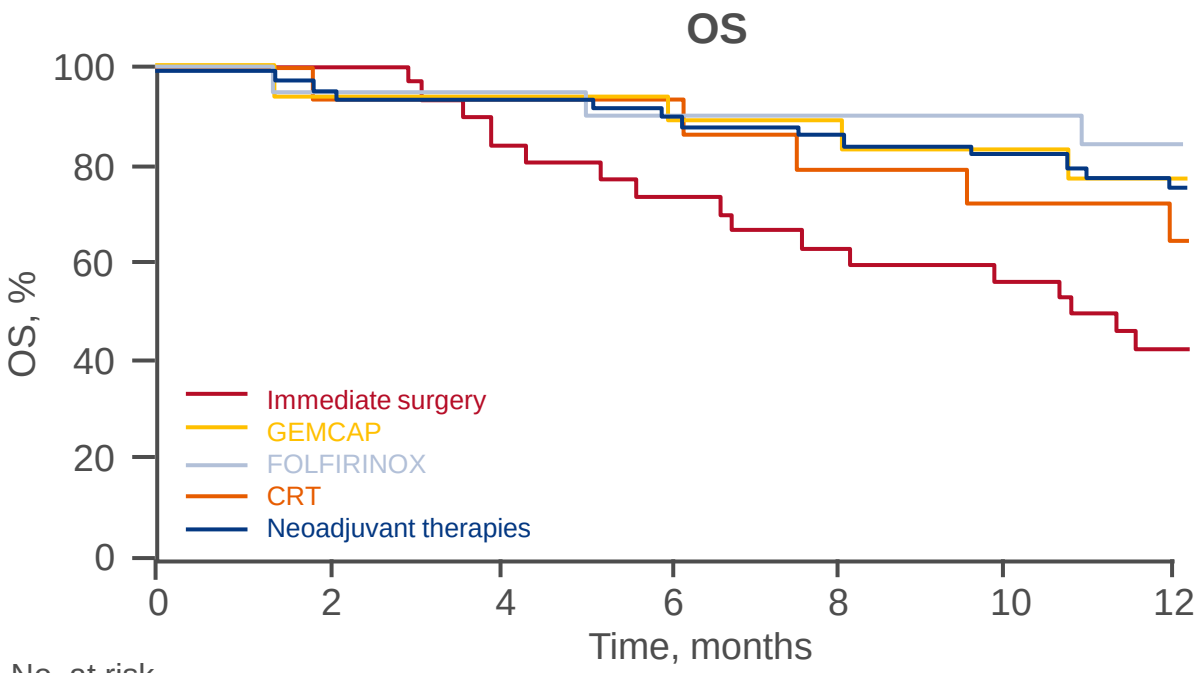
Resection rate	Immediate surgery	Neoadjuvant treatment	Overall
R0 + R1			
n/N†	20/32	31/56	51/88
Rate, % (95%CI)	62 (44, 79)	55 (41, 69)	58 (47, 68)
p-value	0.668		
R0			
n/N†	3/20	7/31	10/51
Rate, % (95%CI)	15 (3, 38)	23 (10, 41)	20 (10, 33)
p-value	0.721		

*Defined as patients recruited divided by time (years) open to recruitment; †n is number of resections/N is number of patients

Ghaneh P, et al. J Clin Oncol 2020;38(suppl);abstr 4505

4505: ESPAC-5F: Four-arm, prospective, multicenter, international randomized phase II trial of immediate surgery compared with neoadjuvant gemcitabine plus capecitabine (GEMCAP) or FOLFIRINOX or chemoradiotherapy (CRT) in patients with borderline resectable pancreatic cancer – Ghaneh P, et al

Key results (cont.)



No. at risk

32	31	25	21	18	16	7
20	20	19	18	17	16	7
20	19	19	17	16	16	14
16	14	14	13	11	10	8
56	53	52	48	44	42	29

	1-y OS, % (95%CI)
Immediate surgery	42 (27, 64)
GEMCAP	79 (62, 100)
FOLFIRINOX	84 (70, 100)
CRT	64 (43, 95)
Neoadjuvant therapy*	77 (66, 89)

HR_{GEMCAP} 0.32 (95%CI 0.12, 0.85)
$HR_{FOLFIRINOX}$ 0.16 (95%CI 0.05, 0.56)
HR_{CRT} 0.41 (95%CI 0.15, 1.10)
X^2 (3) = 14.76, p=0.002

$HR_{Neoadjuvant}$ 0.28 (95%CI 0.14, 0.57)
X^2 (1) = 13.77, p<0.001

*GEMCAP or FOLIRINOX or CRT

Ghaneh P, et al. J Clin Oncol 2020;38(suppl);abstr 4505

4505: ESPAC-5F: Four-arm, prospective, multicenter, international randomized phase II trial of immediate surgery compared with neoadjuvant gemcitabine plus capecitabine (GEMCAP) or FOLFIRINOX or chemoradiotherapy (CRT) in patients with borderline resectable pancreatic cancer – Ghaneh P, et al

Key results (cont.)

Grade ≥3 AEs, n (%)	GEMCAP (n=18)	FOLFIRNOX (n=19)	CRT (n=14)
Any SAEs	1 (6)	5 (26)	3 (21)
Sepsis (grade 5)	0	1 (5)	0
Febrile neutropenia	0	1 (5)	0
Diarrhea	0	1 (5)	0
Gastritis	0	1 (5)	0
Nausea	0	1 (5)	1 (7)
Hepatic infection	1 (6)	0	0
Infection – other	0	0	1 (7)
Wound dehiscence	0	0	1 (7)
Metabolism and nutrition disorders – other	0	0	1 (7)

Conclusions

- **In patients with borderline resectable pancreatic cancer, neoadjuvant therapy showed improved 1-year survival rates compared with immediate surgery**

Ghaneh P, et al. J Clin Oncol 2020;38(suppl);abstr 4505

4515: Phase III APACT trial of adjuvant nab-paclitaxel plus gemcitabine (nab-P + Gem) versus gemcitabine (Gem) alone for patients with resected pancreatic cancer (PC): Outcomes by geographic region – Reni M, et al

Study objective

- To present updated long-term OS and safety data from the APACT study of nab-paclitaxel + gemcitabine compared with gemcitabine in patients with surgically resected pancreatic cancer according to geographical region

Key patient inclusion criteria

- Pancreatic ductal adenocarcinoma (T1–3, N0–1, M0)
- Macroscopic complete resection
- CT: no evidence of disease
- Treatment naïve
- CA19-9 <100 U/mL
- ECOG PS 0–1

(n=866)

R 1:1

nab-paclitaxel 125 mg/m^2 + gemcitabine 1000 mg/m^2 qw for first 3 of 4 weeks for 6 cycles* (n=432) → **PD/ toxicity**

Stratification

- Resection status (R0 vs. R1)
- Lymph node status (positive vs. negative)
- Geographic region (North America, Europe and Australia vs. Asia Pacific)

Gemcitabine 1000 mg/m^2 qw for first 3 of 4 weeks for 6 cycles* (n=434) → **PD/ toxicity**

PRIMARY ENDPOINT

- DFS by ICR

SECONDARY ENDPOINTS

- OS, safety

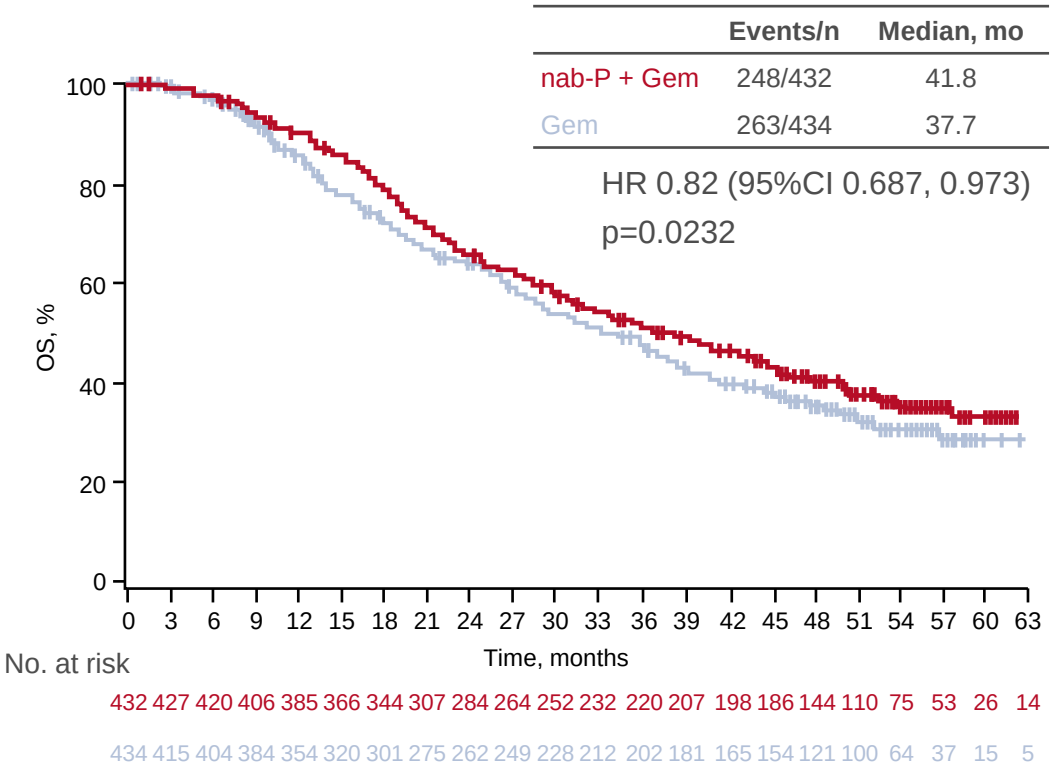
*Treatment initiated ≤12 weeks post-surgery

Reni M, et al. J Clin Oncol 2020;38(suppl);abstr 4515

4515: Phase III APACT trial of adjuvant nab-paclitaxel plus gemcitabine (nab-P + Gem) versus gemcitabine (Gem) alone for patients with resected pancreatic cancer (PC): Outcomes by geographic region – Reni M, et al

Key results

OS (ITT population)



	Median follow-up, months (n at baseline)		4-year OS, %	
	nab-P + Gem	Gem	nab-P + Gem	Gem
Europe	53.9 (203)	53.2 (205)	44	41
North America	53.9 (144)	52.6 (156)	44	37
Asia-Pac	51.1 (55)	52.7 (53)	46	39
Australia	50.6 (30)	54.2 (20)	42	26
Total ITT	53.3 (432)	53.0 (434)	44	38

Reni M, et al. J Clin Oncol 2020;38(suppl);abstr 4515

4515: Phase III APACT trial of adjuvant nab-paclitaxel plus gemcitabine (nab-P + Gem) versus gemcitabine (Gem) alone for patients with resected pancreatic cancer (PC): Outcomes by geographic region – Reni M, et al

Key results (cont.)

Characteristic, n (%)	Europe		N. America		Asia Pac		Australia	
	nab-P + Gem (n=201)	Gem (n=203)	nab-P + Gem (n=143)	Gem (n=148)	nab-P + Gem (n=55)	Gem (n=52)	nab-P + Gem (n=30)	Gem (n=20)
Patients with ≥1 grade ≥3 TEAE	172 (85.6)	131 (64.5)	125 (87.4)	112 (75.7)	47 (85.5)	29 (55.8)	27 (90.0)	14 (70.0)
Patients with ≥1 serious TEAE	73 (36.3)	33 (16.3)	69 (48.3)	47 (31.8)	16 (29.1)	7 (13.5)	18 (60.0)	9 (45.0)

- Safety outcomes, including grade ≥3 hematologic and non-hematologic TEAEs in regional analyses were consistent with those in the full ITT population

Conclusions

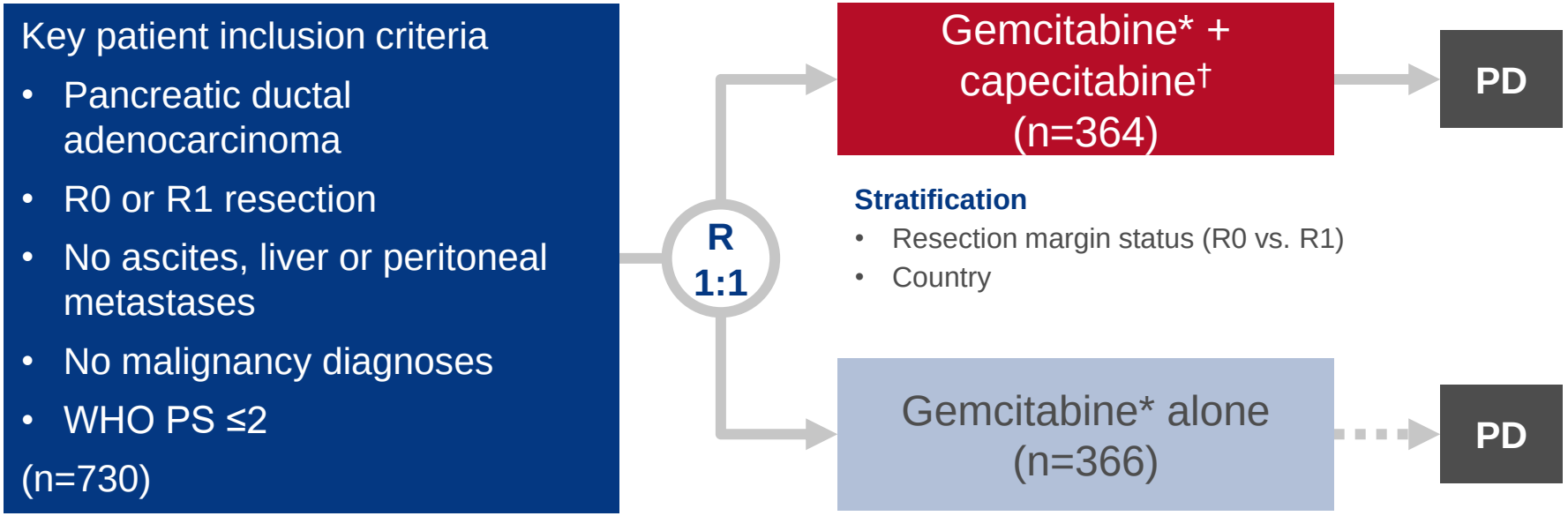
- **In patients with resected pancreatic cancer, this long-term follow-up of the APACT trial showed consistently longer OS with nab-paclitaxel + gemcitabine vs. gemcitabine alone with comparable results across geographic regions**
- **Safety outcomes were consistent with those in the primary analysis**

Reni M, et al. J Clin Oncol 2020;38(suppl);abstr 4515

4516: ESPAC-4: A multicenter, international, open-label randomized controlled phase III trial of adjuvant combination chemotherapy of gemcitabine (GEM) and capecitabine (CAP) versus monotherapy gemcitabine in patients with resected pancreatic ductal adenocarcinoma: Five year follow-up – Neoptolemos JP, et al

Study objective

- To evaluate the long-term efficacy and safety of gemcitabine + capecitabine vs. gemcitabine alone as adjuvant therapy in patients with resected pancreatic cancer



PRIMARY ENDPOINT

- 5-y OS

SECONDARY ENDPOINTS

- RFS, safety

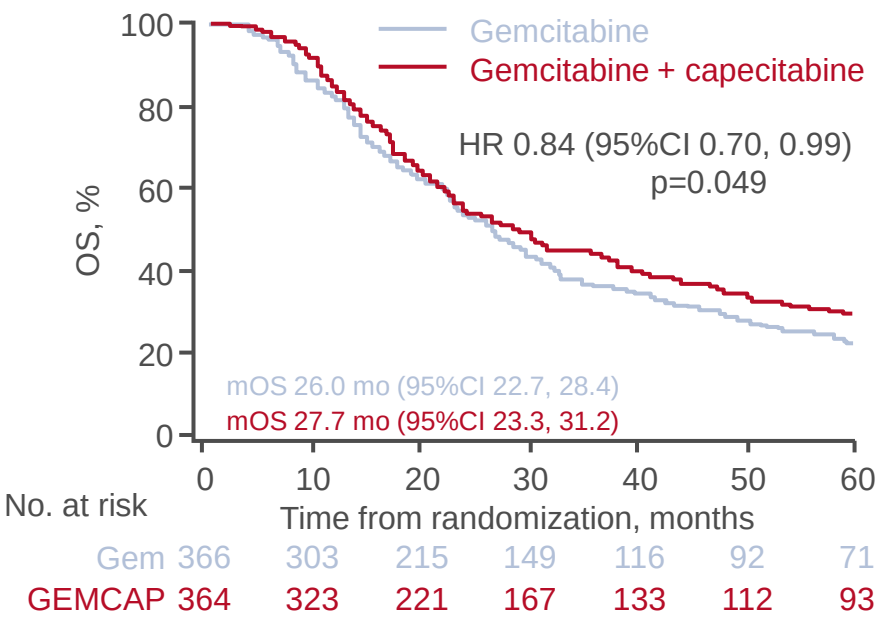
*1000 mg/m^2 D1, 8, 16 (6 cycles); †1660 mg/m^2/day 21/28d

Neoptolemos JP, et al. J Clin Oncol 2020;38(suppl);abstr 4515

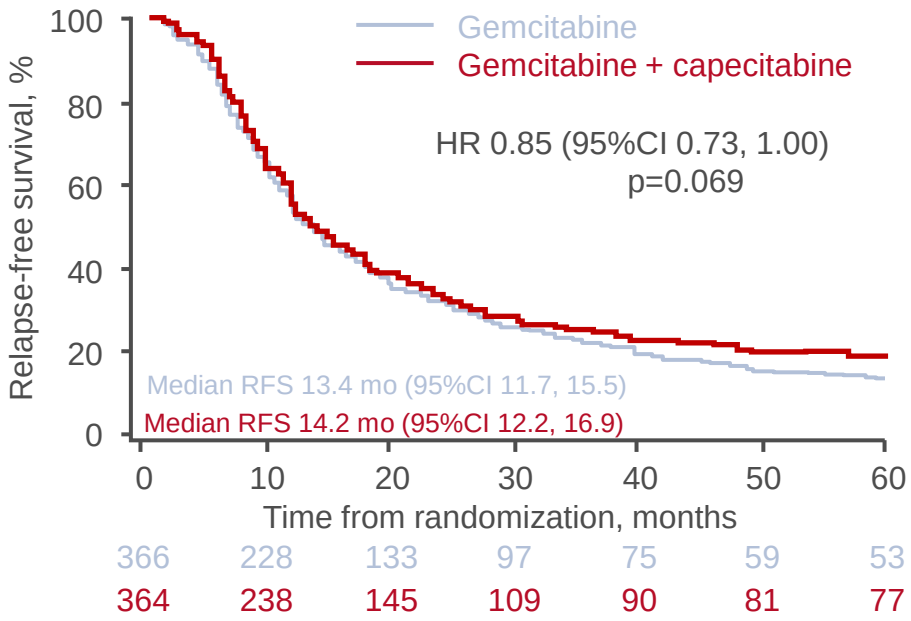
4516: ESPAC-4: A multicenter, international, open-label randomized controlled phase III trial of adjuvant combination chemotherapy of gemcitabine (GEM) and capecitabine (CAP) versus monotherapy gemcitabine in patients with resected pancreatic ductal adenocarcinoma: Five year follow-up – Neoptolemos JP, et al

Key results

OS



Relapse-free survival



OS rate, % (95%CI)	Gemcitabine + capecitabine	Gemcitabine
3-year	0.42 (0.37, 0.47)	0.35 (0.30, 0.39)
4-year	0.33 (0.28, 0.38)	0.27 (0.23, 0.32)
5-year	0.28 (0.23, 0.33)	0.20 (0.16, 0.25)

Salvage therapy:

- Gemcitabine + capecitabine: 84/287 (29%)
- Gemcitabine: 104/313 (33%)

Neoptolemos JP, et al. J Clin Oncol 2020;38(suppl);abstr 4515

4516: ESPAC-4: A multicenter, international, open-label randomized controlled phase III trial of adjuvant combination chemotherapy of gemcitabine (GEM) and capecitabine (CAP) versus monotherapy gemcitabine in patients with resected pancreatic ductal adenocarcinoma: Five year follow-up – Neoptolemos JP, et al

Key results (cont.)

Grade 3/4 AEs, n (%)	Gemcitabine + capecitabine (n=359)	Gemcitabine (n=366)	p-value
Anemia	8 (2)	14 (4)	0.279
Diarrhea	19 (5)	6 (2)	0.008
Fatigue	20 (6)	19 (5)	0.870
Fever	6 (2)	6 (2)	1.000
Infection and infestations, other	9 (3)	24 (7)	0.012
Lymphocytes	9 (3)	11 (3)	0.821
Neutrophils	137 (38)	89 (24)	<0.001
Hand-foot syndrome	26 (7)	0	<0.001
Platelets	8 (2)	7 (2)	0.800
Thromboembolic event	8 (2)	9 (2)	1.000
White blood cells	37 (10)	28 (8)	0.242

Conclusions

- **In patients with pancreatic ductal adenocarcinoma, gemcitabine + capecitabine provides a significantly improved OS compared with gemcitabine alone**

Neoptolemos JP, et al. J Clin Oncol 2020;38(suppl);abstr 4515

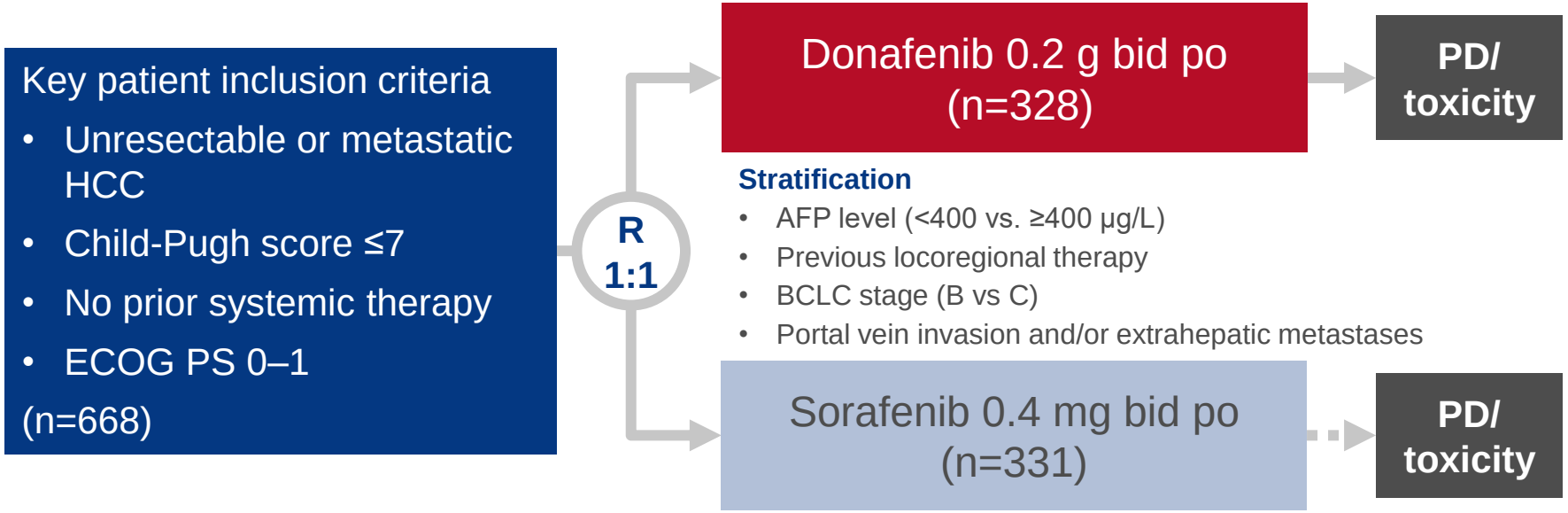
Cancers of the pancreas, small bowel and hepatobiliary tract

HEPATOCELLULAR CARCINOMA

4506: Donafenib versus sorafenib as first-line therapy in advanced hepatocellular carcinoma: An open-label, randomized, multicenter phase II/III trial – Bi F, et al

Study objective

- To evaluate the efficacy and safety of donafenib as a 1L therapy for patients with advanced HCC



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR, DCR, safety

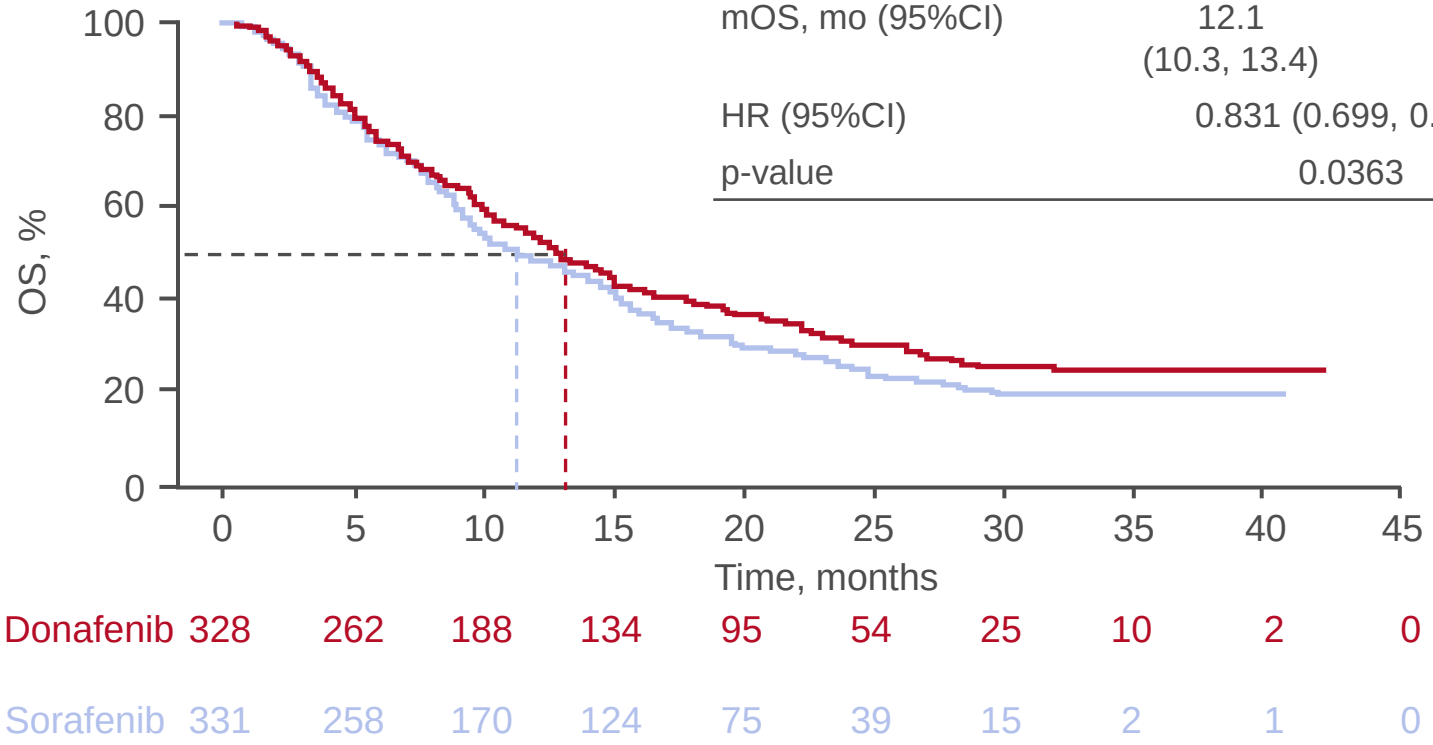
Bi F, et al. J Clin Oncol 2020;38(suppl);abstr 4506

4506: Donafenib versus sorafenib as first-line therapy in advanced hepatocellular carcinoma: An open-label, randomized, multicenter phase II/III trial – Bi F, et al

Key results

OS (full analysis set)

	Donafenib (n=328)	Sorafenib (n=331)
mOS, mo (95%CI)	12.1 (10.3, 13.4)	10.3 (9.2, 12.0)
HR (95%CI)	0.831 (0.699, 0.988)	
p-value	0.0363	



Bi F, et al. J Clin Oncol 2020;38(suppl);abstr 4506

4506: Donafenib versus sorafenib as first-line therapy in advanced hepatocellular carcinoma: An open-label, randomized, multicenter phase II/III trial – Bi F, et al

Key results

Outcome	Donafenib (n=328)	Sorafenib (n=331)
ORR, n (%) [95%CI]	15 (4.6) [2.6, 7.4]	9 (2.7) [1.3, 5.1]
BOR, n (%)		
CR	1 (0.3)	0
PR	19 (5.8)	12 (3.6)
SD	163 (49.7)	166 (50.2)
PD	122 (37.2)	124 (37.5)
NE	23 (7.0)	19 (8.8)
DCR, n (%) [95%CI]	101 (30.8) [25.8, 36.1]	95 (28.7) [23.9, 33.9]
Week 24 DCR, n (%)	68 (20.7)	52 (15.7)
mPFS, months (95%CI)	3.7 (3.0, 3.7)	3.6 (2.4, 3.7)
HR (95%CI); p-value	0.909 (0.763, 1.082); 0.2824	

Bi F, et al. J Clin Oncol 2020;38(suppl);abstr 4506

4506: Donafenib versus sorafenib as first-line therapy in advanced hepatocellular carcinoma: An open-label, randomized, multicenter phase II/III trial – Bi F, et al

Key results (cont.)

AEs, %	Donafenib (n=333)	Sorafenib (n=332)	p-value
Any AE	99.7	99.1	0.3731
Grade ≥3	57.4	67.5	0.0082
SAE	16.5	20.2	0.2307
Led to dose interruption	30.3	42.5	0.0013
Led to discontinuation	10.2	12.7	0.3324
Death	1.8	3.6	0.1610
Any TRAE	94.3	96.7	0.1902
Grade ≥3	37.5	49.7	0.0018
SAE	6.9	6.6	1.0000
Led to dose interruption	25.2	36.1	0.0025
Led to discontinuation	5.7	7.5	0.3544

Conclusions

- **In patients with advanced HCC, donafenib demonstrated superior OS and had a favorable safety profile compared with sorafenib in the 1L setting**

Bi F, et al. J Clin Oncol 2020;38(suppl);abstr 4506

4507: Apatinib as second-line therapy in Chinese patients with advanced hepatocellular carcinoma: A randomized, placebo-controlled, double-blind, phase III study – Li Q, et al

Study objective

- To evaluate the efficacy and safety of apatinib as a 2L treatment for Chinese patients with advanced HCC

Key patient inclusion criteria

- Advanced HCC
- Child-Pugh Class A or B, score ≤7
- ≥1 prior systemic therapy (sorafenib and/or oxaliplatin-based chemotherapy)
- BCLC stage: B or C
- ECOG PS 0–1

(n=400)

R 2:1

Apatinib 750 mg/day po (n=267) → PD/ toxicity

Stratification

- ECOG PS (0 vs. 1)
- Prior sorafenib
- Extrahepatic spread and/or macrovascular invasion (yes vs. no)

Placebo (n=133) → PD/ toxicity

PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

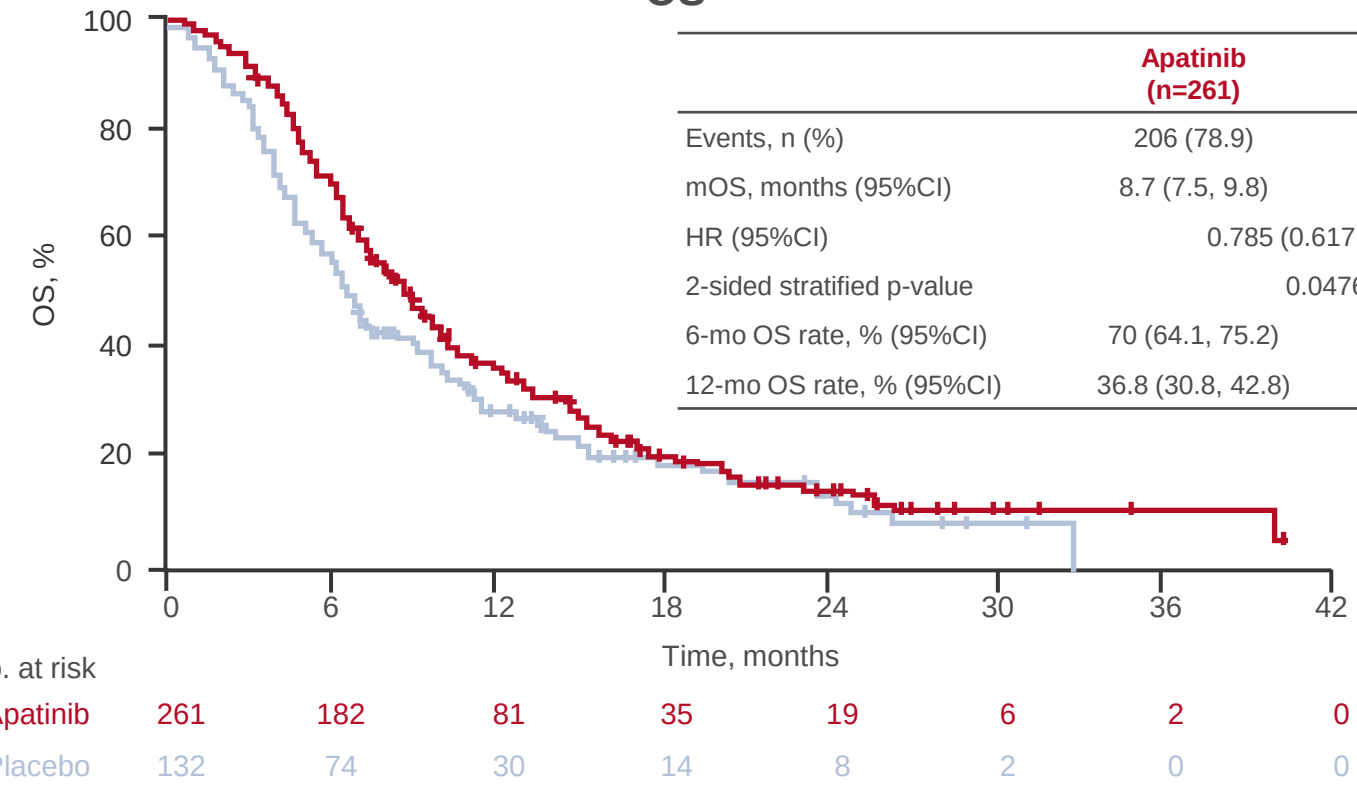
- PFS, TTP, ORR, DoR, DCR, SD ≥6 weeks, safety

Li Q, et al. J Clin Oncol 2020;38(suppl);abstr 4507

4507: Apatinib as second-line therapy in Chinese patients with advanced hepatocellular carcinoma: A randomized, placebo-controlled, double-blind, phase III study – Li Q, et al

Key results

OS



	Apatinib (n=261)	Placebo (n=132)
Events, n (%)	206 (78.9)	106 (80.3)
mOS, months (95%CI)	8.7 (7.5, 9.8)	6.8 (5.7, 9.1)
HR (95%CI)	0.785 (0.617, 0.998)	
2-sided stratified p-value	0.0476	
6-mo OS rate, % (95%CI)	70 (64.1, 75.2)	56.1 (47.2, 64.0)
12-mo OS rate, % (95%CI)	36.8 (30.8, 42.8)	28.9 (21.2, 37.1)

- mPFS: apatinib 4.5 months (95%CI 3.9, 4.7) vs. placebo 1.9 months (9%%CI 1.9, 2.0)
  - HR 0.471 (95%CI 0.369, 0.601); p<0.0001

Li Q, et al. J Clin Oncol 2020;38(suppl);abstr 4507

4507: Apatinib as second-line therapy in Chinese patients with advanced hepatocellular carcinoma: A randomized, placebo-controlled, double-blind, phase III study – Li Q, et al

Key results (cont.)

TRAEs, n (%)	Apatinib (n=257)	Placebo (n=130)
Any grade	250 (97.3)	92 (70.8)
Grade 3–4	199 (77.4)	25 (19.2)
Serious	44 (17.1)	5 (3.8)
Led to dose modifications Dose interruptions Dose reduction	178 (69.3) 155 (60.3) 115 (44.7)	11 (8.5) 11 (8.5) 2 (1.5)
Led to permanent discontinuation	32 (12.5)	0
Led to death	0	0

Conclusions

- **In Chinese patients with pre-treated advanced HCC, apatinib significantly improved survival (OS and PFS) compared with placebo and had a manageable safety profile**

Li Q, et al. J Clin Oncol 2020;38(suppl);abstr 4507

4508: Efficacy, tolerability, and biologic activity of a novel regimen of tremelimumab (T) in combination with durvalumab (D) for patients (pts) with advanced hepatocellular carcinoma (aHCC) – Kelley RK, et al

Study objective

- To evaluate the efficacy and safety of tremelimumab and durvalumab alone or in combination in patients with advanced HCC

Key patient inclusion criteria

- Advanced HCC (unresectable)
- Immune checkpoint inhibitor naïve
- Child-Pugh A
- Progressed on or intolerant of or refused sorafenib

(n=332)

R

- Tremelimumab 300 mg (1 dose) + durvalumab 1500 mg q4w (n=65)
- Tremelimumab 75 mg (4 doses) + durvalumab 1500 mg q4w (n=45)
- Tremelimumab 750 mg q4w (7 doses) then q12w (n=33)
- Durvalumab 1500 mg q4w (n=64)

PRIMARY ENDPOINT

- Safety

SECONDARY ENDPOINTS

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

Kelley RK, et al. J Clin Oncol 2020;38(suppl);abstr 4508

4508: Efficacy, tolerability, and biologic activity of a novel regimen of tremelimumab (T) in combination with durvalumab (D) for patients (pts) with advanced hepatocellular carcinoma (aHCC) – Kelley RK, et al

Key results

AEs, n (%)	Tremelimumab 300 + durvalumab (n=75)	Tremelimumab 75 + durvalumab (n=82)	Tremelimumab (n=69)	Durvalumab (n=101)
Any AE Grade 3–4 Serious	73 (98.6) 43 (58.1) 31 (41.9)	80 (97.6) 50 (61.0) 36 (43.9)	67 (97.1) 46 (66.7) 36 (52.2)	95 (94.1) 56 (55.4) 43 (42.6)
Any TRAE Grade 3–4 Serious	61 (82.4) 26 (35.1) 12 (16.2)	57 (69.5) 19 (23.2) 12 (14.6)	58 (84.1) 30 (43.5) 17 (24.6)	61 (60.4) 18 (17.8) 11 (10.9)
TRAE leading to discontinuation	8 (10.8)	5 (6.1)	9 (13.0)	8 (7.9)
TRAE requiring systemic steroids	18 (24.3)	20 (24.4)	18 (26.1)	10 (9.9)
TRAE leading to death	1 (1.4)	1 (1.2)	0	3 (3.0)

Kelley RK, et al. J Clin Oncol 2020;38(suppl);abstr 4508

4508: Efficacy, tolerability, and biologic activity of a novel regimen of tremelimumab (T) in combination with durvalumab (D) for patients (pts) with advanced hepatocellular carcinoma (aHCC) – Kelley RK, et al

Key results (cont.)

Outcome	Tremelimumab 300 + durvalumab (n=75)	Tremelimumab 75 + durvalumab (n=82)	Tremelimumab (n=69)	Durvalumab (n=101)
mOS, mo (95%CI)	18.73 (10.78, 27.27)	11.30 (8.38, 14.95)	15.11 (11.33, 20.50)	13.57 (8.74, 17.64)
Survival rate, % (95%CI)				
12-mo	60.3 (47.9, 70.6)	49.2 (37.9. 59.6)	60.2 (47.3, 70.9)	51.2 (40.8, 60.8)
18-mo	52.0 (38.9, 63.6)	34.7 (24.4, 45.2)	45.7 (32.8, 57.7)	35.3 (25.0, 45.8)
Median DoT, mo (range)	3.7 (0.8–27.1)	2.4 (0.6–31.4)	3.7 (0.9–31.2)	3.7 (0.7–34.3)
ORR, % (95%CI)	24.0 (14.9, 35.3)	9.5 (4.2, 17.9)	7.2 (2.4, 16.1)	10.6 (5.4, 18.1)
Median DoR, mo	NR	13.21	23.95	11.17
mPFS, mo (95%CI)	2.17 (1.91, 5.42)	1.87 (1.77, 2.43)	2.69 (1.87, 5.29)	2.07 (1.84, 2.83)

Conclusions

- **In patients with advanced HCC, single dose tremelimumab 300 mg plus monthly durvalumab showed encouraging clinical activity and had a manageable safety profile**

Kelley RK, et al. J Clin Oncol 2020;38(suppl);abstr 4508

Cancers of the pancreas, small bowel and hepatobiliary tract

BILIARY TRACT CANCER

108: FOENIX-CCA2: A phase II, open-label, multicenter study of futibatinib in patients (pts) with intrahepatic cholangiocarcinoma (iCCA) harboring FGFR2 gene fusions or other rearrangements – Goyal L, et al

Study objective

- To evaluate the efficacy and safety of futibatinib (an irreversible FGFR1-4 inhibitor) in patients with intrahepatic cholangiocarcinoma (iCCA)

Key patient inclusion criteria

- Locally advanced or metastatic unresectable iCCA
- FGFR2 gene fusions or other rearrangements
- PD after ≥1 line of systemic therapy*
- No prior FGFR inhibitor
- ECOG PS 0–1

(n=103)

→ Futibatinib 20 mg/day po, continuously (21-day cycles)† → **PD/ toxicity**

PRIMARY ENDPOINT

- ORR (RECIST v1.1)

SECONDARY ENDPOINTS

- DCR, DoR, PFS, safety

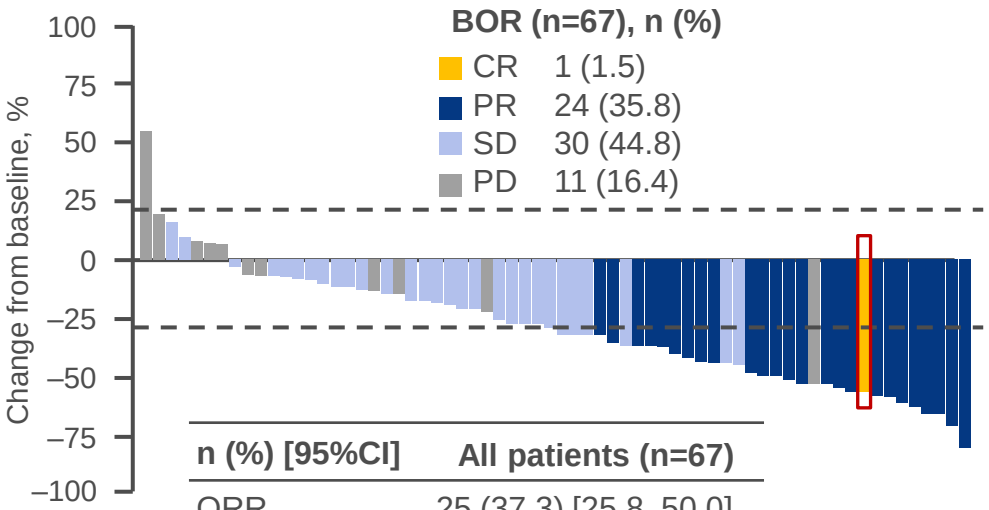
*Gemcitabine + platinum-based chemotherapy; †maximum 2 dose reductions (to 16 and then 12 mg) permitted to manage AEs

Goyal L, et al. J Clin Oncol 2020;38(suppl);abstr 108

108: FOENIX-CCA2: A phase II, open-label, multicenter study of futibatinib in patients (pts) with intrahepatic cholangiocarcinoma (iCCA) harboring FGFR2 gene fusions or other rearrangements – Goyal L, et al

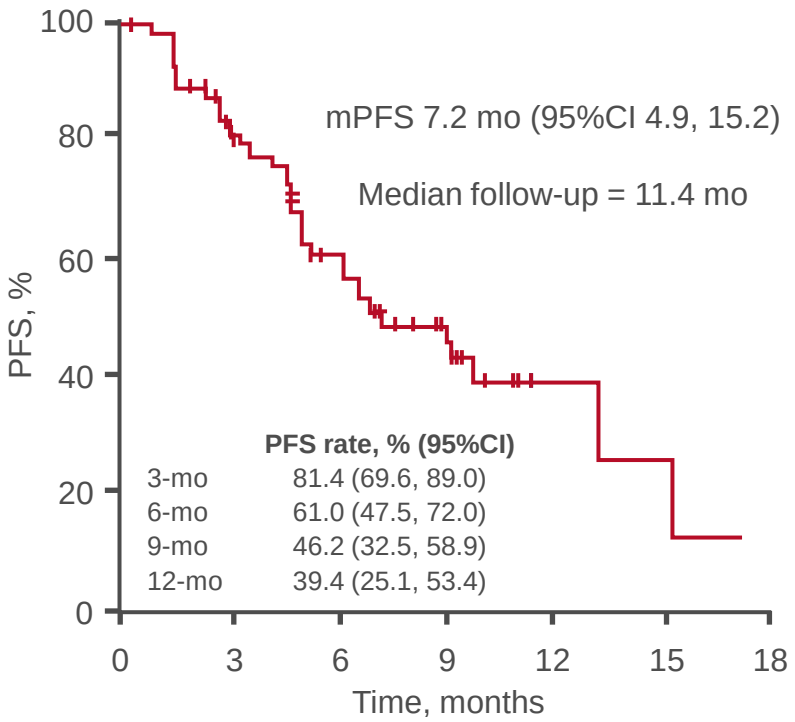
Key results

Change in target lesions



n (%) [95%CI]	All patients (n=67)
ORR	25 (37.3) [25.8, 50.0]
DCR	55 (82.1) [70.8, 90.4]

PFS



- Median (range) DoT: 6.9 mo (0.5–21.2)
- Median (range) DoR: 8.3 mo (6.2–NR)
- Median (range) TTR: 2.5 mo (1.0–6.7)

Goyal L, et al. J Clin Oncol 2020;38(suppl);abstr 108

108: FOENIX-CCA2: A phase II, open-label, multicenter study of futibatinib in patients (pts) with intrahepatic cholangiocarcinoma (iCCA) harboring FGFR2 gene fusions or other rearrangements – Goyal L, et al

Key results (cont.)

AEs, n (%)	Grade 1	Grade 2	Grade 3	Total
TRAEs	6 (9.0)	23 (34.3)	38 (56.7)	67 (100)
Serious TRAEs				7 (10.4)
Modification due to TRAEs				44 (65.7)
Drug interruption				37 (55.2)
Dose reduction				34 (50.7)
Discontinuation				1 (1.5)
TRAEs leading to death				0
TRAEs occurring in ≥25% of patients				
Hyperphosphatemia	4 (6.0)	32 (47.8)	18 (26.9)	54 (80.6)
Diarrhea	18 (26.9)	7 (10.4)	0	25 (37.3)
Dry mouth	19 (28.4)	3 (4.5)	0	22 (32.8)
Alopecia	15 (22.4)	5 (7.5)	0	20 (29.9)
Dry skin	13 (19.4)	5 (7.5)	0	18 (26.9)

Goyal L, et al. J Clin Oncol 2020;38(suppl);abstr 108

108: FOENIX-CCA2: A phase II, open-label, multicenter study of futibatinib in patients (pts) with intrahepatic cholangiocarcinoma (iCCA) harboring FGFR2 gene fusions or other rearrangements – Goyal L, et al

Key results (cont.)

AEs of special interest, n (%)	Any grade	Grade ≥3
Patients with AEs of special interest	64 (95.5)	20 (29.9)
Patients with SAEs of special interest	0	0
Hyperphosphatemia*	59 (88.1)	19 (28.4)
Nail toxicities	28 (41.8)	1 (1.5)
Palmar-plantar erythrodysesthesia syndrome	12 (17.9)	1 (1.5)
Rash	7 (10.4)	0
Central serous retinopathy	6 (9.0)	0
Other eye disorders	34 (50.7)	1 (1.5)
Other skin toxicities	33 (49.3)	0

Conclusions

- **In patients with iCCA with FGFR2 fusions/rearrangements who had progressed after chemotherapy, futibatinib showed promising activity and was well tolerated, highlighting an important role for molecular profiling when treating cholangiocarcinoma**

*Including increased blood phosphorous

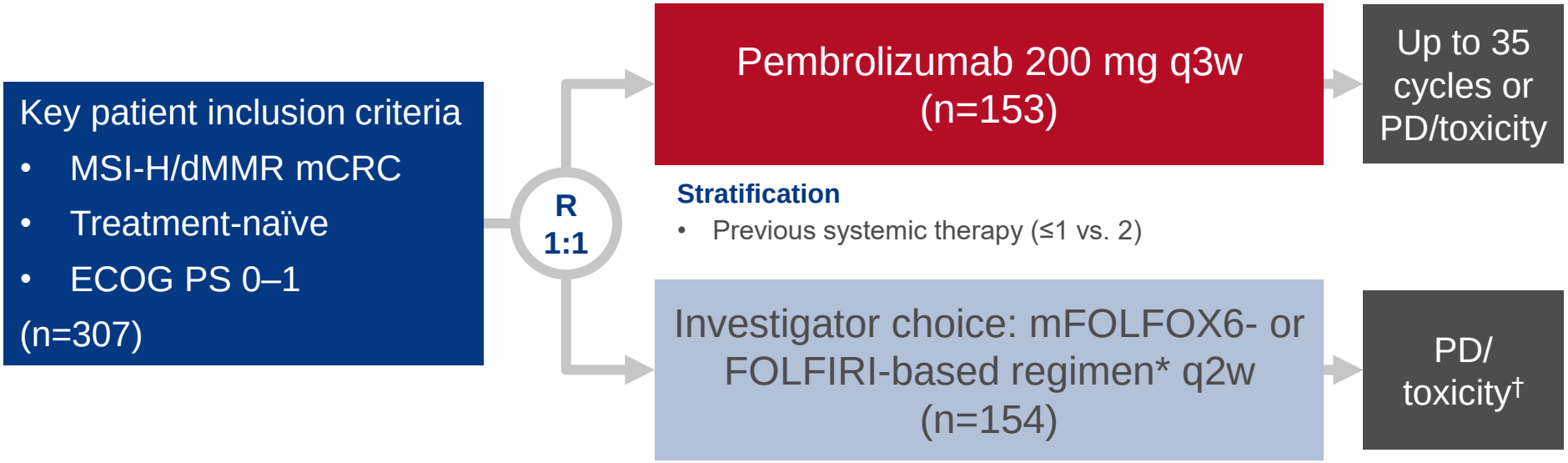
Goyal L, et al. J Clin Oncol 2020;38(suppl);abstr 108

CANCERS OF THE COLON, RECTUM AND ANUS

LBA4: Pembrolizumab versus chemotherapy for microsatellite instability-high/mismatch repair deficient metastatic colorectal cancer: The phase 3 KEYNOTE-177 study – Andre T, et al

Study objective

- To evaluate the efficacy and safety of pembrolizumab vs. standard of care chemotherapy in MSI-H/dMMR mCRC in the 1L setting



CO-PRIMARY ENDPOINTS

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

SECONDARY ENDPOINTS

- ORR (RECIST v1.1 by 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

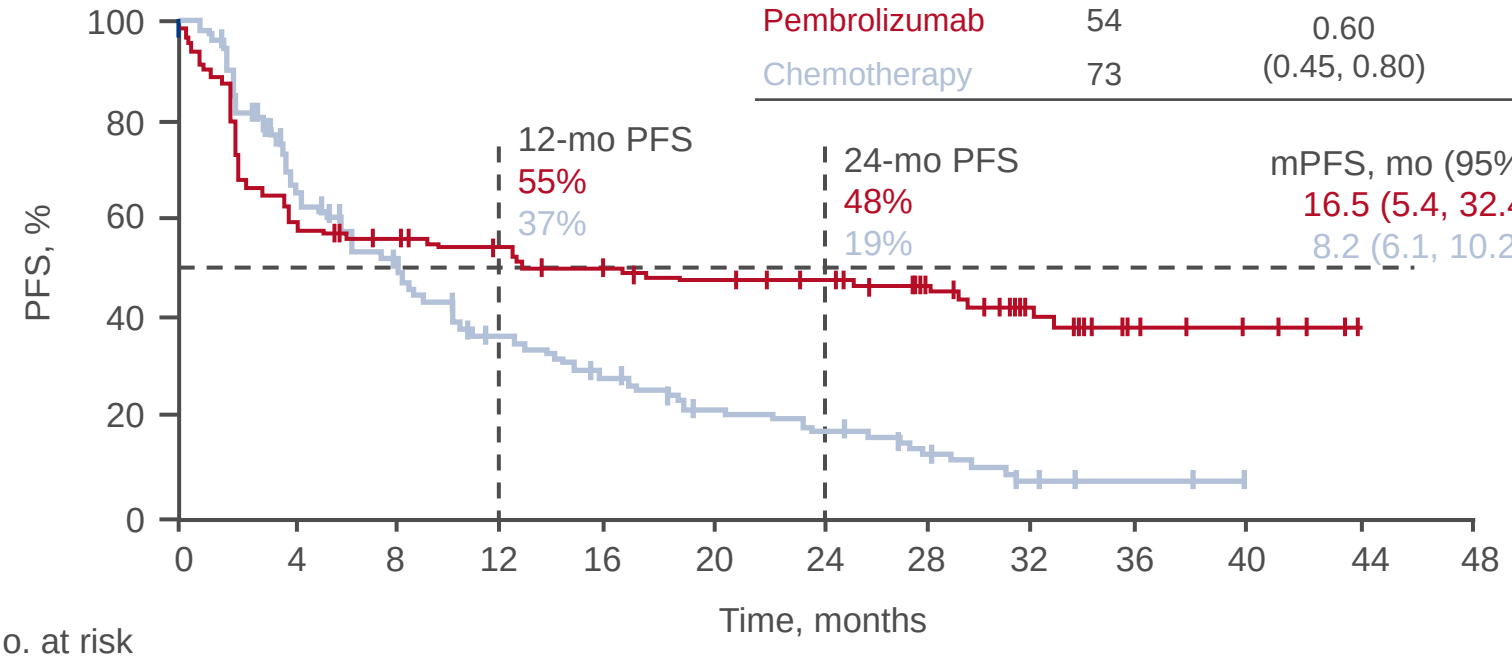
Andre T, et al. J Clin Oncol 2020;38(suppl);abstr LBA4

LBA4: Pembrolizumab versus chemotherapy for microsatellite instability-high/mismatch repair deficient metastatic colorectal cancer: The phase 3 KEYNOTE-177 study – Andre T, et al

Key results

PFS (by BICR)

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



No. at risk

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

- OS not described: DMC recommended reporting OS at final analysis

Median follow-up, mo (range): 32.4 (24.0–48.3)

Andre T, et al. J Clin Oncol 2020;38(suppl);abstr LBA4

LBA4: Pembrolizumab versus chemotherapy for microsatellite instability-high/mismatch repair deficient metastatic colorectal cancer: The phase 3 KEYNOTE-177 study – Andre T, et al

Key results (cont.)

Antitumor response	Pembrolizumab (n=153)	Chemotherapy (n=154)
BOR, n (%)		
CR	17 (11.1)	6 (3.9)
PR	50 (32.7)	45 (29.2)
SD	32 (20.9)	65 (42.2)
PD	45 (29.4)	19 (12.3)
NE	3 (2.0)	2 (1.3)
No assessment	6 (3.9)	17 (11.0)
ORR, n (%)	67 (43.8)	51 (33.1)
% difference, estimate (95%CI); p-value	10.7 (-0.2, 21.3); 0.0275	
DCR, n (%)	99 (64.7)	116 (75.3)
Median TTR, mo (range)	2.2 (1.8–18.8)	2.1 (1.7–24.9)

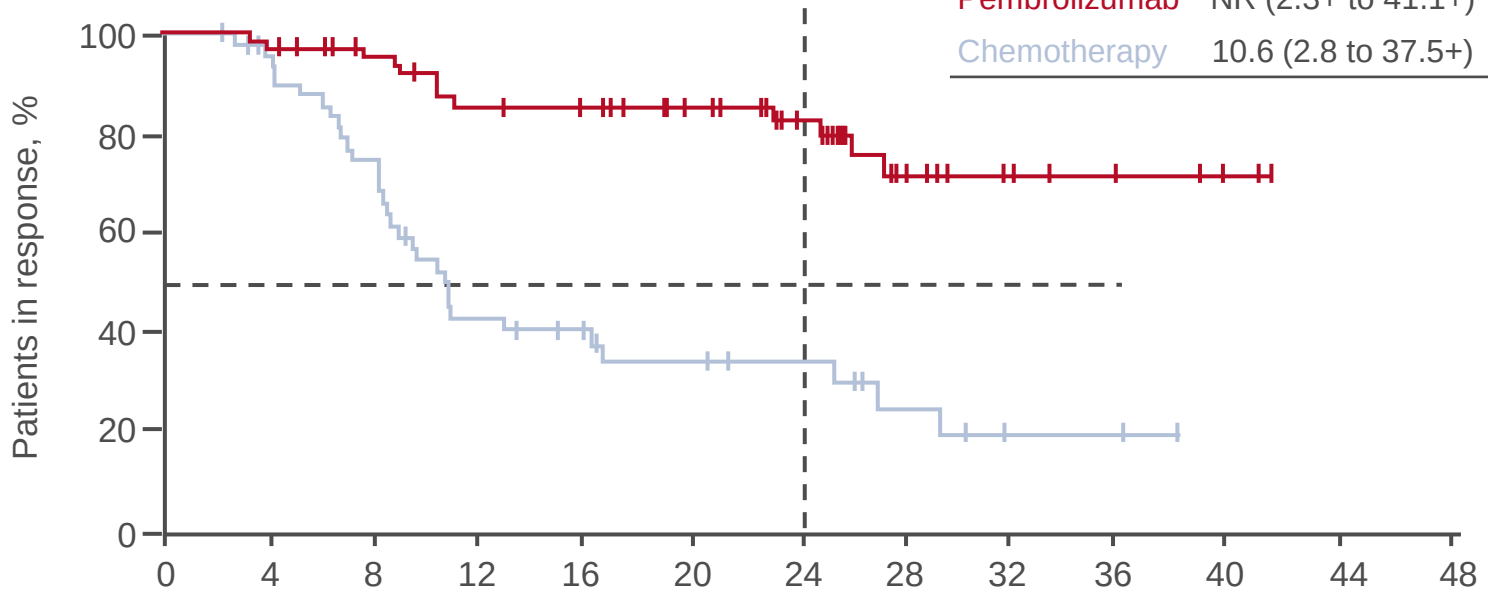
Andre T, et al. J Clin Oncol 2020;38(suppl);abstr LBA4

LBA4: Pembrolizumab versus chemotherapy for microsatellite instability-high/mismatch repair deficient metastatic colorectal cancer: The phase 3 KEYNOTE-177 study – Andre T, et al

Key results (cont.)

DoR

	mDoR, mo (range)	24-mo DoR, %
Pembrolizumab	NR (2.3+ to 41.1+)	83
Chemotherapy	10.6 (2.8 to 37.5+)	35



No. at risk

Pembro	67	64	57	50	48	41	29	13	6	4	2	0	0
Chemo	51	48	35	19	13	11	9	5	2	1	0	0	0

+ denotes ongoing response

Andre T, et al. J Clin Oncol 2020;38(suppl);abstr LBA4

LBA4: Pembrolizumab versus chemotherapy for microsatellite instability-high/mismatch repair deficient metastatic colorectal cancer: The phase 3 KEYNOTE-177 study – Andre T, et al

Key results (cont.)

AEs in all treated patients, %	Pembrolizumab (n=153)	Chemotherapy (n=143)
Any AEs	97	99
TRAEs	80	99
Grade ≥3	22	66
Discontinuations	10	6
Death	0	1
Immune-mediated and transfusion reaction AEs	31	13
Grade ≥3	9	2
Discontinuations	7	0
Death	0	0

Conclusions

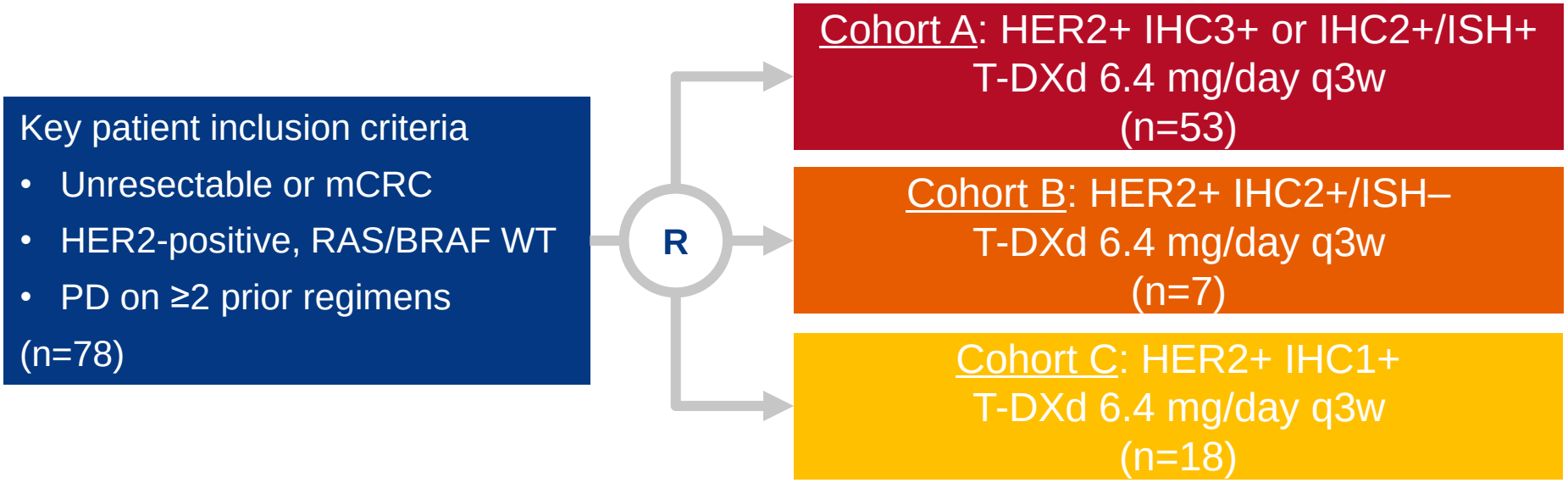
- **In patients with MSI-H/dMMR mCRC, pembrolizumab demonstrated a significant improvement in PFS and more durable responses compared with chemotherapy**

Andre T, et al. J Clin Oncol 2020;38(suppl);abstr LBA4

4000: A phase II, multicenter, open-label study of trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing metastatic colorectal cancer (mCRC): DESTINY-CRC01 – Siena S, et al

Study objective

- To evaluate the efficacy and safety of trastuzumab deruxtecan (T-DXd) in patients with HER2-positive mCRC



PRIMARY ENDPOINT

- ORR by ICR (Cohort A)

SECONDARY ENDPOINTS

- DCR, DoR, PFS, OS, ORR (Cohorts B & C), safety

Siena S, et al. J Clin Oncol 2020;38(suppl);abstr 4000

4000: A phase II, multicenter, open-label study of trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing metastatic colorectal cancer (mCRC): DESTINY-CRC01 – Siena S, et al

Key results

	HER2+ (Cohort A) (n=53)
ORR, % (95%CI)	45.3 (31.6, 59.6)
BOR, n (%)	
CR	1 (1.9)
PR	23 (43.4)
SD	20 (37.7)
PD	5 (9.4)
NE	4 (7.5)
DCR, % (95%CI)	83.0 (70.2, 91.9)
Median DoR, mo (95%CI)	NR (4.2, NE)
Median PFS, mo (95%CI)	6.9 (4.1, NE)

- No responses by ICR in Cohorts B or C
- OS data was immature

Siena S, et al. J Clin Oncol 2020;38(suppl);abstr 4000

4000: A phase II, multicenter, open-label study of trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing metastatic colorectal cancer (mCRC): DESTINY-CRC01 – Siena S, et al

Key results (cont.)

AEs, n (%)	HER2+ Cohort A (n=53)	All patients (n=78)
Any TEAE	53 (100)	78 (100)
Grade ≥3	32 (60.4)	48 (61.5)
Serious	18 (34.0)	26 (33.3)
Led to discontinuation	5 (9.4)	7 (9.0)
Led to dose reductions	11 (20.8)	15 (19.2)
Led to dose interruptions	20 (37.7)	27 (34.6)
Death	5 (9.4)	7 (9.0)
Any TRAE	51 (96.2)	73 (93.6)
Grade ≥3	27 (50.9)	38 (48.7)
Serious	12 (22.6)	14 (17.9)
Led to discontinuation	2 (3.8)	2 (2.6)
Led to dose reductions	10 (18.9)	14 (17.9)
Led to dose interruptions	15 (28.3)	19 (24.4)
Death	2 (3.8)	2 (2.6)

Conclusions

- **In patients with previously treated HER2-positive mCRC, T-DXd 6.4 mg/day q3w demonstrated clinical activity and the safety profile was consistent with prior reports**

Siena S, et al. J Clin Oncol 2020;38(suppl);abstr 4000

4001: Encorafenib plus cetuximab with or without binimetinib for BRAF V600E metastatic colorectal cancer: Updated survival results from a randomized, three-arm, phase III study versus choice of either irinotecan or FOLFIRI plus cetuximab (BEACON CRC) – Kopetz S, et al

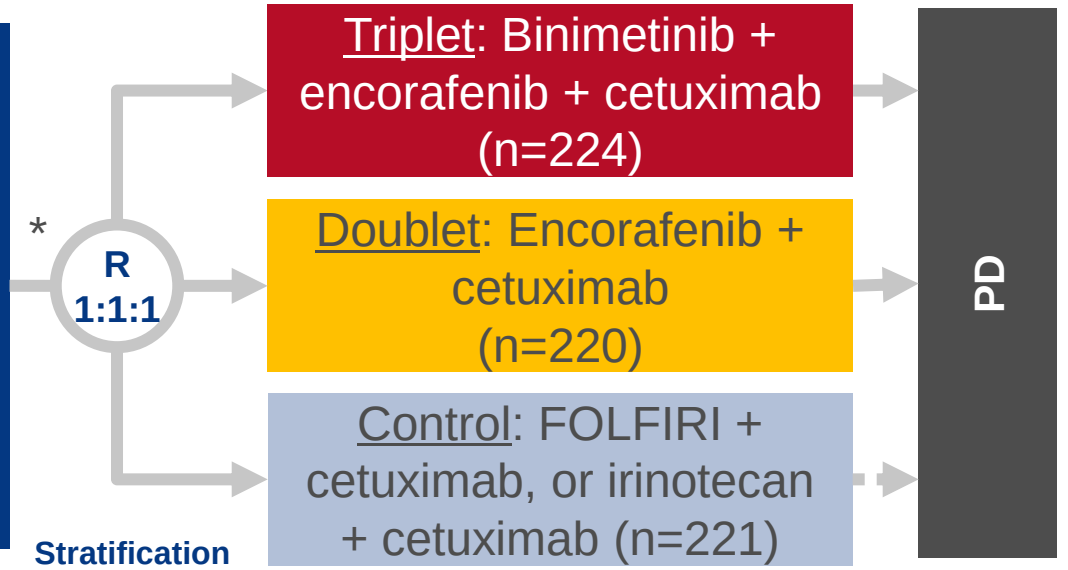
Study objective

- To evaluate the long-term survival in patients with BRAF V600E-mutant mCRC receiving encorafenib + cetuximab ± binimetinib

Key patient inclusion criteria

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

(n=665)



Stratification

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

CO-PRIMARY ENDPOINTS

- OS, ORR (BICR)

SECONDARY ENDPOINTS

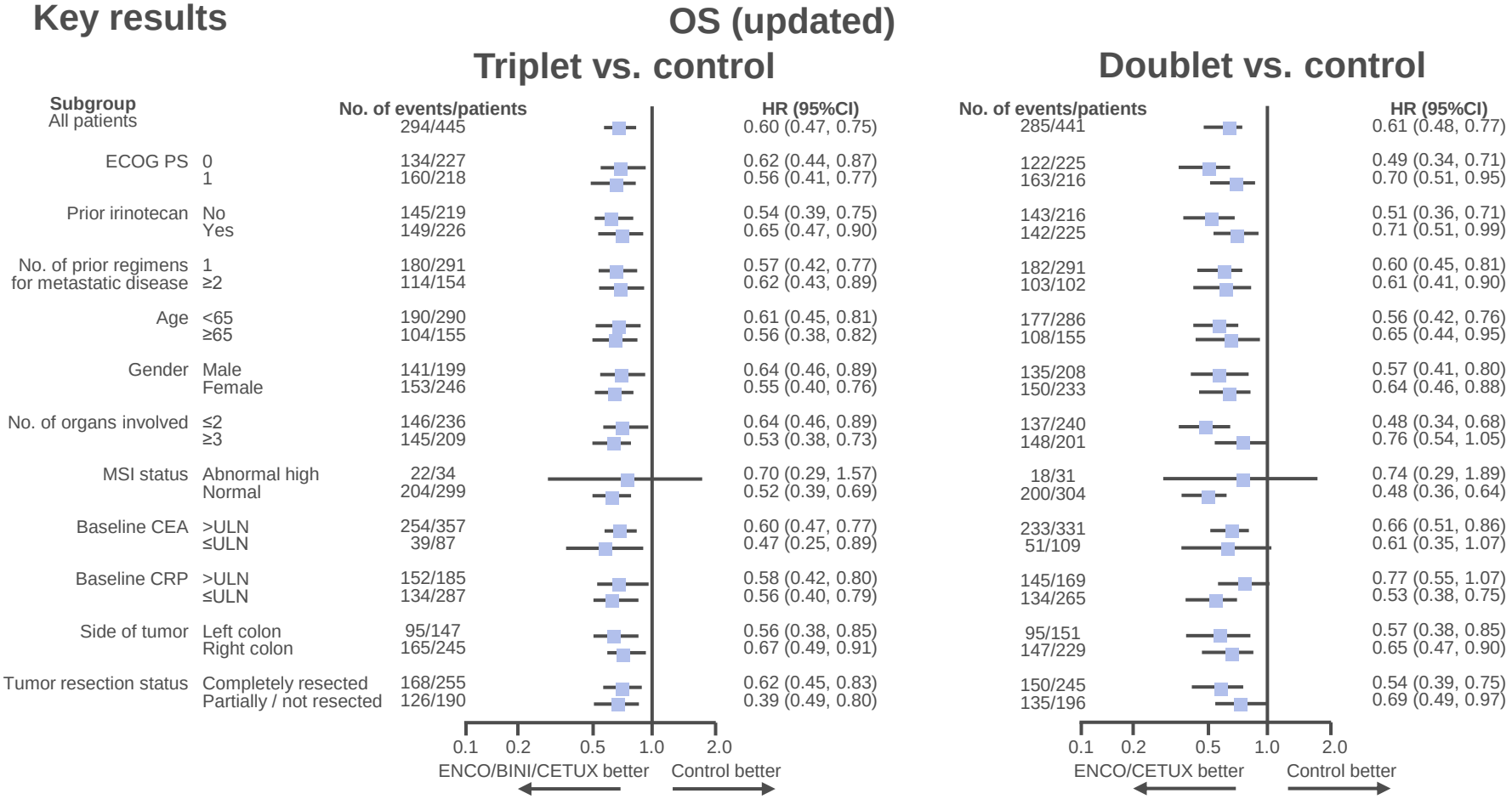
- OS and ORR (for doublet vs control and doublet vs triplet), PFS, QoL safety

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

Kopetz S, et al. J Clin Oncol 2020;38(suppl);abstr 4001

4001: Encorafenib plus cetuximab with or without binimetinib for BRAF V600E metastatic colorectal cancer: Updated survival results from a randomized, three-arm, phase III study versus choice of either irinotecan or FOLFIRI plus cetuximab (BEACON CRC) – Kopetz S, et al

Key results



- mOS, months (95%CI): triplet 9.3 (8.2, 10.8); doublet 9.3 (8.0, 11.3); control 5.9 (5.1, 7.1)
  - HR (95%CI): triplet vs. doublet 0.95 (0.74, 1.21)

Kopetz S, et al. J Clin Oncol 2020;38(suppl);abstr 4001

4001: Encorafenib plus cetuximab with or without binimetinib for BRAF V600E metastatic colorectal cancer: Updated survival results from a randomized, three-arm, phase III study versus choice of either irinotecan or FOLFIRI plus cetuximab (BEACON CRC) – Kopetz S, et al

Key results (cont.)

PFS (BICR)	Triplet (n=224)	Doublet (n=220)	Control (n=221)
Events, n (%)	157 (70.1)	167 (75.9)	147 (66.5)
Median, months (95%CI)	4.5 (4.2, 5.5)	4.3 (4.1, 5.5)	1.5 (1.5, 1.9)
HR vs. control (95%CI)	0.42 (0.33, 0.53)	0.44 (0.35, 0.55)	

Grade ≥3 AEs occurring in ≥5%*, %	Triplet (n=222)	Doublet (n=216)	Control (n=193)
Diarrhea	11	3	10
Abdominal pain	6	3	5
Nausea	5	<1	2
Vomiting	5	1	3
Intestinal obstruction	5	5	3
Pulmonary embolism	4	1	5
Asthenia	4	4	5
Fatigue	2	4	5

Conclusions

- **In patients with BRAF V600E-mutant mCRC, encorafenib + cetuximab significantly improved OS and PFS relevant to standard care and efficacy was similar to triplet regimen**
- **Both the triplet and doublet regimens were well-tolerated and consistent with the known individual safety profiles**

*In ≥5% of patients in any treatment group

Kopetz S, et al. J Clin Oncol 2020;38(suppl);abstr 4001

4002: First-line FOLFOX plus panitumumab versus 5FU plus panitumumab in RAS-BRAF wild-type metastatic colorectal cancer elderly patients: The PANDA study – Lonardi S, et al

Study objective

- To evaluate the efficacy and safety of panitumumab + FOLFOX or 5FU/leucovorin as a 1L treatment for elderly patients with RAS-BRAF WT mCRC

Key patient inclusion criteria

- Unresectable mCRC
- RAS-BRAF WT
- Treatment naïve
- Age ≥70 years
- ECOG PS 1–2 (age 70–75 y); 0–1 (age >75 y)

(n=185)

R 1:1

Panitumumab 6 mg/kg + FOLFOX* (q2w up to 12 cycles) then panitumumab maintenance (n=92) → PD

Stratification

- Age (≤75 vs. >75 years)
- ECOG PS (0–1 vs. 2)
- Geriatric assessment with G8 score (≤14 vs. >14)

Panitumumab 6 mg/kg + 5FU + leucovorin (q2w up to 12 cycles) then panitumumab maintenance (n=93) → PD

PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

- ORR, OS, safety, translational analyses

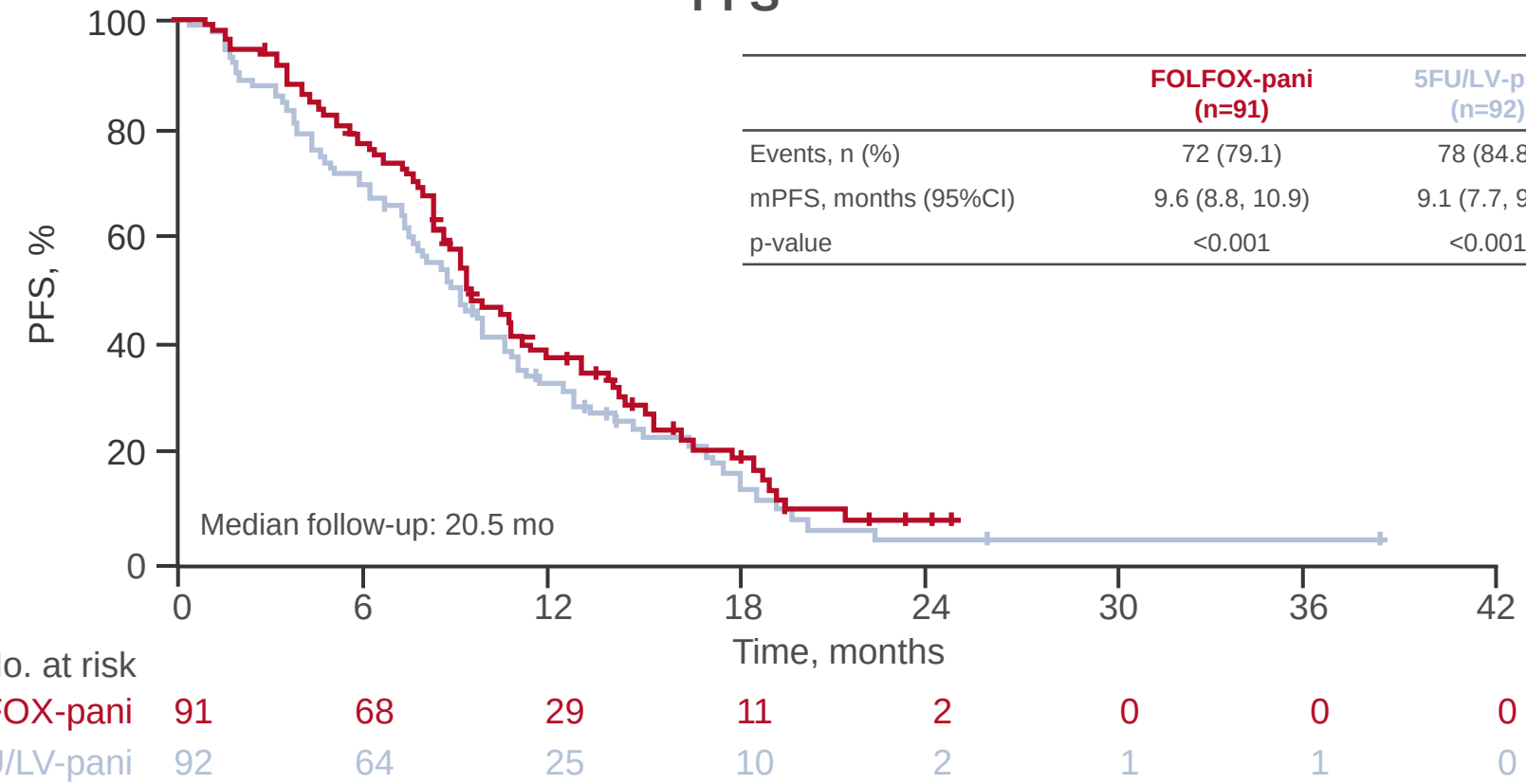
*Oxaliplatin 85 mg/m^2 + 5FU 2400 mg/m^2 + leucovorin 200 mg/m^2

Lonardi S, et al. J Clin Oncol 2020;38(suppl);abstr 4002

4002: First-line FOLFOX plus panitumumab versus 5FU plus panitumumab in RAS-BRAF wild-type metastatic colorectal cancer elderly patients: The PANDA study – Lonardi S, et al

Key results

PFS



	FOLFOX-pani (n=91)	5FU/LV-pani (n=92)
Events, n (%)	72 (79.1)	78 (84.8)
mPFS, months (95%CI)	9.6 (8.8, 10.9)	9.1 (7.7, 9.9)
p-value	<0.001	<0.001

- FOLFOX-pani: ORR 65% (95%CI 54, 74); DCR 88% (95%CI 79, 94)
- 5FU/LV-pani: ORR 57% (95%CI 46, 67); DCR 86% (95%CI 77, 92)

Lonardi S, et al. J Clin Oncol 2020;38(suppl);abstr 4002

4002: First-line FOLFOX plus panitumumab versus 5FU plus panitumumab in RAS-BRAF wild-type metastatic colorectal cancer elderly patients: The PANDA study – Lonardi S, et al

Key results (cont.)

Grade 3–4 AEs, %	FOLFOX-pani (n=92)	5FU/LV-pani (n=91)
Skin rash	25.0	24.2
Diarrhea	16.3	1.1
Stomatitis	9.8	4.4
Neutropenia	9.8	1.1
Fatigue	6.5	4.4
Hypomagnesemia	3.3	7.7
Neurotoxicity	3.3	-

Conclusions

- **In elderly patients with RAS/BRAF WT mCRC, FOLFOX + panitumumab and 5FU/LV + panitumumab showed similar clinical activity**
- **No new safety signals were identified and there was a lower incidence of AEs in the 5FU/LV + panitumumab arm**

Lonardi S, et al. J Clin Oncol 2020;38(suppl);abstr 4002

4003: Celecoxib in addition to standard adjuvant therapy with 5-fluorouracil, leucovorin, oxaliplatin (FOLFOX) in stage III colon cancer: Results from CALGB/SWOG 80702 – Meyerhardt JA, et al

Study objective

- To evaluate the efficacy and safety of celecoxib (a COX-2 inhibitor) + FOLFOX in patients with stage III colon cancer

Key patient inclusion criteria

- Resected stage III colon cancer
- ≥1 positive lymph node or N1c disease
- No regular NSAID or high dose aspirin use*

(n=2526)

R

- Celecoxib 400 mg/day + 3-month FOLFOX (n=618)
- Celecoxib 400 mg/day + 6-month FOLFOX (n=647)
- Placebo + 3-month FOLFOX (n=646)
- Placebo + 6-month FOLFOX (n=615)

Stratification

- Positive lymph nodes (1–3 vs. ≥4); regular low dose aspirin use

PRIMARY ENDPOINT

- DFS

SECONDARY ENDPOINTS

- OS, safety

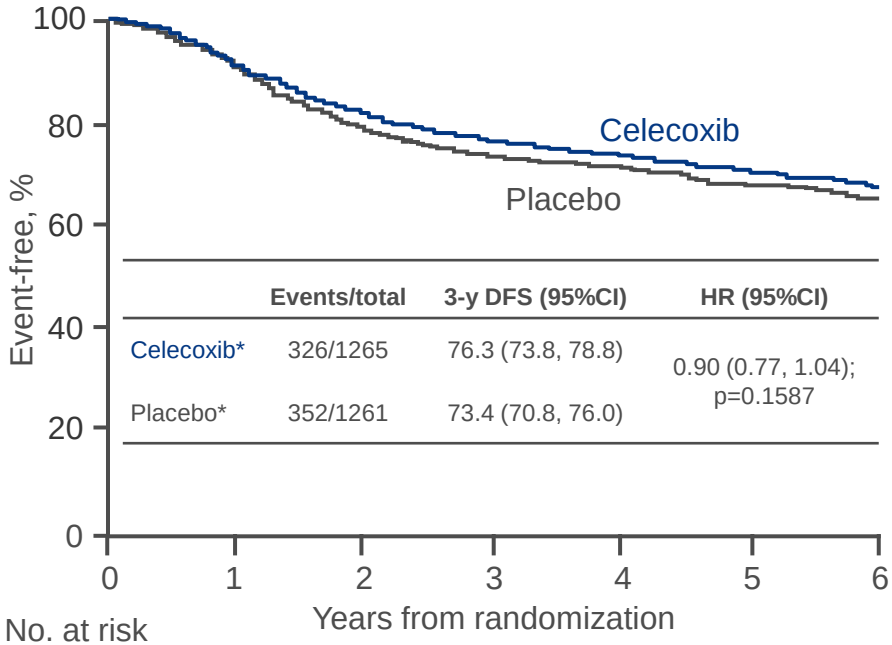
*Patients ineligible if they use NSAIDs ≥x2/week or aspirin at ≥325 mg x3/week; low-dose aspirin ≤100 mg/day permitted

Meyerhardt JA, et al. J Clin Oncol 2020;38(suppl);abstr 4003

4003: Celecoxib in addition to standard adjuvant therapy with 5-fluorouracil, leucovorin, oxaliplatin (FOLFOX) in stage III colon cancer: Results from CALGB/SWOG 80702 – Meyerhardt JA, et al

Key results

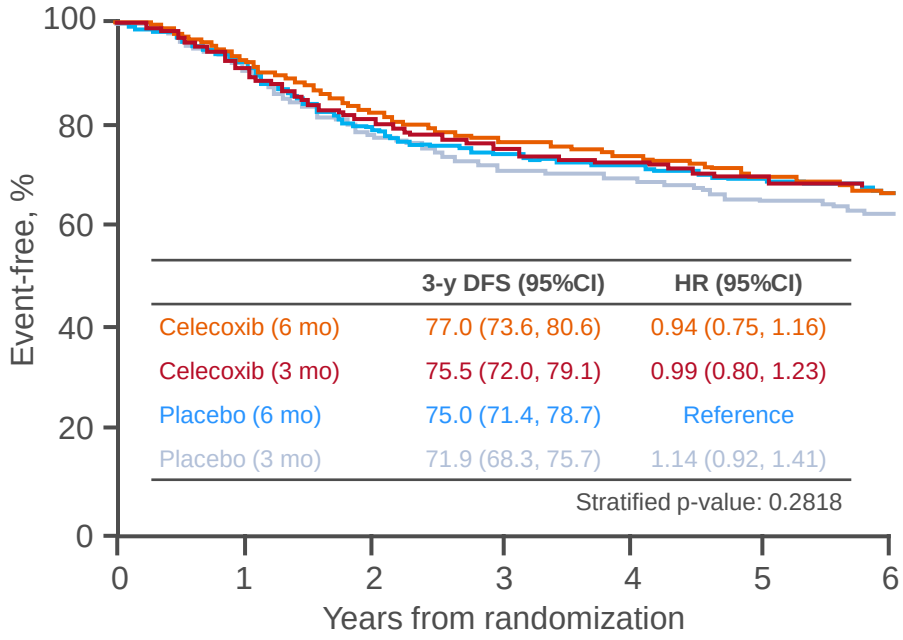
DFS



	Events/total	3-y DFS (95%CI)	HR (95%CI)
Celecoxib*	326/1265	76.3 (73.8, 78.8)	0.90 (0.77, 1.04); p=0.1587
Placebo*	352/1261	73.4 (70.8, 76.0)	

No. at risk

1265	1049	894	768	633	384	109
1261	1041	846	738	608	370	102



	3-y DFS (95%CI)	HR (95%CI)
Celecoxib (6 mo)	77.0 (73.6, 80.6)	0.94 (0.75, 1.16)
Celecoxib (3 mo)	75.5 (72.0, 79.1)	0.99 (0.80, 1.23)
Placebo (6 mo)	75.0 (71.4, 78.7)	Reference
Placebo (3 mo)	71.9 (68.3, 75.7)	1.14 (0.92, 1.41)

Stratified p-value: 0.2818

647	534	450	355	320	188	54
618	515	444	383	313	196	55
615	506	411	360	290	178	46
646	535	435	378	318	192	56

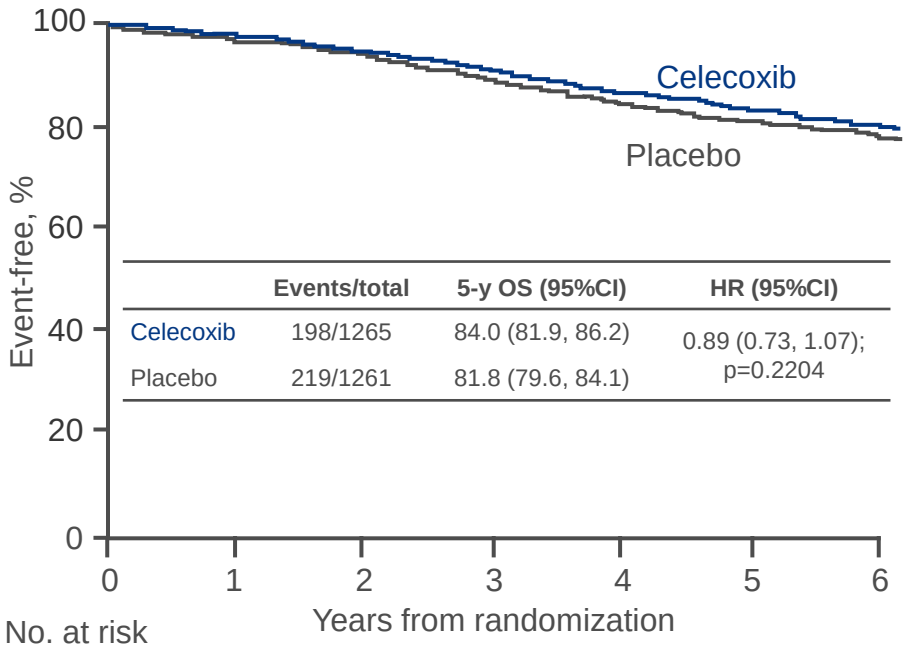
*Combined analyses

Meyerhardt JA, et al. J Clin Oncol 2020;38(suppl);abstr 4003

4003: Celecoxib in addition to standard adjuvant therapy with 5-fluorouracil, leucovorin, oxaliplatin (FOLFOX) in stage III colon cancer: Results from CALGB/SWOG 80702 – Meyerhardt JA, et al

- **Key results (cont.)**

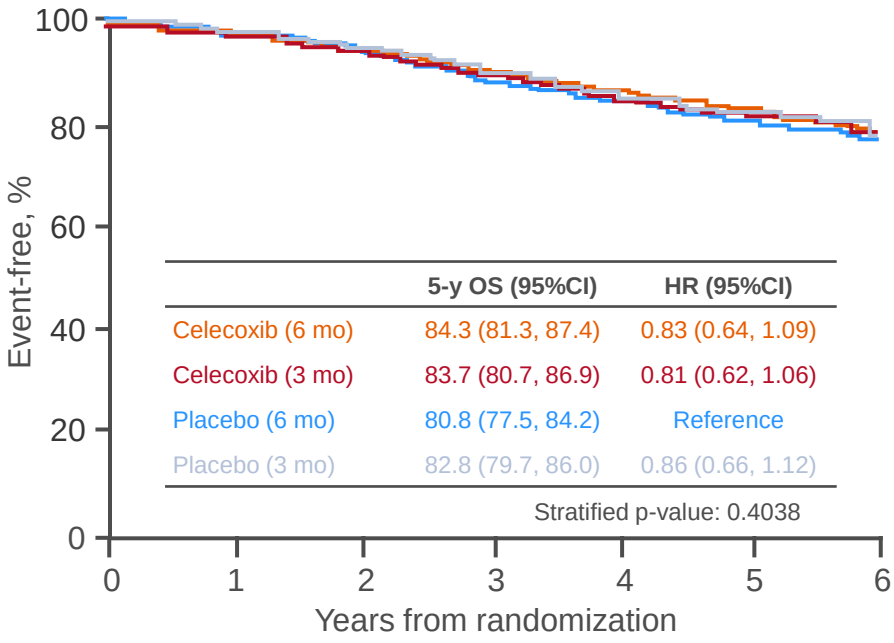
OS



	Events/total	5-y OS (95%CI)	HR (95%CI)
Celecoxib	198/1265	84.0 (81.9, 86.2)	0.89 (0.73, 1.07); p=0.2204
Placebo	219/1261	81.8 (79.6, 84.1)	

No. at risk

1265	1153	1080	1009	929	697	414
1261	1147	1068	989	911	669	393



	5-y OS (95%CI)	HR (95%CI)
Celecoxib (6 mo)	84.3 (81.3, 87.4)	0.83 (0.64, 1.09)
Celecoxib (3 mo)	83.7 (80.7, 86.9)	0.81 (0.62, 1.06)
Placebo (6 mo)	80.8 (77.5, 84.2)	Reference
Placebo (3 mo)	82.8 (79.7, 86.0)	0.86 (0.66, 1.12)

Stratified p-value: 0.4038

647	581	537	503	465	348	201
618	572	543	506	464	349	213
646	595	553	516	475	353	203
615	552	515	473	436	316	190

Meyerhardt JA, et al. J Clin Oncol 2020;38(suppl);abstr 4003

4003: Celecoxib in addition to standard adjuvant therapy with 5-fluorouracil, leucovorin, oxaliplatin (FOLFOX) in stage III colon cancer: Results from CALGB/SWOG 80702 – Meyerhardt JA, et al

Key results (cont.)

Celecoxib-specific AEs, %	During FOLFOX			After FOLFOX therapy		
	Celecoxib	Placebo	χ2 p-value	Celecoxib	Placebo	χ2 p-value
Creatinine increase (grade ≥2)	1.8	1.5	0.51	1.7	0.5	0.01
Cerebral ischemia (any grade)	0.4	0.5	0.52	0.3	0.6	0.32
Diarrhea (grade 3–4)	6.5	6.7	0.82	0.3	0.3	0.99
Gastritis (any grade)	4.2	4.5	0.66	3.0	2.0	0.13
Hypertension (any grade)	14.6	10.9	0.01	13.0	10.0	0.04
Myocardial ischemia (any grade)	0.9	0.9	0.98	0.9	0.3	0.08
Peripheral neuropathy (grade 3–4)	10.3	9.1	0.33	4.9	4.1	0.40

Conclusions

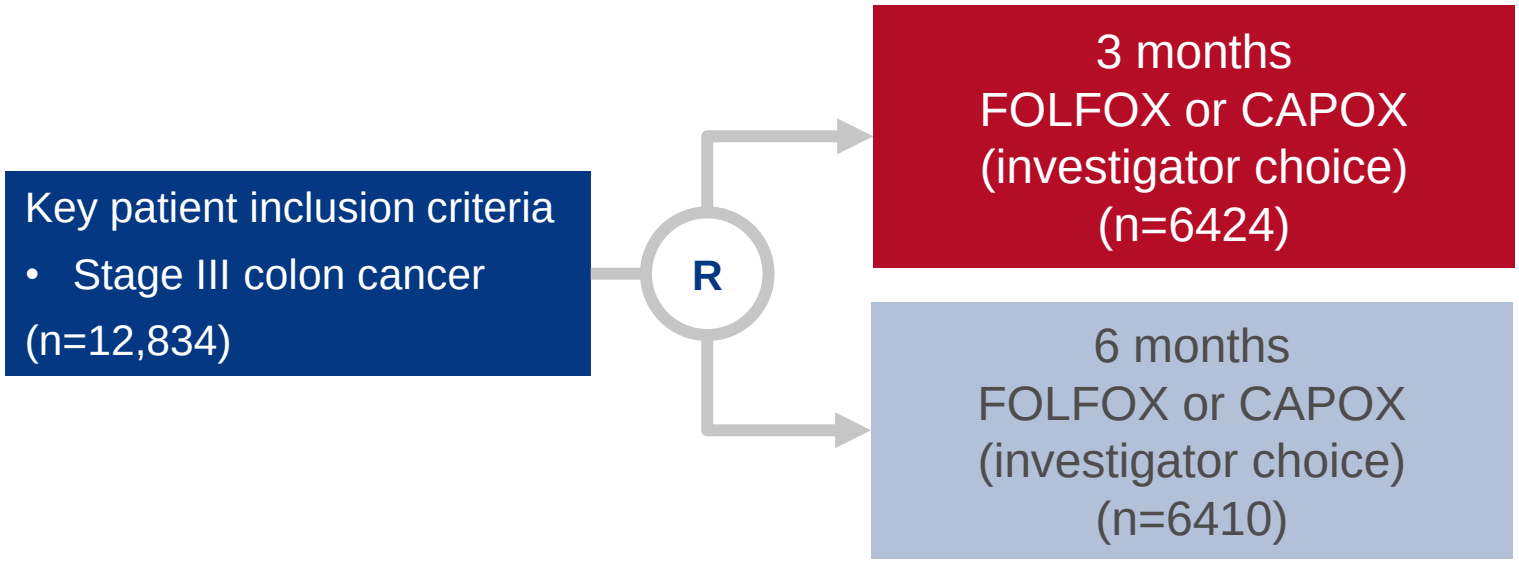
- **In patients with stage III colon cancer, adding celecoxib to FOLFOX adjuvant therapy did not significantly improve survival (DFS or OS)**

Meyerhardt JA, et al. J Clin Oncol 2020;38(suppl);abstr 4003

4004: Overall survival (OS) and long-term disease-free survival (DFS) of three versus six months of adjuvant (adj) oxaliplatin and fluoropyrimidine-based therapy for patients (pts) with stage III colon cancer (CC): Final results from the IDEA (International Duration Evaluation of Adj chemotherapy) collaboration – Sobrero AF, et al

Study objective

- To evaluate the long-term efficacy (non-inferiority) of 3 months compared with 6 months of adjuvant oxaliplatin-based treatment in patients with stage III colon cancer (a pooled analysis of six phase 3 studies*)



PRIMARY ENDPOINT

- DFS

SECONDARY ENDPOINTS

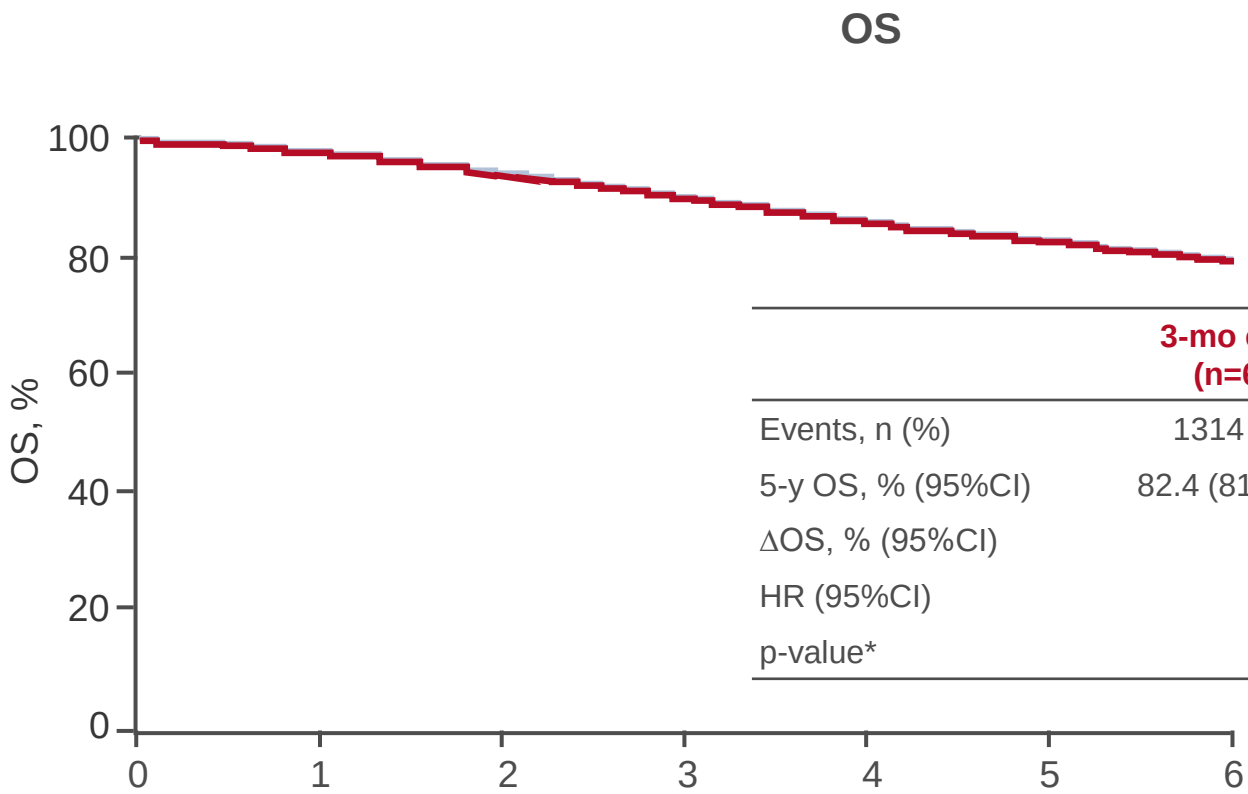
- OS, pre-planned subgroup analyses by regimen and T/N stage

*SCOT, TOSCA, Alliance/SWOG 80702, IDEA France, ACHIEVE, HORG

Sobrero AF, et al. J Clin Oncol 2020;38(suppl);abstr 4004

4004: Overall survival (OS) and long-term disease-free survival (DFS) of three versus six months of adjuvant (adj) oxaliplatin and fluoropyrimidine-based therapy for patients (pts) with stage III colon cancer (CC): Final results from the IDEA (International Duration Evaluation of Adj chemotherapy) collaboration – Sobrero AF, et al

Key results



	3-mo chemo (n=6425)	6-mo chemo (n=6410)
Events, n (%)	1314 (20.5)	1270 (19.8)
5-y OS, % (95%CI)	82.4 (81.4, 83.3)	82.8 (81.8, 83.8)
ΔOS, % (95%CI)	-0.4 (-2.4, 1.5)	
HR (95%CI)	1.02 (0.95, 1.11)	
p-value*	0.0583	

No. at risk

6425	6177	5870	5413	4863	4023	2676
6410	6120	5790	5302	4729	3966	2686

*FDR adjusted stratified NIF

Sobrero AF, et al. J Clin Oncol 2020;38(suppl);abstr 4004

4004: Overall survival (OS) and long-term disease-free survival (DFS) of three versus six months of adjuvant (adj) oxaliplatin and fluoropyrimidine-based therapy for patients (pts) with stage III colon cancer (CC): Final results from the IDEA (International Duration Evaluation of Adj chemotherapy) collaboration – Sobrero AF, et al

Key results (cont.)

OS by subgroups		5-y OS, % (95%CI)		HR* (95%CI)
		3 mo (n=249)	6 mo (n=250)	
Regimen	CAPOX	82.1 (80.5, 83.6)	81.2 (79.7, 82.9)	0.96 (0.85, 1.08)
	FOLFOX	82.6 (81.3, 83.8)	83.8 (82.6, 85.0)	1.07 (0.97, 1.18)
Risk group	Low risk (T1-3, N1)	89.6 (88.6, 90.7)	88.9 (87.8, 90.0)	0.95 (0.84,1.08)
	High risk (T4, N2)	72.0 (70.3, 73.8)	74.1 (72.4, 75.9)	1.08 (0.98, 1.19)
Regimen/risk	CAPOX, Low risk	90.4 (88.9, 92.0)	88.1 (86.3, 89.8)	0.85 (0.69, 1.04)
	CAPOX, High risk	71.4 (68.7, 74.2)	72.4 (69.7, 75.2)	1.03 (0.89, 1.20)
	FOLFOX, Low risk	89.1 (87.8, 90.5)	89.4 (88.1, 90.7)	1.02 (0.87, 1.19)
	FOLFOX, High risk	72.5 (70.2, 74.9)	75.3 (73.1, 77.6)	1.12 (0.98, 1.27)

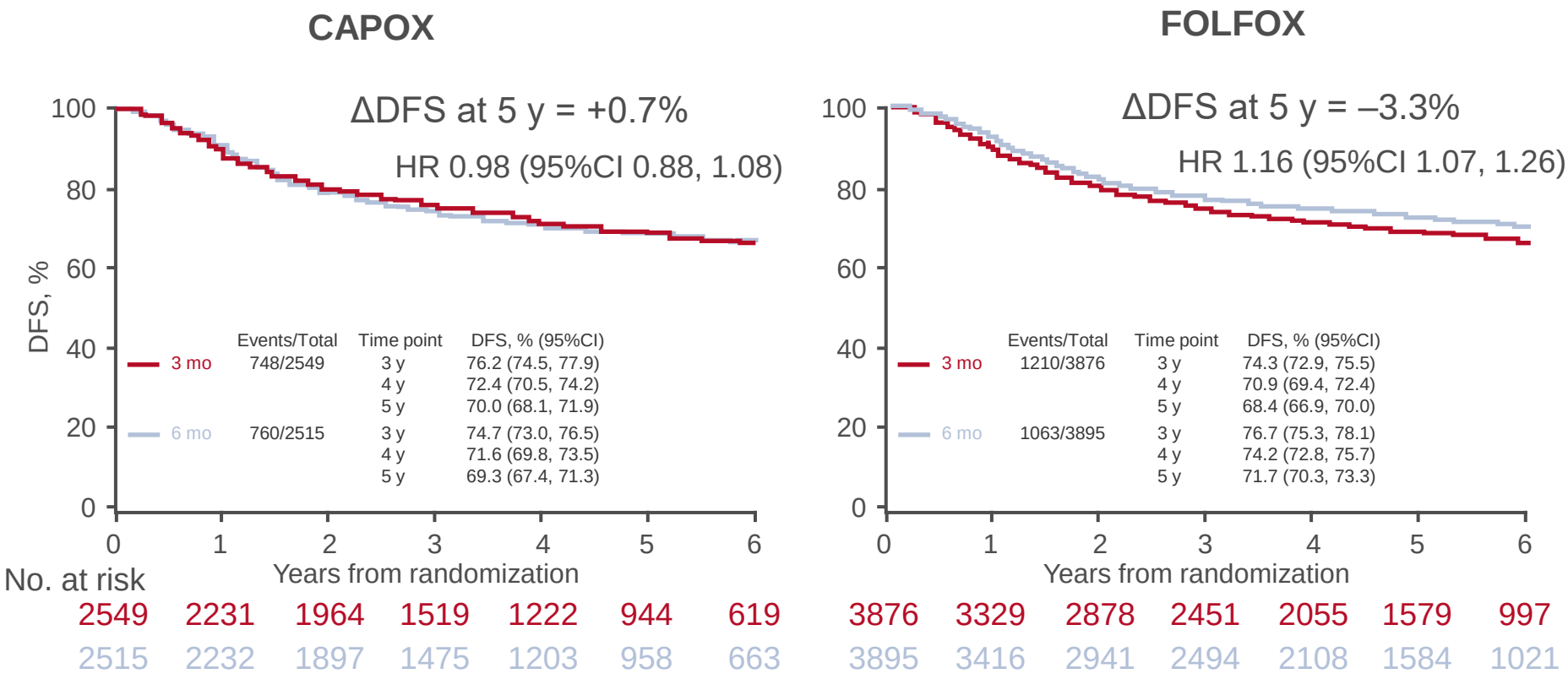
*3 vs. 6 months

Sobrero AF, et al. J Clin Oncol 2020;38(suppl);abstr 4004

4004: Overall survival (OS) and long-term disease-free survival (DFS) of three versus six months of adjuvant (adj) oxaliplatin and fluoropyrimidine-based therapy for patients (pts) with stage III colon cancer (CC): Final results from the IDEA (International Duration Evaluation of Adj chemotherapy) collaboration – Sobrero AF, et al

Key results (cont.)

DFS by regimen



Sobrero AF, et al. J Clin Oncol 2020;38(suppl);abstr 4004

4004: Overall survival (OS) and long-term disease-free survival (DFS) of three versus six months of adjuvant (adj) oxaliplatin and fluoropyrimidine-based therapy for patients (pts) with stage III colon cancer (CC): Final results from the IDEA (International Duration Evaluation of Adj chemotherapy) collaboration – Sobrero AF, et al

Key results (cont.)

AEs, %	FOLFOX		CAPOX	
	3 mo	6 mo	3 mo	6 mo
Any AE				
Grade ≤1	30	11	35	15
Grade 2	32	32	41	48
Grade 3–4	38	57	24	37
p-value*	<0.0001		<0.0001	
Neurotoxicity				
Grade ≤1	83	52	85	55
Grade 2	14	32	12	36
Grade 3–4	3	16	3	9
p-value*	<0.0001		<0.0001	

Conclusions

- **In patients with stage III colon cancer, 3-month adjuvant oxaliplatin-based treatment showed a similar survival and fewer toxicities compared with 6-month treatment**
- **The prolonged follow-up for DFS and OS confirmed the drug regimen effect previously observed**

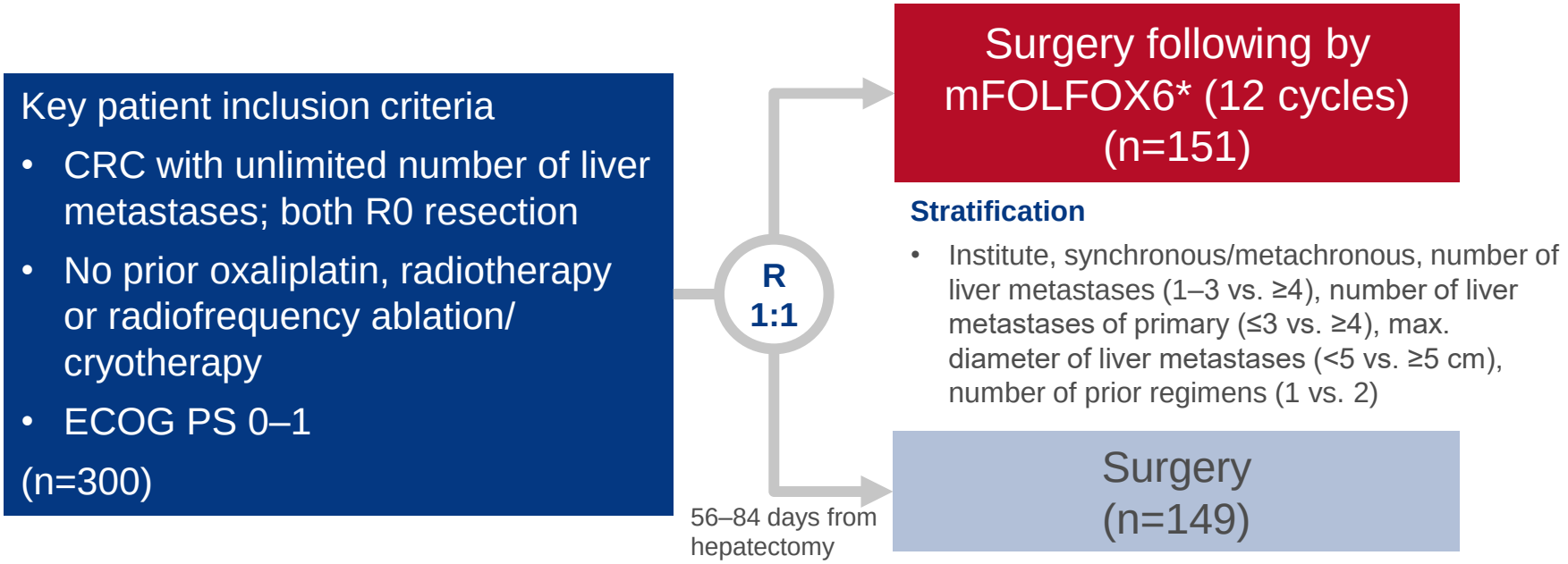
*Chi-squared p-value for trend

Sobrero AF, et al. J Clin Oncol 2020;38(suppl);abstr 4004

4005: A randomized phase II/III trial comparing hepatectomy followed by mFOLFOX6 with hepatectomy alone for liver metastasis from colorectal cancer: JCOG0603 study – Kanemitsu Y, et al

Study objective

- To evaluate the efficacy and safety of adjuvant mFOLFOX6 compared with hepatectomy alone in patients with liver only metastases from CRC



PRIMARY ENDPOINT

- DFS

SECONDARY ENDPOINTS

- OS, sites of relapse, safety

*Oxaliplatin 85 mg/m^2 + leucovorin 200 mg/m^2 + 5FU 400 mg/m^2 bolus then 2400 mg/m^2 over 48 h

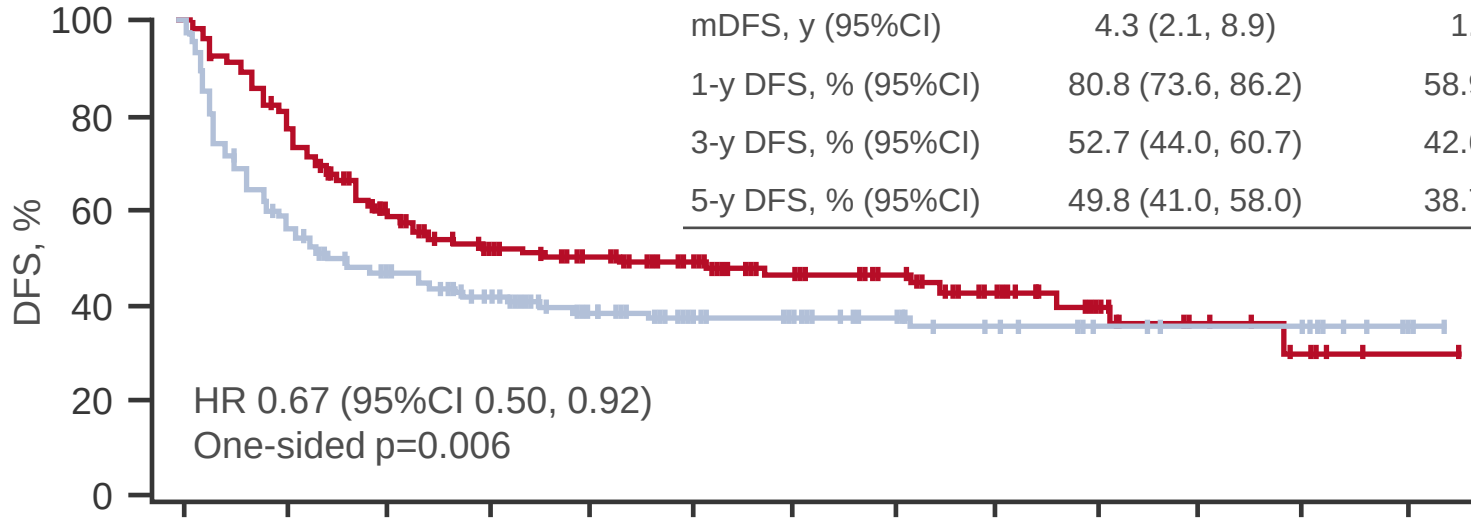
Kanemitsu Y, et al. J Clin Oncol 2020;38(suppl);abstr 4005

4005: A randomized phase II/III trial comparing hepatectomy followed by mFOLFOX6 with hepatectomy alone for liver metastasis from colorectal cancer: JCOG0603 study – Kanemitsu Y, et al

Key results

DFS (ITT – updated)

	mFOLFOX6 (n=151)	Surgery alone (n=149)
Events, n (%)	77 (51.0)	88 (59.1)
mDFS, y (95%CI)	4.3 (2.1, 8.9)	1.7 (1.0, 3.2)
1-y DFS, % (95%CI)	80.8 (73.6, 86.2)	58.9 (50.6, 66.3)
3-y DFS, % (95%CI)	52.7 (44.0, 60.7)	42.6 (34.3, 50.6)
5-y DFS, % (95%CI)	49.8 (41.0, 58.0)	38.7 (30.4, 46.8)



No. at risk
(No. censored)

mFOLFOX6	151(0)	121(1)	75(16)	59(8)	51(6)	42(8)	33(7)	29(4)	19(8)	10(7)	7(3)	3(3)	1(2)	0(1)
Surgery alone	149(0)	86(2)	61(9)	49(6)	39(7)	30(8)	28(2)	21(7)	16(4)	12(4)	10(2)	7(3)	1(6)	0(1)

Median follow-up for DFS was 59.2 months

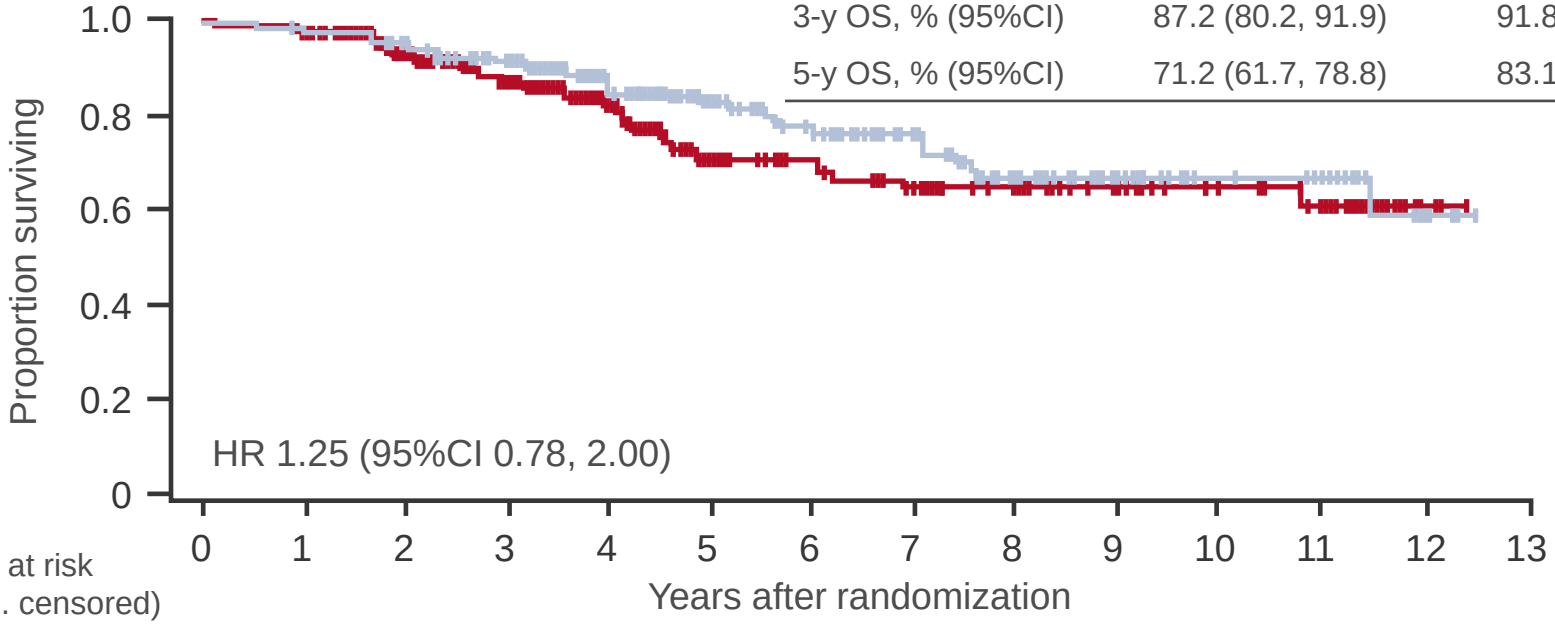
Kanemitsu Y, et al. J Clin Oncol 2020;38(suppl);abstr 4005

4005: A randomized phase II/III trial comparing hepatectomy followed by mFOLFOX6 with hepatectomy alone for liver metastasis from colorectal cancer: JCOG0603 study – Kanemitsu Y, et al

Key results (cont.)

OS (ITT – updated)

	mFOLFOX6 (n=151)	Surgery alone (n=149)
Events, n (%)	38	32
3-y OS, % (95%CI)	87.2 (80.2, 91.9)	91.8 (85.7, 95.4)
5-y OS, % (95%CI)	71.2 (61.7, 78.8)	83.1 (74.9, 88.9)



No; at risk (No. censored)

mFOLFOX6	151(0)	148(1)	121(18)	102(13)	84(13)	61(12)	55(5)	45(7)	35(10)	24(11)	18(6)	12(5)	2(10)	0(2)
Surgery alone	149(0)	144(3)	124(16)	108(11)	86(15)	71(13)	59(7)	50(9)	33(11)	23(10)	19(4)	13(6)	3(9)	0(3)

*DMC recommended the early termination of the trial based given that the OS curve of adjuvant mFOLFOX6 was below that of surgery alone

Kanemitsu Y, et al. J Clin Oncol 2020;38(suppl);abstr 4005

4005: A randomized phase II/III trial comparing hepatectomy followed by mFOLFOX6 with hepatectomy alone for liver metastasis from colorectal cancer: JCOG0603 study – Kanemitsu Y, et al

Key results (cont.)

Tolerance to chemotherapy	mFOLFOX6 (n=151)
Treatment cycles, median (range)	10 (0–12)
Grade 3–4 AEs, n (%)	
Neutropenia	70 (50)
Sensory neuropathy	14 (10)
Allergic reaction	6 (4)
Vomiting	3 (2)
Diarrhea	3 (2)
Nausea	2 (1)
Anorexia	1 (1)
Oral mucositis	1 (1)
Febrile neutropenia	1 (1)
Infection	1 (1)

Postoperative grade 2–4 AEs, n (%)	mFOLFOX6 (n=151)	Surgery alone (n=149)
Constipation	3 (2)	1 (1)
Digestive tract obstruction	2 (1)	2 (1)
Paralytic ileus	2 (1)	1 (1)
Diarrhea	1 (1)	1 (1)
Frequent urination	1 (1)	0
Postoperative death	1 (1)	0

Kanemitsu Y, et al. J Clin Oncol 2020;38(suppl);abstr 4005

4005: A randomized phase II/III trial comparing hepatectomy followed by mFOLFOX6 with hepatectomy alone for liver metastasis from colorectal cancer: JCOG0603 study – Kanemitsu Y, et al

Key results (cont.)

Patterns of recurrence after liver resection, n (%)	mFOLFOX6 (n=68)	Surgery alone (n=83)
Liver only	23 (34)	36 (43)
Lung only	18 (26)	16 (19)
Both liver and lung	2 (3)	7 (8)
Extrahepatic and extrapulmonary	25 (37)	24 (29)

Conclusions

- **In patients with CRC and liver metastases, mFOLFOX6 after hepatectomy significantly prolonged DFS, but did impair OS, leading to early trial termination**
- **Adjuvant mFOLFOX6 altered the pattern of metastases after hepatectomy for liver metastases from CRC**

Kanemitsu Y, et al. J Clin Oncol 2020;38(suppl);abstr 4005

4006: Short-course radiotherapy followed by chemotherapy before TME in locally advanced rectal cancer: The randomized RAPIDO trial – Hospers G, et al

Study objective

- To evaluate the efficacy and safety of short-course radiotherapy followed by chemotherapy before total mesorectal excision (TME) in patients with locally advanced rectal cancer

Key patient inclusion criteria

- Locally advanced rectal cancer, no distant metastases
- cT4a/b, extramural vascular invasion, cN2, involved mesorectal fascia or enlarged lymph nodes

(n=920)

R 1:1

Short-course radiotherapy (5x5 Gy) then CAPOX (6 cycles) or FOLFOX (9 cycles) followed by TME (n=460)

Capecitabine-based chemoradiotherapy (25–28 x 2.0–1.8 Gy) followed by TME then optional CAPOX (8 cycles) or FOLFOX4 (12 cycles) (n=441)

PRIMARY ENDPOINT

- Disease-related treatment failure (DrTF)*

SECONDARY ENDPOINTS

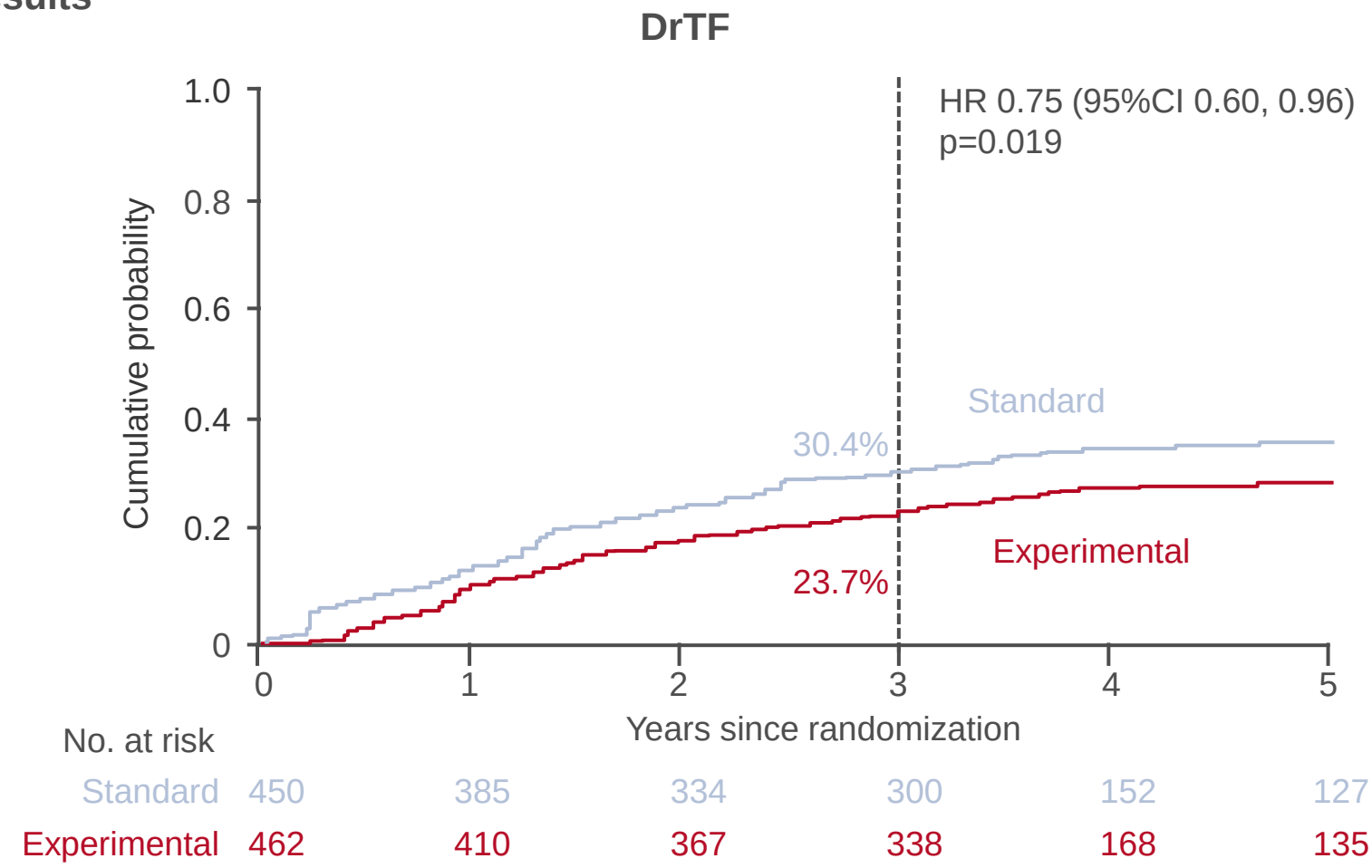
- OS, pCR, R0 rate, safety, QoL at 3 years

*Defined as locoregional failure, distant metastasis, a new primary colon tumor or treatment-related death

Hospers G, et al. J Clin Oncol 2020;38(suppl);abstr 4006

4006: Short-course radiotherapy followed by chemotherapy before TME in locally advanced rectal cancer: The randomized RAPIDO trial – Hospers G, et al

Key results

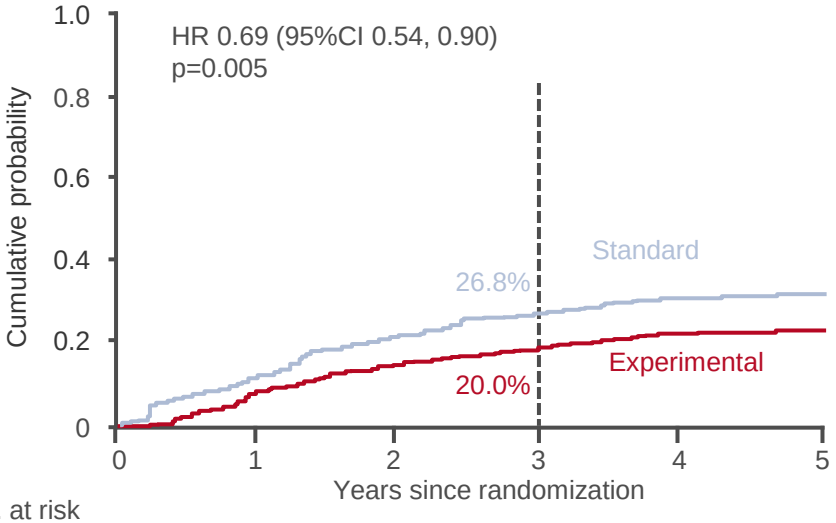


Hospers G, et al. J Clin Oncol 2020;38(suppl);abstr 4006

4006: Short-course radiotherapy followed by chemotherapy before TME in locally advanced rectal cancer: The randomized RAPIDO trial – Hospers G, et al

Key results (cont.)

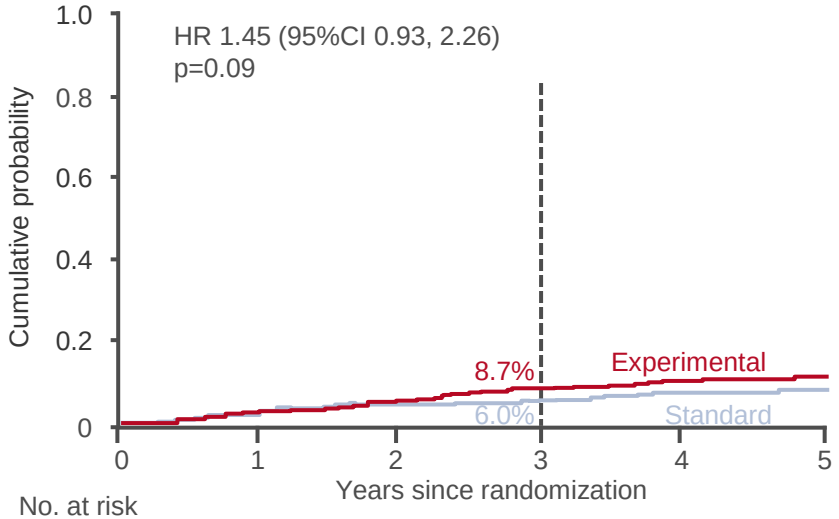
Distant metastases



No. at risk

Standard	450	390	343	311	156	130
Experimental	462	414	372	348	178	144

Locoregional failure



No. at risk

Standard	450	428	405	379	200	162
Experimental	462	434	410	382	192	149

Hospers G, et al. J Clin Oncol 2020;38(suppl);abstr 4006

4006: Short-course radiotherapy followed by chemotherapy before TME in locally advanced rectal cancer: The randomized RAPIDO trial – Hospers G, et al

Key results (cont.)

Pathology of resected tumor, n (%)	Experimental (n=423)	Standard (n=398)	p-value
Residual tumor R0 >1 mm R1 ≤1 mm R2	 383 (90.5) 37 (8.7) 3 (0.7)	 360 (90.5) 37 (9.3) 1 (0.3)	0.62
pCR	120 (28.4)	57 (14.3)	<0.001

Survival	Experimental (n=462)	Standard (n=450)
3-y OS, %	89.1	88.8
HR (95%CI); p-value	0.92 (0.67, 1.25); 0.59	

Hospers G, et al. J Clin Oncol 2020;38(suppl);abstr 4006

4006: Short-course radiotherapy followed by chemotherapy before TME in locally advanced rectal cancer: The randomized RAPIDO trial – Hospers G, et al

Key results (cont.)

Grade ≥3 AEs occurring in ≥2%*, %	Experimental - preop (n=460)	Standard - preop (n=441)	Standard - postop (n=187)
Diarrhea	17.6	9.3	7.0
Neurological toxicity	4.3	0.2	8.6
Vascular disorders	8.5	4.1	0.5
Fatigue/lethargy	3.0	1.4	5.3
Nausea/vomiting	4.1	1.1	2.7
Infections and infestations	3.9	1.6	3.2
Obstruction/constipation	3.3	1.1	1.1
Abdominal pain	3.3	0.9	1.6
Proctitis, rectal bleeding	1.7	3.2	0.5
Hand-foot syndrome	1.7	1.1	2.1
Cardiac disorders	1.5	2.3	0
Blood and lymphatic system	1.1	0.9	2.1

Conclusions

- **In patients with locally advanced rectal cancer, short-course radiotherapy followed by chemotherapy before TME resulted in lower DrTF and improved pCR rate with no unexpected toxicities reported**

*In any treatment arm

Hospers G, et al. J Clin Oncol 2020;38(suppl);abstr 4006

4007: Total neoadjuvant therapy with mFOLFIRINOX versus preoperative chemoradiation in patients with locally advanced rectal cancer: Final results of PRODIGE 23 phase III trial, a UNICANCER GI trial – Conroy T, et al

Study objective

- To evaluate the efficacy and safety of neoadjuvant mFOLFIRINOX compared with preoperative chemoradiotherapy in patients with locally advanced rectal cancer

Key patient inclusion criteria

- cT3 or cT4, M0 rectal adenocarcinomas <15 cm from anal verge
- WHO PS 0–1

(n=461)

Stratification

- Center, T stage, N status, tumor location, perirectal fat extramural extension

R 1:1

mFOLFIRINOX* (6 cycles) then preoperative chemoradiotherapy (50.4 Gy, 2 Gy/fraction; 25 fractions + capecitabine) then surgery followed by adjuvant chemotherapy† (3 months) (n=231)

Preoperative chemoradiotherapy (50.4 Gy, 2 Gy/fraction; 25 fractions + capecitabine) then surgery followed by adjuvant chemotherapy‡ (6 months) (n=230)

PRIMARY ENDPOINT

- 3-year DFS

SECONDARY ENDPOINTS

- pCR (ypT0N0) rate, OS, MFS, safety, QoL

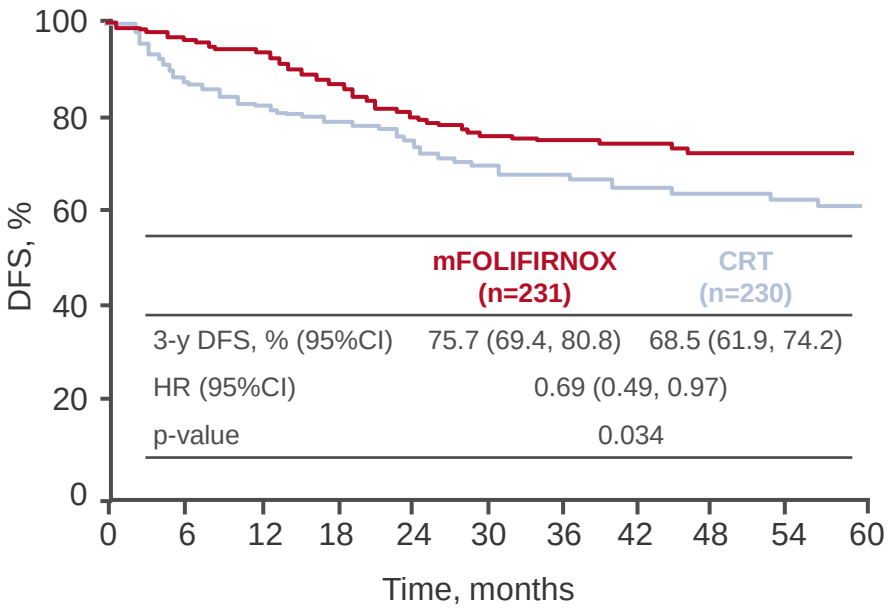
*Oxaliplatin 85 mg/m^2 + leucovorin 400 mg/m^2 + irinotecan 180 mg/m^2 + 5FU 2.4 g/m^2 over 46 h q2w; †mFOLFOX6, 6 cycles; or capecitabine, 4 cycles; ‡mFOLFOX6, 12 cycles; or capecitabine, 8 cycles

Conroy T, et al. J Clin Oncol 2020;38(suppl);abstr 4007

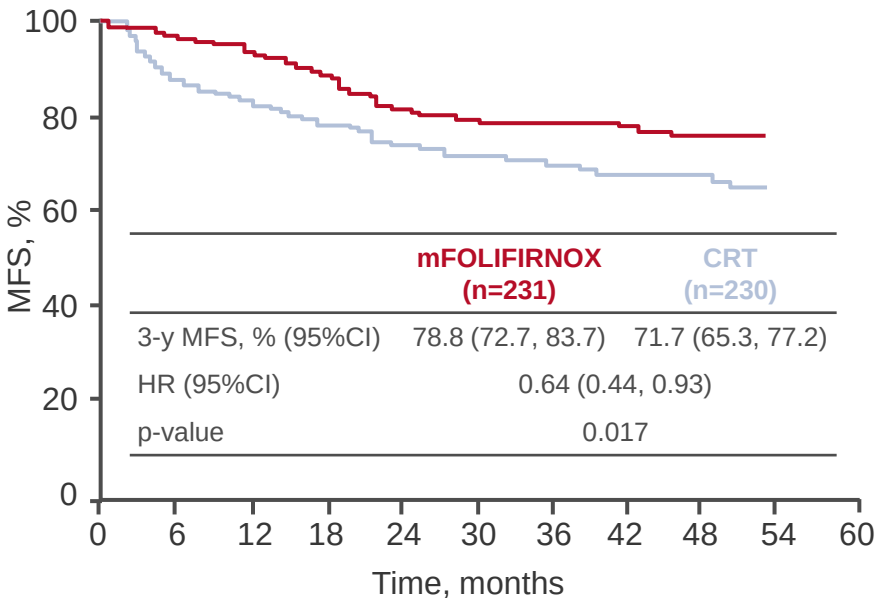
4007: Total neoadjuvant therapy with mFOLFIRINOX versus preoperative chemoradiation in patients with locally advanced rectal cancer: Final results of PRODIGE 23 phase III trial, a UNICANCER GI trial – Conroy T, et al

Key results

DFS



MFS



No. at risk

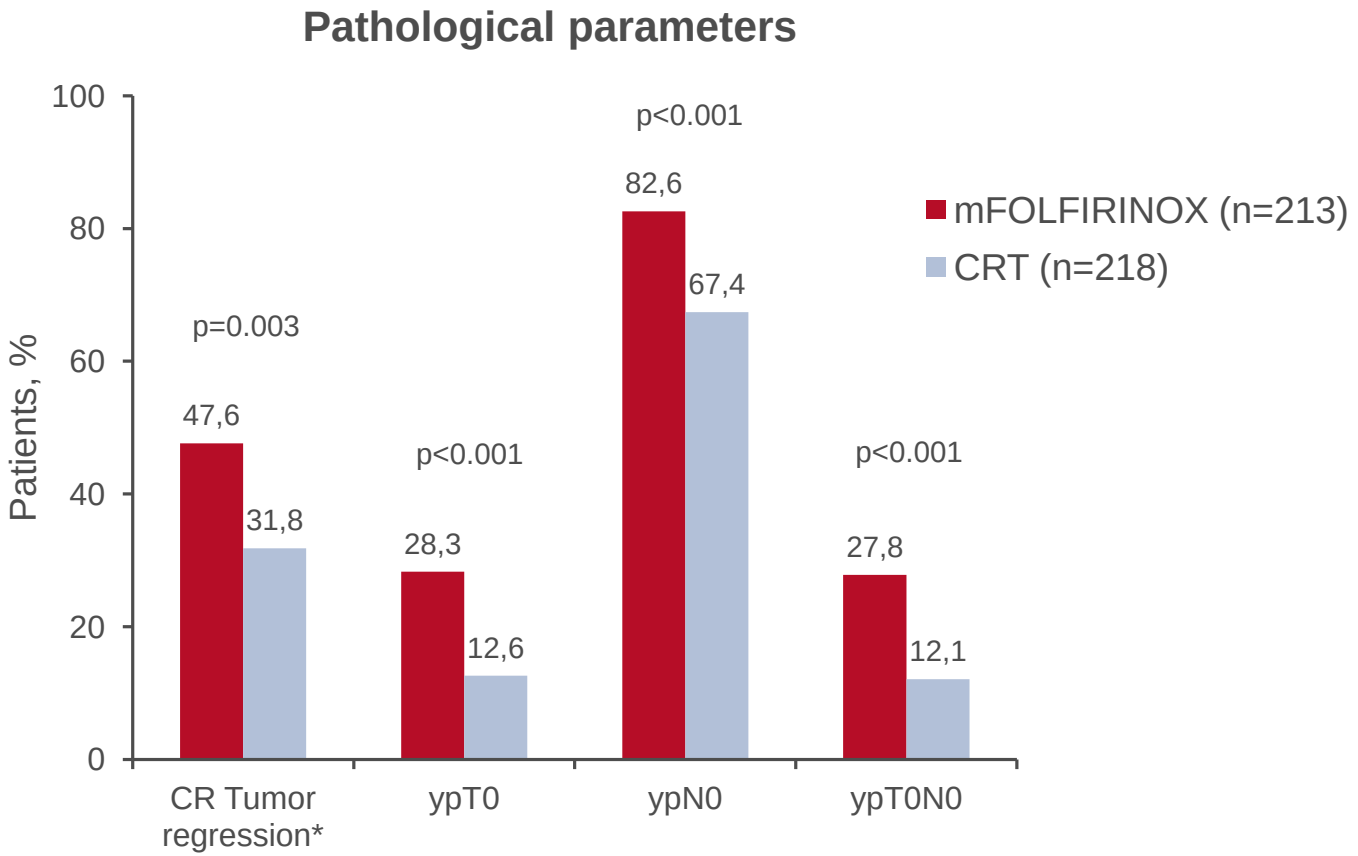
231	217	210	194	176	150	126	104	80	62	51
230	201	188	177	167	146	117	91	65	55	40

231	218	212	200	184	156	131	109	86	65	52
230	202	191	178	170	153	123	96	70	60	43

Conroy T, et al. J Clin Oncol 2020;38(suppl);abstr 4007

4007: Total neoadjuvant therapy with mFOLFIRINOX versus preoperative chemoradiation in patients with locally advanced rectal cancer: Final results of PRODIGE 23 phase III trial, a UNICANCER GI trial – Conroy T, et al

Key results (cont.)



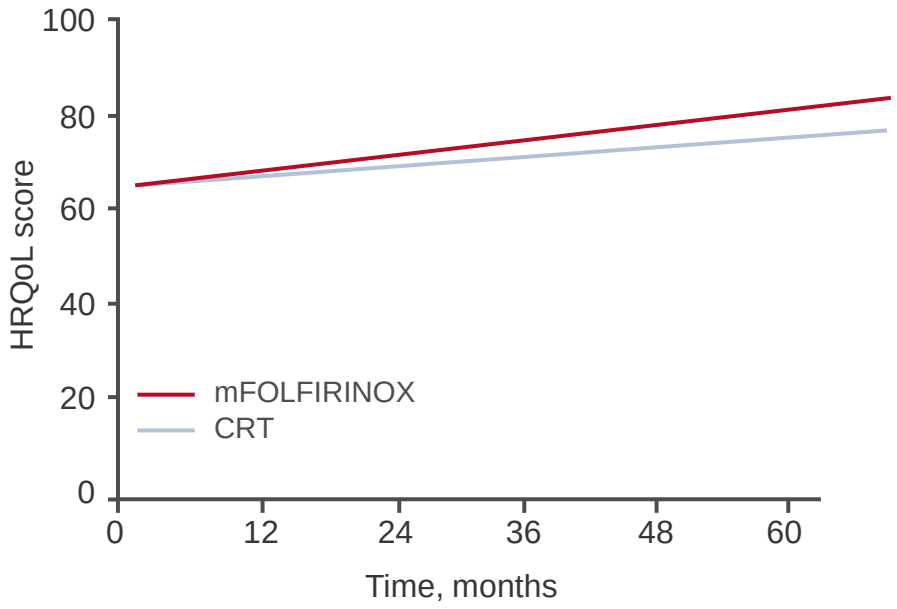
*Grade 1 modified Dworak's tumor regression

Conroy T, et al. J Clin Oncol 2020;38(suppl);abstr 4007

4007: Total neoadjuvant therapy with mFOLFIRINOX versus preoperative chemoradiation in patients with locally advanced rectal cancer: Final results of PRODIGE 23 phase III trial, a UNICANCER GI trial – Conroy T, et al

Key results (cont.)

Global health status/QoL



- Global health status improved over time for both mFOLFIRINOX and CRT arms (p<0.001)
  - Trend in favor of mFOLFIRINOX, p=0.076

Conroy T, et al. J Clin Oncol 2020;38(suppl);abstr 4007

4007: Total neoadjuvant therapy with mFOLFIRINOX versus preoperative chemoradiation in patients with locally advanced rectal cancer: Final results of PRODIGE 23 phase III trial, a UNICANCER GI trial – Conroy T, et al

Key results (cont.)

Safety	mFOLFIRINOX (n=226)
All 6 cycles completed, %	91.6
Grade 3–4 AEs occurring in ≥5%, %	
Neutropenia	16.9
G-CSF use	27.0
Diarrhea	11.1
Fatigue	7.1
Nausea	6.2

Conclusions

- **In patients with stage II/III rectal cancer, neoadjuvant mFOLFIRINOX is well tolerated with a manageable safety profile and significantly increased pCR, 3-year DFS and 3-year MFS**

Conroy T, et al. J Clin Oncol 2020;38(suppl);abstr 4007

4009: Circulating tumor DNA to detect minimal residual disease, response to adjuvant therapy, and identify patients at high risk of recurrence in patients with stage I-III CRC – Tarazona N, et al

Study objective

- To evaluate the use of ctDNA detection and monitoring in patients with CRC during and after adjuvant chemotherapy

Methods

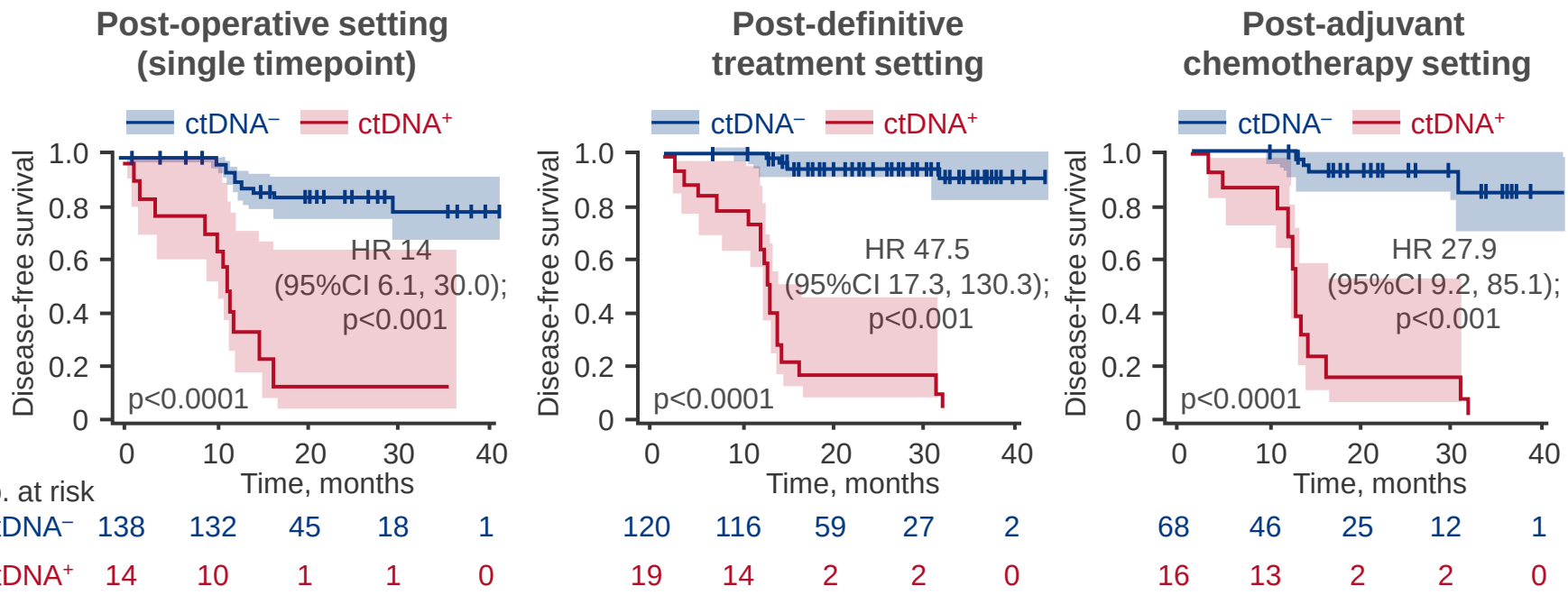
- Plasma samples (n=1052) from patients (n=193) with resected stage I–III CRC were collected
- Whole exome sequencing was used to identify somatic mutations in individual tumors and matched germline DNA
- ctDNA was tracked in plasma samples using multiplex PCR assays designed to 16 tumor-specific nucleotide variants (Signatera™ ctDNA [bespoke mPCR NGS] assay)
- Associations between ctDNA status and clinical outcomes were evaluated using Cox regression for RFS postoperatively and post-adjuvant chemotherapy

Tarazona N, et al. J Clin Oncol 2020;38(suppl);abstr 4009

4009: Circulating tumor DNA to detect minimal residual disease, response to adjuvant therapy, and identify patients at high risk of recurrence in patients with stage I-III CRC – Tarazona N, et al

Key results

- The detection of ctDNA at multiple stages of treatment (post-operative, post-definitive treatment and post-adjuvant chemotherapy) was highly associated with a worse DFS

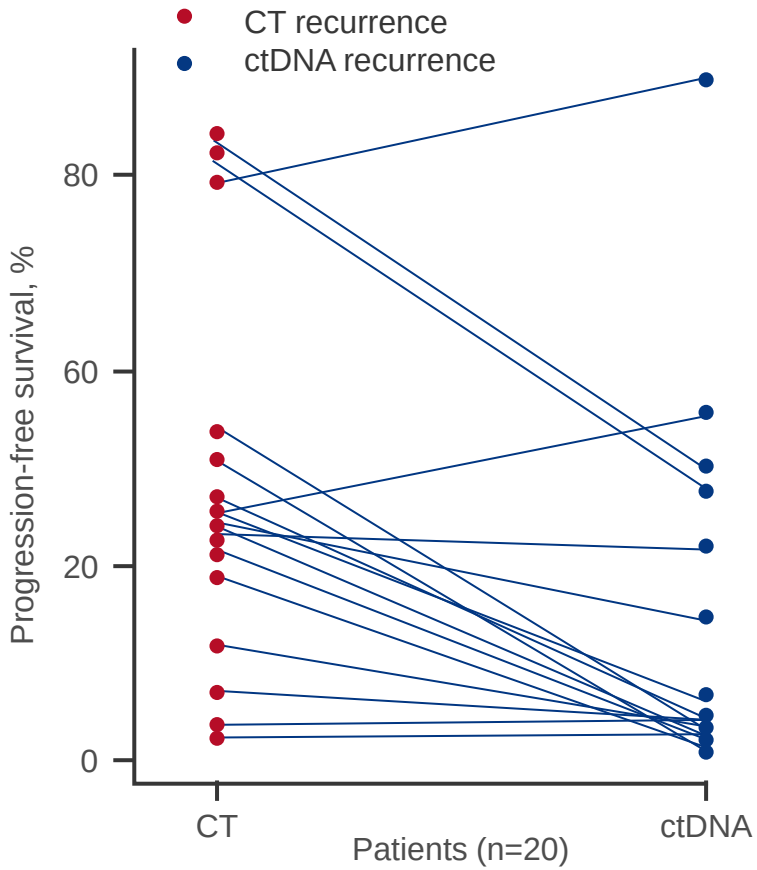


Tarazona N, et al. J Clin Oncol 2020;38(suppl);abstr 4009

4009: Circulating tumor DNA to detect minimal residual disease, response to adjuvant therapy, and identify patients at high risk of recurrence in patients with stage I-III CRC – Tarazona N, et al

Key results (cont.)

- ctDNA detection provides a substantial lead time over radiologic (CT) detection of recurrence (median lead time [IQR] = 8.15 mo [0.56–16.6], p<0.001)
- In a Cox proportional-hazards analysis, which included ctDNA status, age, sex, adjuvant chemotherapy, microsatellite instability, perineural invasion and number of resected lymph nodes, only ctDNA status was predictive of DFS (HR 53.19 [95%CI 18.87, 149.90], p<0.001)



Conclusions

- **SignateraTM ctDNA status is a significant predictor of DFS, and enables detection of relapses substantially earlier than radiologic techniques**

Tarazona N, et al. J Clin Oncol 2020;38(suppl);abstr 4009

4010: A new prognostic and predictive tool to enhance shared decision making in stage III colon cancer – Sobrero AF, et al

Study objective

- To model the potential gain in DFS in different prognostic subgroups of stage III colon cancer after treatment with surgery alone, adjuvant fluoropyrimidine, oxaliplatin-based doublet for 3 months or oxaliplatin-based doublet for 6 months

Methods

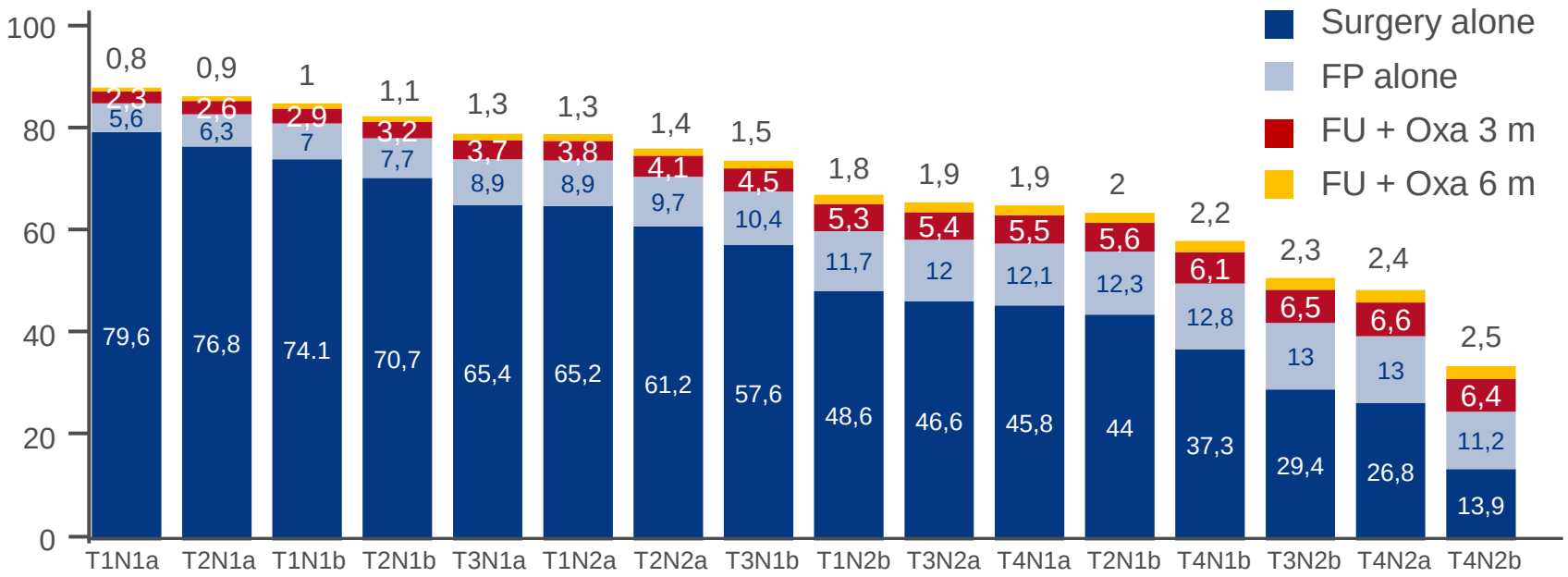
- Outcome data from the IDEA dataset of patients with stage III colon cancer (n=12,834) was used with categorization of patients into 16 sub-stages based on T-N categories
- A meta-regression model to predict the expected 3-year DFS and project 5-year DFS was developed within each T-N subgroup
- The efficacy of each therapy option was evaluated in all sub-stages, working backward with subtraction and using an average HR reported in key trials as a conversion factor

Sobrero AF, et al. J Clin Oncol 2020;38(suppl);abstr 4010

4010: A new prognostic and predictive tool to enhance shared decision making in stage III colon cancer – Sobrero AF, et al

Key results

5-year DFS in patients with stage III colon cancer in different prognostic categories according to treatment



- 5-y DFS varies between 34.0% and 88.3% with maximum adjuvant therapy, according to prognostic subgroup; 5-y DFS for surgery alone varies between 13.9% and 79.6%
- The absolute add-on benefit of maximum adjuvant therapy is between 8.7% and 22.0% according to prognostic subgroup

Sobrero AF, et al. J Clin Oncol 2020;38(suppl);abstr 4010

4010: A new prognostic and predictive tool to enhance shared decision making in stage III colon cancer – Sobrero AF, et al

Conclusions

- **According to this model, the additional benefit of adjuvant therapy after surgery varies greatly according to prognostic subgroup**
- **This model may help physicians to explain the benefits of different treatment approaches to patients and assist in decision making**

Sobrero AF, et al. J Clin Oncol 2020;38(suppl);abstr 4010

4013: FOxTROT: neoadjuvant FOLFOX chemotherapy with or without panitumumab (Pan) for patients (pts) with locally advanced colon cancer (CC) – Seligmann JF, et al

Study objective

- To evaluate the efficacy and safety of neoadjuvant chemotherapy in patients with colon cancer compared with surgery then chemotherapy*

Key patient inclusion criteria
- Operable, non-obstructed colon cancer
- T3-4, N0-2, M0

(n=1053)

R 2:1

Neoadjuvant chemotherapy FOLFOX for 6 weeks followed by surgery then FOLFOX for 18 weeks (n=698)

Surgery then FOLFOX for 24 weeks (n=354)

PRIMARY ENDPOINT

- 2-year DFS

SECONDARY ENDPOINTS

- Resection rate, perioperative safety, downstaging, tumor regression

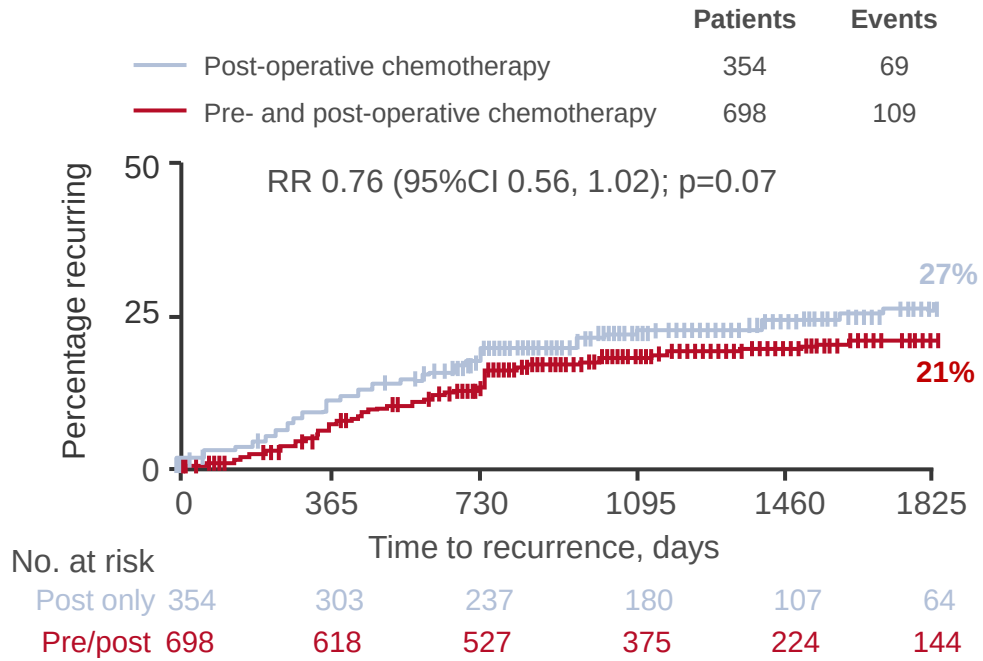
*Note that the results of an optional panitumumab substudy in KRAS-WT (c12-13, 61) patients were not presented

Seligmann JF, et al. J Clin Oncol 2020;38(suppl);abstr 4013

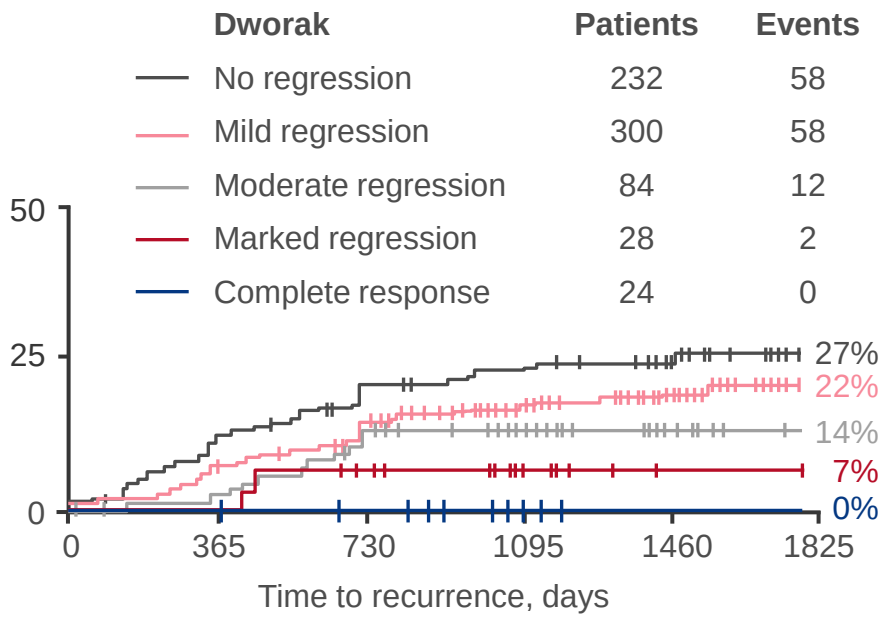
4013: FOxTROT: neoadjuvant FOLFOX chemotherapy with or without panitumumab (Pan) for patients (pts) with locally advanced colon cancer (CC) – Seligmann JF, et al

Key results

Recurrence-free survival



Regression grade in patients in neoadjuvant arm



Seligmann JF, et al. J Clin Oncol 2020;38(suppl);abstr 4013

4013: FOxTROT: neoadjuvant FOLFOX chemotherapy with or without panitumumab (Pan) for patients (pts) with locally advanced colon cancer (CC) – Seligmann JF, et al

Key results (cont.)

- Site of primary tumor and radiologic stage influenced benefit from neoadjuvant chemotherapy

	Site of primary tumor			Radiologic T-stage			
	Left	Right	Sub-total	T3 <5 mm	T3 ≥5 mm	T4	Sub-total
Recurrences, n/N (%)							
Pre/post-op chemo	53/358 (14.8)	56/340 (16.5)	101/698 (15.6)	25/177 (14.1)	50/344 (14.5)	34/177 (19.2)	109/698 (15.6)
Post-op chemo	40/180 (22.2)	29/174 (16.7)	69/354 (19.5)	11/88 (12.5)	30/175 (17.1)	28/91 (30.8)	69/354 (19.5)
OR (95%CI)	**0.58 (0.38, 0.91)**	0.97 (0.62, 1.52)	0.75 (0.55, 1.02)	1.07 (0.53, 2.17)	0.78 (0.49, 1.25)	**0.59 (0.35, 1.00)**	0.75 (0.55, 1.03)

- MMR status also influenced benefit from neoadjuvant chemotherapy
  - Tumor regression after neoadjuvant chemotherapy was slower with dMMR vs. pMMR tumors
  - Time to recurrence was longer with pre-/post-operative chemo vs. post-operative chemo in pMMR tumors (RR 0.72 [95%CI 0.52, 1.00], p=0.05), but not in dMMR tumors (p=NS)

Conclusions

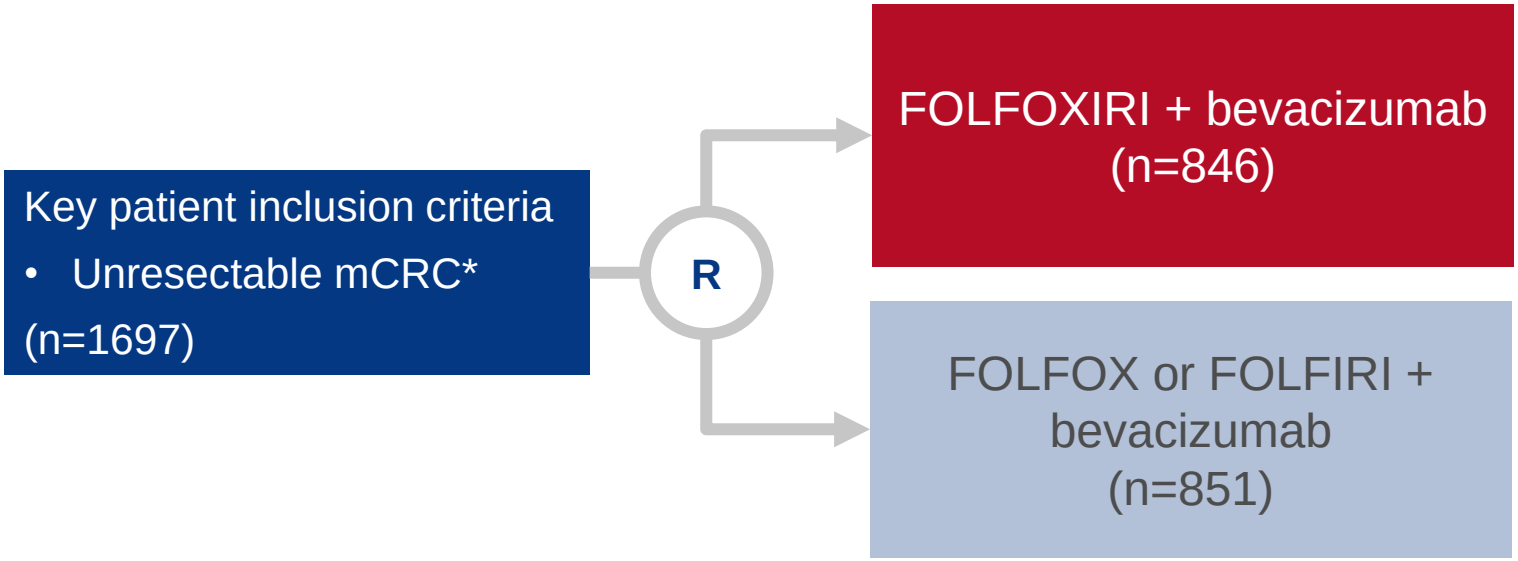
- **Neoadjuvant chemotherapy can be considered for locally advanced colon cancer, although dMMR tumors showed no response to neoadjuvant chemotherapy**
- **Left colon primary tumor location and T4 disease showed particular benefit from neoadjuvant chemotherapy**

Seligmann JF, et al. J Clin Oncol 2020;38(suppl);abstr 4013

4015: FOLFOXIRI/bevacizumab (bev) versus doublets/bev as initial therapy of unresectable metastatic colorectal cancer (mCRC): A meta-analysis of individual patient data (IPD) from five randomized trials – Cremolini C, et al

Study objective

- To evaluate the efficacy and safety of FOLFOXIRI + bevacizumab as 1L treatment for patients with unresectable mCRC



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR, R0 rate, safety

*Data collected from 5 trials: CHARTA, OLIVIA, STEAM, TRIBE and TRIBE2

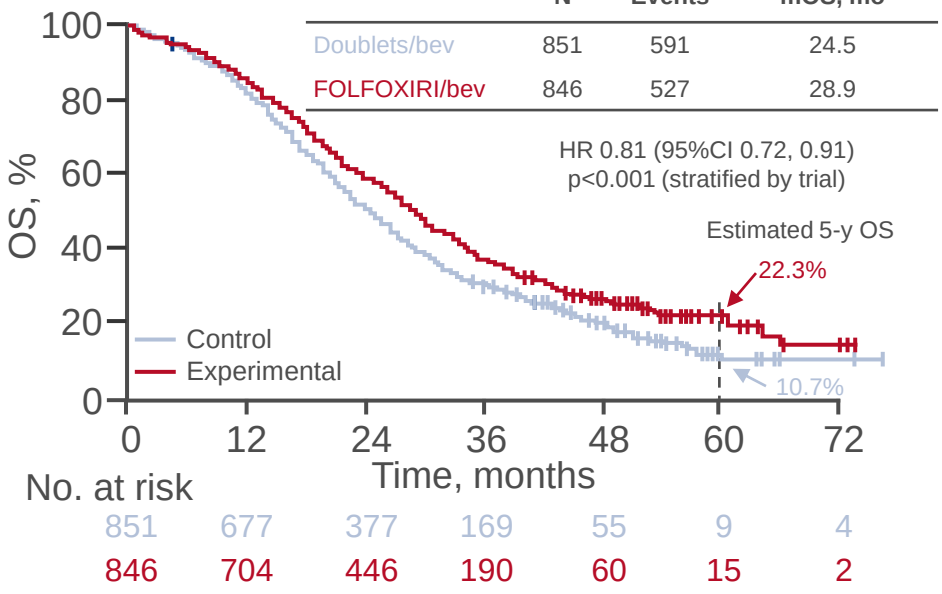
Cremolini C, et al. J Clin Oncol 2020;38(suppl);abstr 4015

4015: FOLFOXIRI/bevacizumab (bev) versus doublets/bev as initial therapy of unresectable metastatic colorectal cancer (mCRC): A meta-analysis of individual patient data (IPD) from five randomized trials – Cremolini C, et al

Key results

OS

	N	Events	mOS, mo
Doublets/bev	851	591	24.5
FOLFOXIRI/bev	846	527	28.9

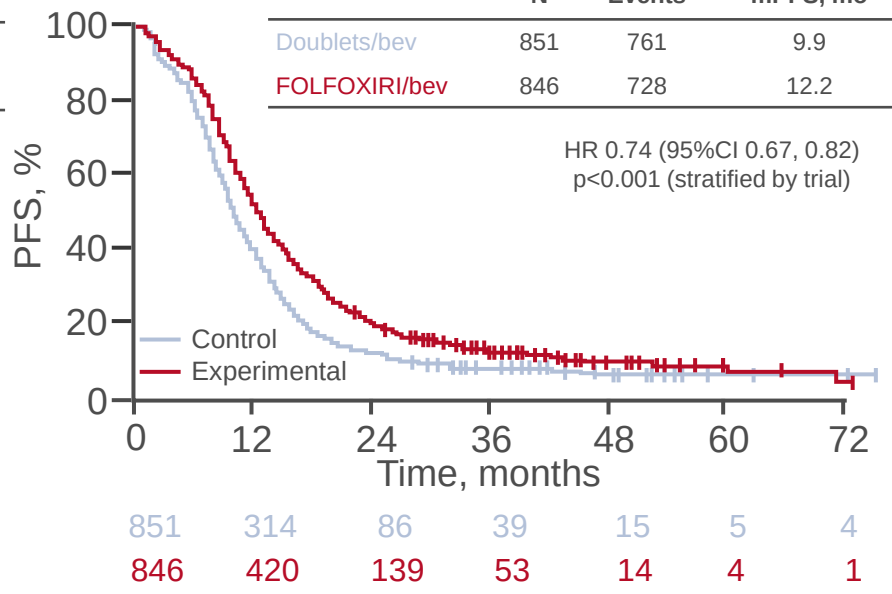


No. at risk

Doublets/bev	851	677	377	169	55	9	4
FOLFOXIRI/bev	846	704	446	190	60	15	2

PFS

	N	Events	mPFS, mo
Doublets/bev	851	761	9.9
FOLFOXIRI/bev	846	728	12.2



Doublets/bev	851	314	86	39	15	5	4
FOLFOXIRI/bev	846	420	139	53	14	4	1

FOLFOXIRI/bev treatment was also associated with:

- Higher ORR (64.5% vs. 53.6%, p<0.001)
- Higher R0 rate (16.4% vs. 11.8%, p=0.007)
- Higher rates of grade 3/4 neutropenia (p<0.001), febrile neutropenia (p=0.019), mucositis (p=0.024), nausea (p=0.016) and diarrhea (p<0.001)

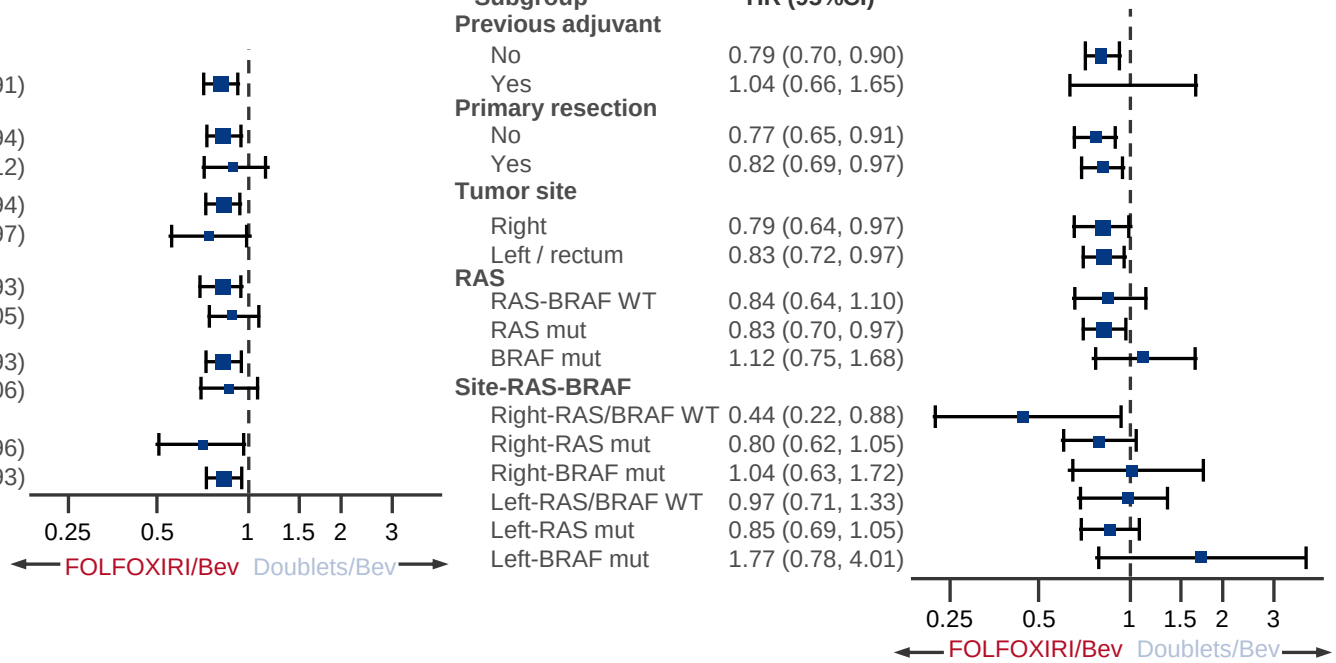
Cremolini C, et al. J Clin Oncol 2020;38(suppl);abstr 4015

4015: FOLFOXIRI/bevacizumab (bev) versus doublets/bev as initial therapy of unresectable metastatic colorectal cancer (mCRC): A meta-analysis of individual patient data (IPD) from five randomized trials – Cremolini C, et al

Key results (cont.)

Subgroup analyses for OS

Subgroup	HR (95%CI)
ITT population	0.81 (0.72, 0.91)
ECOG PS	
0	0.82 (0.71, 0.94)
0–1	0.88 (0.69, 1.12)
Age	
<70 years	0.82 (0.72, 0.94)
>70 years	0.72 (0.54, 0.97)
Gender	
Male	0.80 (0.68, 0.93)
Female	0.87 (0.72, 1.05)
Liver only	
No	0.81 (0.70, 0.93)
Yes	0.85 (0.68, 1.06)
Time to metastases	
Metachronous	0.69 (0.49, 0.96)
Synchronous	0.82 (0.72, 0.93)
Previous adjuvant	
No	0.79 (0.70, 0.90)
Yes	1.04 (0.66, 1.65)
Primary resection	
No	0.77 (0.65, 0.91)
Yes	0.82 (0.69, 0.97)
Tumor site	
Right	0.79 (0.64, 0.97)
Left / rectum	0.83 (0.72, 0.97)
RAS	
RAS-BRAF WT	0.84 (0.64, 1.10)
RAS mut	0.83 (0.70, 0.97)
BRAF mut	1.12 (0.75, 1.68)
Site-RAS-BRAF	
Right-RAS/BRAF WT	0.44 (0.22, 0.88)
Right-RAS mut	0.80 (0.62, 1.05)
Right-BRAF mut	1.04 (0.63, 1.72)
Left-RAS/BRAF WT	0.97 (0.71, 1.33)
Left-RAS mut	0.85 (0.69, 1.05)
Left-BRAF mut	1.77 (0.78, 4.01)



- The benefit of FOLFOXIRI/bevacizumab on OS was consistent across all subgroups analysed

Conclusions

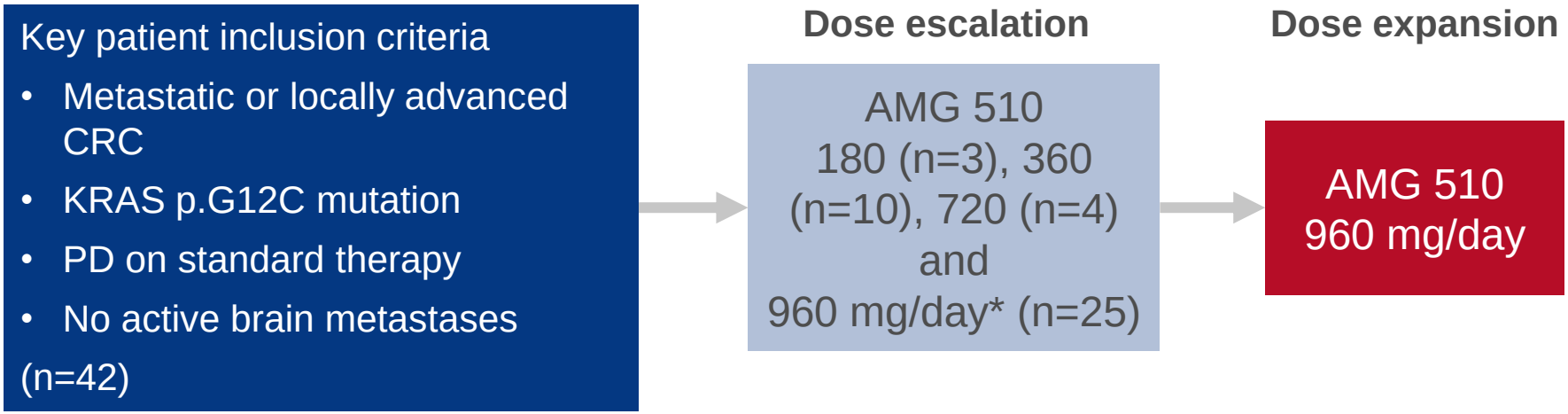
- **In patients with mCRC, 1L FOLFOXIRI/bevacizumab significantly improved survival compared with doublets/bevacizumab**

Cremolini C, et al. J Clin Oncol 2020;38(suppl);abstr 4015

4018: CodeBreak 100: Activity of AMG 510, a novel small molecule inhibitor of KRAS^{G12C}, in patients with advanced colorectal cancer – Fakih M, et al

Study objective

- To evaluate the efficacy and safety of AMG 510 (a KRAS^{G12C} inhibitor) in patients with advanced CRC



PRIMARY ENDPOINTS

- DLTs, safety

SECONDARY ENDPOINTS

- ORR, DoR, DCR, PFS, duration of SD

*21-day cycles until PD

Fakih M, et al. J Clin Oncol 2020;38(suppl);abstr 4018

4018: CodeBreak 100: Activity of AMG 510, a novel small molecule inhibitor of KRAS^{G12C}, in patients with advanced colorectal cancer – Fakih M, et al

Key results

n (%)	All patients (n=42)	
	TEAEs	TRAEs
Any grade	38 (90.5)	20 (47.6)
Grade ≥2	29 (69.0)	9 (21.4)
Grade ≥3	13 (31.0)	2 (4.8)
Grade ≥4	3 (7.1)	0
DLTs	0	0
SAEs	10 (23.8)	0
Fatal AEs	3 (7.1)	0
AEs leading to discontinuation	2 (4.8)	0

TRAEs occurring in >1 patient, n (%)	All patients (n=42)
Diarrhea	8 (19.0)
Fatigue	4 (9.5)
Nausea	2 (4.8)
Blood creatinine phosphokinase increase	2 (4.8)
Anemia	2 (4.8)
Vomiting	2 (4.8)

Fakih M, et al. J Clin Oncol 2020;38(suppl);abstr 4018

4018: CodeBreak 100: Activity of AMG 510, a novel small molecule inhibitor of KRAS^{G12C}, in patients with advanced colorectal cancer – Fakih M, et al

Key results (cont.)

Efficacy outcome	All doses (n=42)	960 mg (n=25)
BOR, n (%)		
Confirmed PR	3 (7.1)	3 (12.0)
SD	29 (69.0)	17 (68.0)
PD	9 (21.4)	4 (16.0)
Not assessed	1 (2.4)	1 (4.0)
ORR, % (95%CI)	7.1 (1.50, 19.48)	12.0 (2.55, 31.22)
DCR, % (95%CI)	76.2 (60.55, 87.95)	80.0 (59.30, 93.17)
DoR for the 3 responders, months	1.4+, 4.2+, 4.3+	1.4+, 4.2+, 4.3+
Duration of SD, months (min, max)	4.2 (2.5+, 11.0)	4.2 (2.6, 5.7+)

Conclusions

- **In heavily pre-treated patients with KRAS p.G12C mutant mCRC, AMG 510 showed activity with 3 (7.1%) patients achieving durable PRs**
- **AMG 510 was well tolerated, with no DLTs observed**

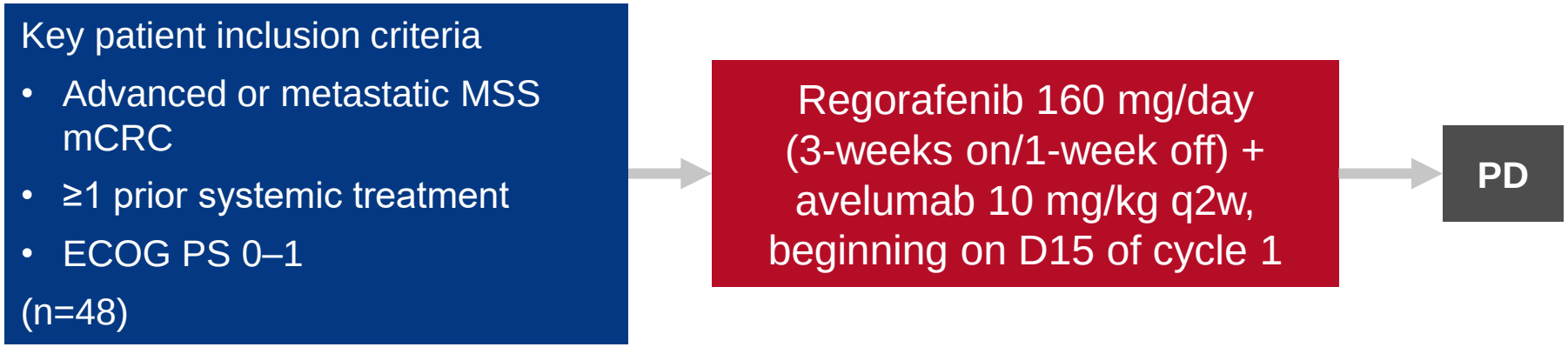
+ denotes ongoing

Fakih M, et al. J Clin Oncol 2020;38(suppl);abstr 4018

4019: REGOMUNE: A phase II study of regorafenib plus avelumab in solid tumors—Results of the non-MSI-H metastatic colorectal cancer (mCRC) cohort – Cousin S, et al

Study objective

- To evaluate the efficacy and safety of regorafenib + avelumab in patients with MSS mCRC



PRIMARY ENDPOINT

- 6-mo ORR (RECIST v1.1)

SECONDARY ENDPOINTS

- PFS, OS, safety

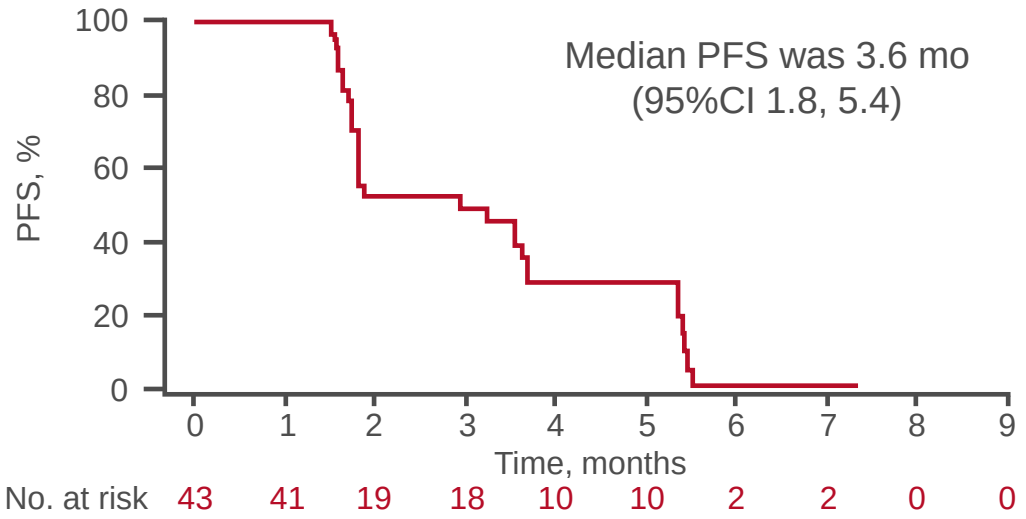
Cousin S, et al. J Clin Oncol 2020;38(suppl);abstr 4019

4019: REGOMUNE: A phase II study of regorafenib plus avelumab in solid tumors—Results of the non-MSI-H metastatic colorectal cancer (mCRC) cohort – Cousin S, et al

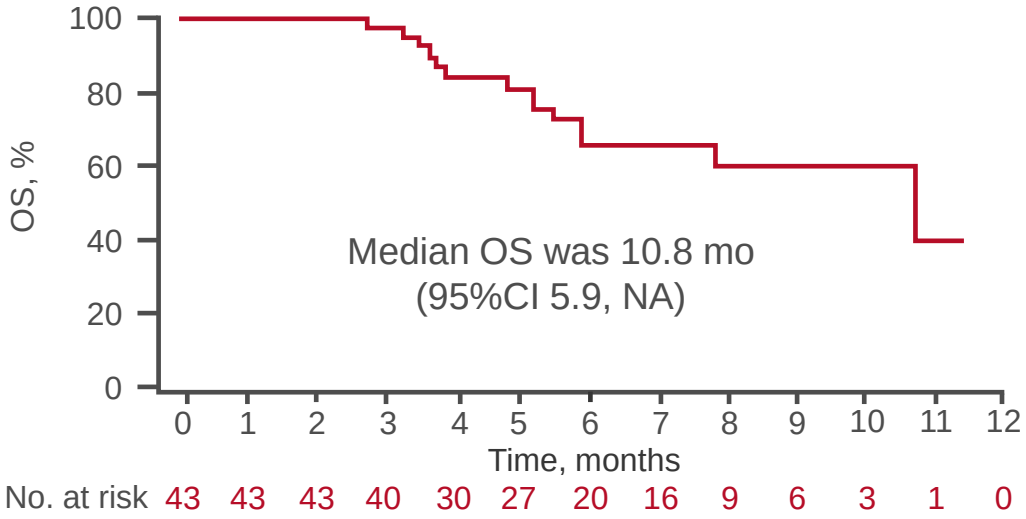
Key results

Response, n (%)	n=43
ORR	0
CR/PR	0
SD	23 (53.5)
PD	17 (39.5)
NA	3 (7)

PFS



OS



Cousin S, et al. J Clin Oncol 2020;38(suppl);abstr 4019

4019: REGOMUNE: A phase II study of regorafenib plus avelumab in solid tumors—Results of the non-MSI-H metastatic colorectal cancer (mCRC) cohort – Cousin S, et al

Key results (cont.)

AEs, n (%)	n=47
Patients with ≥1 AE	47 (100)
Grade 3–4 AEs	41 (87)
TRAEs	47 (100)
SAEs	22 (47)
AEs leading to withdrawal of treatment Withdrawal of regorafenib Withdrawal of avelumab	9 (19) 8 (17) 5 (11)
Grade 5 TRAEs	0

AEs of special interest occurring in ≥5%, n (%)	Grade 1–2	Grade 3–4
Palmoplantar erythrodysesthesia	21 (45)	14 (30)
Hypertension	9 (19)	11 (23)
AST and/or ALT increased	14 (30)	6 (13)
Diarrhea	17 (36)	6 (13)
Maculopapular rash	4 (9)	4 (9)
Fatigue	29 (62)	3 (6)

Conclusions

- **In patients with advanced or metastatic MSS CRC, a combination of regorafenib + avelumab demonstrated activity and was generally well-tolerated**

Cousin S, et al. J Clin Oncol 2020;38(suppl);abstr 4019

4020: Pembrolizumab for previously treated advanced anal squamous cell carcinoma: Pooled results from the KEYNOTE-028 and KEYNOTE-158 studies – Marabelle A, et al

Study objective

- To evaluate the efficacy and safety of pembrolizumab monotherapy in previously treated patients with ASCC

Key patient inclusion criteria

- Metastatic, unresectable ASCC
- Prior failure of, or intolerance to, standard therapy or no standard therapy option
- Tissue sample for PD-L1/biomarker testing
- PD-L1 positive (KEYNOTE-028 only)
- ECOG PS 0–1

(n=137)

<u>KEYNOTE-028</u>
Pembrolizumab
10 mg/kg q2w
(n=25)
or
<u>KEYNOTE-158</u>
Pembrolizumab
200 mg q3w
(n=112)

For 2 years or until PD/ toxicity

PRIMARY ENDPOINT

- ORR (RECIST v1.1)

SECONDARY ENDPOINTS

- DoR, PFS, OS, safety

Marabelle A, et al. J Clin Oncol 2020;38(suppl);abstr 4020

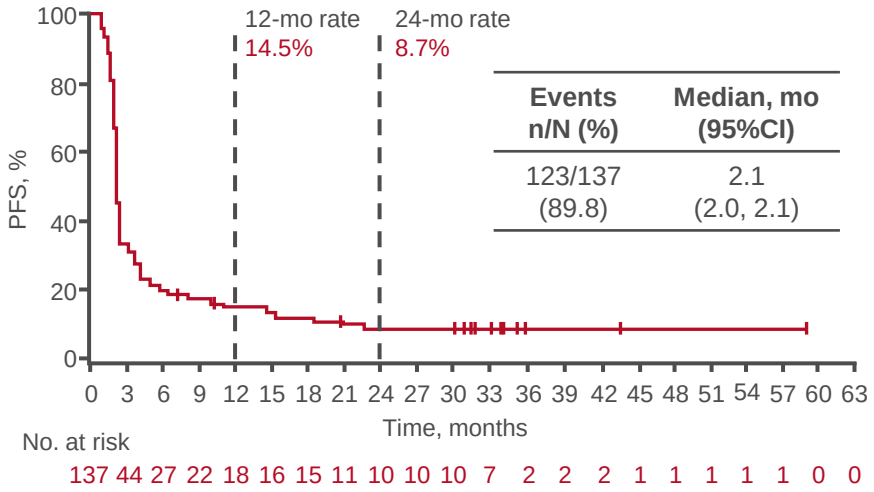
4020: Pembrolizumab for previously treated advanced anal squamous cell carcinoma: Pooled results from the KEYNOTE-028 and KEYNOTE-158 studies – Marabelle A, et al

Key results

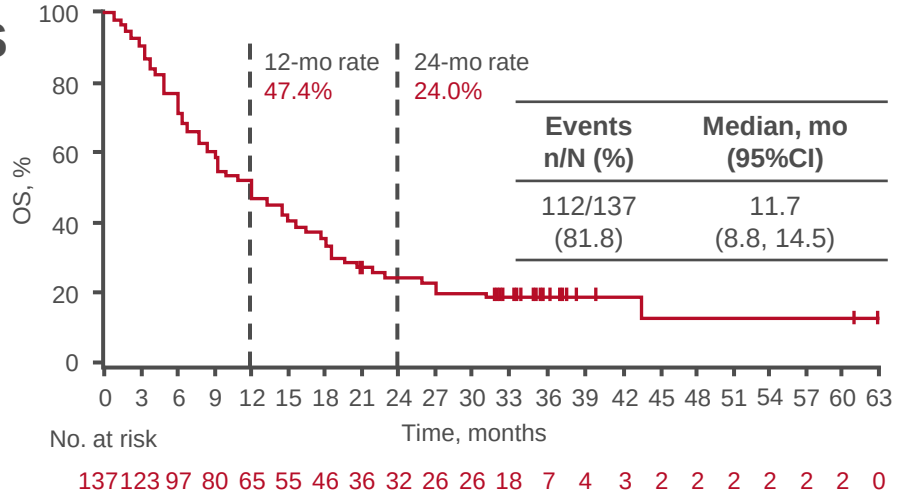
	All patients (n=137*)
ORR, % (95%CI)	
Total	10.9 (6.3, 17.4)
PD-L1^{+}	14.0
PD-L1^{-}	3.3
CR, n (%)	8 (5.8)
PR, n (%)	7 (5.1)
SD, n (%)	27 (19.7)
PD, n (%)	84 (61.3)
DoR	
Median, months (range)	NR (6.0+ to 57.5+)
12 mo, %	84.6
24 mo, %	84.6

*n=100 for PD-L1^{+}; n=30 for PD-L1^{-}

PFS



OS



Marabelle A, et al. J Clin Oncol 2020;38(suppl);abstr 4020

4020: Pembrolizumab for previously treated advanced anal squamous cell carcinoma: Pooled results from the KEYNOTE-028 and KEYNOTE-158 studies – Marabelle A, et al

Key results (cont.)

	All patients (n=137)	
TRAEs, n (%)	**Any grade**	**Grade 3–4**
Any	85 (62.0)	24 (17.5)
Leading to discontinuation	6 (4.4)	5 (3.6)
Leading to death	0	0
Immune-related AEs or infusion reaction, n (%)	**Any grade**	**Grade 3–5**
Any immune-related or infusion reaction	33 (24.1)	7 (5.1)
Immune-mediated	31 (22.6)	7 (5.1)
Infusion reactions	3 (2.2)	0

Conclusions

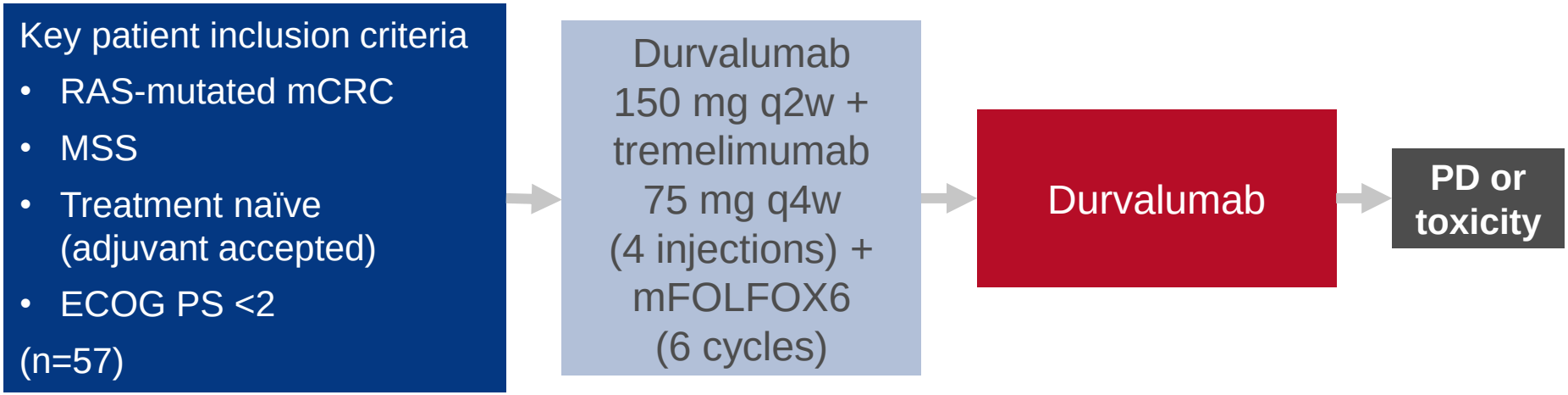
- **In previously treated patients with ASCC, pembrolizumab showed activity, with durable responses and promising OS data**
- **The safety profile was consistent with previous reports**

Marabelle A, et al. J Clin Oncol 2020;38(suppl);abstr 4020

3006: Durvalumab and tremelimumab in combination with FOLFOX in patients with RAS-mutated, microsatellite-stable, previously untreated metastatic colorectal cancer (MCRC): Results of the first intermediate analysis of the phase Ib/II MEDETREME trial – Ghiringhelli F, et al

Study objective

- To evaluate the efficacy and safety of durvalumab + tremelimumab + FOLFOX in treatment naïve patients with RAS-mutated, MSS, mCRC*



PRIMARY ENDPOINT

- 6-month PFS

SECONDARY ENDPOINTS

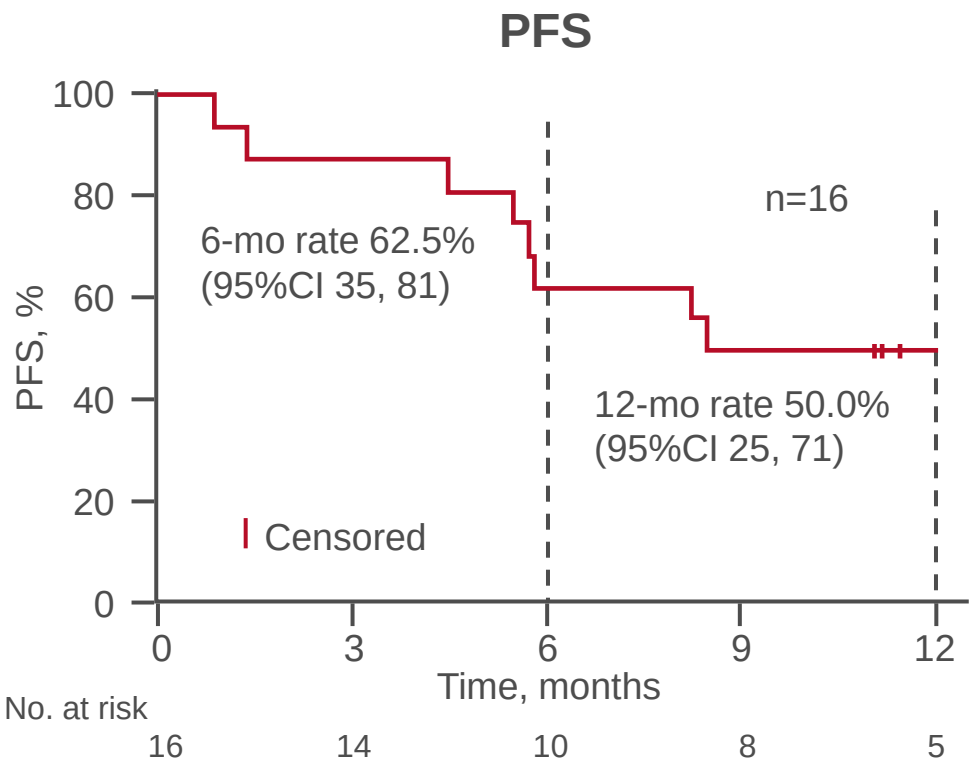
- Response rate, safety

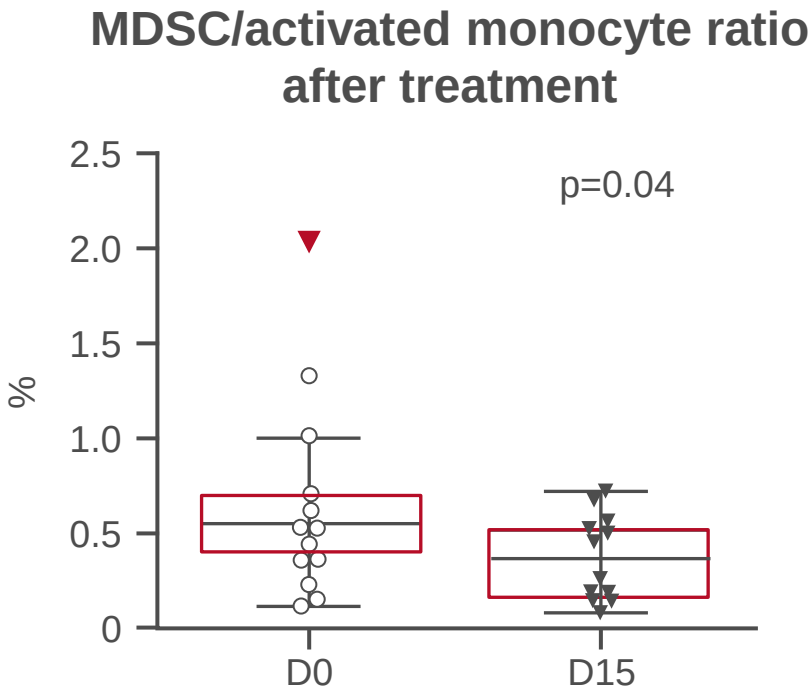
*Intermediate analysis of the first 16 patients who had 1 year of follow-up

Ghiringhelli F, et al. J Clin Oncol 2020;38(suppl);abstr 3006

3006: Durvalumab and tremelimumab in combination with FOLFOX in patients with RAS-mutated, microsatellite-stable, previously untreated metastatic colorectal cancer (MCRC): Results of the first intermediate analysis of the phase Ib/II MEDETREME trial – Ghiringhelli F, et al

Key results





At 12 months

- DRR (CR + PR + SD): 87.5%
- ORR (CR + PR): 62.5%
- CR: 25%

- Responders had fewer immunosuppressive MDS cells at baseline
- Treatment induced a decrease in MDSC and an increase in activated monocytes

Ghiringhelli F, et al. J Clin Oncol 2020;38(suppl);abstr 3006

3006: Durvalumab and tremelimumab in combination with FOLFOX in patients with RAS-mutated, microsatellite-stable, previously untreated metastatic colorectal cancer (MCRC): Results of the first intermediate analysis of the phase Ib/II MEDETREME trial – Ghiringhelli F, et al

Key results (cont.)

Chemotherapy-related AEs, n (%)	n=16	
	Any	Grade 3–5
All	16 (100)	11 (68.75)
Led to death	0	0
Incidence ≥5%		
Neuropathy	14 (87.50)	0
Asthenia	13 (81.25)	3 (18.75)
Nausea/vomiting	10 (62.50)	0
Neutropenia	10 (62.50)	8 (50.00)
Rash	7 (43.75)	0
Blood pressure	4 (25.00)	4 (25)
Cholestasis	3 (18.75)	3 (18.75)
Anemia	3 (18.75)	0
Thrombocytopenia	3 (18.75)	0
Headache	2 (12.50)	0

Immune-mediated AEs and infusion reactions, n (%)	n=16	
	Any	Grade 3–5
All	12 (75.00)	6 (37.50)
Led to death	0	0
Incidence ≥5%		
Dysthyroidism	14 (87.50)	1 (6.25)
Diarrhea	9 (56.25)	2 (12.50)
Infusion reactions	3 (18.75)	0
Pruritus	2 (12.50)	0
Hepatitis	3 (18.75)	1 (6.25)
Hypophysitis	1 (6.25)	1 (6.25)
Pancreatitis	1 (6.25)	0
Type 1 diabetes	1 (6.25)	1 (6.25)

Conclusions

- **In previously untreated patients with RAS-mutated, MSS mCRC, FOLFOX + durvalumab + tremelimumab showed promising efficacy and induced a decrease in myeloid immunosuppressive cells, with a similar toxicity profile to FOLFOX or immunotherapy**

Ghiringhelli F, et al. J Clin Oncol 2020;38(suppl);abstr 3006

7009: Survival outcomes among older adults (OA) receiving second-line therapy for metastatic CRC (mCRC): 5,289 patients (pts) from the ARCAD Clinical Trials Program – McCleary NJ, et al

Study objective

- To evaluate survival outcomes of 2L therapy in elderly (>70 years) patients with mCRC

Methods

- Available progression data from 10 ARCAD 1L trials were collected to assess whether there were any associations between clinical characteristics and time to initial progression as well as 2L therapy
- Comparisons were made between those aged >70 years and ≤70 years
- Cox regression was used with adjustments for age, sex, ECOG PS, number of metastatic sites, presence of metastasis in lung, liver or peritoneum

McCleary NJ, et al. J Clin Oncol 2020;38(suppl);abstr 7009

7009: Survival outcomes among older adults (OA) receiving second-line therapy for metastatic CRC (mCRC): 5,289 patients (pts) from the ARCAD Clinical Trials Program – McCleary NJ, et al

Key results

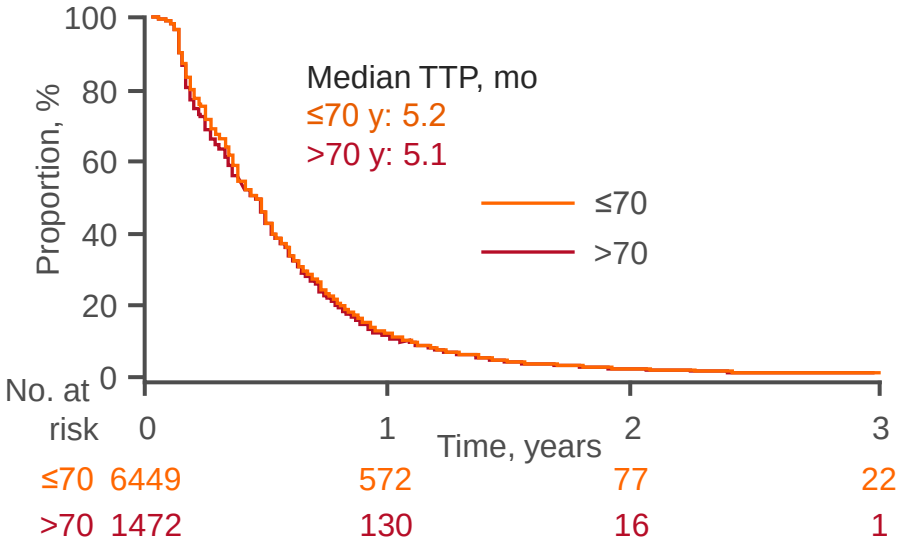
Characteristic			1L therapy Time to initial progression (n=5289; 5121 evaluable)			2L therapy Time to progression (n=7921; 7408 evaluable)		2L therapy OS (n=8280; 7764 evaluable)	
			OR (95%CI)	p-value		HR (95%CI)	p-value	HR (95%CI)	p-value
Enrollment age, mean (SD)		59.8 (10.7)	1.11 (1.02, 1.21)	0.012	Age, per 10 y	0.97 (0.94, 0.99)	0.005	0.99 (0.97, 1.02)	0.618
Sex, n (%)	Male	2880 (87.2)	1.15 (0.96, 1.38) (♀ referent)	0.121		0.98 (0.94, 1.04)	0.54	0.97 (0.92, 1.02)	0.204
ECOG PS, n (%)	0	2566 (90.4)	Referent						
	1	1815 (85.8)	1.55 (1.30, 1.84)			1.22 (1.16, 1.28)		1.51 (1.43, 1.59)	
	>1	115 (69.7)	4.07 (2.85, 5.82)	<0.0001		1.59 (1.38, 1.83)	<0.001	3.54 (3.13, 4.02)	<0.0001
Metastasis	Lung	1562 (87.4)	1.03 (0.86, 1.23)	0.761		1.10 (1.04, 1.18)	0.003	1.08 (1.01, 1.16)	0.02
	Liver	3421 (88.0)	0.90 (0.75, 1.09)	0.291		1.36 (1.28, 1.45)	<0.001	1.62 (1.52, 1.74)	<0.001
	Peritoneum	407 (88.1)	0.92 (0.68, 1.24)	0.571		1.27 (1.03, 1.57)	0.025	1.42 (1.14, 1.75)	0.001

McCleary NJ, et al. J Clin Oncol 2020;38(suppl);abstr 7009

7009: Survival outcomes among older adults (OA) receiving second-line therapy for metastatic CRC (mCRC): 5,289 patients (pts) from the ARCAD Clinical Trials Program – McCleary NJ, et al

Key results (cont.)

TTP



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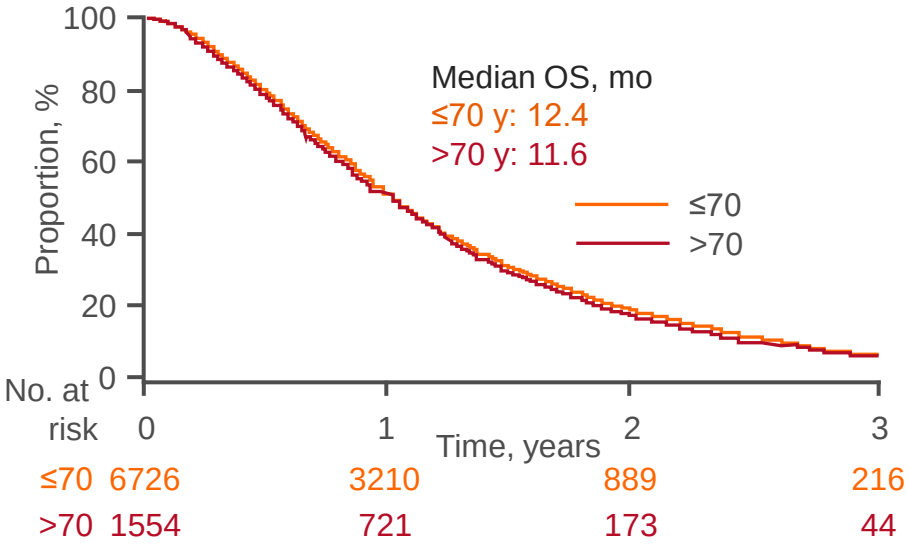

Conclusions

- **In patients with mCRC, the likelihood of receiving 2L therapy is lower in older patients (>70 years) and those with ECOG PS >0 compared with younger patients (≤70 years)**
- **Older patients (>70 years) experienced similar TTP and OS in 2L setting as younger patients (≤70 years)**

McCleary NJ, et al. J Clin Oncol 2020;38(suppl);abstr 7009

GASTROINTESTINAL CANCERS

3504: Phase I monotherapy dose escalation of RGX-202, a first-in-class oral inhibitor of the SLC6a8/CKB pathway, in patients with advanced gastrointestinal (GI) solid tumors – Bendell JC, et al

Study objective

- To evaluate the efficacy and safety of RGX-202 (an SLC6a8/CKB inhibitor) in patients with advanced GI solid tumors

Key patient inclusion criteria

- Metastatic or locally advanced and unresectable GI tumors of adenocarcinoma or poorly differentiated histology
- PD following standard systemic therapy
- ECOG PS ≤1

(n=17)

Dose escalation (3+3)

RGX-202
600 mg (n=3; colorectal [2], pancreatic [1]), 1200 mg (n=4; colorectal [4]), 2400 mg (n=5; colorectal [4], pancreatic [1]), 3600 mg (n=5; colorectal [3], pancreatic [2]) PO BID

Dose expansion*

RGX-202 ± FOLFIRI

PRIMARY ENDPOINTS

- MTD (or maximum tested dose without DLTs), antitumor activity

SECONDARY ENDPOINTS

- PK, PD, safety

*Ongoing

Bendell JC, et al. J Clin Oncol 2020;38(suppl);abstr 3504

3504: Phase I monotherapy dose escalation of RGX-202, a first-in-class oral inhibitor of the SLC6a8/CKB pathway, in patients with advanced gastrointestinal (GI) solid tumors – Bendell JC, et al

Key results

AEs, n (%)	All (n=17)		600 mg BID (n=3)		1200 mg BID (n=4)		2400 mg BID (n=5)		3600 mg BID (n=5)	
	Gr ≤2	Gr 3	Gr ≤2	Gr 3	Gr ≤2	Gr 3	Gr ≤2	Gr 3	Gr ≤2	Gr 3
Nausea	7 (41)	1 (6)				1 (25)	2 (40)		5 (100)	
Vomiting	6 (35)	1 (6)			1 (25)	1 (25)	1 (20)		4 (80)	
Diarrhea	5 (29)		1 (33)		1 (25)		1 (20)		2 (40)	
Decreased appetite	4 (23)				1 (25)		1 (20)		2 (40)	
Fatigue	4 (23)				1 (25)				3 (60)	
Blood alkaline phosphate increased	2 (12)								2 (40)	
Muscle spasms	2 (12)						1 (20)		1 (20)	
Weight decreased	2 (12)						1 (20)		1 (20)	
Lymphocyte count decreased		1 (6)								1 (20)

- No DLTs were observed
- Most AEs were Grade 1 (69.8%) and there were no Grade 4 or 5 AEs

Bendell JC, et al. J Clin Oncol 2020;38(suppl);abstr 3504

3504: Phase I monotherapy dose escalation of RGX-202, a first-in-class oral inhibitor of the SLC6a8/CKB pathway, in patients with advanced gastrointestinal (GI) solid tumors – Bendell JC, et al

Key results (cont.)

Efficacy findings	
Total evaluable patients	n=10 all colorectal; KRAS mutant (n=5), KRAS WT/unknown (n=5)
BOR by RECIST 1.1	
PR	1 (10%); $KRAS^{G12V}$
SD	3 (30%); $KRAS^{G13D}$ (n=2), KRAS WT (n=1)
PD	6 (60%)
ORR	10%; KRAS mutant 20%, KRAS WT/unknown 0%
DCR	40%; KRAS mutant 60%, KRAS WT/unknown 20%

Conclusions

- **In patients with KRAS-mutant CRC, RGX-202 monotherapy was well tolerated, with an efficacy signal detected**
- **A combination dose escalation study with FOLFIRI is ongoing**

Bendell JC, et al. J Clin Oncol 2020;38(suppl);abstr 3504