GI SLIDE DECK 2020

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esdo european society of digestive oncology

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Letter from ESDO

DEAR COLLEAGUES

It is our pleasure to present this ESDO slide set which has been designed to highlight and summarize key findings in digestive cancers from the major congresses in 2020. This slide set specifically focuses on the **2020 Gastrointestinal Cancers Symposium** and is available in English, French, Chinese and Japanese.

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

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

Yours sincerely,

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

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

(ESDO Governing Board)

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european society of digestive oncology

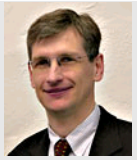
ESDO Medical Oncology Slide Deck
Editors 2020

COLORECTAL CANCERS



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

PANCREATIC CANCER AND HEPATOBILIARY TUMOURS

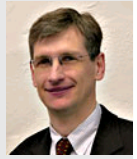



Prof Thomas Seufferlein	Clinic of Internal Medicine I, University of Ulm, Ulm, Germany
Prof Jean-Luc Van Laethem	Digestive Oncology, Erasme University Hospital, Brussels, Belgium

GASTRO-OESOPHAGEAL AND NEUROENDOCRINE TUMOURS


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

BIOMARKERS

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

esdo

Glossary

1L	first-line
2L	second-line
5FU	5-fluouracil
AC	adenocarcinoma
AE	adverse event
AFP	alpha-fetoprotein
ALT	alanine aminotransferase
ASCC	anal squamous cell carcinoma
AST	aspartate aminotransferase
Atezo	atezolizumab
AUC	area under the curve
Bev	bevacizumab
BICR	blinded-independent central review
bid	twice daily
BOR	best overall response
BSC	best supportive care
CA19-9	carbohydrate antigen 19-9
CAPTEM	capecitabine + temozolomide
CBR	clinical benefit rate
Chemo	chemotherapy
CI	confidence interval
CNS	central nervous system
CR	complete response
CRC	colorectal cancer
CTCAE	Common Terminology Criteria for Adverse Events
D	day
DCR	disease control rate
DFS	disease-free survival
dMMR	deficient mismatch repair
DoR	duration of response
ECOG	Eastern Cooperative Oncology Group
EGFR	epidermal growth factor receptor
EIPL	extensive intraoperative peritoneal lavage
EORTC QLQ	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire
EQ-5D-5l	EuroQol five dimensions questionnaire
ESMO	European Society of Medical Oncology
FACT-C	Functional Assessment of Cancer Therapy – Colon Cancer
FOLFIRI	folinic acid + 5-fluouracil + irinotecan
(m)FOLFOX	(modified) leucovorin + 5-fluorouracil + oxaliplatin
FOLFOXIRI	5-fluouracil + leucovorin + oxaliplatin + irinotecan
GEJ	gastro-esophageal junction
GI	gastrointestinal
Gy	Gray
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HER2	human epidermal growth factor receptor 2
HR	hazard ratio
ITT	intent-to-treat
iv	intravenous
mCRC	metastatic colorectal cancer
mo	months
MSI-H	high microsatellite instability
NA	not available
NE	not evaluable/estimable
NET	neuroendocrine tumor
NR	not reached
OMD	oligometastatic disease
ORR	overall/objective response rate
OR	odds ratio
(m)OS	(median) overall survival
PD	progressive disease
PDAC	pancreatic ductal adenocarcinoma
PD-L1	programmed death-ligand 1
PEGPH20	pegvorhyaluronidase alfa
(m)PFS	(median) progression-free survival
PGIC	Patient Global Impression of Change
po	orally
PR	partial response
PRO	patient-reported outcome
PRRT	peptide receptor radionuclide therapy
PS	performance status
PTR	primary tumor resection
q(2/3/4/6)w	every (2/3/4/6) week(s)
QoL	quality of life
R	randomized
R0	resection 0
RECIST	Response Evaluation Criteria In Solid Tumors
RP2D	recommended phase 2 dose
RR	response rate
SCC	squamous cell carcinoma
SD	stable disease
TB	tumor burden
TEAE	treatment-emergent adverse event
TRAE	treatment-related adverse event
TTD	time to deterioration
TTP	time to progression
TTR	time to response
WHO	World Health Organization

Contents

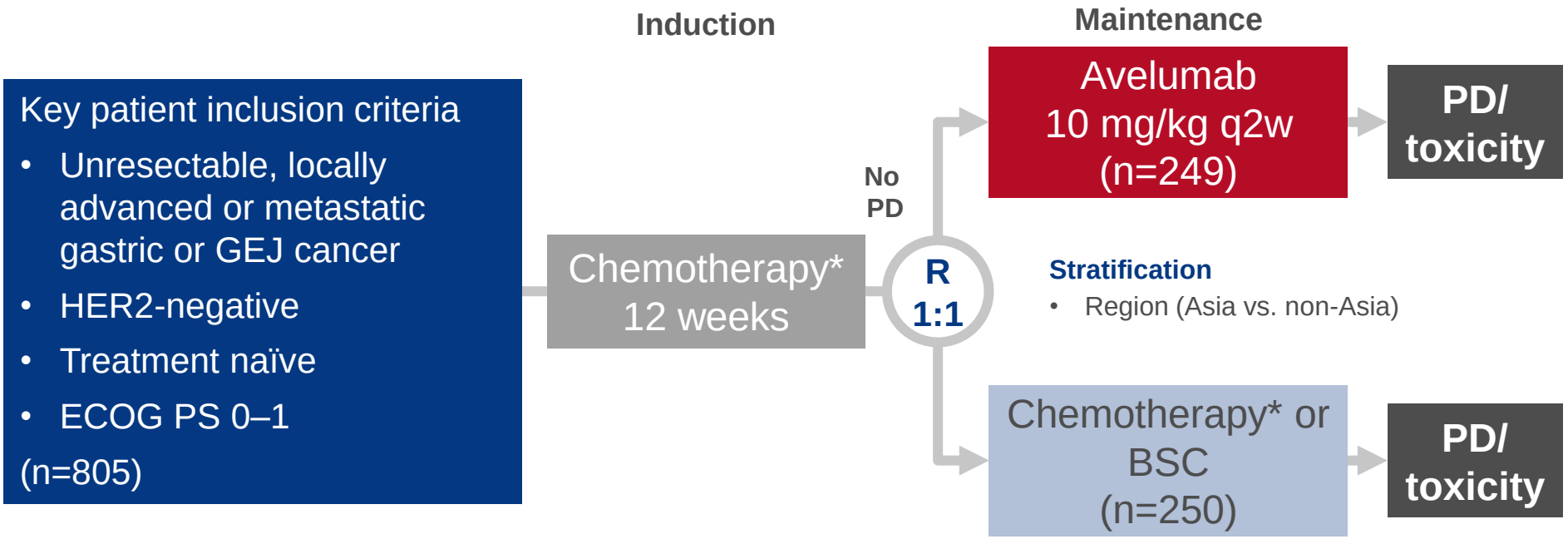
Note: To jump to a section, right click on the number and ‘Open Hyperlink’

CANCERS OF THE OESOPHAGUS AND STOMACH

278: Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2– advanced gastric or gastroesophageal junction cancer (GC/GEJC) – Moehler MH, et al

Study objective

- To evaluate the efficacy and safety of maintenance avelumab following 1L chemotherapy in patients with HER2-negative advanced gastric or GEJ cancer



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, BOR, QoL, safety

*Oxaliplatin 85 mg/m^2 D1 with 5FU 2600 mg/m^2 D1 and leucovorin 400 mg/m^2 D1 or capecitabine 1000 mg/m^2 (2-weeks on/1-week off)

Moehler MH, et al. J Clin Oncol 2020;38(suppl):abstr 278

278: Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2– advanced gastric or gastroesophageal junction cancer (GC/GEJC) – Moehler MH, et al

Key results

Patient characteristics		Avelumab (n=249)	Chemotherapy (n=250)
Median age, years		62.0	61.0
Sex, n (%)	Male Female	164 (65.9) 85 (34.1)	167 (66.8) 83 (33.2)
Region, n (%)	North America Europe Asia Rest of the world	34 (13.7) 110 (44.2) 57 (22.9) 48 (19.3)	23 (9.2) 123 (49.2) 57 (22.8) 47 (18.8)
ECOG PS, n (%)	0 1	102 (41.0) 147 (59.0)	108 (43.2) 142 (56.8)
Site of primary tumor, n (%)	Stomach GEJ	174 (69.9) 75 (30.1)	181 (72.4) 69 (27.6)
Prior gastrectomy, n (%)		69 (27.7)	66 (26.4)
No. of metastatic sites, n (%)	0 1 2 ≥3	31 (12.5) 43 (17.3) 59 (23.7) 116 (46.6)	29 (11.6) 55 (22.0) 57 (22.8) 109 (43.6)

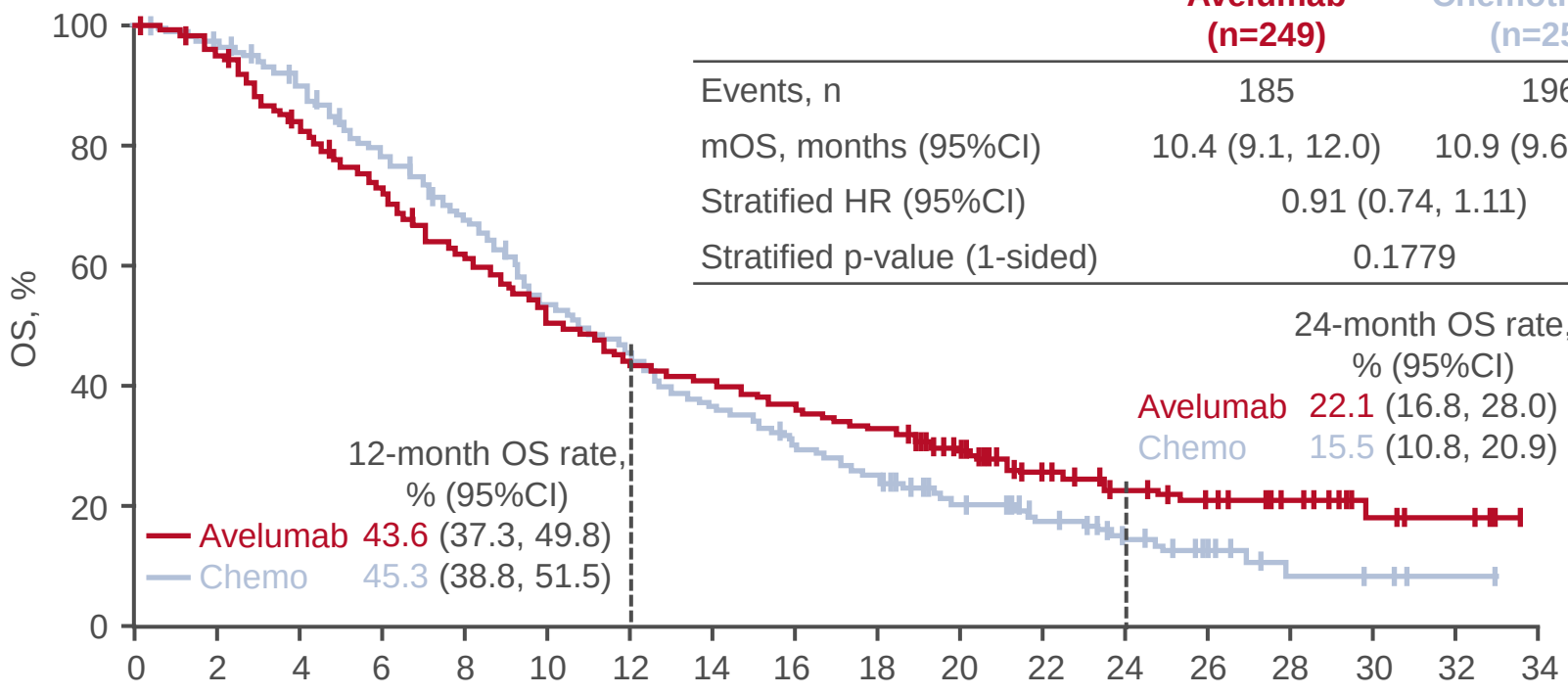
Moehler MH, et al. J Clin Oncol 2020;38(suppl):abstr 278

278: Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2– advanced gastric or gastroesophageal junction cancer (GC/GEJC) – Moehler MH, et al

Key results (cont.)

OS from randomization* (ITT)

	Avelumab (n=249)	Chemotherapy (n=250)
Events, n	185	196
mOS, months (95%CI)	10.4 (9.1, 12.0)	10.9 (9.6, 12.4)
Stratified HR (95%CI)	0.91 (0.74, 1.11)	
Stratified p-value (1-sided)	0.1779	



No. at risk

Avelumab	249	235	201	176	147	123	104	96	87	77	60	41	29	20	14	6	4	0
Chemo	250	237	215	187	158	123	104	85	70	58	39	28	19	12	5	3	1	0

*After 12 weeks of induction chemotherapy

Moehler MH, et al. J Clin Oncol 2020;38(suppl):abstr 278

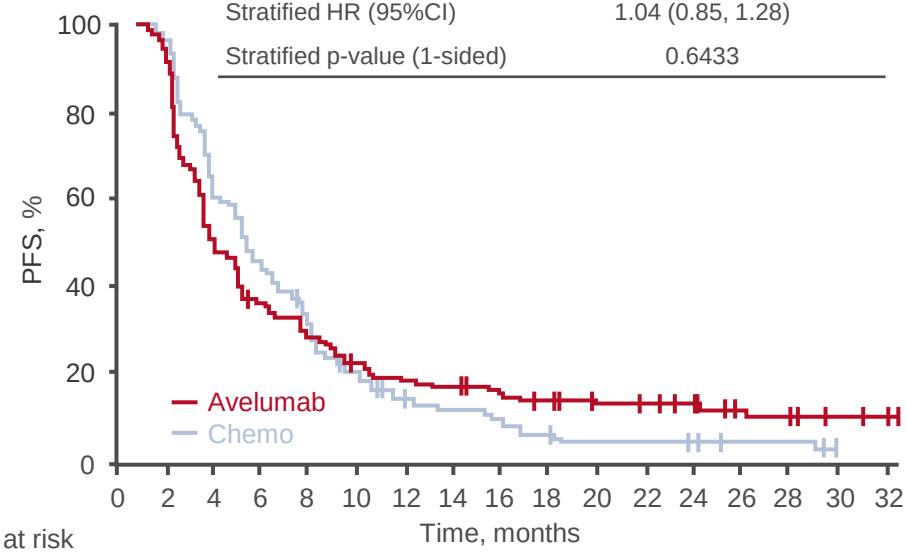
278: Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2– advanced gastric or gastroesophageal junction cancer (GC/GEJC) – Moehler MH, et al

Key results (cont.)

PFS from randomization* (investigator assessed)

All randomized patients

	Avelumab (n=249)	Chemotherapy (n=250)
Events, n	189	188
mPFS, months (95%CI)	3.2 (2.8, 4.1)	4.4 (4.0, 5.5)
Stratified HR (95%CI)	1.04 (0.85, 1.28)	
Stratified p-value (1-sided)	0.6433	

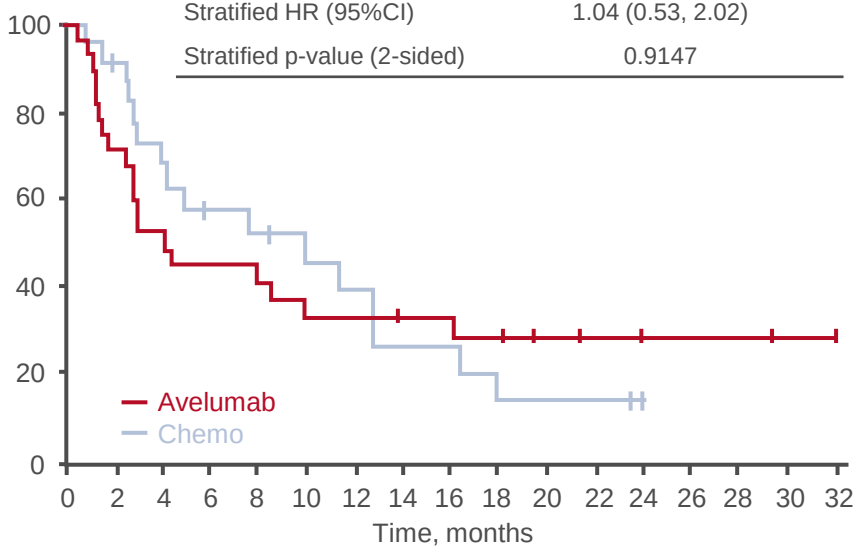


No. at risk

Avelumab	249	153	98	64	51	35	33	29	24	18	15	14	9	6	4	3	1
Chemo	250	181	118	71	42	27	19	17	12	6	6	6	4	3	3	0	0

PD-L1+ population (≥1% of tumor cells)*

	Avelumab (n=30)	Chemotherapy (n=24)
Events, n	19	16
mPFS, months (95%CI)	4.1 (1.6, 16.0)	9.7 (2.8, 12.5)
Stratified HR (95%CI)	1.04 (0.53, 2.02)	
Stratified p-value (2-sided)	0.9147	



Avelumab	30	19	14	11	10	8	8	7	6	5	4	3	2	2	2	1	0
Chemo	24	19	14	10	9	7	6	4	4	2	2	2	0	0	0	0	0

*After 12 weeks of induction chemotherapy

Moehler MH, et al. J Clin Oncol 2020;38(suppl):abstr 278

278: Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2– advanced gastric or gastroesophageal junction cancer (GC/GEJC) – Moehler MH, et al

Key results (cont.)

OS in PD-L1+ population	Avelumab	Chemotherapy
73-10 pharmDx assay		
Events, n/N	19/30	15/24
mOS, months (95%CI)	16.2 (8.2, NR)	17.7 (9.6, NR)
HR (95%CI); p-value	1.13 (0.57, 2.23); 0.6352	
22C3 pharmDx assay		
Events, n/N	55/74	55/63
mOS, months (95%CI)	14.9 (8.7, 17.3)	11.6 (8.4, 12.6)
HR (95%CI), unstratified	0.72 (0.49, 1.05)	

	Avelumab (n=249)	Chemotherapy (n=250)
ORR, % (95%CI)	13.3 (9.3, 18.1)	14.4 (10.3, 19.4)
OR (95%CI); p-value	0.91 (0.55, 1.51); 0.6443	
DCR, % (95%CI)	54.2 (47.8, 60.5)	65.6 (59.4, 71.5)

Moehler MH, et al. J Clin Oncol 2020;38(suppl):abstr 278

278: Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2– advanced gastric or gastroesophageal junction cancer (GC/GEJC) – Moehler MH, et al

Key results (cont.)

AEs, n (%)	Avelumab (n=243)	Chemotherapy (n=238)
Any AE Grade ≥3	223 (91.8) 132 (54.3)	214 (89.9) 128 (53.8)
Any TRAE Grade ≥3	149 (61.3) 31 (12.8)	184 (77.3) 78 (32.8)
TRAE leading to discontinuation	25 (10.3)	65 (27.3)
Serious TRAE	19 (7.8)	23 (9.7)
TRAE leading to death	0 (0)	1 (0.4)
Any infusion-related reaction AE	48 (19.8)	17 (7.1)

Conclusions

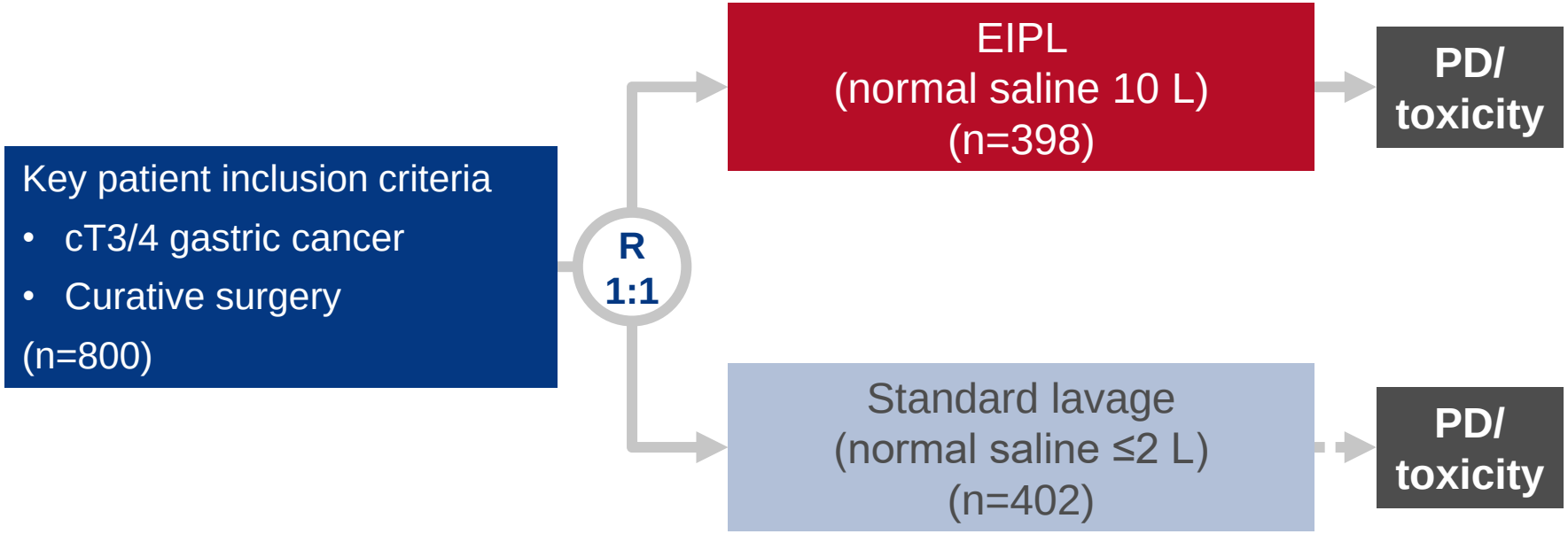
- **In patients with advanced gastric or GEJ cancer, maintenance avelumab demonstrated a favorable safety profile, but did not provide any survival benefit compared with chemotherapy or BSC**

Moehler MH, et al. J Clin Oncol 2020;38(suppl):abstr 278

279: Extensive peritoneal lavage after curative gastrectomy for gastric cancer study (EXPEL): An international multicenter randomized controlled trial – So JB, et al

Study objective

- To evaluate the efficacy and safety of surgery + extensive intraoperative peritoneal lavage (EIPL) in patients with gastric cancer



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- DFS, peritoneal recurrence, safety

Trial terminated early after futility analysis

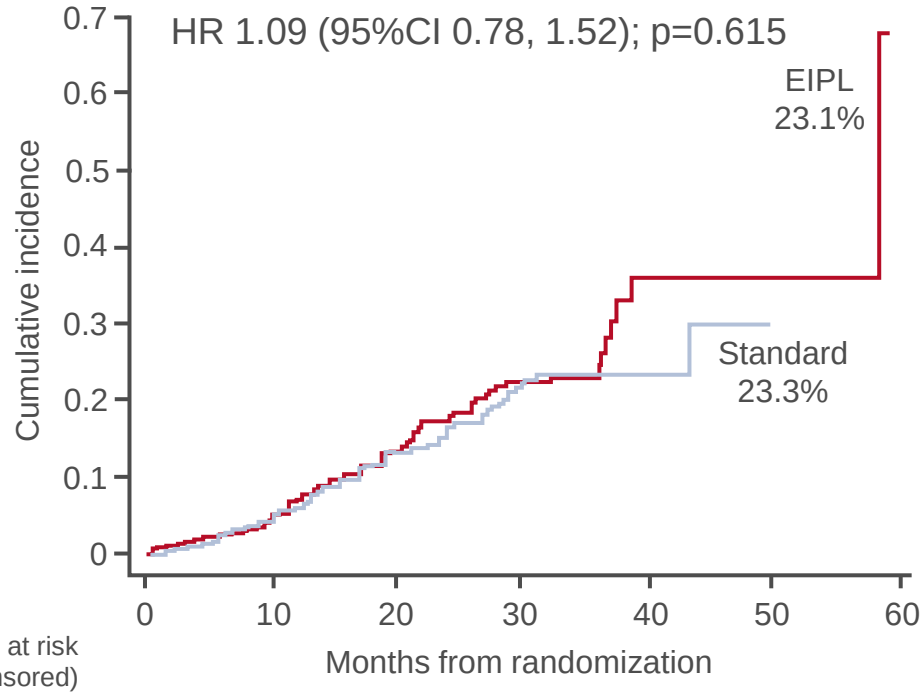
So JB, et al. J Clin Oncol 2020;38(suppl):abstr 279

279: Extensive peritoneal lavage after curative gastrectomy for gastric cancer study (EXPEL): An international multicenter randomized controlled trial – So JB, et al

Key results

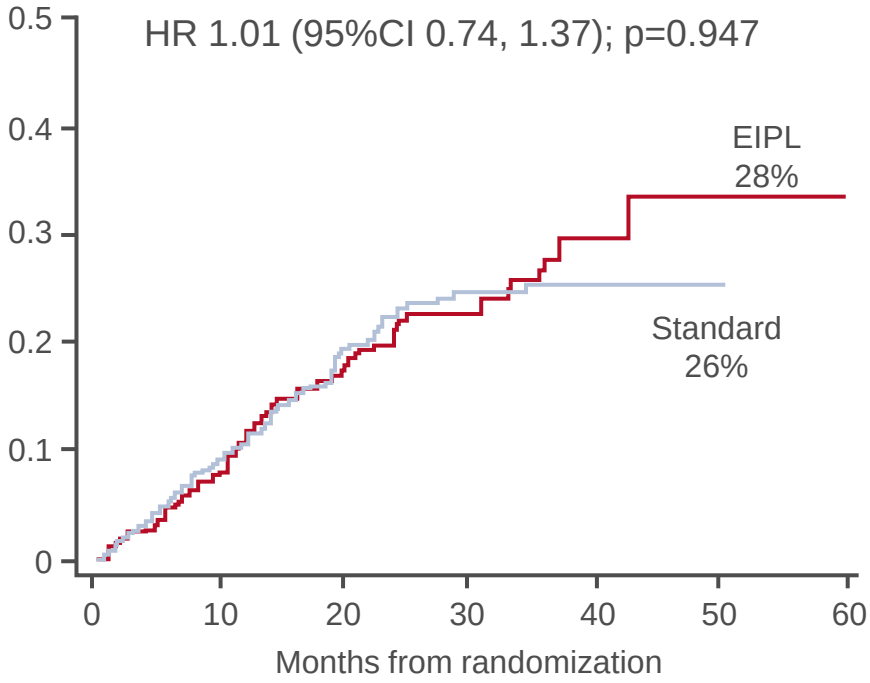
OS

Cumulative incidence of mortality



DFS

Cumulative incidence of recurrence



No. at risk (censored)													
EIPL	396 (0)	351 (16)	234 (30)	142 (20)	22 (7)	6 (0)	0 (1)	396 (0)	327 (32)	203 (31)	126 (10)	21 (7)	5 (1)	0 (0)
Standard	401 (0)	348 (17)	233 (28)	142 (19)	16 (2)	0 (1)	0 (0)	401 (0)	325 (37)	205 (32)	131 (11)	15 (2)	0 (0)	0 (0)

So JB, et al. J Clin Oncol 2020;38(suppl):abstr 279

279: Extensive peritoneal lavage after curative gastrectomy for gastric cancer study (EXPEL): An international multicenter randomized controlled trial – So JB, et al

Key results (cont.)

- The 3-year cumulative incidence of peritoneal recurrence was 7.9% for EIPL and 6.6% for standard lavage (HR 1.33 [95%CI 0.73, 2.42]; p=0.347

AEs, n	EIPL			Standard lavage		
	Mild	Moderate	Severe	Mild	Moderate	Severe
Anastomotic stump leak	2	6	2	0	5	1
Bleeding	1	2	3	2	2	2
Intra-abdominal abscess	3	1	0	2	3	0
Superficial wound infection	5	1	1	1	0	0
Abnormal liver function	3	3	0	0	1	0
Bowel perforation	0	2	1	0	1	0
Pancreatic fistula	1	0	0	0	1	0
Myocardial infarction	0	1	1	0	0	0
Other	6	5	10	7	12	1

Conclusions

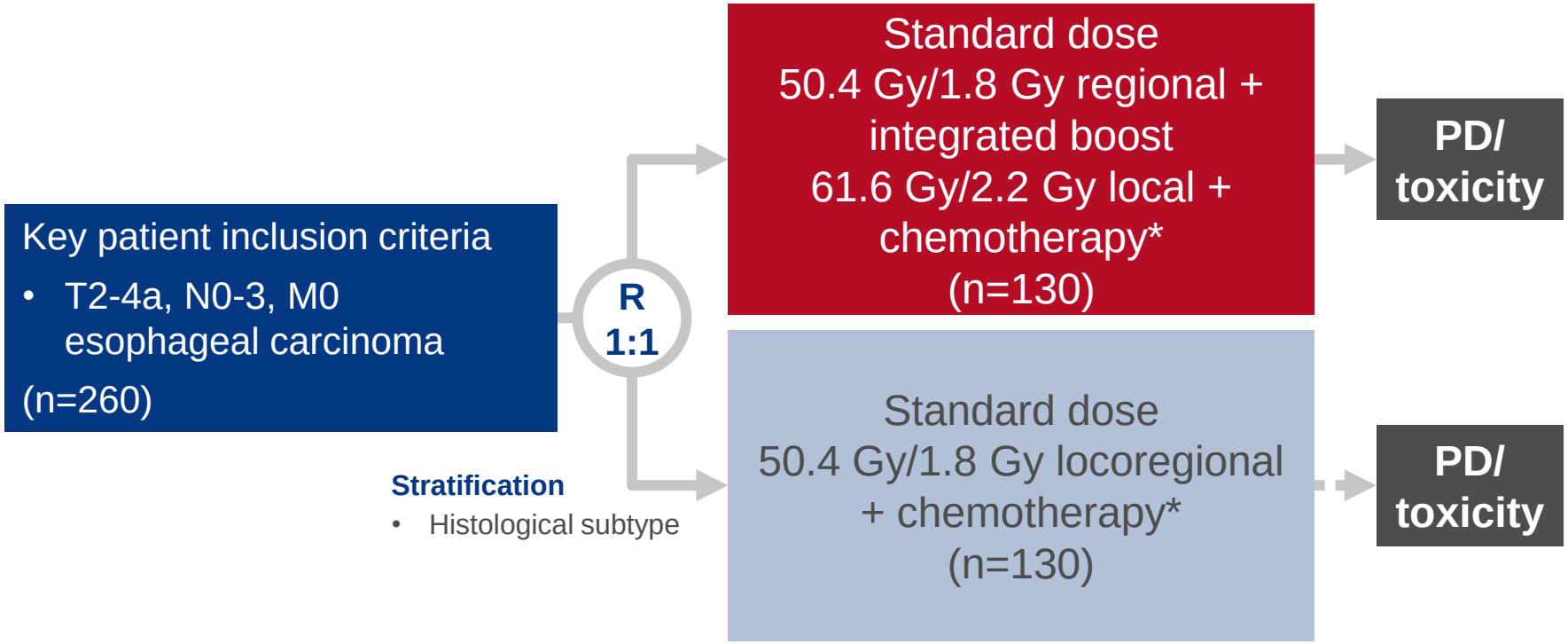
- **In patients with gastric cancer, EIPL failed to reduce the risk of peritoneal recurrence and did not improve survival after surgery**

So JB, et al. J Clin Oncol 2020;38(suppl):abstr 279

281: A randomized controlled phase III multicenter study on dose escalation in definitive chemoradiation for patients with locally advanced esophageal cancer: ARTDECO study – Hulshof MCCM, et al

Study objective

- To evaluate the efficacy and safety of radiation dose escalation in definitive chemoradiation in patients with esophageal cancer



PRIMARY ENDPOINT

- Local tumor control

SECONDARY ENDPOINTS

- Locoregional control, OS, safety

*Concurrent carboplatin AUC2 + paclitaxel 50 mg/m^2 weekly (6 times)

Hulshof MCCM, et al. J Clin Oncol 2020;38(suppl):abstr 281

281: A randomized controlled phase III multicenter study on dose escalation in definitive chemoradiation for patients with locally advanced esophageal cancer: ARTDECO study – Hulshof MCCM, et al

Key results

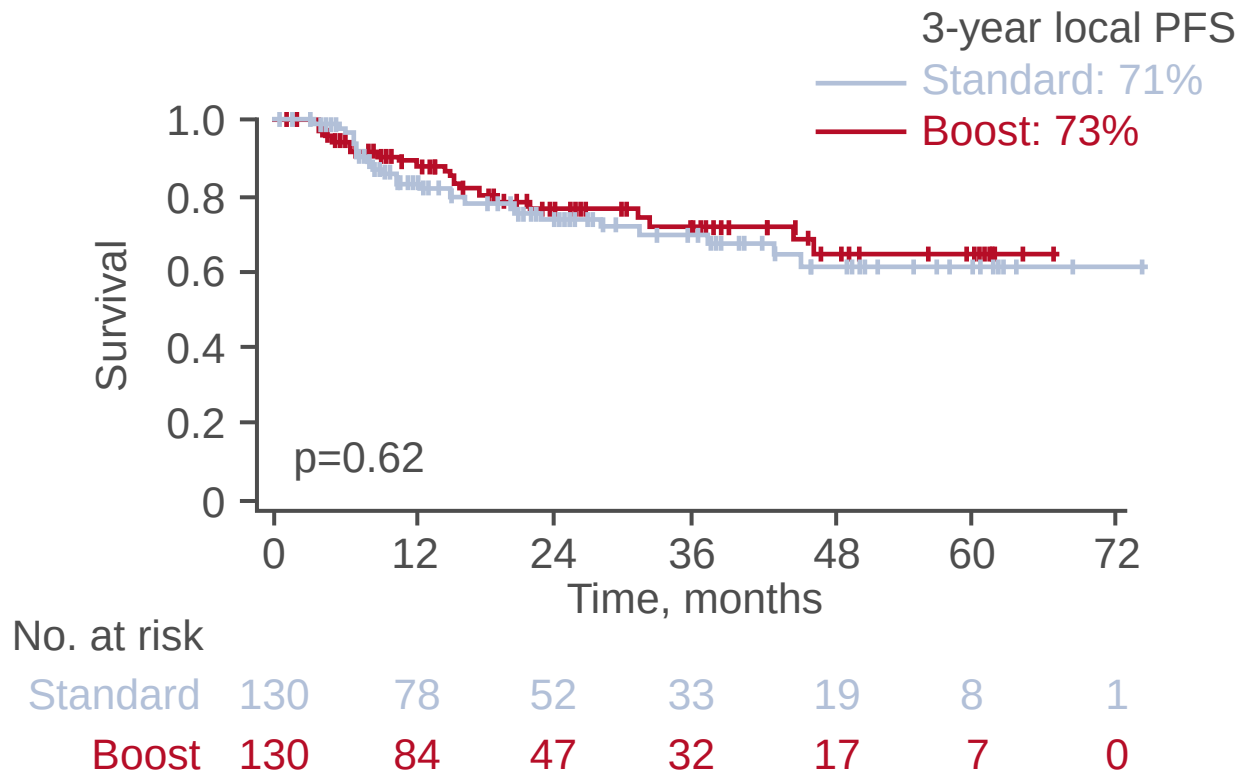
Baseline characteristics		Standard dose + boost (n=130)	Standard dose (n=130)
Mean age, years		71	70
WHO PS, %	0 1 2	32 59 9	44 45 10
Tumor site, %	Squamous cell carcinoma Adenocarcinoma	63 37	61 39
Localization, %	Cervical Upper thoracic Mid thoracic Lower thoracic GEJ	3 21 31 39 6	6 25 21 40 7
T stage, %	T2-3 T4	88 8	86 6
N stage, %	N0 N1 N2 N3	28 43 25 4	25 45 22 7
Medically unfit, %		31	28

Hulshof MCCM, et al. J Clin Oncol 2020;38(suppl):abstr 281

281: A randomized controlled phase III multicenter study on dose escalation in definitive chemoradiation for patients with locally advanced esophageal cancer: ARTDECO study – Hulshof MCCM, et al

Key results (cont.)

Local progression by arm

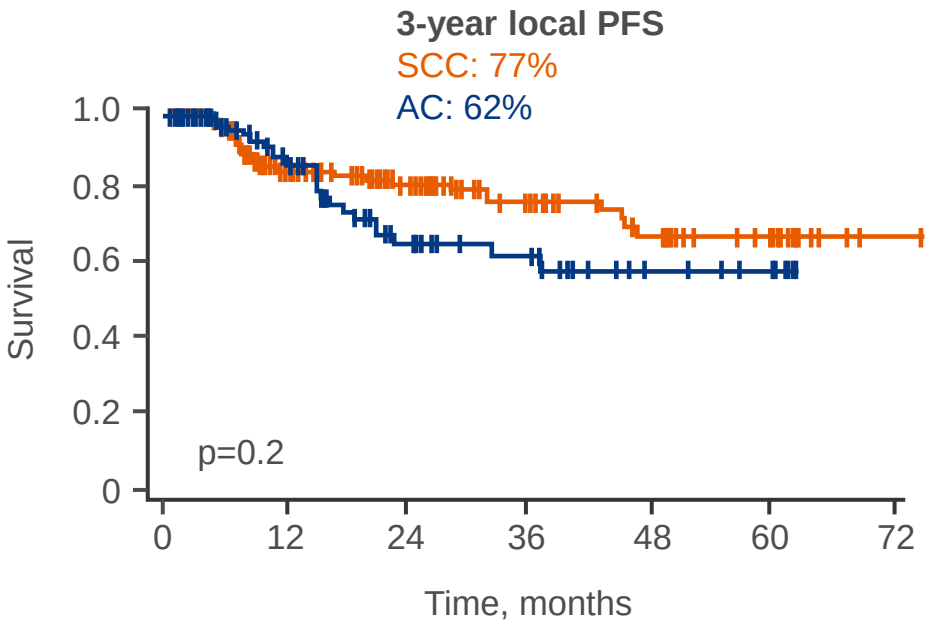


Hulshof MCCM, et al. J Clin Oncol 2020;38(suppl):abstr 281

281: A randomized controlled phase III multicenter study on dose escalation in definitive chemoradiation for patients with locally advanced esophageal cancer: ARTDECO study – Hulshof MCCM, et al

Key results (cont.)

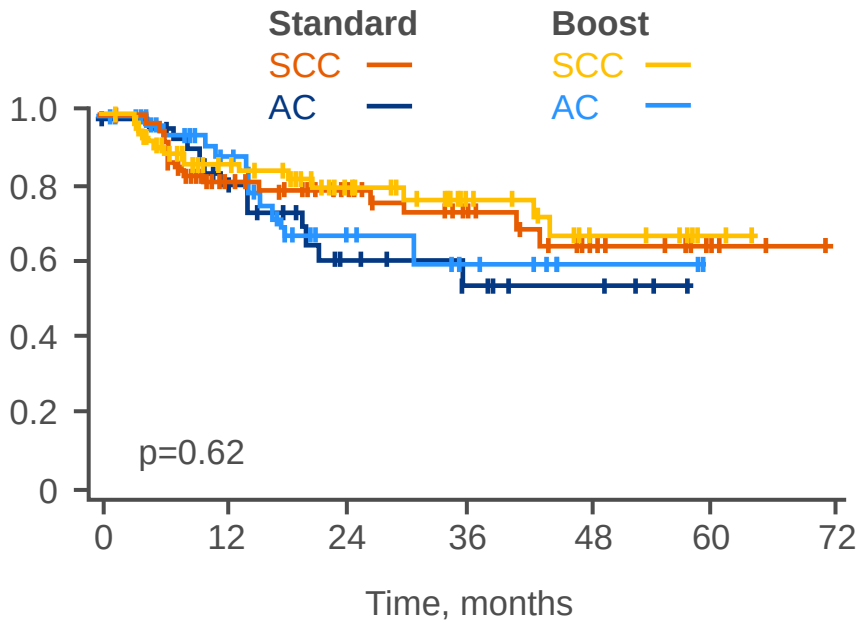
Local progression by histological type



No. at risk

SCC	160	105	73	47	29	12	1
AC	100	57	26	18	7	3	0

Local progression by arm stratified by histological type



No. at risk

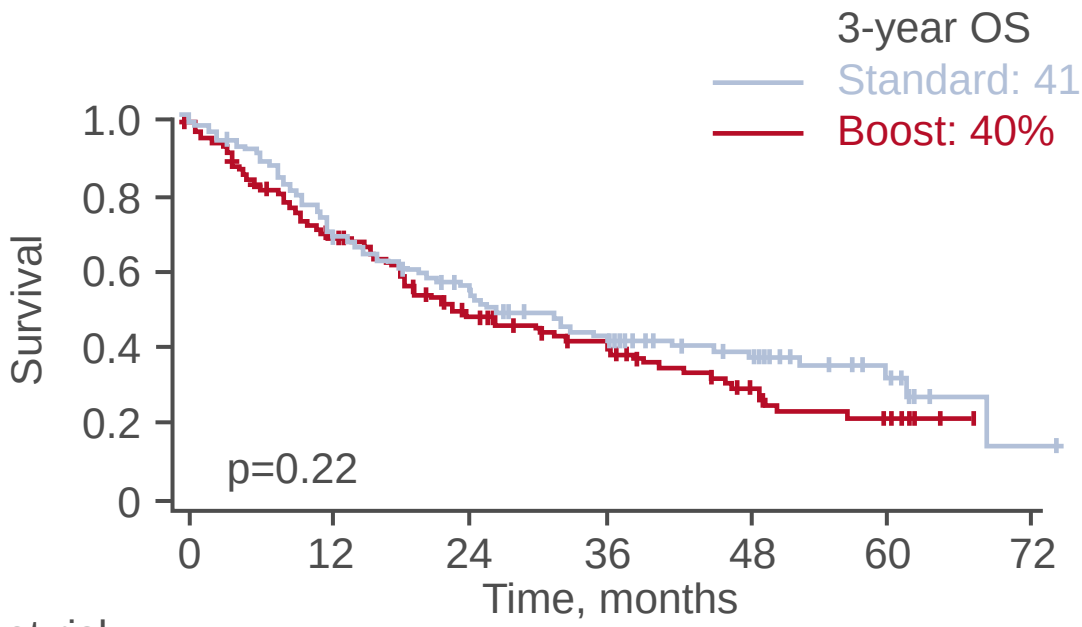
Standard SCC	80	52	38	23	14	7	1
Standard AC	50	26	14	10	5	1	0
Boost SCC	80	53	35	24	15	5	0
Boost AC	50	31	12	8	2	2	0

Hulshof MCCM, et al. J Clin Oncol 2020;38(suppl):abstr 281

281: A randomized controlled phase III multicenter study on dose escalation in definitive chemoradiation for patients with locally advanced esophageal cancer: ARTDECO study – Hulshof MCCM, et al

Key results (cont.)

Overall survival



No. at risk							
Standard	130	89	83	38	24	11	1
Boost	130	88	50	35	19	7	0

Hulshof MCCM, et al. J Clin Oncol 2020;38(suppl):abstr 281

281: A randomized controlled phase III multicenter study on dose escalation in definitive chemoradiation for patients with locally advanced esophageal cancer: ARTDECO study – Hulshof MCCM, et al

Key results (cont.)

CTCAE scoring, %	Standard dose + boost (n=118)	Standard dose (n=120)
1	3.3	0
2	25.8	15.3
3	55.0	61.0
4	10.8	13.6
5	5.0	8.5

Conclusions

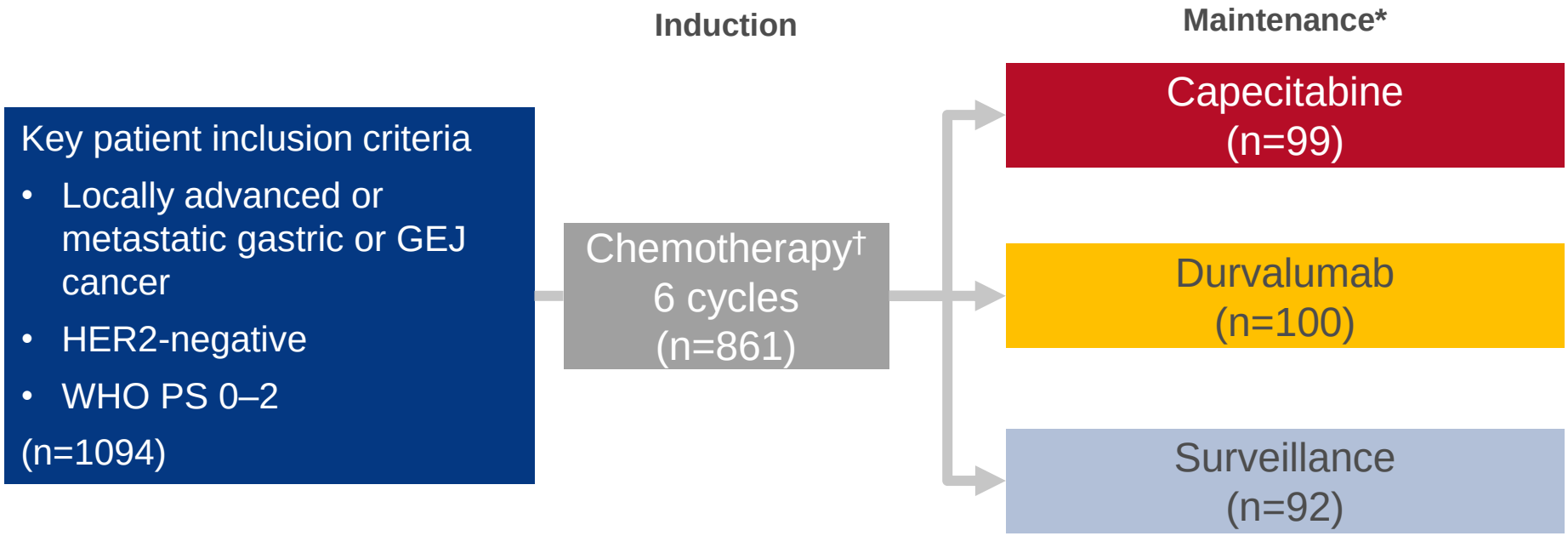
- In patients with locally advanced esophageal cancer, the use of dose escalation in definitive chemoradiation did not provide any improvement in local tumor control
- The standard dose should remain as the standard of care

Hulshof MCCM, et al. J Clin Oncol 2020;38(suppl):abstr 281

282: Evaluating maintenance therapies in advanced oesophago-gastric adenocarcinoma (OGA): Interim analysis and biomarker results from the PLATFORM study – Cunningham D, et al

Study objective

- To evaluate the efficacy and safety of maintenance therapy in patients with advanced esophago-gastric adenocarcinoma who have achieved disease control (interim analysis)



PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

- OS, ORR, safety

*Adaptive design, other arms include rucaparib, capecitabine + ramucirumab in HER2-negative and trastuzumab ± durvalumab in HER2-positive; †platinum-based chemotherapy

Cunningham D, et al. J Clin Oncol 2020;38(suppl):abstr 282

282: Evaluating maintenance therapies in advanced oesophago-gastric adenocarcinoma (OGA): Interim analysis and biomarker results from the PLATFORM study – Cunningham D, et al

Key results

	Capecitabine (n=61)	Durvalumab (n=61)	Surveillance (n=61)
12-week PFS rate, n (%) [95%CI]	34 (56) [45, 66]	29 (48) [37, 58]	30 (49) [39, 60]
PFS rate vs. surveillance, % (95%CI)	+6.6 (-8.3, 21.4)	-1.6 (-16.5, 13.3)	
Response, n (%)			
CR	0 (0)	0 (0)	0 (0)
PR	0 (0)	3 (5)	0 (0)
SD	34 (56)	26 (43)	30 (49)
PD	25 (41)	31 (51)	28 (46)
Clinical PD	2 (3)	1 (2)	3 (5)

Cunningham D, et al. J Clin Oncol 2020;38(suppl):abstr 282

282: Evaluating maintenance therapies in advanced oesophago-gastric adenocarcinoma (OGA): Interim analysis and biomarker results from the PLATFORM study – Cunningham D, et al

Key results (cont.)

Maximum reported TRAEs, n (%)	Capecitabine (n=61)	Durvalumab (n=61)	Surveillance (n=61)
Grade 3	8 (13)	7 (11)	0 (0)
Grade 4	0 (0)	2 (3)	0 (0)
Grade 5	0 (0)	0 (0)	0 (0)

Conclusions

- **In this interim analysis, in patients with advanced esophago-gastric cancer, maintenance with capecitabine or durvalumab did not demonstrate futility compared with surveillance and further analysis is ongoing**

Cunningham D, et al. J Clin Oncol 2020;38(suppl):abstr 282

383: A phase III study of nivolumab (Nivo) in previously treated advanced gastric or gastric esophageal junction (G/GEJ) cancer (ATTRACTION-2): Three-year update data – Chen L-T, et al

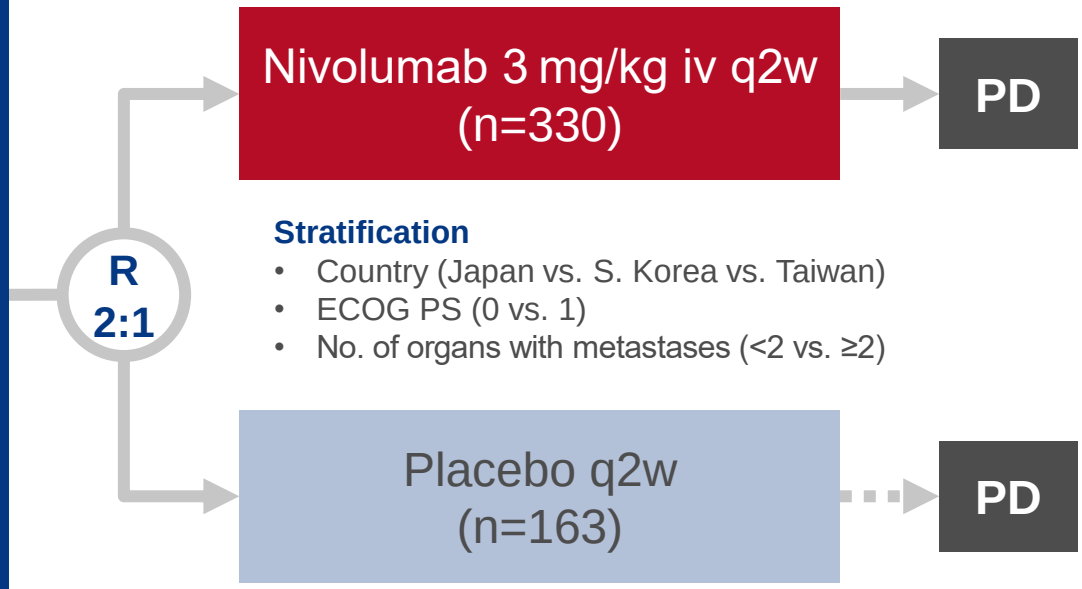
Study objective

- To evaluate the long-term efficacy and safety of nivolumab in patients with previously treated advanced gastric or GEJ cancer

Key patient inclusion criteria

- Unresectable advanced or recurrent gastric or GEJ cancer
- Refractory to or intolerant of ≥2 standard therapy regimens
- ECOG PS 0–1

(n=493)



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, BOR, ORR, TTR, DoR, DCR, safety

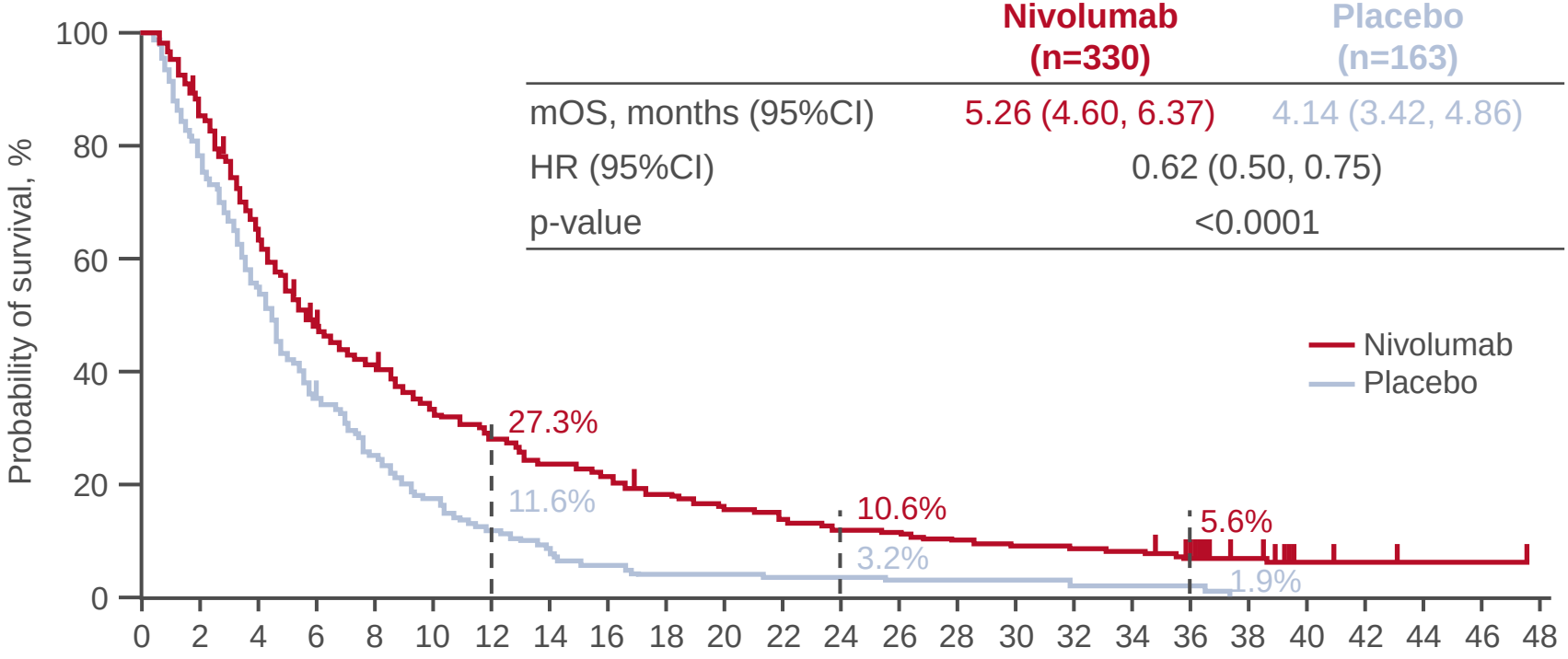
Chen L-T, et al. J Clin Oncol 2020;38(suppl):abstr 383

383: A phase III study of nivolumab (Nivo) in previously treated advanced gastric or gastric esophageal junction (G/GEJ) cancer (ATTRACTION-2): Three-year update data – Chen L-T, et al

Key results

OS

	Nivolumab (n=330)	Placebo (n=163)
mOS, months (95%CI)	5.26 (4.60, 6.37)	4.14 (3.42, 4.86)
HR (95%CI)	0.62 (0.50, 0.75)	
p-value	<0.0001	



No. at risk

Nivolumab	330	275	192	143	123	97	84	70	60	51	44	37	32	30	26	23	22	21	15	8	3	2	1	1	0
Placebo	163	121	82	54	37	24	18	10	9	6	6	5	5	4	4	4	3	3	3	0	0	0	0	0	0

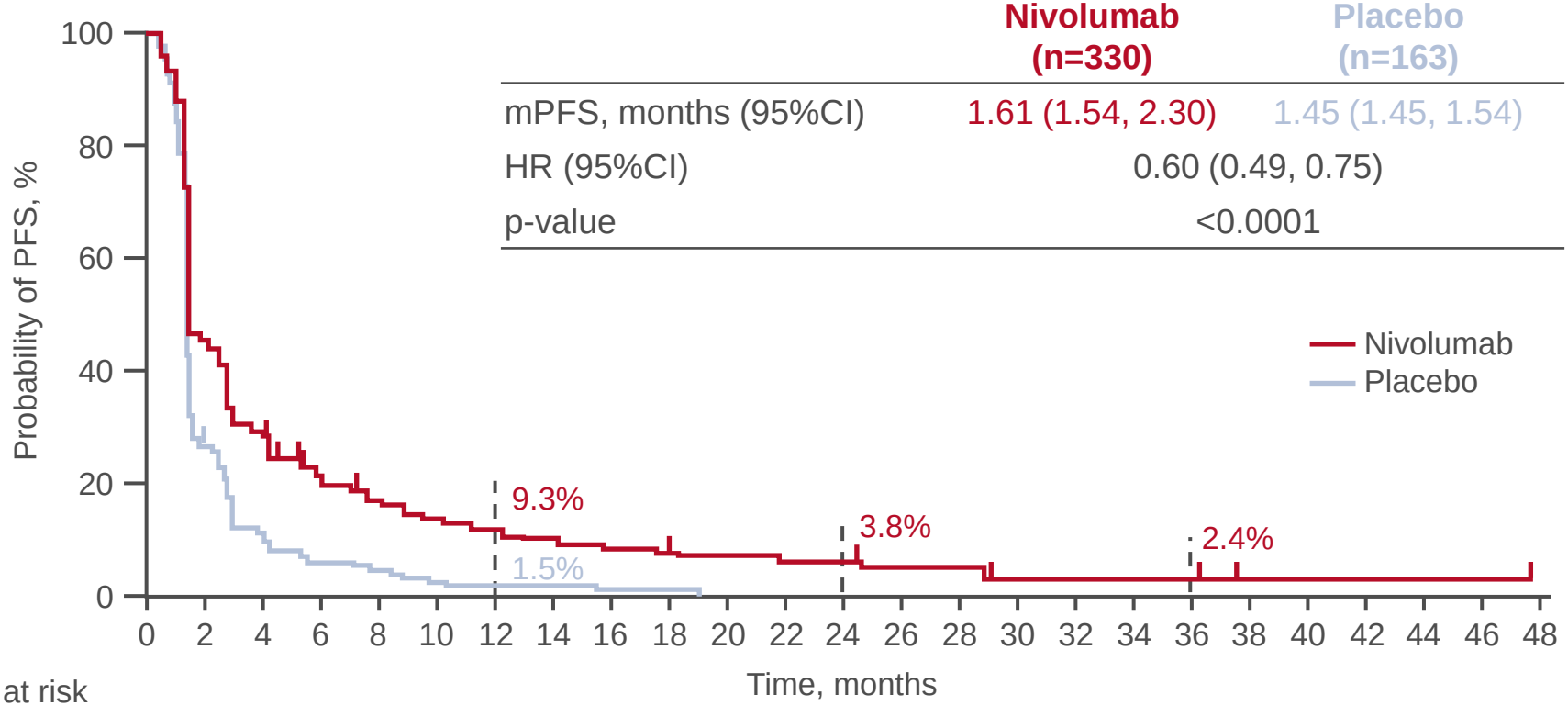
Chen L-T, et al. J Clin Oncol 2020;38(suppl):abstr 383

383: A phase III study of nivolumab (Nivo) in previously treated advanced gastric or gastric esophageal junction (G/GEJ) cancer (ATTRACTION-2): Three-year update data – Chen L-T, et al

Key results (cont.)

PFS

	Nivolumab (n=330)	Placebo (n=163)
mPFS, months (95%CI)	1.61 (1.54, 2.30)	1.45 (1.45, 1.54)
HR (95%CI)	0.60 (0.49, 0.75)	
p-value	<0.0001	



No. at risk

Nivolumab	330	131	83	54	41	31	24	20	16	13	11	9	9	6	6	4	4	4	4	1	1	1	1	1	0
Placebo	163	41	17	9	7	4	2	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

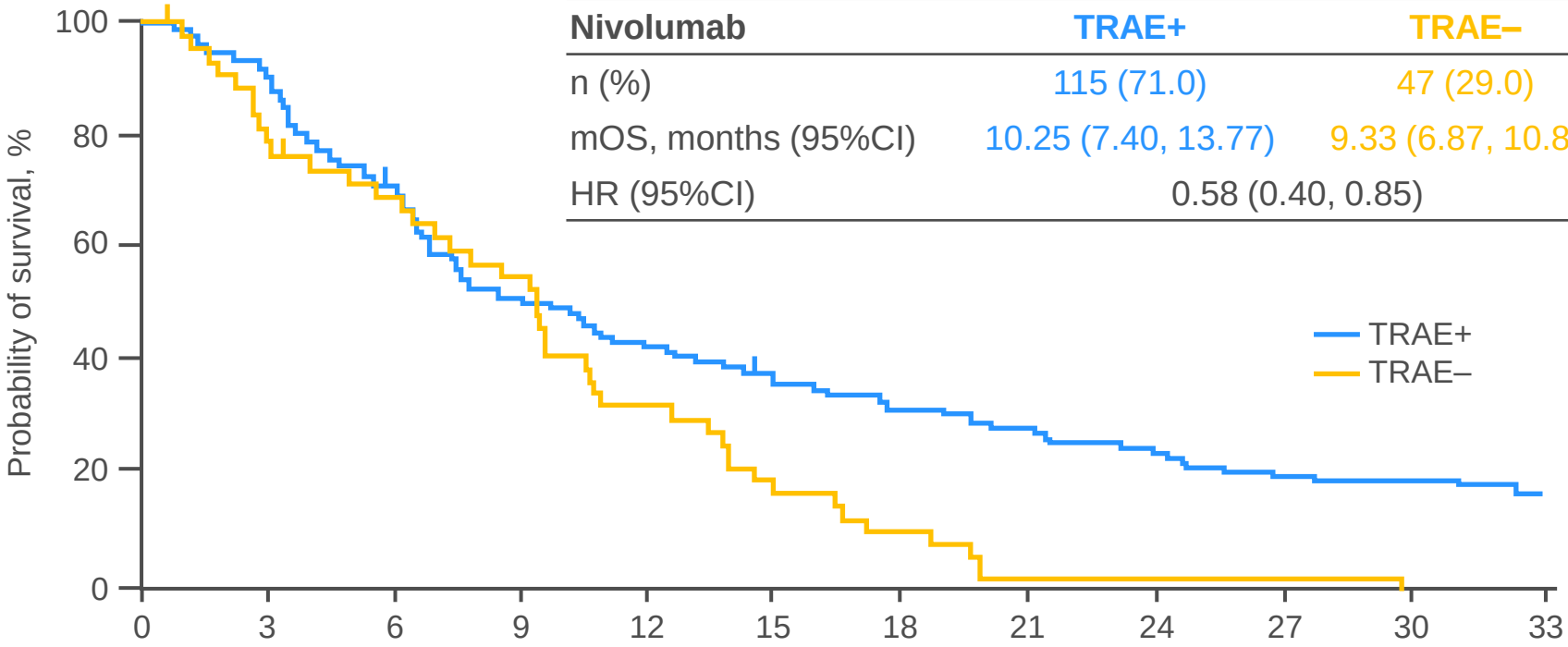
Chen L-T, et al. J Clin Oncol 2020;38(suppl):abstr 383

383: A phase III study of nivolumab (Nivo) in previously treated advanced gastric or gastric esophageal junction (G/GEJ) cancer (ATTRACTION-2): Three-year update data – Chen L-T, et al

Key results (cont.)

OS by TRAEs of special interest in patients who continued nivolumab for >2 months

Nivolumab	TRAE+	TRAE–
n (%)	115 (71.0)	47 (29.0)
mOS, months (95%CI)	10.25 (7.40, 13.77)	9.33 (6.87, 10.81)
HR (95%CI)	0.58 (0.40, 0.85)	



No. at risk

TRAE+	115	102	81	60	50	41	36	32	27	22	21	18
TRAE–	47	37	31	25	15	8	5	1	1	1	0	0

Chen L-T, et al. J Clin Oncol 2020;38(suppl):abstr 383

383: A phase III study of nivolumab (Nivo) in previously treated advanced gastric or gastric esophageal junction (G/GEJ) cancer (ATTRACTION-2): Three-year update data – Chen L-T, et al

Key results (cont.)

- TRAEs of special interest* occurred in 21 of 32 patients who had CR or PR and 9 of these 21 patients experienced the TRAE before the first response to nivolumab
- In the majority of cases, the first TRAEs of special interest occurred within 3 months of initiating nivolumab
- Over the 3 years of follow-up, there were no new safety signals reported

Conclusions

- **In patients with previously treated advanced gastric or GEJ cancer, nivolumab provided significant long-term survival benefit with no new safety signals**
- **A longer mOS was observed in those patients who experienced TRAEs of special interest compared with those who did not**
- **TRAEs of special interest should be carefully monitored both during and after nivolumab treatment**

*Endocrine, gastrointestinal, hepatic, hypersensitivity reaction, pulmonary, renal or skin

Chen L-T, et al. J Clin Oncol 2020;38(suppl):abstr 383

CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

Cancers of the pancreas, small bowel and hepatobiliary tract

PANCREATIC CANCER

637: Randomized phase III study of FOLFOX alone and with pegilodecakin as second-line therapy in patients with metastatic pancreatic cancer (SEQUOIA) – Hecht JR, et al

Study objective

- To evaluate the efficacy and safety of pegilodecakin + FOLFOX as a 2L treatment for patients with metastatic pancreatic cancer

Key patient inclusion criteria

- Metastatic pancreatic adenocarcinoma
- Progression on or after gemcitabine-containing regimen
- ECOG PS 0–1

(n=566)

R 1:1

Pegilodecakin* + FOLFOX† followed by pegilodecakin maintenance‡ (n=283) → PD

FOLFOX† (n=284) → PD

Stratification

- Prior gemcitabine monotherapy or gemcitabine/nab-paclitaxel
- North America vs. Europe vs. Asia-Pacific

PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR, DCR, safety

*0.4 mg/day if ≤80 kg or 0.8 mg/day if >80 kg; †leucovorin 400 mg/m^2 + oxaliplatin 85 mg/m^2 followed by bolus 5FU 400 mg/m^2 then 5FU 2400 mg/m^2 D1 q2w; ‡0.8 mg/day if ≤80 kg or 1.6 mg/day if >80 kg

Presented by Johanna Bendell

Hecht JR, et al. J Clin Oncol 2020;38(suppl):abstr 637

637: Randomized phase III study of FOLFOX alone and with pegilodecakin as second-line therapy in patients with metastatic pancreatic cancer (SEQUOIA) – Hecht JR, et al

Key results

Baseline characteristics		Pegilodecakin + FOLFOX (n=283)	FOLFOX (n=284)
Median age, years (range)		65 (33–88)	65 (34–88)
Gender, n (%)	Female Male	135 (47.7) 148 (52.3)	132 (46.5) 152 (53.5)
Region, n (%)	Asia Europe North America	67 (23.6) 121 (42.8) 95 (33.6)	67 (23.6) 121 (42.6) 96 (33.8)
Prior therapy*, n (%)		267 (94.3)	270 (95.1)
No. of metastatic sites, n (%)	1 2 ≥3	113 (40.1) 104 (36.9) 65 (23.0)	103 (36.5) 92 (32.6) 87 (30.9)
Liver metastases, n (%)		235 (84.2)	228 (82.6)
Primary lesion location, n (%)	Head Body Tail	99 (35.0) 72 (25.4) 70 (24.7)	109 (38.4) 74 (26.1) 69 (24.3)
ECOG PS 0, n (%)		84 (29.8)	100 (35.2)
CA19-9, n (%)	>59 ULN >Normal – ≤59 ULN Normal	110 (38.9) 124 (43.8) 44 (15.5)	122 (43.0) 120 (42.3) 40 (14.1)

*Gemcitabine + nab-paclitaxel

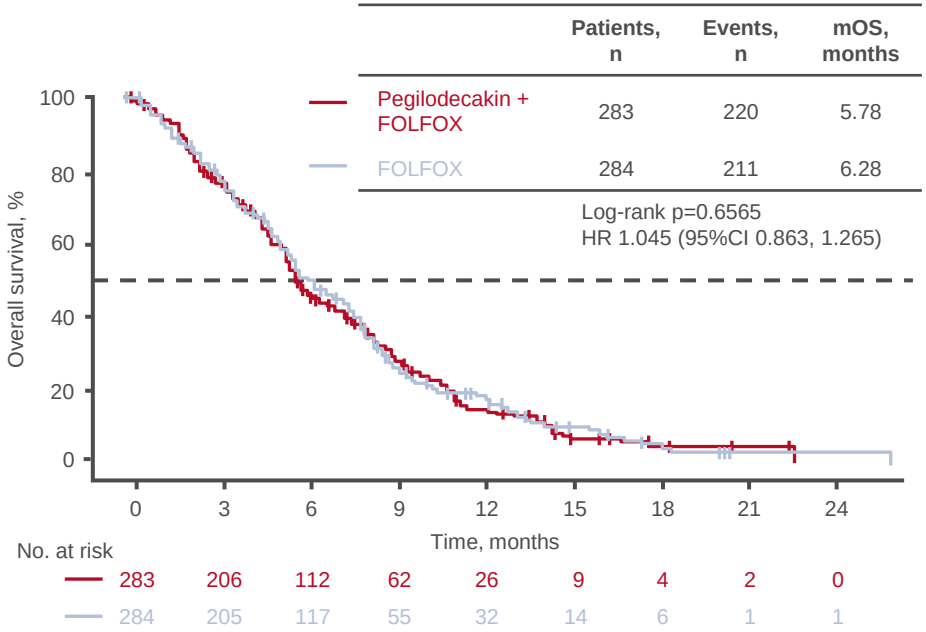
Presented by Johanna Bendell

Hecht JR, et al. J Clin Oncol 2020;38(suppl):abstr 637

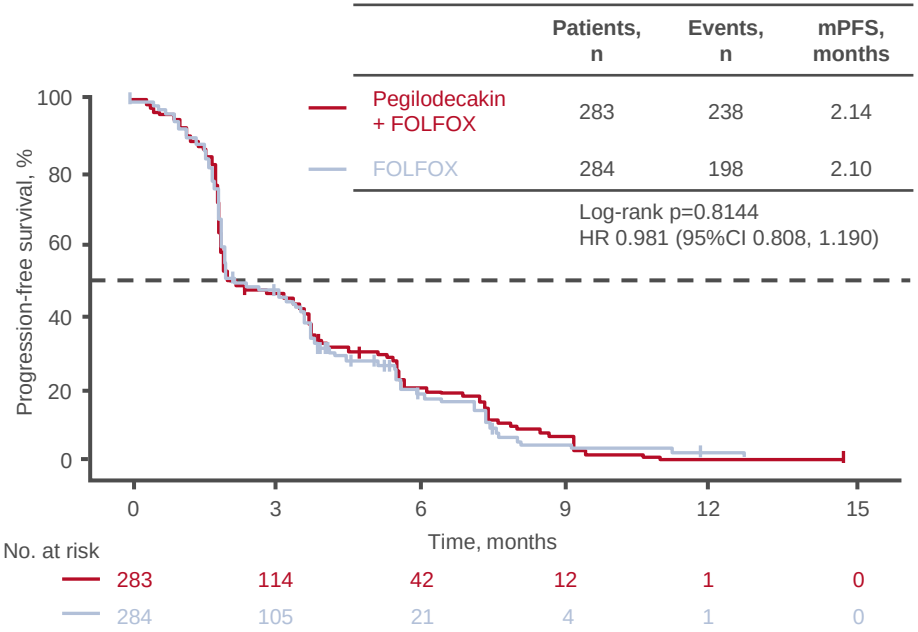
637: Randomized phase III study of FOLFOX alone and with pegilodecakin as second-line therapy in patients with metastatic pancreatic cancer (SEQUOIA) – Hecht JR, et al

Key results (cont.)

OS (ITT)



PFS* (ITT)



Response	Pegilodecakin + FOLFOX (n=283)	FOLFOX (n=284)
ORR (CR/PR), n (%)	13 (4.6)	16 (5.6)
DCR, n (%)	121 (42.8)	104 (36.6)
Median DoR, months (95%CI)	5.0 (3.5, 7.1)	5.2 (3.8, 5.7)
Median TTR, months (range)	1.9 (1.7–4.0)	1.9 (1.5–5.3)

*Investigator assessed (RECIST v1.1)

Presented by Johanna Bendell

Hecht JR, et al. J Clin Oncol 2020;38(suppl):abstr 637

637: Randomized phase III study of FOLFOX alone and with pegilodecakin as second-line therapy in patients with metastatic pancreatic cancer (SEQUOIA) – Hecht JR, et al

Key results (cont.)

Grade ≥3 TEAEs occurring in ≥10%, %	Pegilodecakin + FOLFOX (n=278)	FOLFOX (n=251)
Any	81.3	66.9
Fatigue	17.6	10.8
Thrombocytopenia	25.5	3.6
Anemia	16.2	4.0
Neutropenia	29.5	22.7

Conclusions

- **In patients with metastatic pancreatic cancer, combining pegilodecakin with FOLFOX did not provide any additional survival benefit over FOLFOX alone**
- **Pegilodecakin + FOLFOX was generally well-tolerated and had a manageable safety profile**

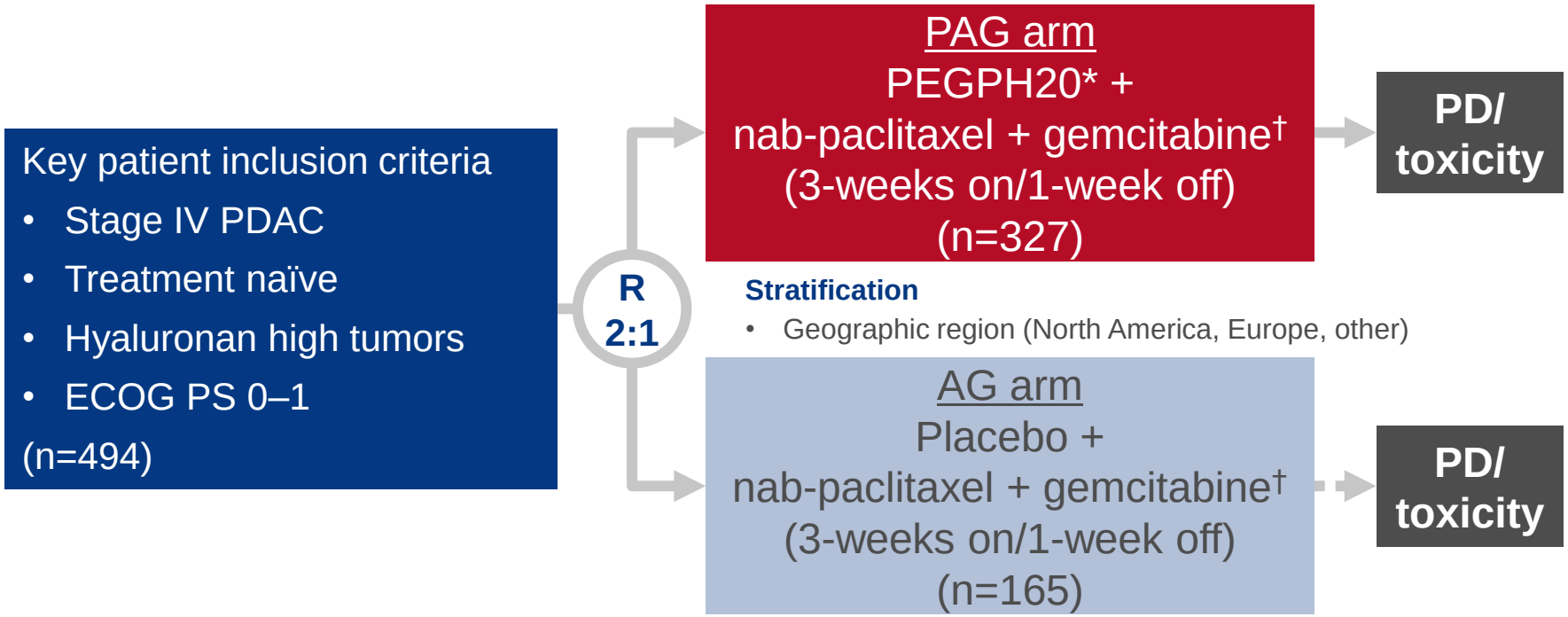
Presented by Johanna Bendell

Hecht JR, et al. J Clin Oncol 2020;38(suppl):abstr 637

638: HALO 109-301: A randomized, double-blind, placebo-controlled, phase 3 study of pegvorhyaluronidase alfa (PEGPH20) + nab-paclitaxel/gemcitabine (AG) in patients (pts) with previously untreated hyaluronan (HA)-high metastatic pancreatic ductal adenocarcinoma (mPDA) – Tempero MA, et al

Study objective

- To evaluate the efficacy and safety of PEGPH20 + nab-paclitaxel + gemcitabine in treatment naïve patients with hyaluronan-high metastatic PDAC



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR, DoR, safety

*PEGPH20 3 µg/kg twice weekly for cycle 1 then weekly; †nab-paclitaxel 125 mg/m^2 + gemcitabine 1000 mg/m^2 with prophylactic dexamethasone 8 mg + enoxaparin 1 mg/kg/day

Tempero MA, et al. J Clin Oncol 2020;38(suppl):abstr 638

638: HALO 109-301: A randomized, double-blind, placebo-controlled, phase 3 study of pegvorhyaluronidase alfa (PEGPH20) + nab-paclitaxel/gemcitabine (AG) in patients (pts) with previously untreated hyaluronan (HA)-high metastatic pancreatic ductal adenocarcinoma (mPDA) – Tempero MA, et al

Key results

Baseline characteristics		PAG (n=327)	AG (n=165)
Age, years	Mean (SD)	63.8 (9.62)	62.3 (9.50)
Gender, n (%)	Female Male	147 (45.0) 180 (55.0)	85 (51.5) 80 (48.5)
Race/ethnicity, n (%)	White Asian	266 (81.3) 33 (10.1)	126 (76.4) 24 (14.5)
ECOG PS, n (%)	0 1	160 (48.9) 167 (51.1)	79 (47.9) 86 (52.1)
No. of metastatic sites, n (%)	1 2 ≥3	206 (63.0) 71 (21.7) 50 (15.3)	92 (55.8) 38 (23.0) 35 (21.2)
Liver metastases, n (%)	Yes	254 (77.7)	124 (75.2)
Biopsy location, n (%)	Primary tumor	117 (35.8)	70 (42.4)
Serum level of CA19-9, U/mL	Mean (SD)	16,012 (47,295)	21,775 (57,806)
Prior PDAC diagnosis, n (%)	Yes	39 (11.9)	14 (8.5)
Time to metastatic PDAC diagnosis, years	Mean (SD)	1.5 (0.85)	1.6 (1.76)
Prior cancer medication, n (%)	Yes	26 (8.0)	9 (5.5)

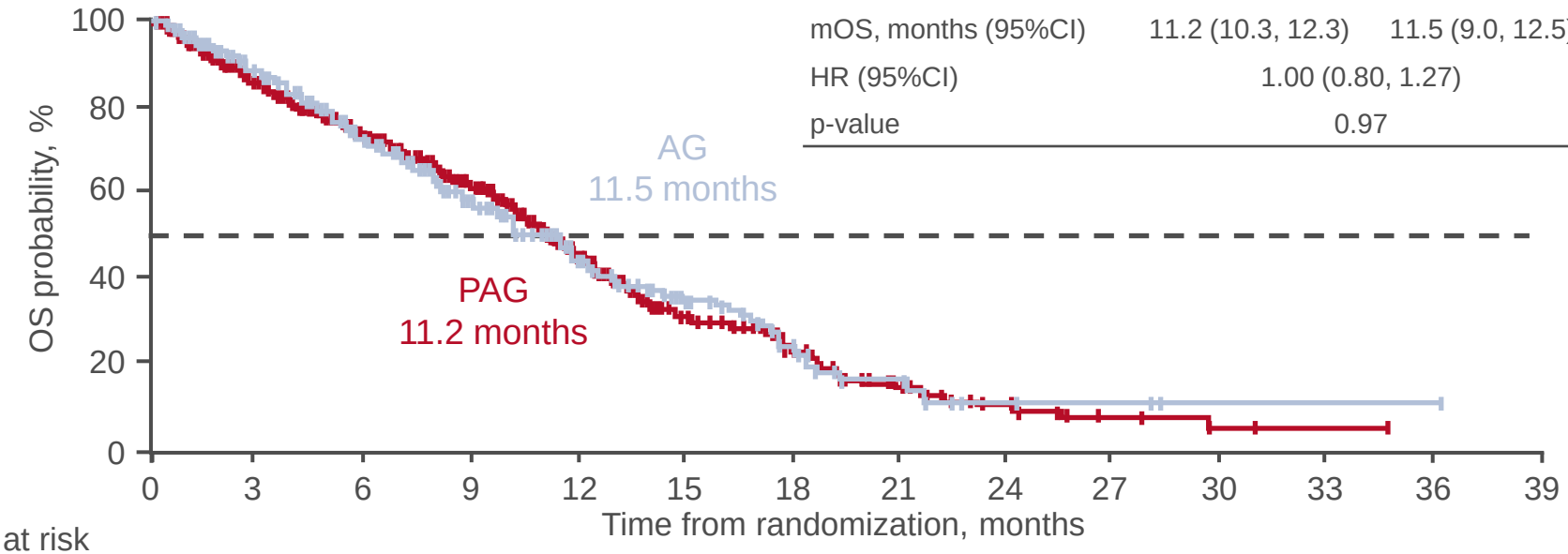
Tempero MA, et al. J Clin Oncol 2020;38(suppl):abstr 638

638: HALO 109-301: A randomized, double-blind, placebo-controlled, phase 3 study of pegvorhyaluronidase alfa (PEGPH20) + nab-paclitaxel/gemcitabine (AG) in patients (pts) with previously untreated hyaluronan (HA)-high metastatic pancreatic ductal adenocarcinoma (mPDA) – Tempero MA, et al

Key results (cont.)

OS

	PAG (n=327)	AG (n=165)
Deaths, n (%)	223 (68)	107 (65)
mOS, months (95%CI)	11.2 (10.3, 12.3)	11.5 (9.0, 12.5)
HR (95%CI)	1.00 (0.80, 1.27)	
p-value	0.97	



No. at risk

PAG	327	277	229	175	112	58	34	17	10	4	2	1	0	0
AG	165	139	109	77	51	32	16	11	4	3	1	1	1	0

Data cut-off: 20 May 2019; 330 deaths

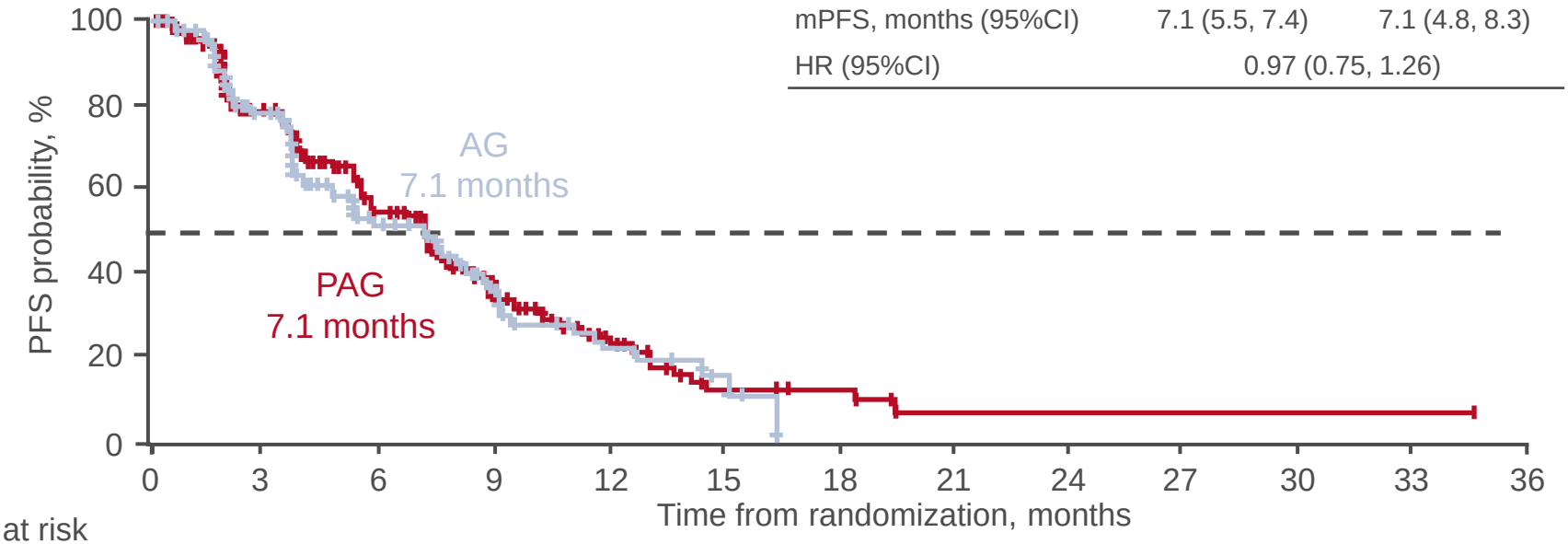
Tempero MA, et al. J Clin Oncol 2020;38(suppl):abstr 638

638: HALO 109-301: A randomized, double-blind, placebo-controlled, phase 3 study of pegvorhyaluronidase alfa (PEGPH20) + nab-paclitaxel/gemcitabine (AG) in patients (pts) with previously untreated hyaluronan (HA)-high metastatic pancreatic ductal adenocarcinoma (mPDA) – Tempero MA, et al

Key results (cont.)

PFS

	PAG (n=327)	AG (n=165)
mPFS, months (95%CI)	7.1 (5.5, 7.4)	7.1 (4.8, 8.3)
HR (95%CI)	0.97 (0.75, 1.26)	



No. at risk

PAG	327	200	103	46	21	7	5	1	1	1	1	1	0
AG	165	99	52	23	11	3	0	0	0	0	0	0	1

Tempero MA, et al. J Clin Oncol 2020;38(suppl):abstr 638

638: HALO 109-301: A randomized, double-blind, placebo-controlled, phase 3 study of pegvorhyaluronidase alfa (PEGPH20) + nab-paclitaxel/gemcitabine (AG) in patients (pts) with previously untreated hyaluronan (HA)-high metastatic pancreatic ductal adenocarcinoma (mPDA) – Tempero MA, et al

Key results (cont.)

Response	PAG arm (n=327)	AG arm (n=165)
ORR*, %	47	36
ORR ratio (95%CI)	1.29 (1.03, 1.63)	
BOR, n (%)		
CR	2 (0.6)	1 (0.6)
PR	152 (46.5)	59 (35.8)
SD	71 (21.7)	54 (32.7)
Non-CR/non-PD	9 (2.8)	2 (1.2)
PD	47 (14.4)	22 (13.3)
NE/unknown	46 (14.1)	27 (16.4)
Median DoR, months	6.1	7.4
Confirmed ORR, %	34	27
Confirmed ORR ratio (95%CI)	1.22 (0.91, 1.62)	

*BICR (RECIST v1.1)

Tempero MA, et al. J Clin Oncol 2020;38(suppl):abstr 638

638: HALO 109-301: A randomized, double-blind, placebo-controlled, phase 3 study of pegvorhyaluronidase alfa (PEGPH20) + nab-paclitaxel/gemcitabine (AG) in patients (pts) with previously untreated hyaluronan (HA)-high metastatic pancreatic ductal adenocarcinoma (mPDA) – Tempero MA, et al

Key results (cont.)

Grade ≥3 AEs occurring in ≥5% and with a ≥2% higher rate on PAG arm, n (%)	PAG arm (n=325)	AG arm (n=156)
Thrombocytopenia/platelet count decreased	68 (20.9)	25 (16.1)
Fatigue	52 (16.0)	15 (9.6)
Asthenia	28 (8.6)	9 (5.8)
Hyponatremia	26 (8.0)	6 (3.8)
Sepsis	24 (7.4)	6 (3.8)
Muscle spasms	21 (6.5)	1 (0.6)

Conclusions

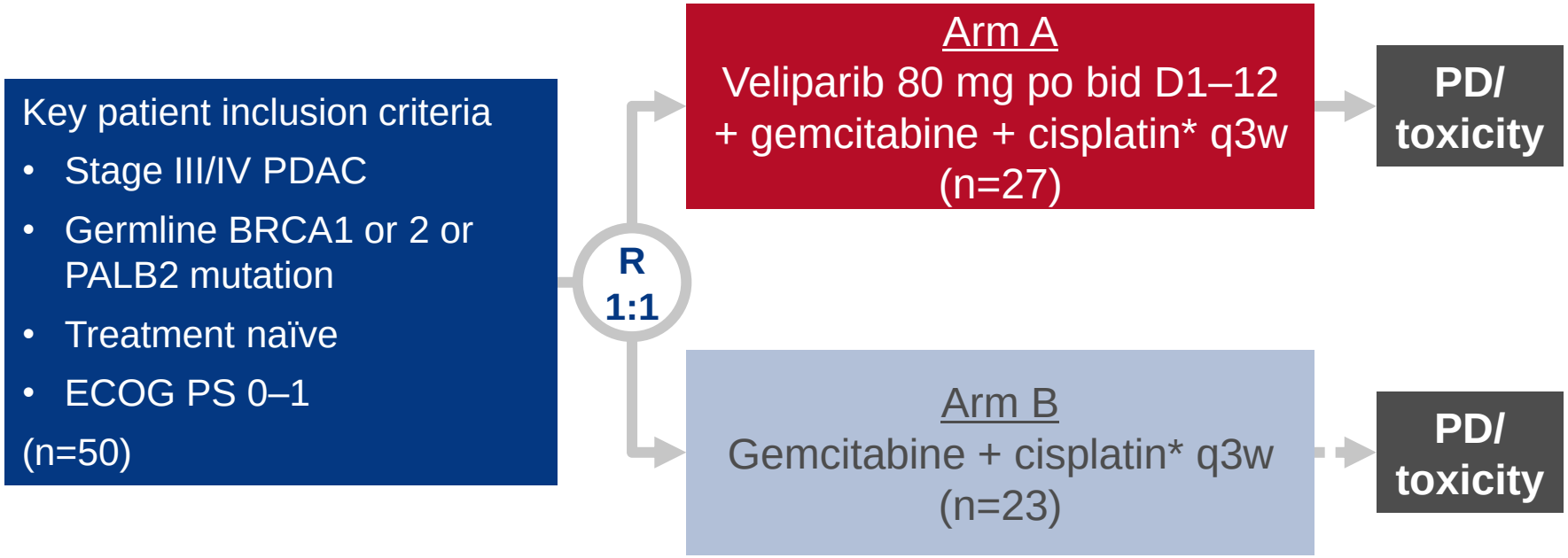
- **In patients with metastatic PDAC, combining PEGPH20 with nab-paclitaxel + gemcitabine did not provide any additional survival benefit to nab-paclitaxel + gemcitabine**
- **Toxicity was consistent with the known safety profiles**

Tempero MA, et al. J Clin Oncol 2020;38(suppl):abstr 638

639: A randomized, multicenter, phase II trial of gemcitabine (G), cisplatin (C) +/- veliparib (V) in patients with pancreas adenocarcinoma (PDAC) and a known germline (g)BRCA/ PALB2 mutation – O'Reilly EM, et al

Study objective

- To evaluate the efficacy and safety of gemcitabine + cisplatin ± veliparib in patients with PDAC and germline BRCA/PALB2 mutation



PRIMARY ENDPOINT

- RR (RECIST v1.1)

SECONDARY ENDPOINTS

- PFS, OS, DCR, safety

*Gemcitabine 600 mg/m^2 + cisplatin 25 mg/m^2 D3, 10

O'Reilly EM, et al. J Clin Oncol 2020;38(suppl):abstr 639

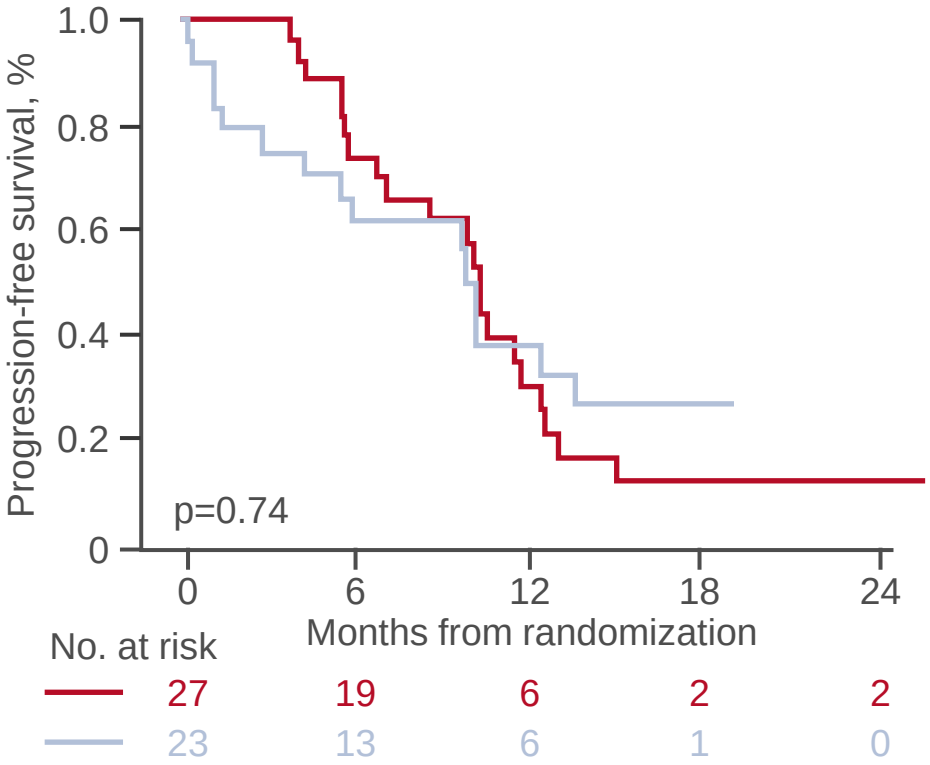
639: A randomized, multicenter, phase II trial of gemcitabine (G), cisplatin (C) +/- veliparib (V) in patients with pancreas adenocarcinoma (PDAC) and a known germline (g)BRCA/ PALB2 mutation – O'Reilly EM, et al

Key results

PFS

Arm A: 10.1 months (95%CI 6.7, 11.5)

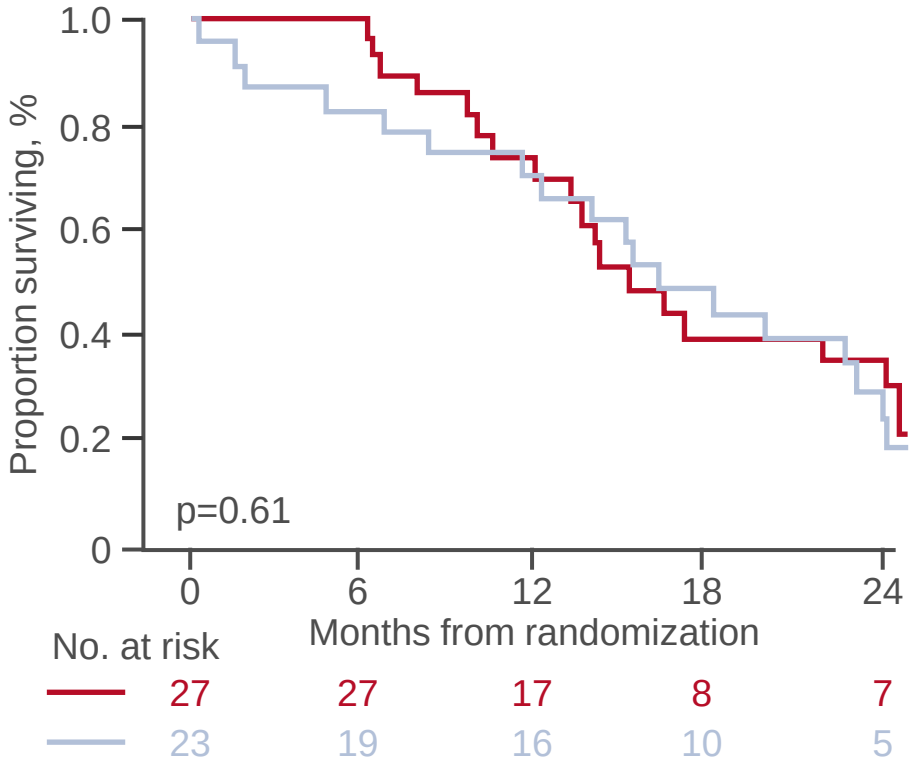
Arm B: 9.7 months (95%CI 4.2, 13.6)



OS

Arm A: 15.5 months (95%CI 12.2, 25.3)

Arm B: 16.4 months (95%CI 11.7, 23.4)



O'Reilly EM, et al. J Clin Oncol 2020;38(suppl):abstr 639

639: A randomized, multicenter, phase II trial of gemcitabine (G), cisplatin (C) +/- veliparib (V) in patients with pancreas adenocarcinoma (PDAC) and a known germline (g)BRCA/ PALB2 mutation – O'Reilly EM, et al

Key results (cont.)

Toxicity	Arm A (n=27)	Arm B (n=23)
Grade 3–4 AEs, n (%)		
Anemia	14 (52)	8 (35)
Thrombocytopenia	15 (55)	2 (9)
Neutropenia	13 (41)	7 (30)
Dose reductions, n (%)		
Heme toxicity	18 (90)	4 (17)

Conclusions

- **In patients with PDAC and germline BRCA or PALB2 mutation, gemcitabine + cisplatin with or without veliparib demonstrated promising activity although the triplet arm had a higher rate of hematologic toxicity than the doublet arm**

O'Reilly EM, et al. J Clin Oncol 2020;38(suppl):abstr 639

Cancers of the pancreas, small bowel and hepatobiliary tract

HEPATOCELLULAR CARCINOMA

476: Patient-reported outcomes (PROs) from the Phase III IMbrave150 trial of atezolizumab (atezo) + bevacizumab (bev) vs sorafenib (sor) as first-line treatment (tx) for patients (pts) with unresectable hepatocellular carcinoma (HCC) – Galle PR, et al

Study objective

- To evaluate PROs with atezolizumab + bevacizumab when used as a 1L treatment for patients with unresectable HCC

Key patient inclusion criteria
- Locally advanced or metastatic and/or unresectable HCC
- Child-Pugh class A
- No prior systemic therapy
- ECOG PS 0–1

(n=501)

R 2:1

Atezolizumab 1200 mg D1 + bevacizumab 15 mg/kg D1 q3w (n=336) → PD/ toxicity

Stratification
- Region (Asia, excluding Japan* vs. rest of world)
- ECOG PS (0 vs. 1)
- Macrovascular invasion and/or extrahepatic spread (presence vs. absence)
- Baseline AFP (<400 vs. ≥400 ng/mL)

Sorafenib 400 mg bid D1–21 q3w (n=165) → PD/ toxicity

CO-PRIMARY ENDPOINTS†
- OS, PFS (RECIST v1.1)

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

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

Galle PR, et al. J Clin Oncol 2020;38(suppl):abstr 476

476: Patient-reported outcomes (PROs) from the Phase III IMbrave150 trial of atezolizumab (atezo) + bevacizumab (bev) vs sorafenib (sor) as first-line treatment (tx) for patients (pts) with unresectable hepatocellular carcinoma (HCC) – Galle PR, et al

Key results

Median TTD[a], months (95%CI)	Atezolizumab + bevacizumab (n=336)	Sorafenib (n=165)
QoL/global health status scale of EORTC QLQ-C30	11.2 (6.0, NE)	3.6 (3.0, 7.0)
HR (95%CI)	0.63 (0.46, 0.85)	
Physical functioning scale of EORTC QLQ-C30	13.1 (9.7, NE)	4.9 (3.5, 6.2)
HR (95%CI)	0.53 (0.39, 0.73)	
Role functioning scale of EORTC QLQ-C30	9.1 (6.5, NE)	3.6 (2.2, 6.0)
HR (95%CI)	0.62 (0.46, 0.84)	

[a]Time to deterioration defined as the time from randomization to first decrease from baseline of ≥10 points in the particular scale/questionnaire maintained for 2 consecutive assessments or 1 assessment followed by death from any cause within 3 weeks

Galle PR, et al. J Clin Oncol 2020;38(suppl):abstr 476

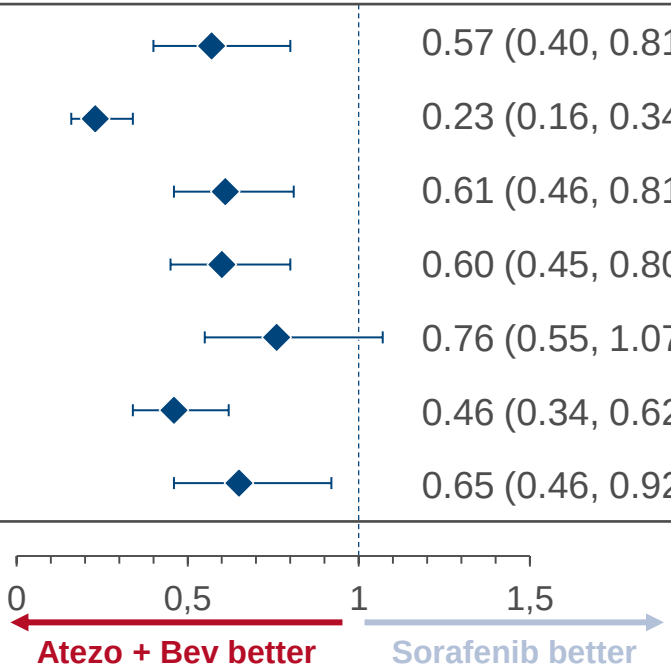
476: Patient-reported outcomes (PROs) from the Phase III IMbrave150 trial of atezolizumab (atezo) + bevacizumab (bev) vs sorafenib (sor) as first-line treatment (tx) for patients (pts) with unresectable hepatocellular carcinoma (HCC) – Galle PR, et al

Key results (cont.)

TTD in symptoms

Median time to event[a], months (95%CI)

Scale (questionnaire)	Atezo + Bev (n=336)	Sorafenib (n=165)	HR (95%CI)
Appetite loss	NE	7.62 (3.48, NE)	0.57 (0.40, 0.81)
Diarrhea	NE	4.44 (3.48, 5.59)	0.23 (0.16, 0.34)
Fatigue (QLQ-C30)	5.68 (4.30, 7.10)	2.10 (1.45, 4.83)	0.61 (0.46, 0.81)
Fatigue (QLQ-HCC18)	5.65 (4.30, 9.03)	2.14 (1.64, 2.83)	0.60 (0.45, 0.80)
Jaundice	10.55 (6.93, NE)	6.47 (5.55, NE)	0.76 (0.55, 1.07)
Pain (QLQ-C30)	9.72 (7.16, NE)	2.79 (2.14, 4.30)	0.46 (0.34, 0.62)
Pain (QLQ-HCC18)	NE	9.82 (4.27, NE)	0.65 (0.46, 0.92)



Conclusions

- **In patients with unresectable HCC, atezolizumab + bevacizumab provided benefits in all PROs including QoL, functioning and key symptoms compared with sorafenib**

[a]Exploratory endpoint

Galle PR, et al. J Clin Oncol 2020;38(suppl):abstr 476

478: Nivolumab (NIVO) + ipilimumab (IPI) + cabozantinib (CABO) combination therapy in patients (pts) with advanced hepatocellular carcinoma (aHCC): Results from CheckMate 040 – Yau T, et al

Study objective

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

Key patient inclusion criteria

- Advanced HCC
- Sorafenib naïve or progression after or intolerant to sorafenib
- Child-Pugh A5 or A6
- HBV, HCV or non-viral HCC
- ECOG PS 0–1

(n=71)

R 1:1

Triplet arm
Nivolumab 3 mg/kg q2w + cabozantinib 40 mg/day po + ipilimumab 1 mg/kg q6w (n=35)

Doublet arm
Nivolumab 240 mg q2w + cabozantinib 40 mg/day po (n=36)

PD/ toxicity

PD/ toxicity

PRIMARY ENDPOINTS

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

SECONDARY ENDPOINTS

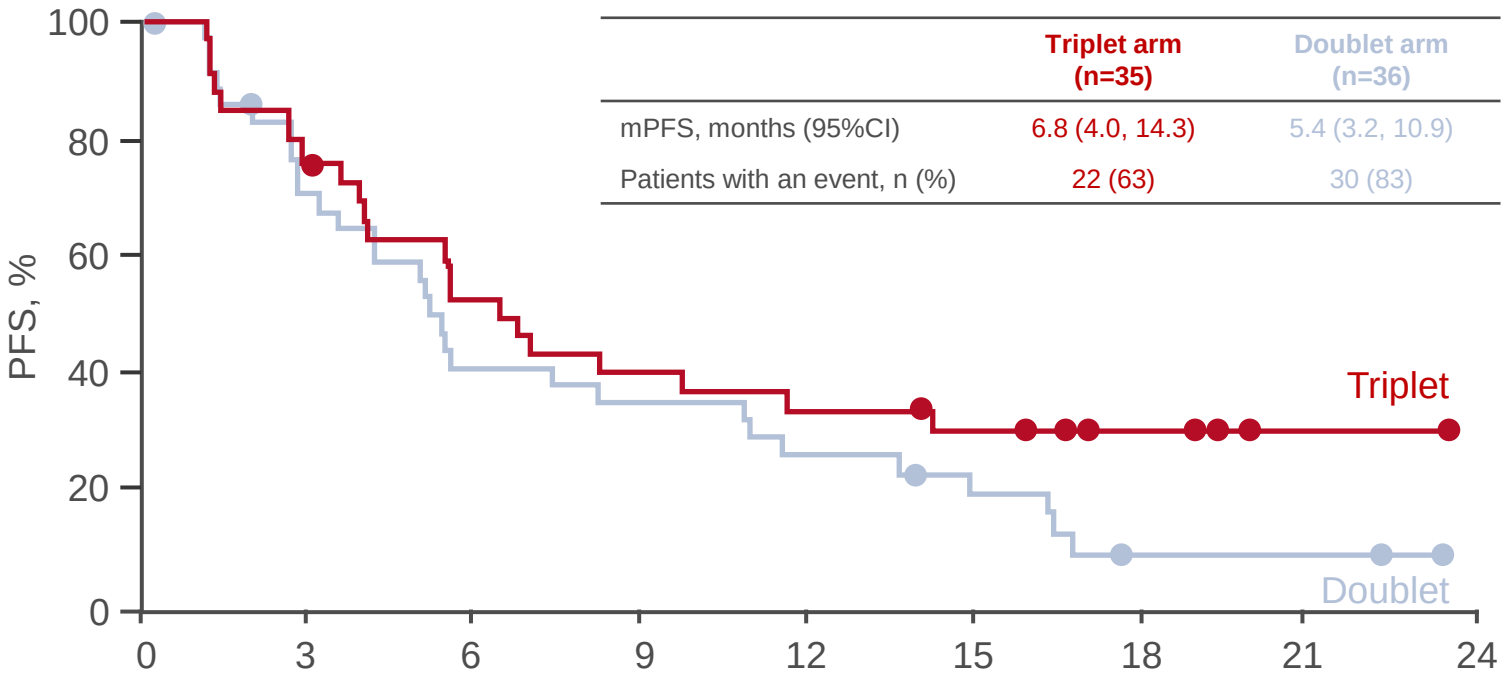
- DCR, DoR, TTR, TTP, PFS, OS

Yao T, et al. J Clin Oncol 2020;38(suppl):abstr 478

478: Nivolumab (NIVO) + ipilimumab (IPI) + cabozantinib (CABO) combination therapy in patients (pts) with advanced hepatocellular carcinoma (aHCC): Results from CheckMate 040 – Yau T, et al

Key results

PFS (investigator assessed)



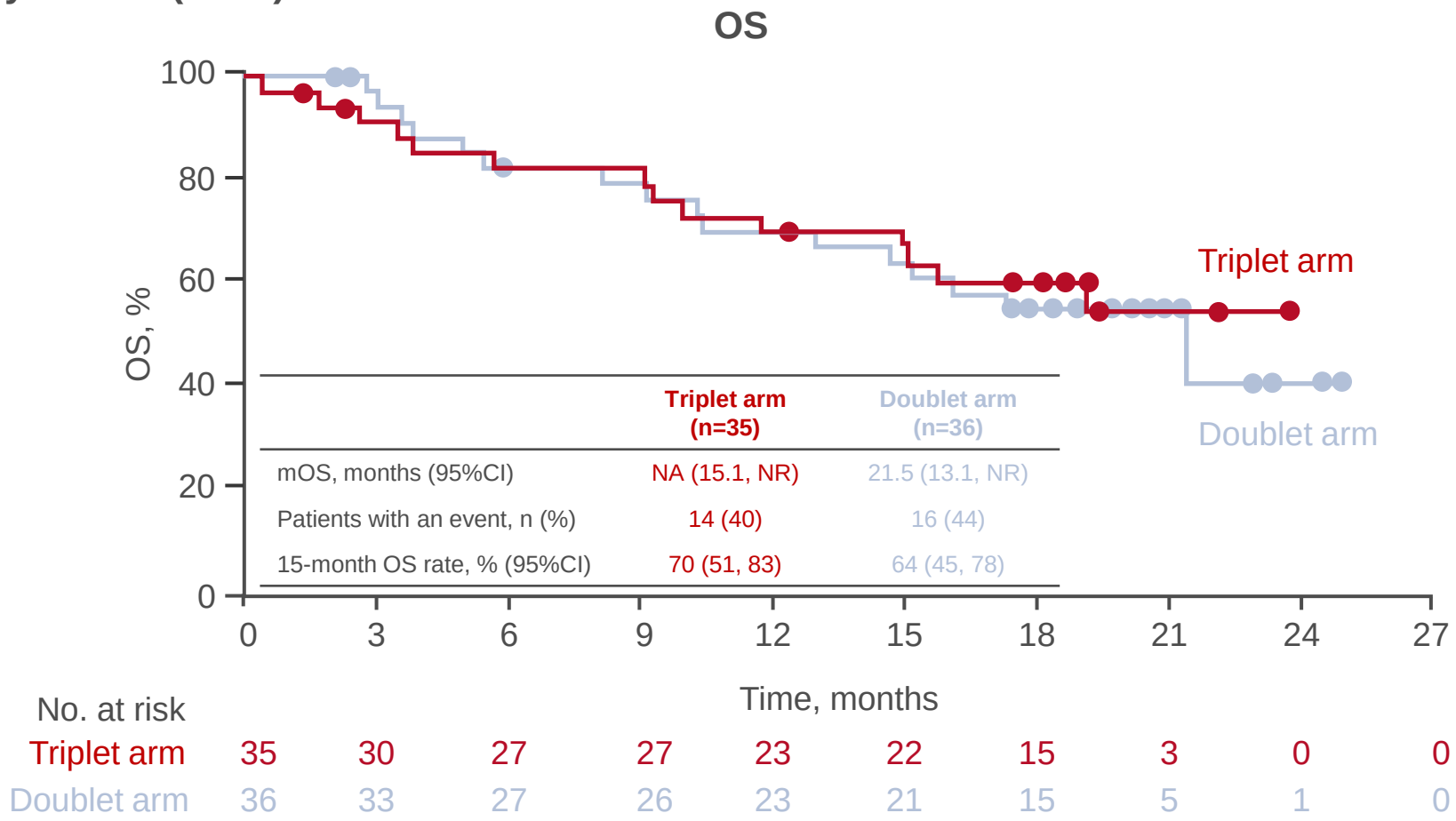
	Triplet arm (n=35)	Doublet arm (n=36)
mPFS, months (95%CI)	6.8 (4.0, 14.3)	5.4 (3.2, 10.9)
Patients with an event, n (%)	22 (63)	30 (83)

No. at risk									
Triplet arm	35	25	17	13	11	9	5	1	0
Doublet arm	36	24	14	12	9	6	2	2	0

Yao T, et al. J Clin Oncol 2020;38(suppl):abstr 478

478: Nivolumab (NIVO) + ipilimumab (IPI) + cabozantinib (CABO) combination therapy in patients (pts) with advanced hepatocellular carcinoma (aHCC): Results from CheckMate 040 – Yau T, et al

Key results (cont.)



Yao T, et al. J Clin Oncol 2020;38(suppl):abstr 478

478: Nivolumab (NIVO) + ipilimumab (IPI) + cabozantinib (CABO) combination therapy in patients (pts) with advanced hepatocellular carcinoma (aHCC): Results from CheckMate 040 – Yau T, et al

Key results (cont.)

Grade 3–4 TRAEs occurring in ≥5%, n (%)	Triplet arm (n=35)	Doublet arm (n=36)
Any	25 (71)	17 (47)
Diarrhea	1 (3)	4 (11)
Palmar-plantar erythrodysesthesia syndrome	3 (9)	1 (3)
Hypertension	6 (17)	4 (11)
AST increased	8 (23)	3 (8)
ALT increased	6 (17)	1 (3)
Lipase increased	6 (17)	2 (6)

Conclusions

- **In patients with advanced HCC, nivolumab + cabozantinib with or without ipilimumab demonstrated encouraging antitumor activity and there were no new safety signals**

Yao T, et al. J Clin Oncol 2020;38(suppl):abstr 478

Cancers of the pancreas, small bowel and hepatobiliary tract

BILIARY TRACT CANCER

477: Ramucirumab (RAM) or merestinib (MER) or placebo (PL) plus gemcitabine (GEM) and cisplatin (CIS) as first-line treatment for advanced or metastatic biliary tract cancer (BTC): A randomized, double-blind, phase II study – Valle JW, et al

Study objective

- To evaluate the efficacy and safety of ramucirumab or merestinib as 1L treatment for patients with advanced or metastatic biliary tract cancer

Key patient inclusion criteria

- Locally advanced or metastatic biliary tract adenocarcinoma*
- Treatment naïve
- ECOG PS 0–1

(n=309)

R 1:1

Arm A iv

R 2:1

- Arm A1: Ramucirumab† + gemcitabine + cisplatin# (n=106) → PD/ other
- Arm A2: Placebo + gemcitabine + cisplatin# (n=52) → PD/ other

Stratification

- Region
- Pathologic diagnosis
- Metastatic disease

Arm B po

R 2:1

- Arm B1: Merestinib‡ + gemcitabine + cisplatin# (n=102) → PD/ other
- Arm B2: Placebo + gemcitabine + cisplatin# (n=49) → PD/ other

PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

- OS, ORR, safety

*Intrahepatic or extrahepatic cholangiocarcinoma, gallbladder cancer or Ampulla of Vater; †8 mg iv D1, 8 q3w; ‡80 mg po; #gemcitabine 1000 mg/m^2 + cisplatin 25 mg/m^2 D1, 8 q3w

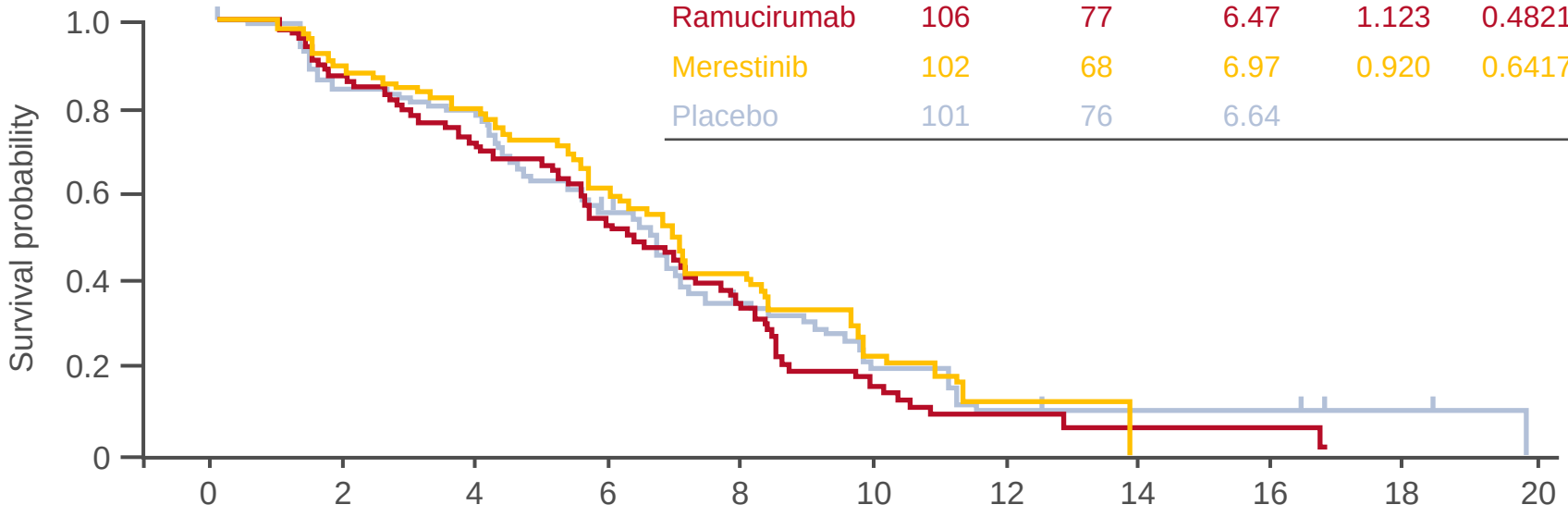
Valle JW, et al. J Clin Oncol 2020;38(suppl):abstr 477

477: Ramucirumab (RAM) or merestinib (MER) or placebo (PL) plus gemcitabine (GEM) and cisplatin (CIS) as first-line treatment for advanced or metastatic biliary tract cancer (BTC): A randomized, double-blind, phase II study – Valle JW, et al

Key results

PFS

	Patients, n	Events, n	mPFS, months	HR	p-value
Ramucirumab	106	77	6.47	1.123	0.4821
Merestinib	102	68	6.97	0.920	0.6417
Placebo	101	76	6.64		



No. at risk											
Ramucirumab	106	87	68	46	27	10	6	2	2	0	0
Merestinib	102	84	72	48	29	12	4	0	0	0	0
Placebo	101	80	73	50	24	13	6	4	4	2	0

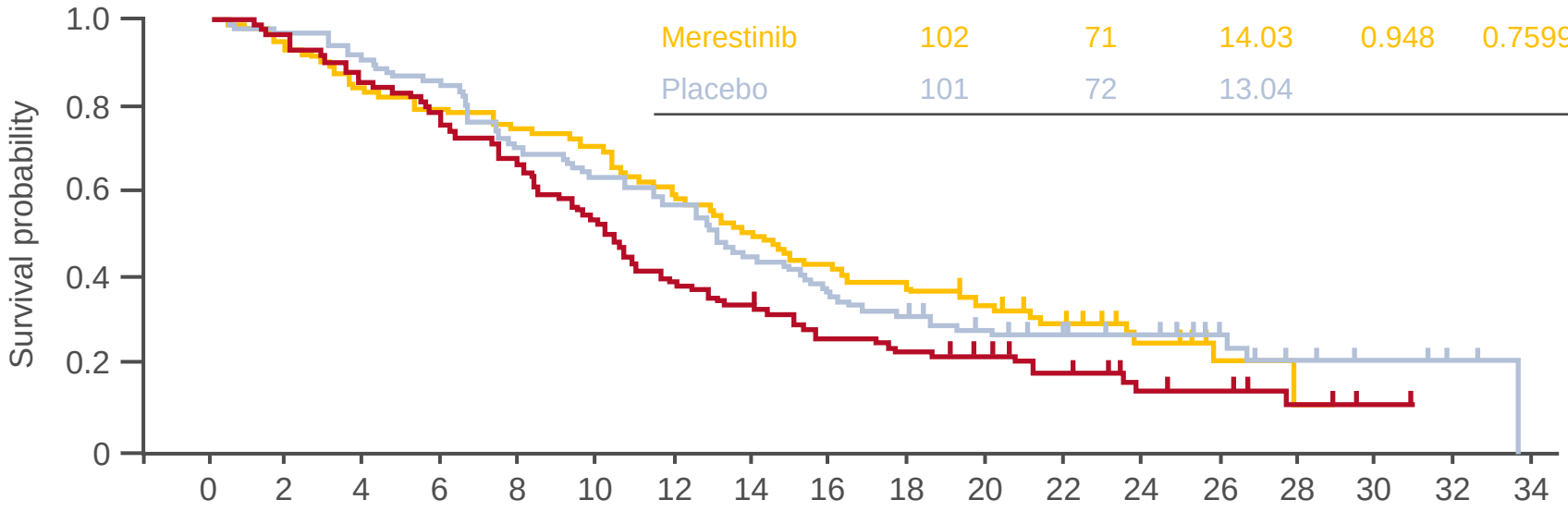
Valle JW, et al. J Clin Oncol 2020;38(suppl):abstr 477

477: Ramucirumab (RAM) or merestinib (MER) or placebo (PL) plus gemcitabine (GEM) and cisplatin (CIS) as first-line treatment for advanced or metastatic biliary tract cancer (BTC): A randomized, double-blind, phase II study – Valle JW, et al

Key results (cont.)

OS

	Patients, n	Events, n	mOS, months	HR	p-value
Ramucirumab	106	84	10.45	1.336	0.0870
Merestinib	102	71	14.03	0.948	0.7599
Placebo	101	72	13.04		



No. at risk																		
Ramucirumab	106	101	89	78	67	52	39	33	25	22	18	13	8	6	3	1	0	0
Merestinib	102	92	83	76	71	67	56	47	40	35	28	19	11	5	1	0	0	0
Placebo	101	95	89	81	65	59	53	42	34	27	22	19	14	10	6	4	2	0

Valle JW, et al. J Clin Oncol 2020;38(suppl):abstr 477

477: Ramucirumab (RAM) or merestinib (MER) or placebo (PL) plus gemcitabine (GEM) and cisplatin (CIS) as first-line treatment for advanced or metastatic biliary tract cancer (BTC): A randomized, double-blind, phase II study – Valle JW, et al

Key results (cont.)

	Ramucirumab (n=106)	Merestinib (n=102)	Pooled placebo (n=101)
BOR, n (%) [95%CI]			
CR	0 (0) [NA]	3 (2.9) [0.0, 6.2]	2 (2.0) [0.0, 4.7]
PR	33 (31.1) [22.3, 39.9]	17 (16.7) [9.4, 23.9]	31 (30.7) [21.7, 39.7]
SD	53 (50.0) [40.5, 59.5]	65 (63.7) [54.4, 73.1]	46 (45.5) [35.8, 55.3]
PD	13 (12.3) [6.0, 18.5]	9 (8.8) [3.3, 14.3]	26 (25.8) [8.7, 23.0]
NE	7 (6.6) [1.9, 11.3]	8 (7.8) [2.6, 13.1]	6 (5.9) [1.3, 10.6]
ORR (CR/PR), n (%) [95%CI]	33 (31.1) [22.3, 39.9]	20 (19.6) [11.9, 27.3]	33 (32.7) [23.5, 41.8]
OR vs. placebo (95%CI); p-value	1.0 (0.6, 1.9); 0.8779	0.5 (0.2, 0.9); 0.0235	-
DCR (CR/PR/SD), n (%) [95%CI]	86 (81.1) [73.7, 88.6]	85 (83.3) [76.1, 90.6]	79 (78.2) [70.2, 86.3]
OR vs. placebo (95%CI); p-value	1.2 (0.6, 2.4); 0.6809	1.3 (0.6, 2.6); 0.4996	-

Valle JW, et al. J Clin Oncol 2020;38(suppl):abstr 477

477: Ramucirumab (RAM) or merestinib (MER) or placebo (PL) plus gemcitabine (GEM) and cisplatin (CIS) as first-line treatment for advanced or metastatic biliary tract cancer (BTC): A randomized, double-blind, phase II study – Valle JW, et al

Key results (cont.)

Grade ≥3 TEAEs occurring in ≥10%, n (%)	Ramucirumab (n=104)	Merestinib (n=102)	Pooled placebo (n=100)
Any	90 (86.5)	87 (85.3)	81 (81.0)
Neutropenia	51 (49.0)	48 (47.1)	33 (33.0)
Fatigue	11 (10.6)	10 (9.8)	5 (5.0)
Thrombocytopenia	36 (34.6)	19 (18.6)	17 (17.0)
Anemia	28 (26.9)	16 (15.7)	19 (19.0)
ALT increased	5 (4.8)	11 (10.8)	5 (5.0)
Hypertension	17 (16.3)	4 (3.9)	1 (1.0)

Conclusions

- **In patients with locally advanced or metastatic biliary tract cancer, neither ramucirumab nor merestinib provided any additional survival benefit when added to gemcitabine + cisplatin**
- **All treatments were generally well-tolerated and consistent with their individual known safety profiles**

Valle JW, et al. J Clin Oncol 2020;38(suppl):abstr 477

Cancers of the pancreas, small bowel and hepatobiliary tract

NEUROENDOCRINE TUMOUR

604: First results for Australasian Gastrointestinal Trials Group (AGITG) control net study: Phase II study of ^{177}Lu-octreotate peptide receptor radionuclide therapy (LuTate PRRT) +/- capecitabine, temozolomide (CAPTEM) for midgut neuroendocrine tumors (mNETs) – Pavlakis N, et al

Study objective

- To evaluate the efficacy and safety of ^{177}Lu-octreotate peptide receptor radionuclide therapy (PRRT) alone or combined with capecitabine + temozolomide (CAPTEM) in patients with midgut NETs (mNETs)

Key patient inclusion criteria

- Unresectable grade 1/2 midgut NETs
- Ki-67 ≤20%
- Progression on or after ≤2 prior systemic therapies
- ECOG PS 0–2

(n=45)

R 2:1

PRRT + CAPTEM
^{177}Lu-octreotate* + CAPTEM†
(n=18 pancreatic NETs; n=30 mNETs)

→ Up to 4 cycles/ toxicity

Stratification

- Previous systemic therapy (≤1 vs. 2)
- WHO tumor grade (1 low [Ki-67 ≤2% and/or mitotic count <2] vs. 2 intermediate [Ki-67 3–20% and/or mitotic count 2–20])
- Visceral only vs. visceral with bone metastases
- Institution

PRRT
^{177}Lu-octreotate*
(n=15)

→ Up to 4 cycles/ toxicity

PRIMARY ENDPOINT

- PFS at 15 months†

SECONDARY ENDPOINTS

- ORR, OS, safety

*^{177}Lu-octreotate 7.8 GBq D1 q8w; †capecitabine 750 mg/m^2 bid D1–14 + temozolomide 75 mg/m^2 bid D10–14 q4w; †original analysis plan was PFS at 24 months (amended due to funding)

Pavlakis N, et al. J Clin Oncol 2020;38(suppl):abstr 604

604: First results for Australasian Gastrointestinal Trials Group (AGITG) control net study: Phase II study of ^{177}Lu-octreotate peptide receptor radionuclide therapy (LuTate PRRT) +/- capecitabine, temozolomide (CAPTEM) for midgut neuroendocrine tumors (mNETs) – Pavlakis N, et al

Key results

Outcome	PRRT + CAPTEM (n=32)	PRRT (n=13)
15-month PFS rate, % (95%CI)	90.2 (72.7, 96.8)	92.3 (56.6, 98.9)
Difference, % (95%CI)	2.1 (-15.8, 19.9)	
BOR, n (%)		
CR	0 (0)	0 (0)
PR	8 (25)	2 (15)
SD	23 (72)	10 (77)
PD	0 (0)	1 (8)
Early withdrawal	1 (3)	0 (0)

Pavlakis N, et al. J Clin Oncol 2020;38(suppl):abstr 604

604: First results for Australasian Gastrointestinal Trials Group (AGITG) control net study: Phase II study of ^{177}Lu-octreotate peptide receptor radionuclide therapy (LuTate PRRT) +/- capecitabine, temozolomide (CAPTEM) for midgut neuroendocrine tumors (mNETs) – Pavlakis N, et al

Key results (cont.)

Outcome	PRRT + CAPTEM (n=32)	PRRT (n=13)
ORR (CR/PR), n (%)		
ITT population	8 (25.0)	2 (15.4)
Difference, % (95%CI)	9.6 (-15.0, 34.3)	
Excluding unknown/early withdrawals*	8 (25.8)	2 (15.4)
Difference, % (95%CI)	10.4 (-15.0, 35.4)	
CBR (CR/PR/SD), n (%)		
ITT population	31 (96.9)	12 (92.3)
Difference, % (95%CI)	4.6 (-11.0, 20.3)	
Excluding unknown/early withdrawals*	31 (100)	12 (92.3)
Difference, % (95%CI)	7.7 (-6.8, 22.2)	

*Due to toxicity, drug intolerance or treatment-related death

Pavlakis N, et al. J Clin Oncol 2020;38(suppl):abstr 604

604: First results for Australasian Gastrointestinal Trials Group (AGITG) control net study: Phase II study of ^{177}Lu-octreotate peptide receptor radionuclide therapy (LuTate PRRT) +/- capecitabine, temozolomide (CAPTEM) for midgut neuroendocrine tumors (mNETs) – Pavlakis N, et al

Key results (cont.)

Grade 3–4 AEs occurring in ≥10%, n (%)	PRRT + CAPTEM (n=32)	PRRT (n=13)
Neutrophil count decreased	6 (19)	0 (0)
Platelet count decreased	8 (25)	1 (8)
White blood cell decreased	5 (16)	0 (0)
Lymphocyte count decreased	18 (56)	4 (31)

Conclusions

- **In patients with midgut NETs, PRRT with or without CAPTEM demonstrated encouraging PFS rates at 15 months, although there were higher rates of grade 3–4 toxicity, particularly hematologic disorders, in the combination arm**

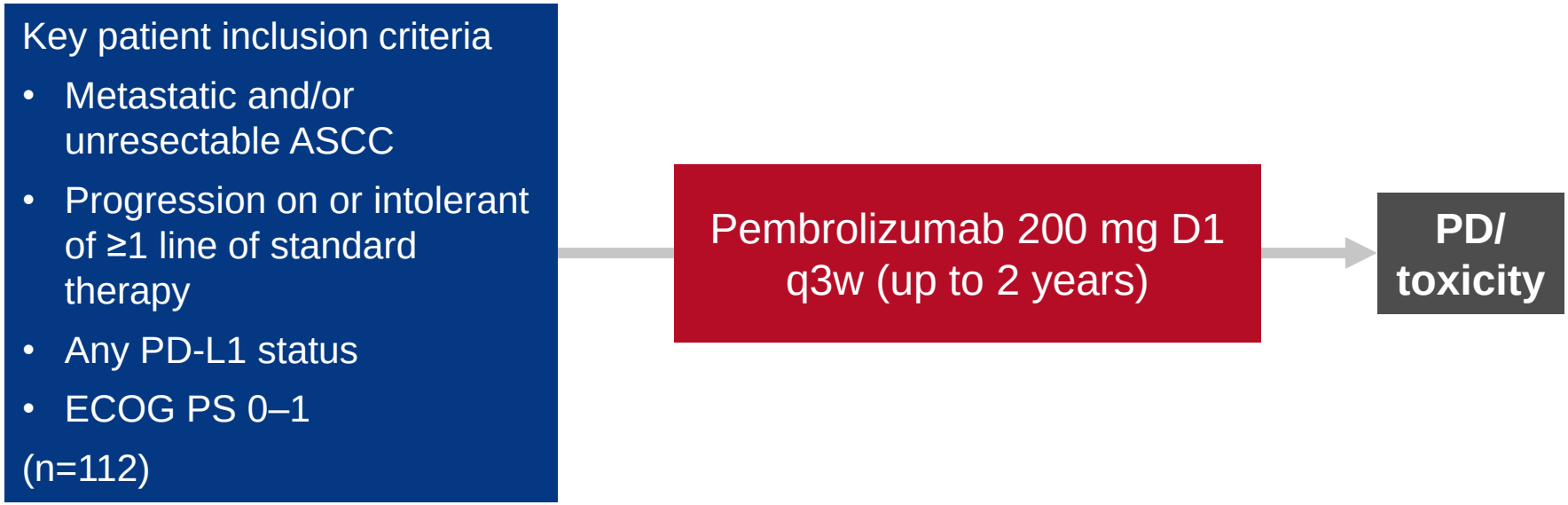
Pavlakis N, et al. J Clin Oncol 2020;38(suppl):abstr 604

CANCERS OF THE COLON, RECTUM AND ANUS

1: Pembrolizumab for advanced anal squamous cell carcinoma (ASCC): Results from the multicohort, phase II KEYNOTE-158 study – Marabelle A, et al

Study objective

- To evaluate the efficacy and safety of pembrolizumab in a cohort of patients with advanced ASCC



PRIMARY ENDPOINT

- ORR (RECIST v1.1, central review)

SECONDARY ENDPOINTS

- DoR, OS, PFS, safety

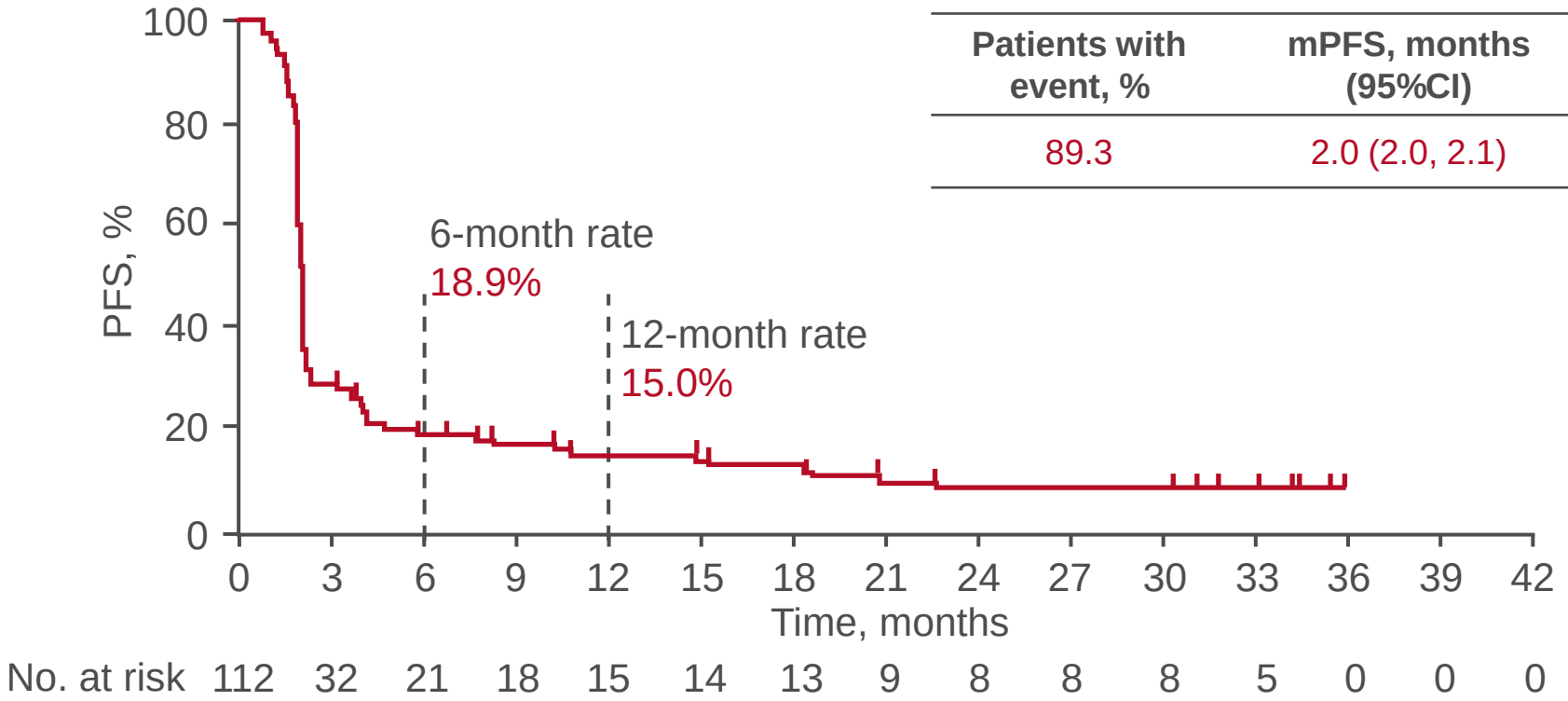
Marabelle A, et al. J Clin Oncol 2020;38(suppl):abstr 1

1: Pembrolizumab for advanced anal squamous cell carcinoma (ASCC): Results from the multicohort, phase II KEYNOTE-158 study – Marabelle A, et al

Key results

- ORR was 10.7% (95%CI 5.7, 18.0) in total population and 14.7% (95%CI 7.6, 24.7) in PD-L1-positive (n=75) and 3.3% (95%CI 0.1, 17.2) in PD-L1 negative (n=30) populations

PFS (central review)

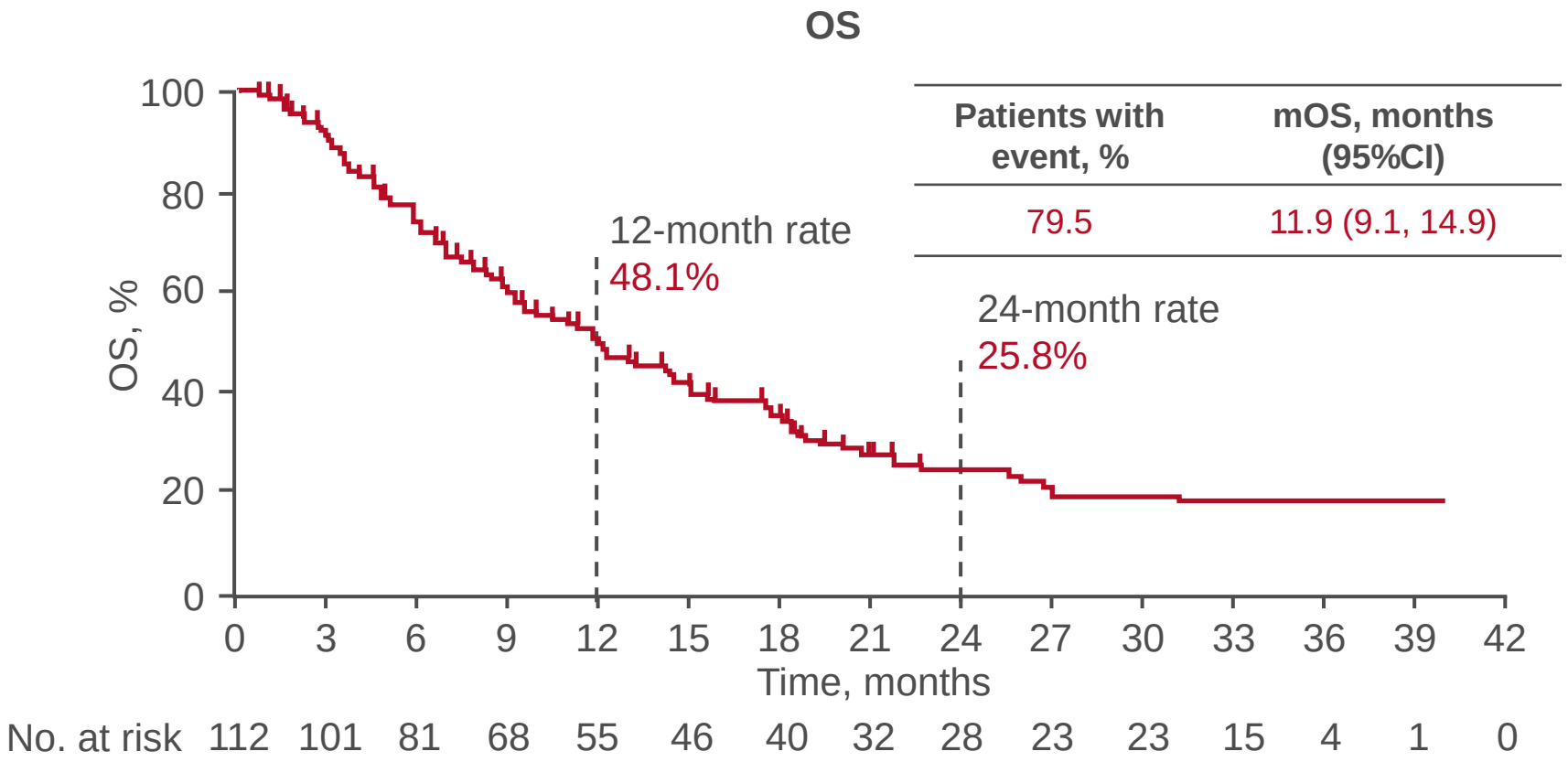


Patients with event, %	mPFS, months (95%CI)
89.3	2.0 (2.0, 2.1)

Marabelle A, et al. J Clin Oncol 2020;38(suppl):abstr 1

1: Pembrolizumab for advanced anal squamous cell carcinoma (ASCC): Results from the multicohort, phase II KEYNOTE-158 study – Marabelle A, et al

Key results (cont.)



Patients with event, %	mOS, months (95%CI)
79.5	11.9 (9.1, 14.9)

Marabelle A, et al. J Clin Oncol 2020;38(suppl):abstr 1

1: Pembrolizumab for advanced anal squamous cell carcinoma (ASCC): Results from the multicohort, phase II KEYNOTE-158 study – Marabelle A, et al

Key results (cont.)

AEs, n (%)	All patients (n=112)
Any TRAE	68 (60.7)
Grade 3–4	20 (17.9)
Led to treatment discontinuation	5 (4.5)
Any immune-mediated AE or infusion reaction	26 (23.2)
Grade 3–4	5 (4.5)
Led to treatment discontinuation	3 (2.7)

Conclusions

- **In patients with ASCC regardless of PD-L1 status, pembrolizumab showed promising antitumor activity, OS and durable response along with a manageable safety profile**

Marabelle A, et al. J Clin Oncol 2020;38(suppl):abstr 1

7: A randomized phase III trial comparing primary tumor resection plus chemotherapy with chemotherapy alone in incurable stage IV colorectal cancer: JCOG1007 study (iPACS) – Kanemitsu Y, et al

Study objective

- To evaluate the efficacy and safety of primary tumor resection + chemotherapy compared with chemotherapy alone in patients with asymptomatic unresectable stage IV CRC

Key patient inclusion criteria

- Unresectable stage IV CRC
- Asymptomatic
- Presence of ≤3 synchronous unresectable metastatic disease
- No prior chemotherapy or radiotherapy
- ECOG PS 0–1

(n=160‡)

R 1:1

Primary tumor resection* followed by chemotherapy† after 8–56 days (n=78) → **PD/ toxicity**

Stratification

- Institute
- Location of primary tumor
- ECOG PS
- Sex

Chemotherapy† (n=82) → **PD/ toxicity**

PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, R0 resection rate, safety

*Open or laparoscopic colectomy/high anterior resection with D1-D3 lymph node dissection; †bevacizumab with either mFOLFOX6 or capecitabine + oxaliplatin; ‡original sample size was for 770 patients and study terminated early after futility analysis

Kanemitsu Y, et al. J Clin Oncol 2020;38(suppl):abstr 7

7: A randomized phase III trial comparing primary tumor resection plus chemotherapy with chemotherapy alone in incurable stage IV colorectal cancer: JCOG1007 study (iPACS) – Kanemitsu Y, et al

Key results

Baseline characteristics		PTR + chemo (n=82)	Chemotherapy (n=78)
Median age, years (range)		65 (29–74)	65 (44–74)
Male, n (%)		44 (54)	43 (55)
Tumor location, n (%)	Colon Upper rectum	76 (93) 6 (7)	72 (92) 6 (8)
ECOG PS, n (%)	0 1	75 (91) 7 (9)	70 (92) 6 (8)
Unresectable factors, n (%)	Liver Lung Distant lymph node Peritoneum	58 (71) 17 (21) 23 (28) 4 (5)	57 (73) 20 (26) 15 (19) 6 (8)
Depth of primary tumor, n (%)	cT2 cT3 cT4a	3 (4) 41 (50) 38 (46)	2 (3) 43 (55) 33 (42)

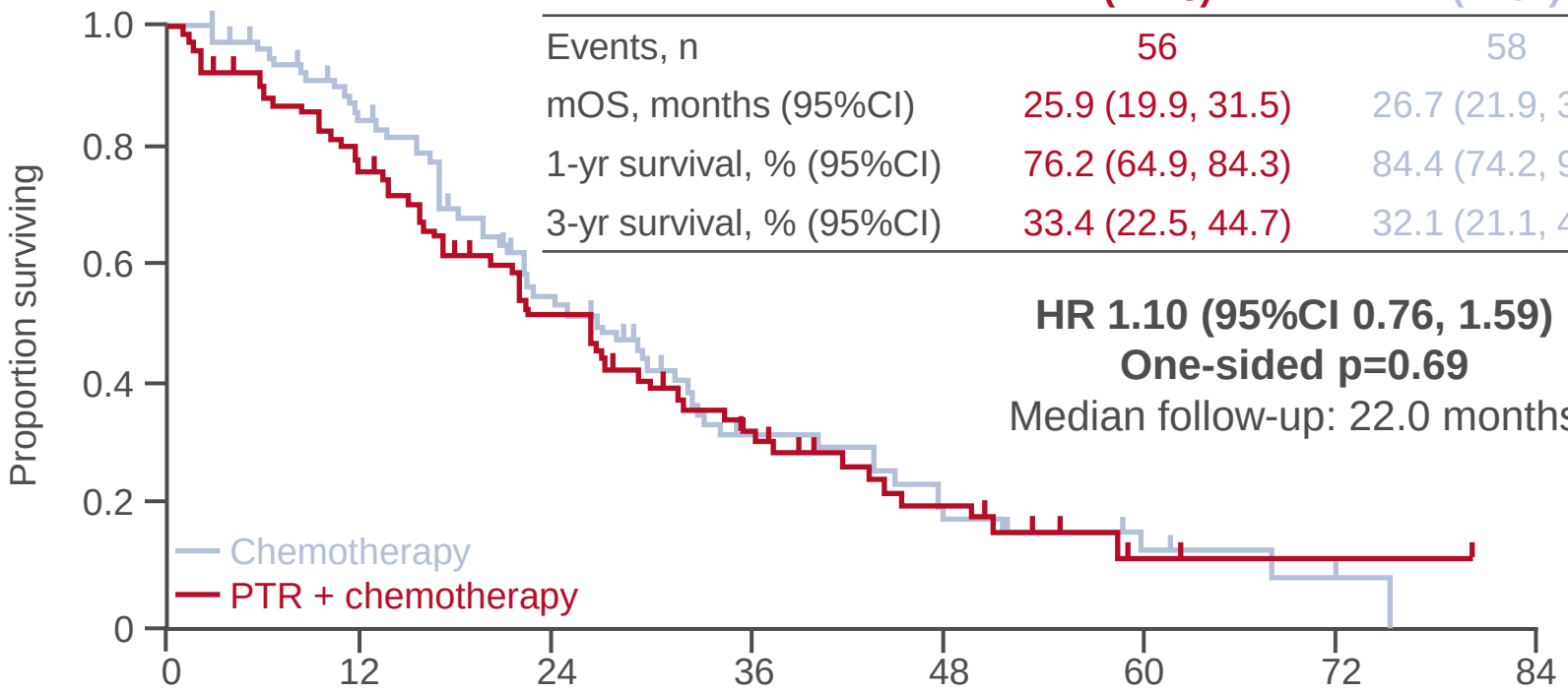
Kanemitsu Y, et al. J Clin Oncol 2020;38(suppl):abstr 7

7: A randomized phase III trial comparing primary tumor resection plus chemotherapy with chemotherapy alone in incurable stage IV colorectal cancer: JCOG1007 study (iPACS) – Kanemitsu Y, et al

Key results (cont.)

OS (ITT)

	PTR + chemo (n=78)	Chemo (n=82)
Events, n	56	58
mOS, months (95%CI)	25.9 (19.9, 31.5)	26.7 (21.9, 32.5)
1-yr survival, % (95%CI)	76.2 (64.9, 84.3)	84.4 (74.2, 90.8)
3-yr survival, % (95%CI)	33.4 (22.5, 44.7)	32.1 (21.1, 43.6)



HR 1.10 (95%CI 0.76, 1.59)
One-sided p=0.69
Median follow-up: 22.0 months

No. at risk (censored)								
PTR + chemo	78 (0)	56 (4)	35 (4)	19 (4)	10 (3)	2 (5)	1 (1)	0 (1)
Chemo	82 (0)	63 (7)	36 (5)	17 (6)	9 (1)	4 (3)	1 (2)	0 (0)

Kanemitsu Y, et al. J Clin Oncol 2020;38(suppl):abstr 7

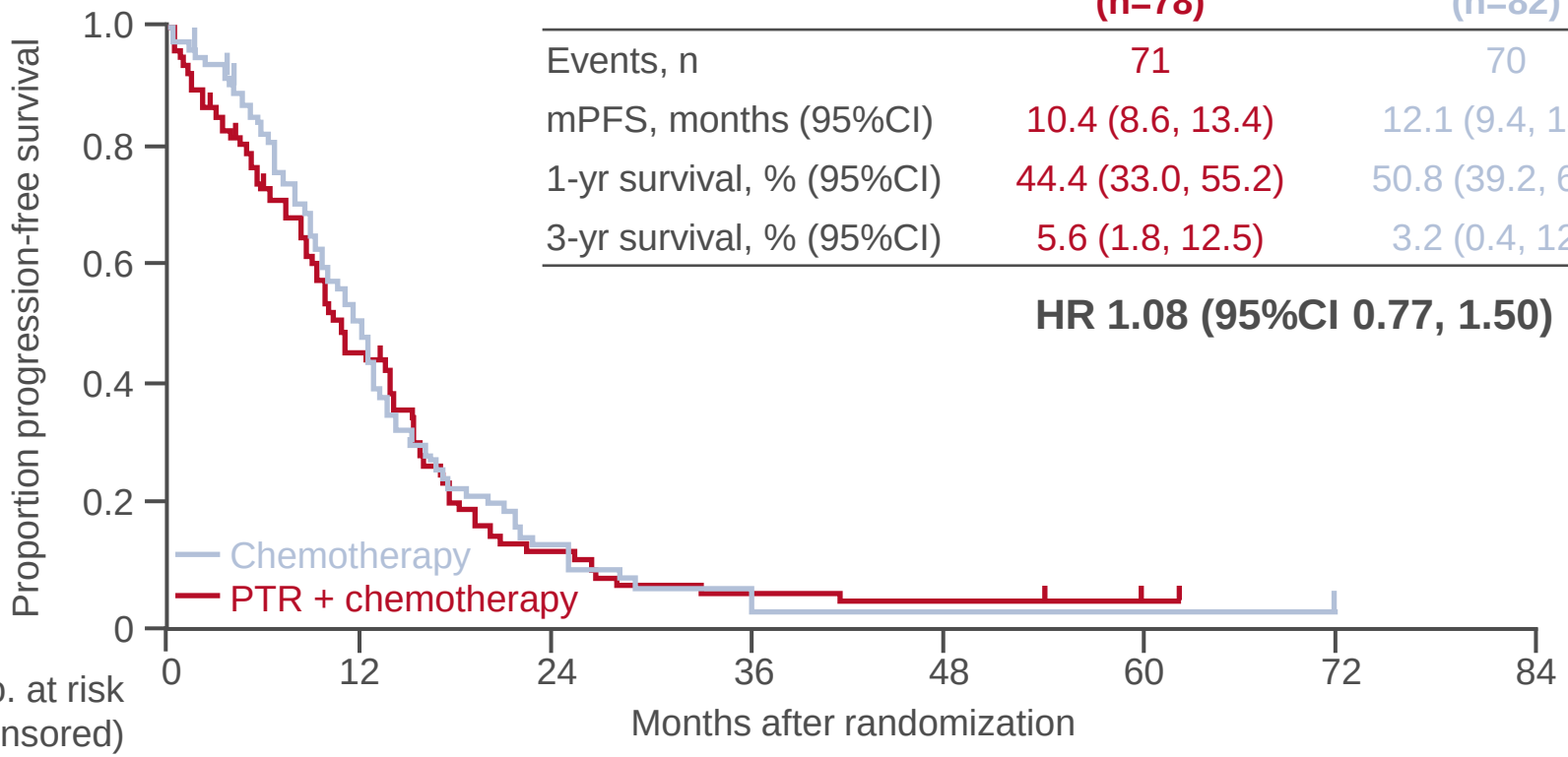
7: A randomized phase III trial comparing primary tumor resection plus chemotherapy with chemotherapy alone in incurable stage IV colorectal cancer: JCOG1007 study (iPACS) – Kanemitsu Y, et al

Key results (cont.)

PFS (ITT)

	PTR + chemo (n=78)	Chemo (n=82)
Events, n	71	70
mPFS, months (95%CI)	10.4 (8.6, 13.4)	12.1 (9.4, 13.2)
1-yr survival, % (95%CI)	44.4 (33.0, 55.2)	50.8 (39.2, 61.3)
3-yr survival, % (95%CI)	5.6 (1.8, 12.5)	3.2 (0.4, 12.0)

HR 1.08 (95%CI 0.77, 1.50)



No. at risk (censored)							
PTR + chemo 78 (0)	33 (3)	9 (1)	4 (0)	3 (0)	1 (2)	0 (1)	0 (0)
Chemo 82 (0)	37 (7)	8 (2)	1 (2)	1 (0)	1 (0)	0 (1)	0 (0)

Kanemitsu Y, et al. J Clin Oncol 2020;38(suppl):abstr 7

7: A randomized phase III trial comparing primary tumor resection plus chemotherapy with chemotherapy alone in incurable stage IV colorectal cancer: JCOG1007 study (iPACS) – Kanemitsu Y, et al

Key results (cont.)

Mortality and morbidity, n (%)	PTR + chemotherapy (n=78)
Primary tumor resection performed	74 (95)
Open surgery	41 (55)
Postoperative mortality	3 (4)
Early postoperative morbidity	
Grade 2–4	28 (38)
Grade 3–4	15 (2)
Grade 4	2 (3)

Grade 3–4 AEs, n (%)	PTR + chemotherapy* (n=65)	Chemotherapy (n=77)
Leukopenia	7 (11)	8 (10)
Anemia	3 (5)	3 (4)
Neutropenia	22 (35)	27 (35)
Allergic reaction	1 (2)	1 (1)
Paresthesia	3 (5)	1 (1)
Hypertension	11 (17)	6 (8)
Nausea	1 (2)	2 (3)
Diarrhea	3 (5)	1 (1)
Neuropathy	9 (14)	7 (9)

*Two patients missing

Kanemitsu Y, et al. J Clin Oncol 2020;38(suppl):abstr 7

7: A randomized phase III trial comparing primary tumor resection plus chemotherapy with chemotherapy alone in incurable stage IV colorectal cancer: JCOG1007 study (iPACS) – Kanemitsu Y, et al

Key results (cont.)

Secondary surgery, n (%)	PTR + chemotherapy* (n=78)	Chemotherapy† (n=82)
R0 resection for responders to chemotherapy		
No	72 (92)	72 (88)
Yes	2 (3)	4 (5)
Palliative surgery		
No		65 (79)
Yes		11 (13)

Conclusions

- **In patients with asymptomatic unresectable stage IV CRC, primary tumor resection prior to chemotherapy did not provide any survival benefit and was associated with higher rates of AEs including 3 treatment-related deaths from postoperative complications**
- **Chemotherapy alone remains the standard of care in this patient population**

*Four patients missing; †six patients missing

Kanemitsu Y, et al. J Clin Oncol 2020;38(suppl):abstr 7

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

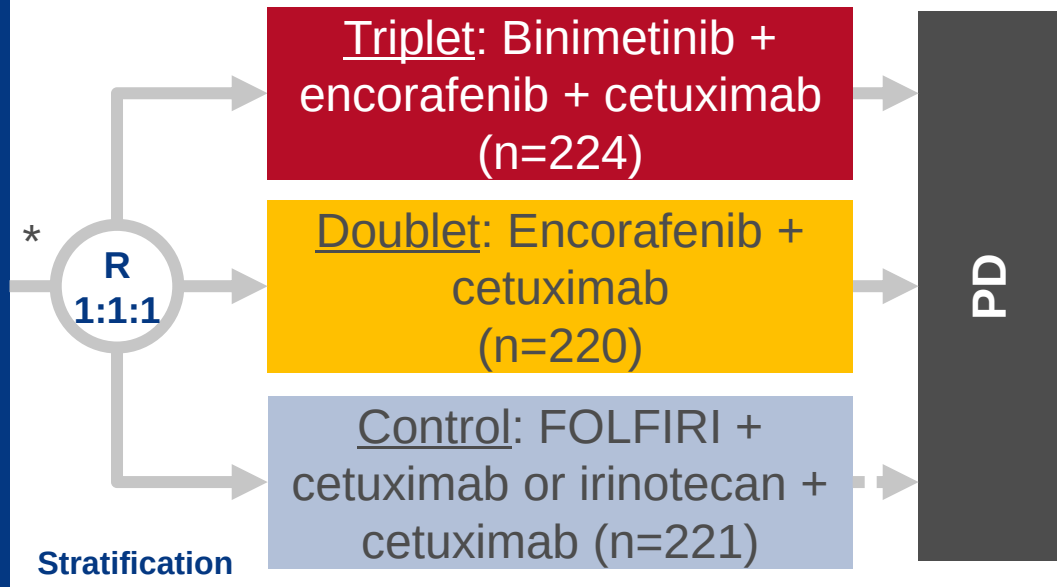
Study objective

- To evaluate the QoL of patients with BRAF V600E-mutant mCRC receiving encorafenib + cetuximab ± binimetinib

Key patient inclusion criteria

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

(n=665)



Stratification

- BRAF V600E mutation status, ECOG PS, no. of prior regimens (1/2)

CO-PRIMARY ENDPOINTS

- OS, ORR (BICR)

*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

SECONDARY ENDPOINTS

- OS, PFS, QoL (EORTC QLQ-C30, FACT-C, EQ-5D-5L, PGIC), safety

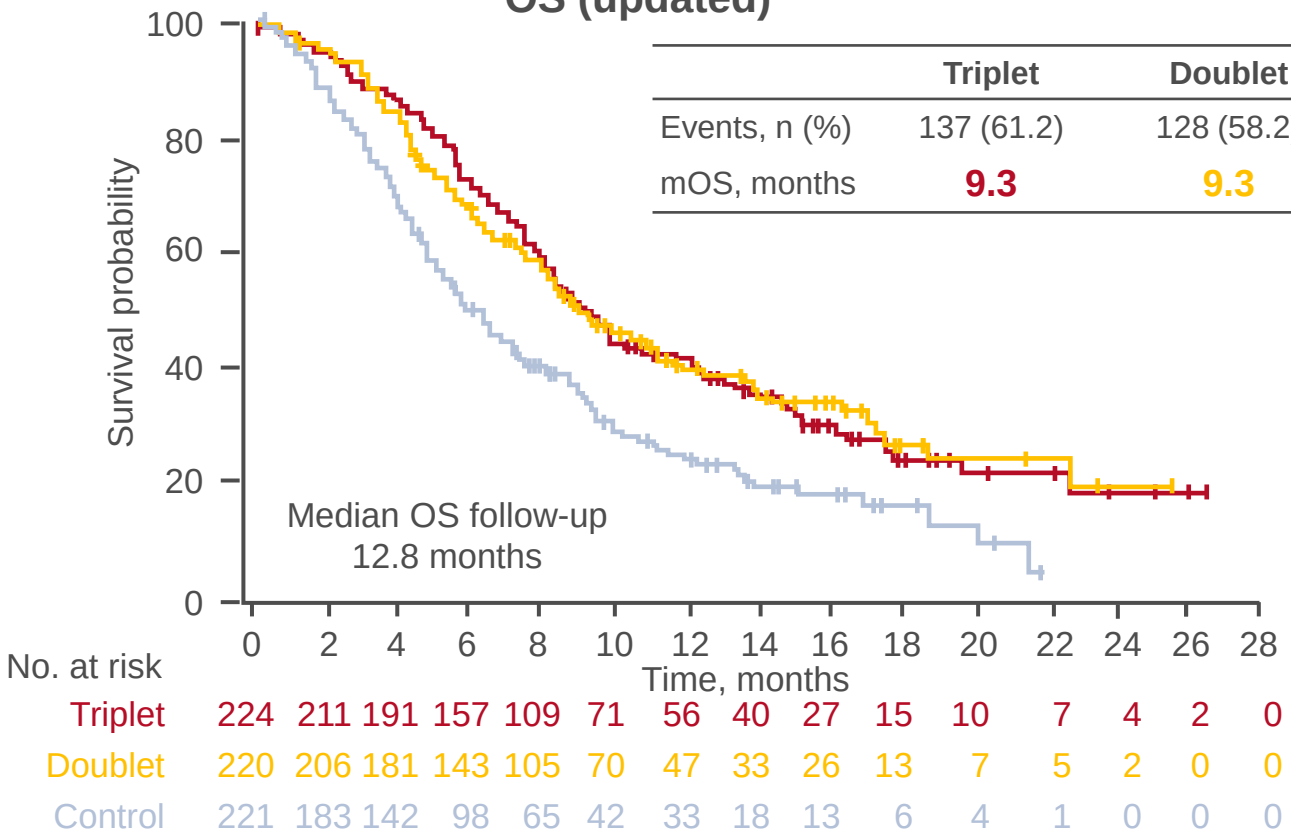
Kopetz S, et al. J Clin Oncol 2020;38(suppl):abstr 8

8: Encorafenib plus cetuximab with or without binimetinib for BRAF V600E-mutant metastatic colorectal cancer: Quality-of-life 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

OS (updated)

	Triplet	Doublet	Control
Events, n (%)	137 (61.2)	128 (58.2)	157 (71.0)
mOS, months	**9.3**	**9.3**	**5.9**



Response (BICR)	Triplet (n=224)	Doublet (n=220)	Control (n=221)
ORR, % (95%CI)	27 (21, 33)	20 (15, 25)	2 (<1, 5)
p-value vs. control	<0.001	<0.0001	

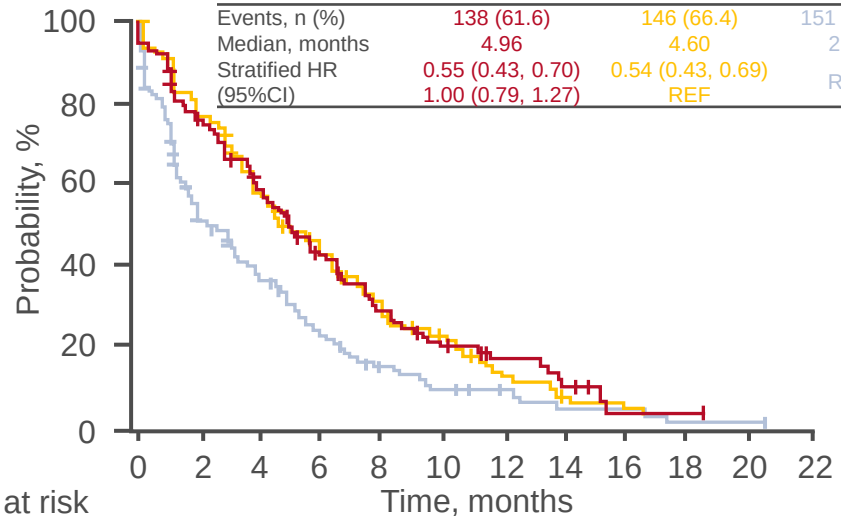
Kopetz S, et al. J Clin Oncol 2020;38(suppl):abstr 8

8: Encorafenib plus cetuximab with or without binimetinib for BRAF V600E-mutant metastatic colorectal cancer: Quality-of-life 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.)

Time to definitive deterioration in EORTC QLQ-C30 Global Health Status

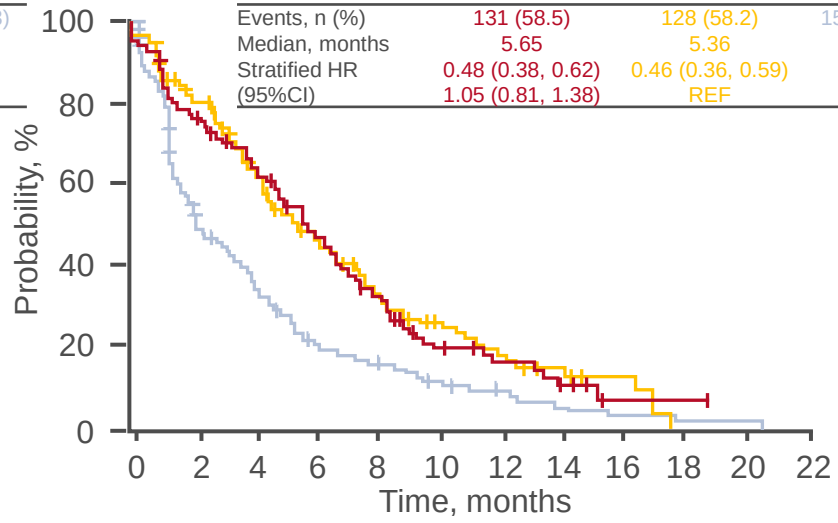
	Triplet	Doublet	Control
Events, n (%)	138 (61.6)	146 (66.4)	151 (68.3)
Median, months	4.96	4.60	2.20
Stratified HR (95%CI)	0.55 (0.43, 0.70) 1.00 (0.79, 1.27)	0.54 (0.43, 0.69) REF	REF



No. at risk												
Triplet	224	143	87	57	33	16	10	5	1	1	0	0
Doublet	220	142	90	61	35	23	11	6	3	1	1	0
Control	221	79	50	28	16	9	6	3	2	1	1	0

Time to definitive deterioration in FACT-C Colorectal Cancer Subscale

	Triplet	Doublet	Control
Events, n (%)	131 (58.5)	128 (58.2)	154 (69.7)
Median, months	5.65	5.36	2.00
Stratified HR (95%CI)	0.48 (0.38, 0.62) 1.05 (0.81, 1.38)	0.46 (0.36, 0.59) REF	REF



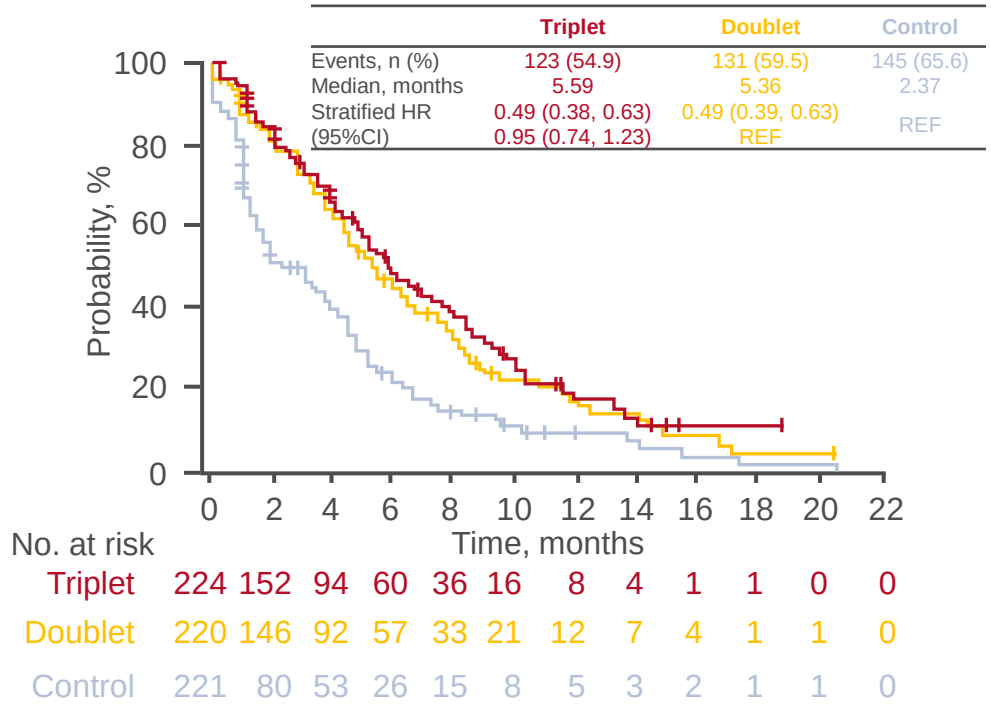
Triplet	224	148	98	61	33	16	9	5	1	1	0	0
Doublet	220	147	97	59	33	21	12	7	4	0	0	0
Control	221	82	48	25	18	10	7	3	2	1	1	0

Kopetz S, et al. J Clin Oncol 2020;38(suppl):abstr 8

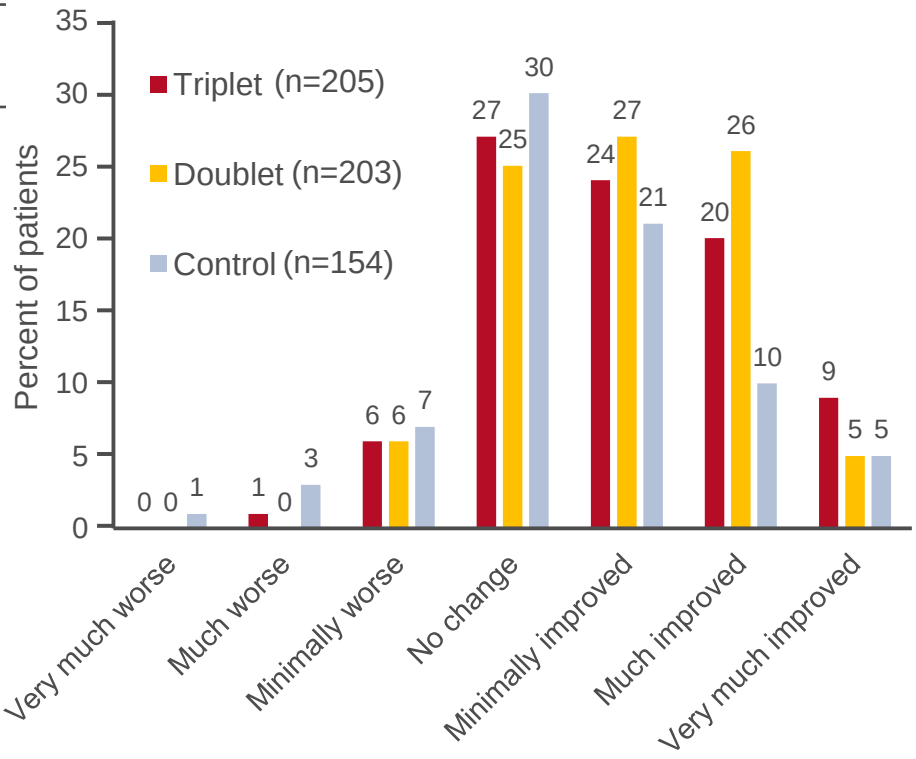
8: Encorafenib plus cetuximab with or without binimetinib for BRAF V600E-mutant metastatic colorectal cancer: Quality-of-life results from a randomized, three-arm, phase III study versus choice of either irinotecan or FOLFIRI plus cetuximab (BEACON CRC) – Kopetz S, et al

Key results (cont.)

Time to definitive deterioration in EQ-5D-5L Visual Analog Scale



Patient global impression of change – Cycle 2, Day 1



Kopetz S, et al. J Clin Oncol 2020;38(suppl):abstr 8

8: Encorafenib plus cetuximab with or without binimetinib for BRAF V600E-mutant metastatic colorectal cancer: Quality-of-life 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.)

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	3	4	5
Fatigue	2	4	5

Conclusions

- **In patients with BRAF V600E-mutant mCRC, significant improvement in survival as well as a longer maintenance of QoL was observed for encorafenib + cetuximab with or without binimetinib compared with standard of care**
- **Both the triplet and doublet regimens were well-tolerated and consistent with the known individual safety profiles**

Kopetz S, et al. J Clin Oncol 2020;38(suppl):abstr 8

11: Nivolumab plus low-dose ipilimumab as first-line therapy in microsatellite instability-high/DNA mismatch repair deficient metastatic colorectal cancer: Clinical update – Lenz H-J, et al

Study objective

- To evaluate the efficacy and safety of nivolumab + low-dose ipilimumab as a 1L treatment for patients with MSI-H/dMMR mCRC

Key patient inclusion criteria
- Recurrent or metastatic CRC
- MSI-H/dMMR
- No prior therapy for metastatic disease
- ECOG PS 0–1

(n=45)

→ Nivolumab 3 mg/kg q2w + low-dose ipilimumab 1 mg/kg q6w → **PD/ toxicity**

PRIMARY ENDPOINT

- ORR (RECIST v1.1, investigator assessed)

SECONDARY ENDPOINTS

- ORR (BICR), DCR, DoR, PFS, OS, safety

Lenz H-J, et al. J Clin Oncol 2020;38(suppl):abstr 11

11: Nivolumab plus low-dose ipilimumab as first-line therapy in microsatellite instability-high/DNA mismatch repair deficient metastatic colorectal cancer: Clinical update – Lenz H-J, et al

Key results

Outcome	Nivolumab + ipilimumab (n=45)	
	Investigator assessed	BICR assessed
ORR, n (%) [95%CI]	29 (64) [49, 78]	25 (58) [42, 72]
BOR, n (%)		
CR	4* (9)	8 (18)
PR	25 (56)	18 (40)
SD	9 (20)	10 (22)
PD	6 (13)	7 (16)
Not determined	1 (2)	2 (4)
DCR, n (%) [95%CI]	38 (84) [71, 94]	35 (78) [63, 89]
Median TTR, months (range)	2.6 (1.2–13.8)	1.6 (1.2–16.3)
Median DoR, months (range)	NR (1.4+–20.8+)	NR (3.3+–20.8+)

*One patient incorrectly reported as CR instead of PR

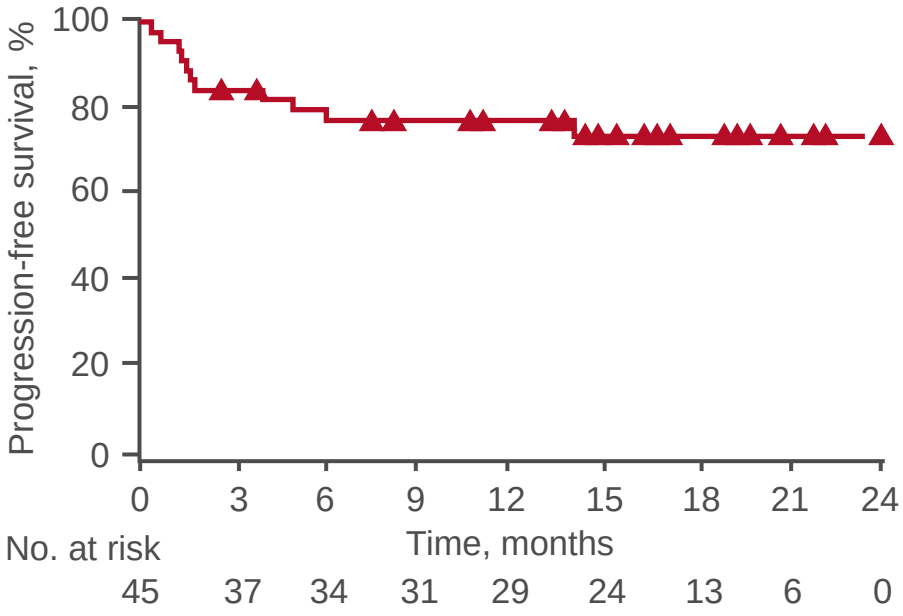
Lenz H-J, et al. J Clin Oncol 2020;38(suppl):abstr 11

11: Nivolumab plus low-dose ipilimumab as first-line therapy in microsatellite instability-high/DNA mismatch repair deficient metastatic colorectal cancer: Clinical update – Lenz H-J, et al

Key results

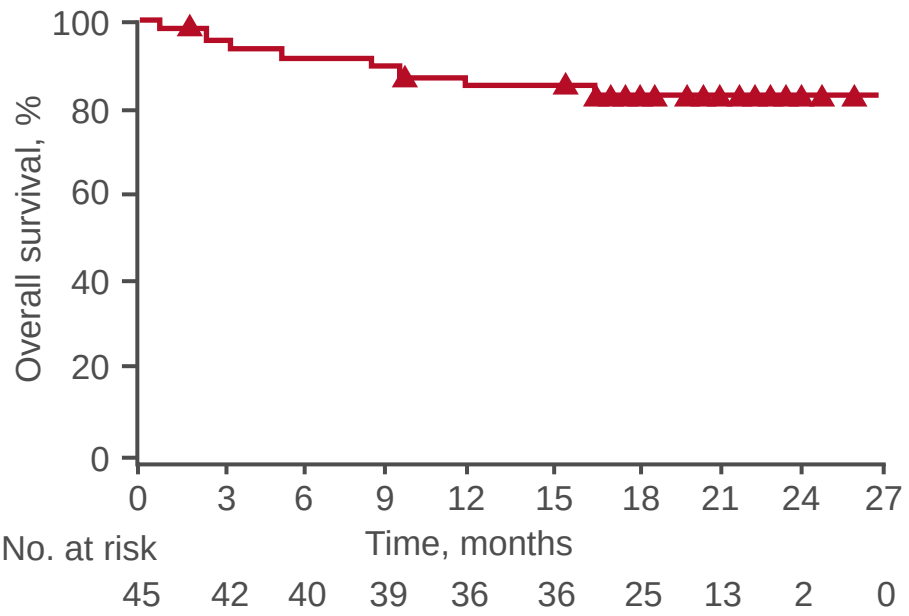
PFS*

	All patients (n=45)
mPFS, months (95%CI)	NR (NE)
12-mo PFS rate, % (95%CI)	77 (62, 87)
15-mo PFS rate, % (95%CI)	75 (59, 85)



OS

	All patients (n=45)
mOS, months (95%CI)	NR (NE)
12-mo OS rate, % (95%CI)	84 (70, 92)
15-mo OS rate, % (95%CI)	84 (70, 92)



*Investigator assessed

Lenz H-J, et al. J Clin Oncol 2020;38(suppl):abstr 11

11: Nivolumab plus low-dose ipilimumab as first-line therapy in microsatellite instability-high/DNA mismatch repair deficient metastatic colorectal cancer: Clinical update – Lenz H-J, et al

Key results (cont.)

TRAEs, n (%)	Nivolumab + ipilimumab (n=45)	
	Any grade	Grade 3–4
Any TRAE	35 (78)	9 (20)
Any serious TRAE	7 (16)	5 (11)
Any TRAE leading to discontinuation	5 (11)	2 (4)
TRAEs reported in >15%		
Pruritus	15 (33)	0 (0)
Hypothyroidism	8 (18)	1 (2)
Arthralgia	8 (18)	0 (0)
Asthenia	7 (16)	1 (2)

Conclusions

- **In patients with MSI-H/dMMR mCRC, nivolumab + ipilimumab provided robust and durable clinical activity and was generally well-tolerated with no new safety signals**

Lenz H-J, et al. J Clin Oncol 2020;38(suppl):abstr 11

12: Oligometastatic colorectal cancer: Prognostic implications of tumor load, role of locoregional treatments, and of first-line therapy intensification—A pooled analysis of TRIBE and TRIBE2 studies by GONO – Zucchelli G, et al

Study objective

- To evaluate the impact of having oligometastatic disease and low tumor burden compared with non-oligometastatic disease and low tumor burden on prognosis and efficacy in patients with CRC

Methods

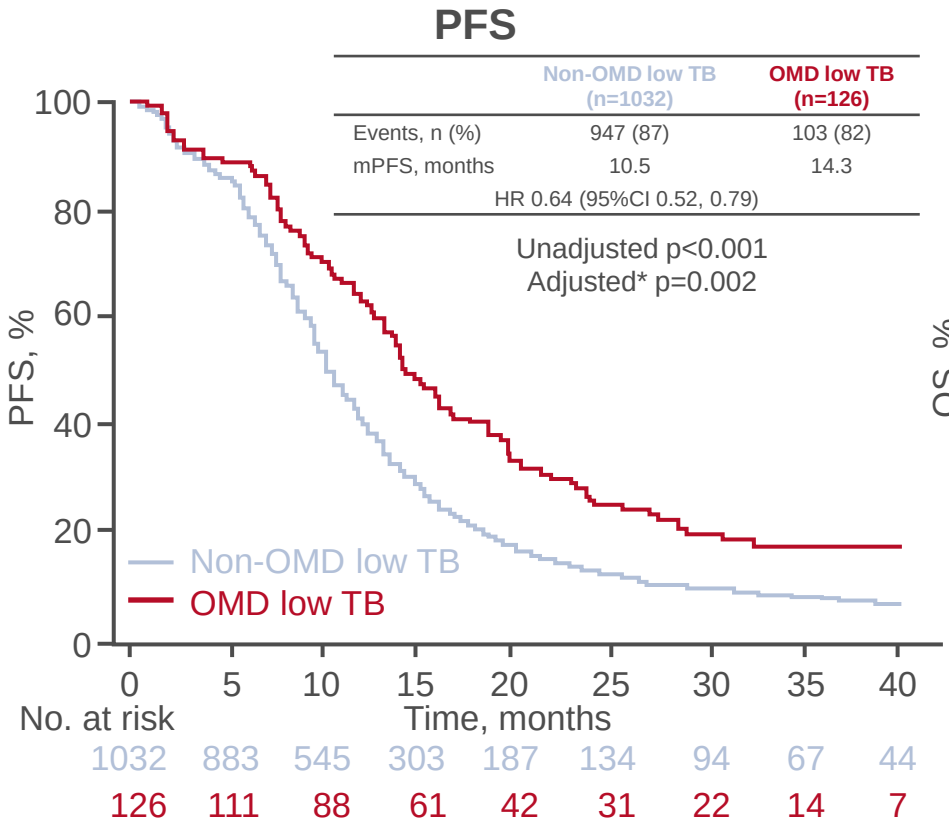
- Data from 1187 patients with mCRC in the TRIBE and TRIBE2 studies were analyzed
- In the two studies patients were randomly allocated to receive 1L treatment with FOLFOXIRI/bevacizumab or a doublet (FOLFIRI in TRIBE and FOLFOX in TRIBE2)/bevacizumab
- In this analysis, patients were split into two groups: those with oligometastatic disease and low tumor burden (OMD low TB, n=126) and those without oligometastatic disease and low tumor burden (non-OMD low TB, n=1032)
- OMD low TB was defined as having all of the following characteristics: up to 3 involved organs, up to 5 metastases, up to 3 metastases per organ, maximum size of metastases ≤3 cm and absence of ascites and peritoneal, bone and CNS metastases; while non-OMD low TB was defined as not having at least one of them
- The impact of OMD low TB vs. non-OMD low TB on prognosis, weight of intensification of upfront chemotherapy backbone (ORR, PFS and OS) and radical locoregional treatment efficacy was assessed

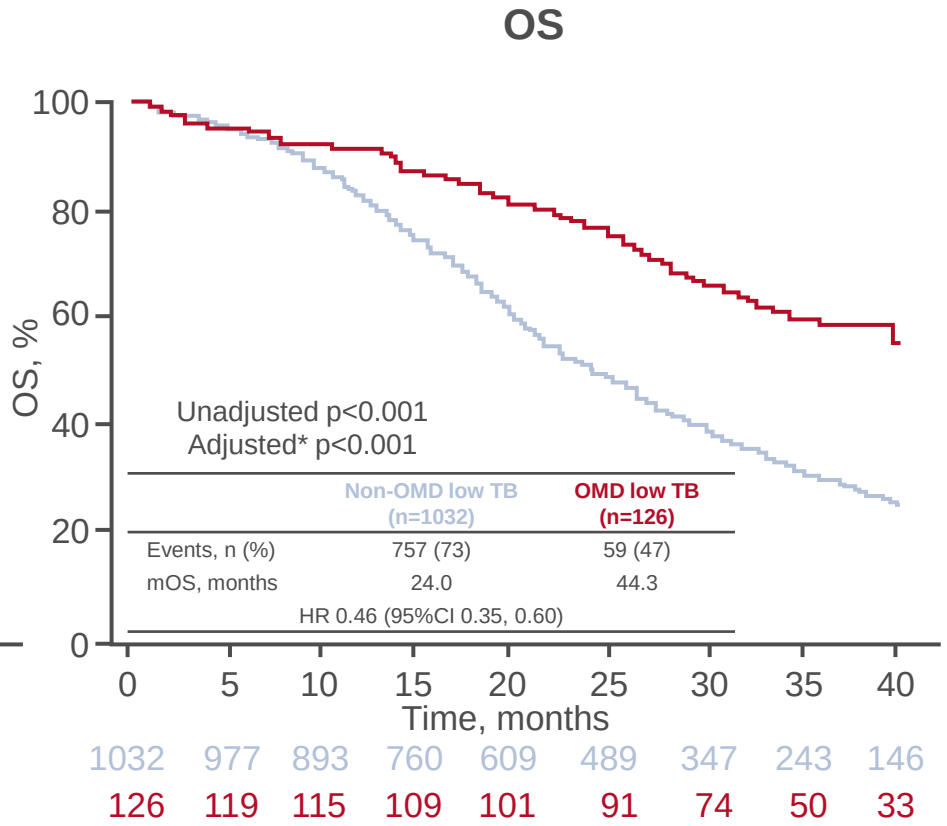
Zucchelli G, et al. J Clin Oncol 2020;38(suppl):abstr 12

12: Oligometastatic colorectal cancer: Prognostic implications of tumor load, role of locoregional treatments, and of first-line therapy intensification—A pooled analysis of TRIBE and TRIBE2 studies by GONO – Zucchelli G, et al

Key results

Prognostic role





*Covariates: treatment, previous adjuvant chemotherapy, time to metastases, resected primary tumor, liver only disease, site of primary tumor, mutational status and 1L radical locoregional treatments

Zucchelli G, et al. J Clin Oncol 2020;38(suppl):abstr 12

12: Oligometastatic colorectal cancer: Prognostic implications of tumor load, role of locoregional treatments, and of first-line therapy intensification—A pooled analysis of TRIBE and TRIBE2 studies by GONO – Zucchelli G, et al

Key results (cont.)

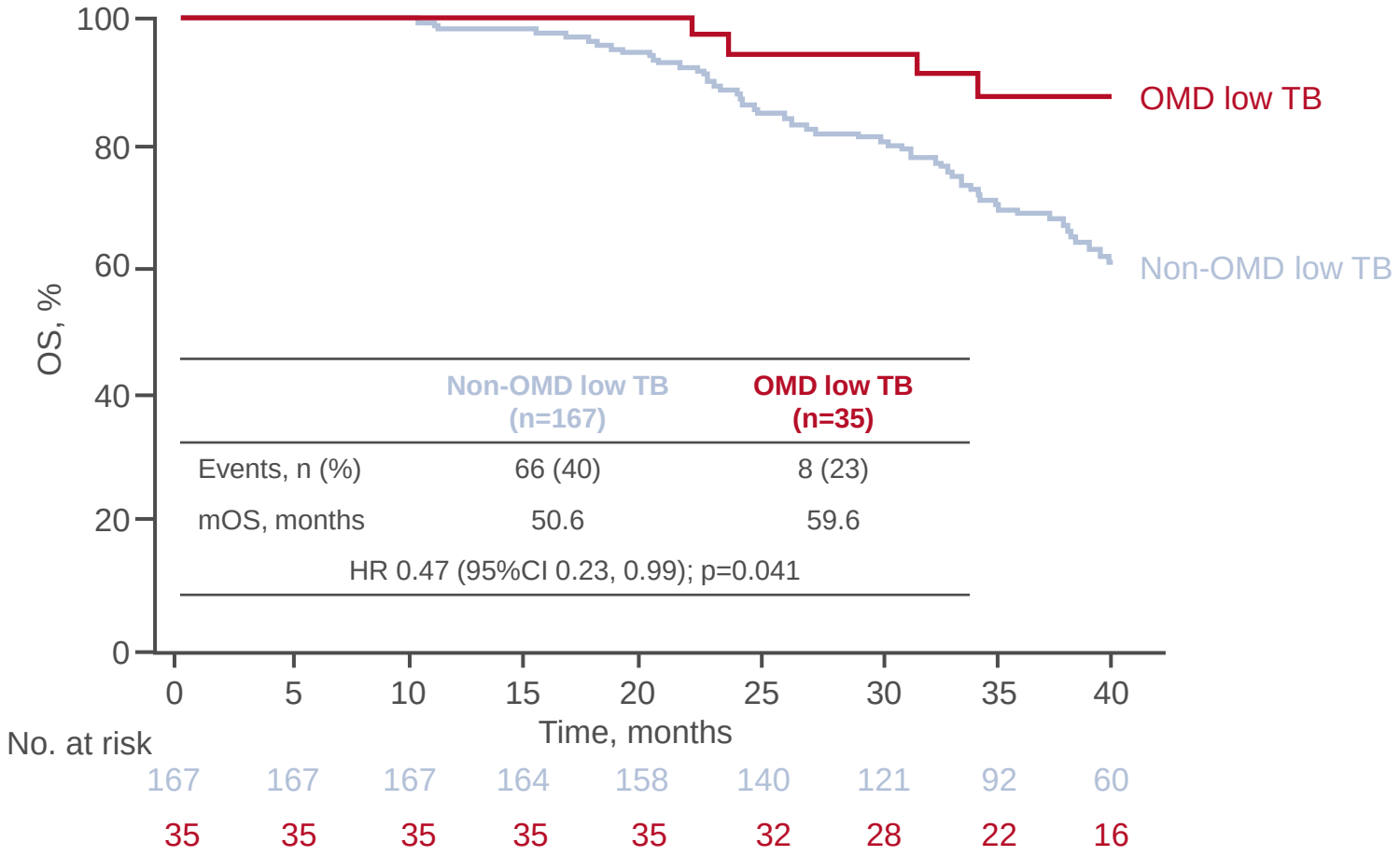
Impact of chemo-intensification	Non-OMD low TB (n=1032)		OMD low TB (n=126)	
	Doublet/bev (n=523)	FOLFOXIRI/bev (n=509)	Doublet/bev (n=59)	FOLFOXIRI/bev (n=67)
ORR, %	52	61	51	75
OR (95%CI); p-value	1.46 (1.14, 1.87); 0.003		2.84 (1.43, 6.02); <0.001	
PFS events, n (%)	482 (92)	465 (91)	51 (86)	52 (78)
mPFS, months	9.6	11.7	13.9	15.9
HR (95%CI)	0.76 (0.67, 0.87)		0.84 (0.57, 1.25)	
OS events, n (%)	402 (77)	355 (70)	28 (86)	31 (78)
mOS, months	22.5	26.3	48.4	43.7
HR (95%CI)	0.82 (0.71, 0.95)		1.20 (0.71, 2.01)	
1L locoregional therapy, n (%)	167 (16)		35 (28)	
Locoregional re-treatment after PD, n/N (%)	24/128 (19)		13/25 (52)	

Zucchelli G, et al. J Clin Oncol 2020;38(suppl):abstr 12

12: Oligometastatic colorectal cancer: Prognostic implications of tumor load, role of locoregional treatments, and of first-line therapy intensification—A pooled analysis of TRIBE and TRIBE2 studies by GONO – Zucchelli G, et al

Key results (cont.)

Impact on locoregional treatment efficacy: OS



Zucchelli G, et al. J Clin Oncol 2020;38(suppl):abstr 12

12: Oligometastatic colorectal cancer: Prognostic implications of tumor load, role of locoregional treatments, and of first-line therapy intensification—A pooled analysis of TRIBE and TRIBE2 studies by GONO – Zucchelli G, et al

Conclusions

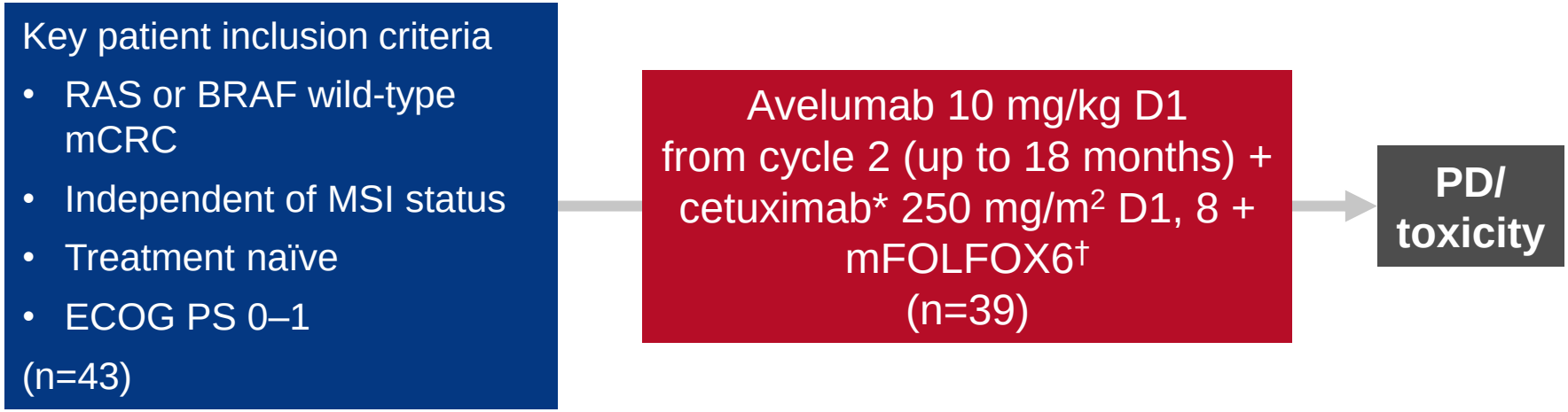
- **In patients with mCRC, FOLFOXIRI/bevacizumab was more effective than doublet/bevacizumab in both the OMD low TB and non-OMD low TB groups**
- **Patients with OMD low TB should not be excluded from receiving intensified upfront chemotherapy and to prolong survival locoregional treatments should be considered across all treatment lines**

Zucchelli G, et al. J Clin Oncol 2020;38(suppl):abstr 12

96: Avelumab and cetuximab in combination with FOLFOX in patients with previously untreated metastatic colorectal cancer (mCRC): Final results of the phase II AVETUX trial (AIO-KRK-0216) – Stein A, et al

Study objective

- To evaluate the efficacy and safety of avelumab + cetuximab + FOLFOX in previously untreated patients with mCRC



PRIMARY ENDPOINT

- 12-month PFS

SECONDARY ENDPOINTS

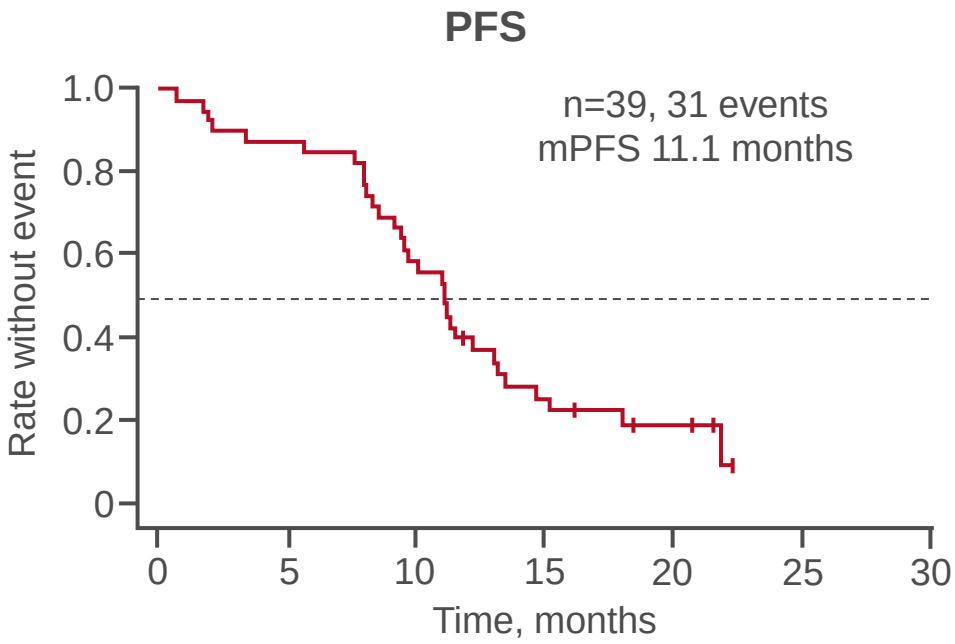
- RR, PFS (RECIST v1.1), OS, safety

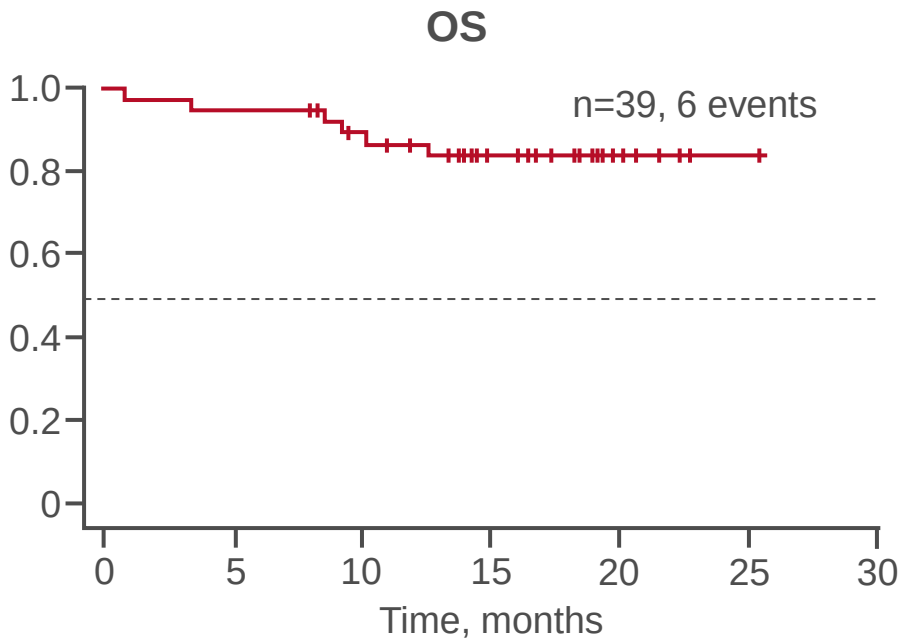
*Cetuximab first dose 400 mg/m^2; †oxaliplatin 85 mg/m^2 D1, 5FU 400 mg/m^2 bolus D1 then 2400 mg/m^2 D1–3, leucovorin 400 mg/m^2 D1

Stein A, et al. J Clin Oncol 2020;38(suppl):abstr 96

96: Avelumab and cetuximab in combination with FOLFOX in patients with previously untreated metastatic colorectal cancer (mCRC): Final results of the phase II AVETUX trial (AIO-KRK-0216) – Stein A, et al

Key results





Stein A, et al. J Clin Oncol 2020;38(suppl):abstr 96

96: Avelumab and cetuximab in combination with FOLFOX in patients with previously untreated metastatic colorectal cancer (mCRC): Final results of the phase II AVETUX trial (AIO-KRK-0216) – Stein A, et al

Key results (cont.)

Outcome	
Response, n/N (%) CR PR SD PD	 4/37 (11) 26 (70) 4 (11) 3 (8)
Early tumor shrinkage, %	81
Secondary resection rate, n/N (%)	6/39 (15)
12-month PFS rate, %	40

Grade 3–4 AEs occurring in ≥10%, n (%)	
Infections	12 (32)
Neutropenia	12 (32)
Rash	7 (18)
Peripheral sensory neuropathy	5 (13)
Diarrhea	4 (11)
Leukopenia	4 (11)
Thromboembolic event	4 (11)

Conclusions

- **In patients with previously untreated mCRC, avelumab + cetuximab + mFOLFOX6 is feasible and demonstrated an acceptable safety profile, although these findings need to be confirmed in a randomized controlled trial**

Stein A, et al. J Clin Oncol 2020;38(suppl):abstr 96