GI SLIDE DECK 2019

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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 summarise key findings in digestive cancers from the major congresses in 2019. This slide set specifically focuses on the **2019 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 realisation of this activity.

Yours sincerely,

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ESDO Medical Oncology Slide Deck
Editors 2019

COLORECTAL CANCERS




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GASTRO-OESOPHAGEAL AND NEUROENDOCRINE TUMOURS


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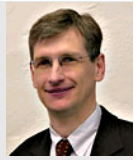

Prof Eric Van Cutsem	Digestive Oncology, University Hospitals, Leuven, Belgium
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esdo

Glossary

1L	first-line
2L	second-line
5FU	5-fluorouracil
AE	adverse event
ADX	andecaliximab
AFP	alpha-fetoprotein
ALT	alanine aminotransferase
AST	aspartate aminotransferase
bid	twice daily
BCLC	Barcelona Clinic Liver Cancer
BOR	best overall response
BSA	body surface area
BSC	best supportive care
BTC	biliary tract carcinoma
BW	body weight
CA19.9	cancer antigen 19.9
CAPOX	capecitabine + oxaliplatin
CI	confidence interval
CR	complete response
CRC	colorectal cancer
CRT	chemoradiation
CPS	combined positive score
D	day
DCR	disease control rate
DFS	disease-free survival
DoR	duration of response
ECOG	Eastern Cooperative Oncology Group
EHS	extrahepatic spread
FISH	fluorescence in situ hybridization
(m)FOLFOX	(modified) leucovorin + 5-fluorouracil + oxaliplatin
GEJ	gastroesophageal junction
Gy	Gray
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HER2	human epidermal growth factor receptor 2
HR	hazard ratio
ICI	immune checkpoint inhibition
IHC	immunohistochemistry
iv	intravenous
LN	lymph node
mo	months
MMP9	matrix metalloproteinase 9
MSI	microsatellite instability
MSS	microsatellite stable
MUC1	mucin 1
MVI	macroscopic portal vein invasion
NA	not available
NAR	neoadjuvant rectal (score)
NE	not evaluable
NET	neuroendocrine tumor
NLR	neutrophil-to-lymphocyte ratio
NR	not reached
OR(R)	objective response (rate)
OS	overall survival
pCR	pathological complete response
PD	progressive disease
PD-(L)1	programmed death-(ligand) 1
PFS	progression-free survival
PR	partial response
PS	performance status
q(2/3/4)w	every (2/3/4) week(s)
R	randomized
R0/1	resection 0/1
(m)RECIST	(modified) Response Evaluation Criteria In Solid Tumors
RFS	relapse-free survival
SAE	serious adverse event
SBRT	stereotactic body radiation therapy
sc	subcutaneous
SCC	squamous cell carcinoma
SD	stable disease
SLD	sum of the longest diameters
SoC	standard of care
SOX	S-1 + oxaliplatin
TMB	tumor mutation burden
TNM	tumor, node, metastasis
TRAE	treatment-related adverse event
TTP	time to progression
UFT	tegafur + uracil

Contents

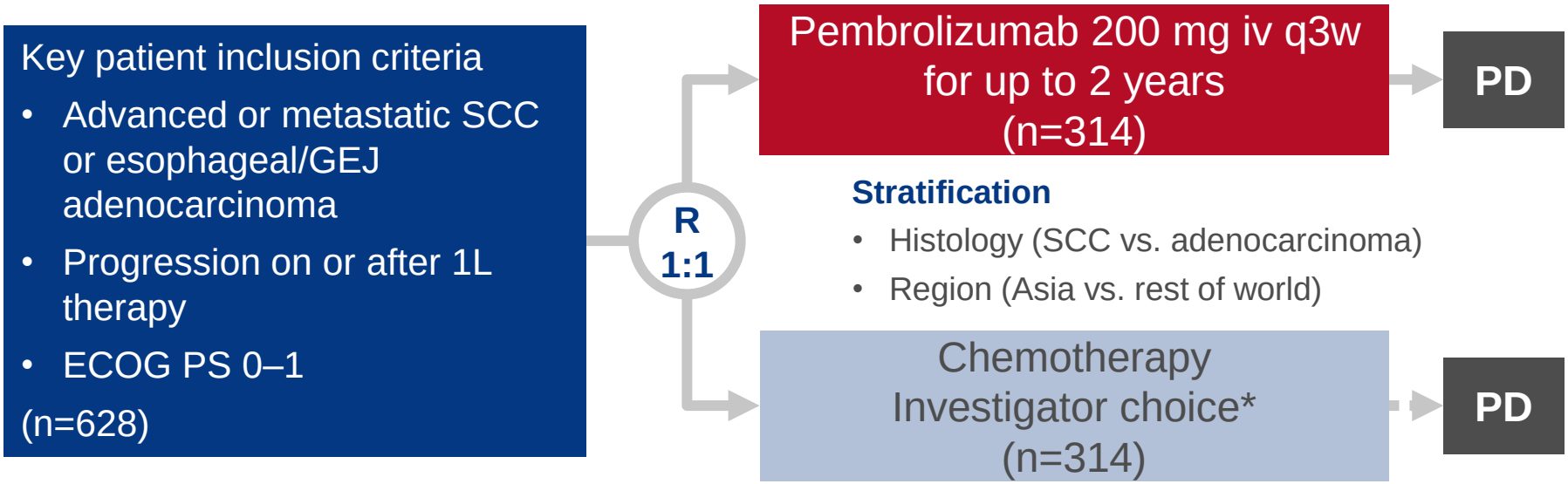
Note: To jump to a section, right click on the number and ‘Open Hyperlink’

CANCERS OF THE OESOPHAGUS AND STOMACH

2: Pembrolizumab versus chemotherapy as second-line therapy for advanced esophageal cancer: Phase III KEYNOTE-181 study – Kojima T, et al

Study objective

- To assess the efficacy and safety of pembrolizumab as a 2L treatment for patients with advanced or metastatic SCC and esophageal or GEJ adenocarcinoma in KEYNOTE-181



PRIMARY ENDPOINT

- OS in PD-L1 CPS ≥10, SCC, total population

SECONDARY ENDPOINTS

- PFS, ORR (RECIST v1.1), safety

*Paclitaxel 80–100 mg/m^2 D1, 8, 15 q4w; docetaxel 75 mg/m^2 q3w; or irinotecan 180 mg/m^2 q2w

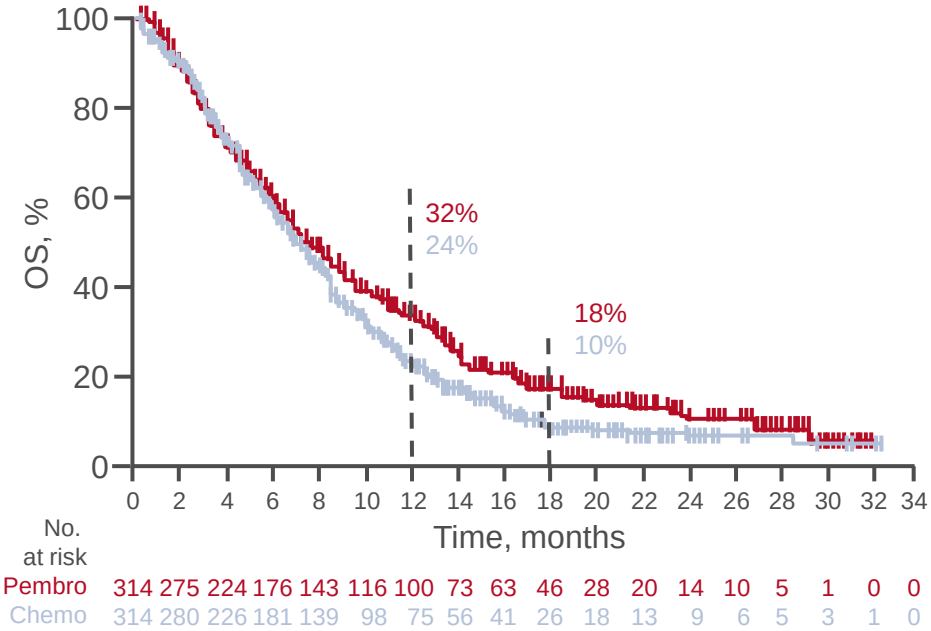
Kojima T, et al. J Clin Oncol 2019;37(Suppl):Abstr 2

2: Pembrolizumab versus chemotherapy as second-line therapy for advanced esophageal cancer: Phase III KEYNOTE-181 study – Kojima T, et al

Key results

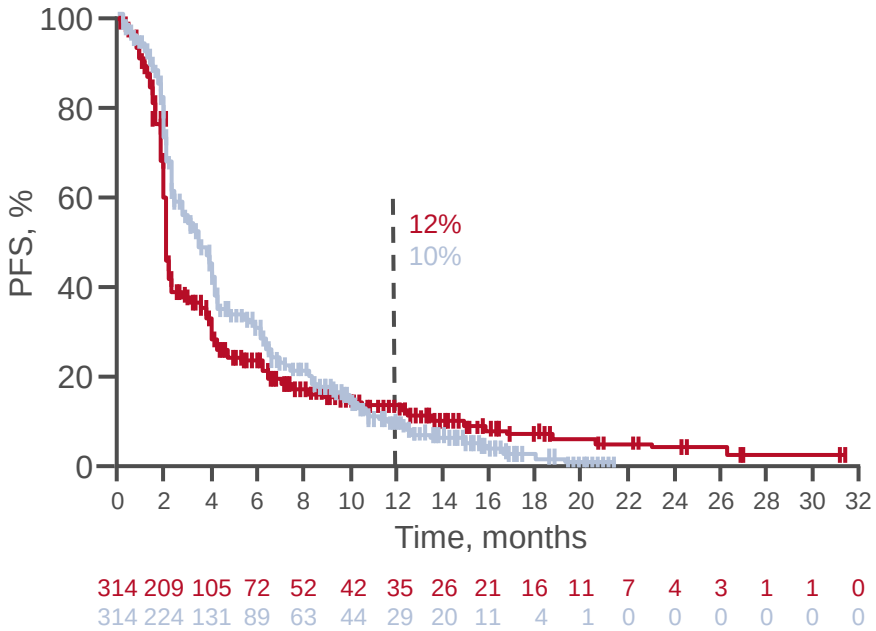
OS in total population

	Events, n	Median, mo (95%CI)	HR[a] (95%CI)	p-value
Pembrolizumab	314	7.1 (6.2, 8.1)	0.89 (0.75, 1.05)	0.0560
Chemotherapy	314	7.1 (6.3, 8.0)	–	



PFS in total population

	Median, mo (95%CI)	HR (95%CI)
Pembrolizumab	2.1 (2.1, 2.2)	1.11 (0.94, 1.31)
Chemotherapy	3.4 (2.8, 3.9)	



[a]Based on Cox regression model with treatment as a covariate stratified by region and histology

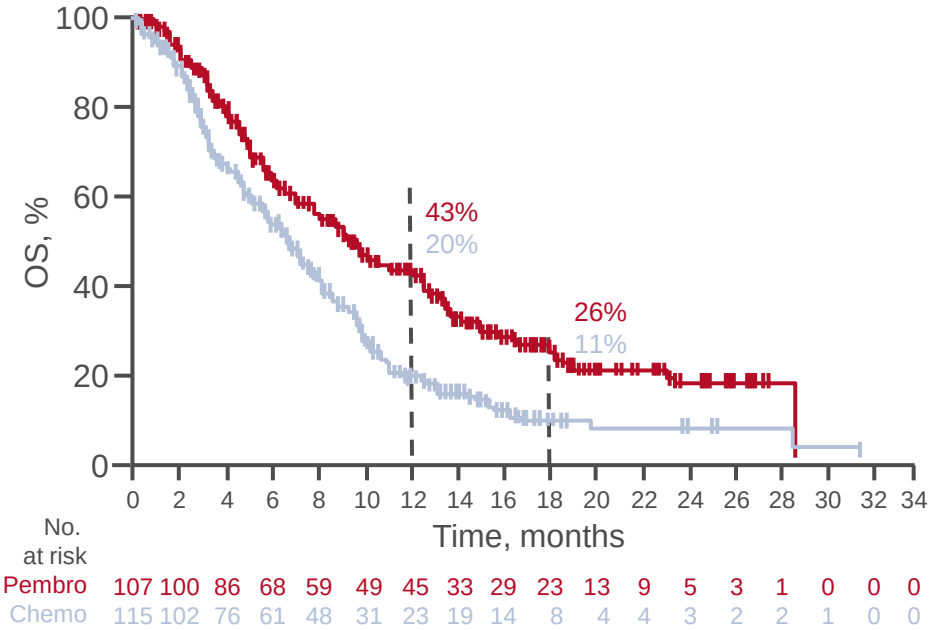
Kojima T, et al. J Clin Oncol 2019;37(Suppl):Abstr 2

2: Pembrolizumab versus chemotherapy as second-line therapy for advanced esophageal cancer: Phase III KEYNOTE-181 study – Kojima T, et al

Key results (cont.)

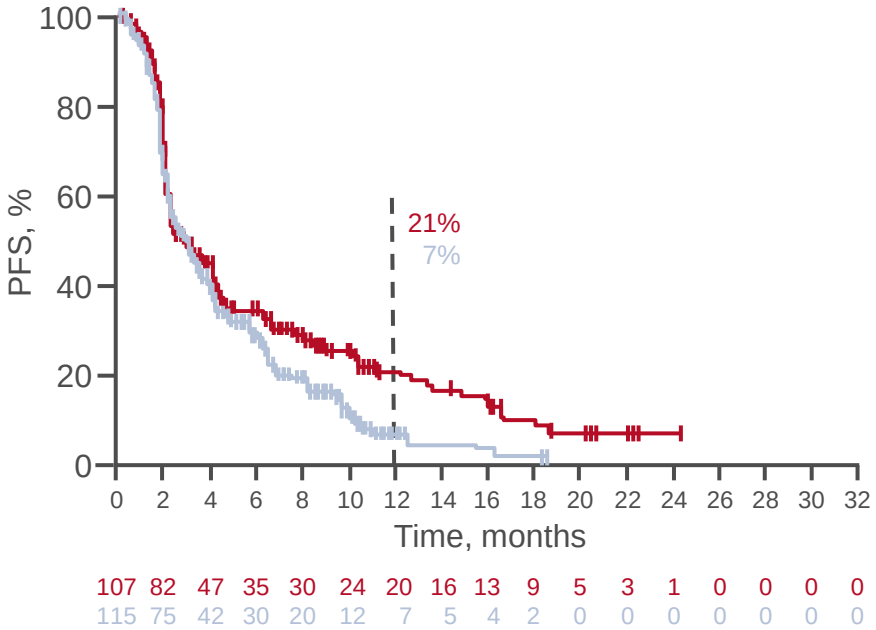
OS in PD-L1 CPS ≥10

	Events, n	Median, mo (95%CI)	HR[a] (95%CI)	p-value
Pembrolizumab	107	9.3 (6.6, 12.5)	0.69 (0.52, 0.93)	0.0074
Chemotherapy	115	6.7 (5.1, 8.2)	–	



PFS in PD-L1 CPS ≥10

	Median, mo (95%CI)	HR (95%CI)
Pembrolizumab	2.6 (2.1, 4.1)	0.73 (0.54, 0.97)
Chemotherapy	3.0 (2.1, 3.7)	



[a]Based on Cox regression model with treatment as a covariate stratified by region and histology

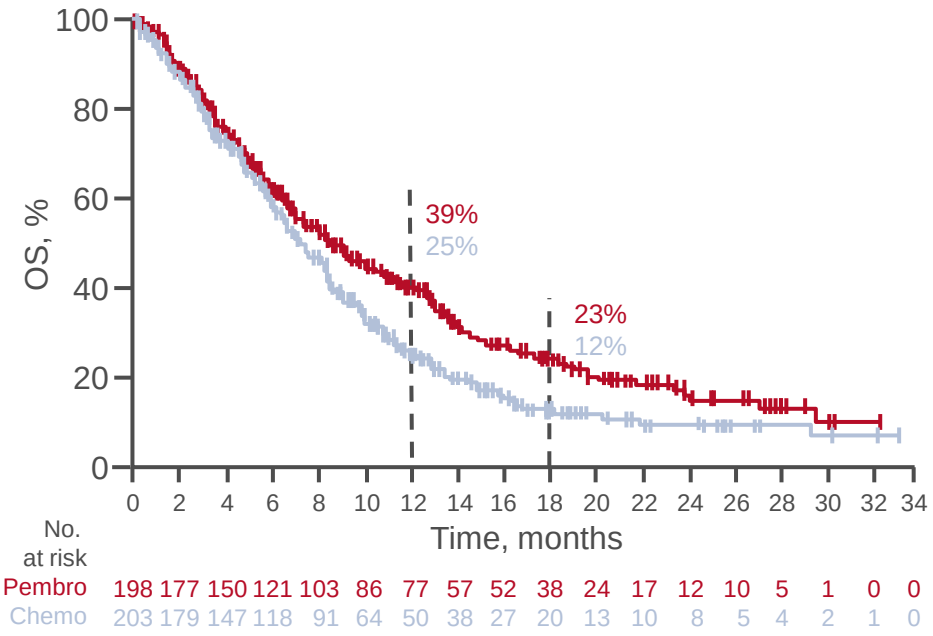
Kojima T, et al. J Clin Oncol 2019;37(Suppl):Abstr 2

2: Pembrolizumab versus chemotherapy as second-line therapy for advanced esophageal cancer: Phase III KEYNOTE-181 study – Kojima T, et al

Key results (cont.)

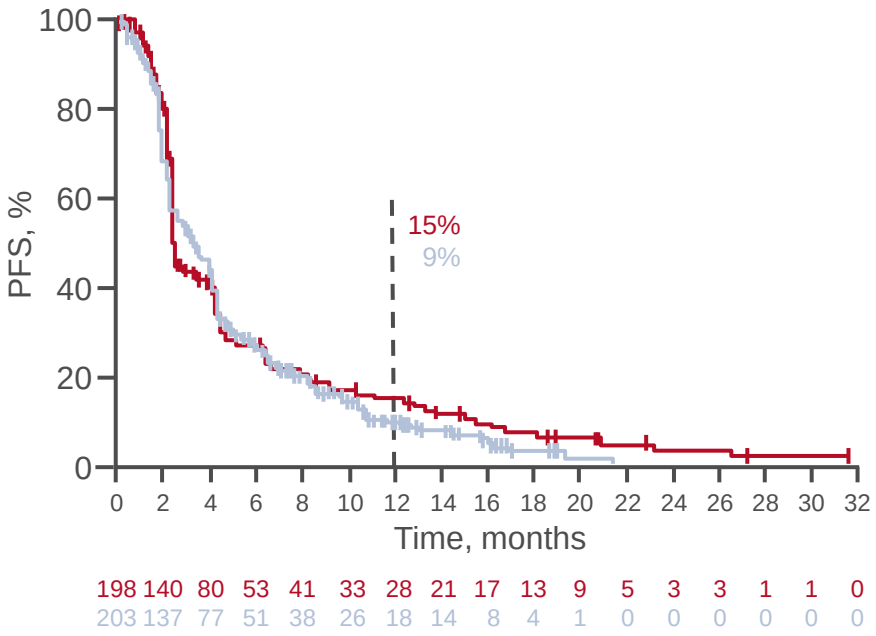
OS in SCC

	Events, n	Median, mo (95%CI)	HR[a] (95%CI)	p-value
Pembrolizumab	198	8.2 (6.7, 10.3)	0.78 (0.63, 0.96)	0.0095[b]
Chemotherapy	203	7.1 (6.1, 8.2)	–	



PFS in SCC

	Median, mo (95%CI)	HR (95%CI)
Pembrolizumab	2.2 (2.1, 3.2)	0.92 (0.75, 1.13)
Chemotherapy	3.1 (2.2, 3.9)	



[a]Based on Cox regression model with treatment as a covariate stratified by region and histology; [b]not significant based on pre-specified statistical boundaries

Kojima T, et al. J Clin Oncol 2019;37(Suppl):Abstr 2

2: Pembrolizumab versus chemotherapy as second-line therapy for advanced esophageal cancer: Phase III KEYNOTE-181 study – Kojima T, et al

Key results (cont.)

ORR, %	Pembrolizumab	Chemotherapy	p-value
Total population	13.1	6.7	0.0037
PD-L1 CPS ≥10	21.5	6.1	0.0006
SCC	16.7	7.4	0.0022

TRAE, n (%)	Pembrolizumab (n=314)	Chemotherapy (n=296)
Treatment-related	202 (64.3)	255 (86.1)
Grade 3–5	57 (18.2)	121 (40.9)
Led to discontinuation	19 (6.1)	19 (6.4)
Led to death	5 (1.5)	5 (1.7)

Conclusions

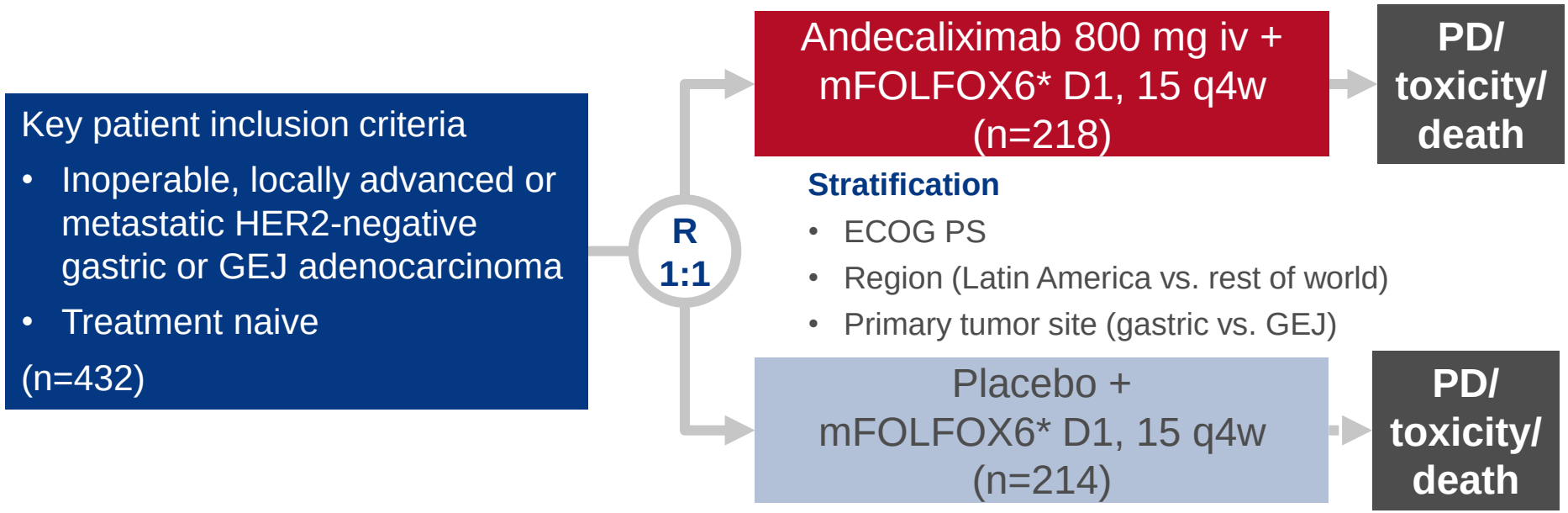
- **In patients with metastatic esophageal cancer and PD-L1 CPS ≥10 who had progressed after 1 prior therapy, pembrolizumab provided significant improvement in OS and higher ORR when compared with chemotherapy**
- **The pembrolizumab safety profile was more favorable than chemotherapy**
- **In patients with metastatic esophageal cancer and PD-L1 CPS ≥10, pembrolizumab may be a new 2L SoC**

Kojima T, et al. J Clin Oncol 2019;37(Suppl):Abstr 2

4: A phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of andecaliximab combined with mFOLFOX6 as first-line treatment in patients with advanced gastric or gastroesophageal junction adenocarcinoma (GAMMA-1) – Shah MA, et al

Study objective

- To assess the efficacy and safety of andecaliximab, an MMP9 inhibitor, combined with mFOLFOX6 in patients with advanced gastric or GEJ adenocarcinoma



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR (RECIST v1.1), safety

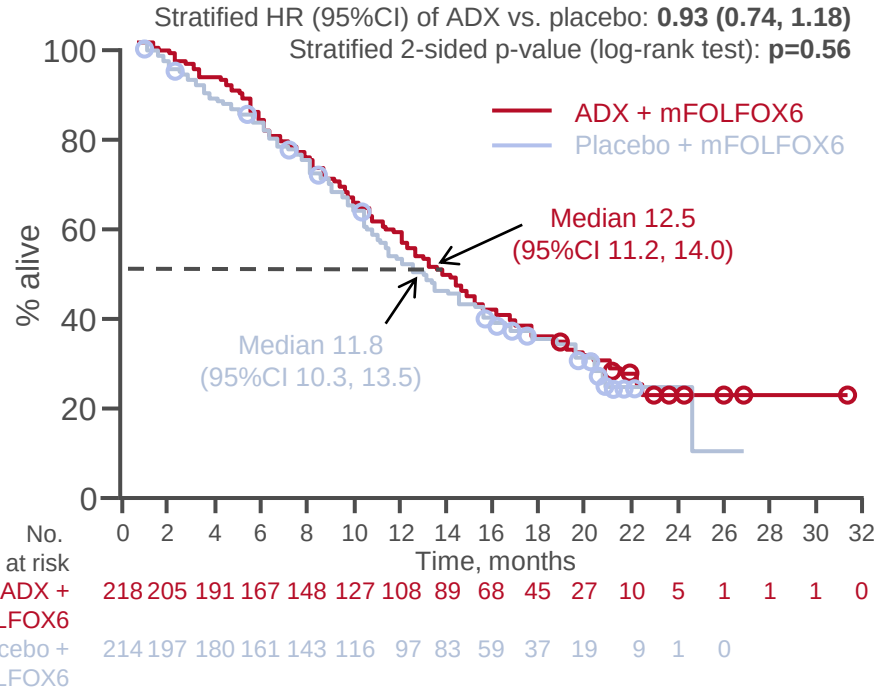
*Oxaliplatin D1, 15 followed by leucovorin + 5FU D1, 15 of 28-day cycle

Shah MA, et al. J Clin Oncol 2019;37(Suppl):Abstr 4

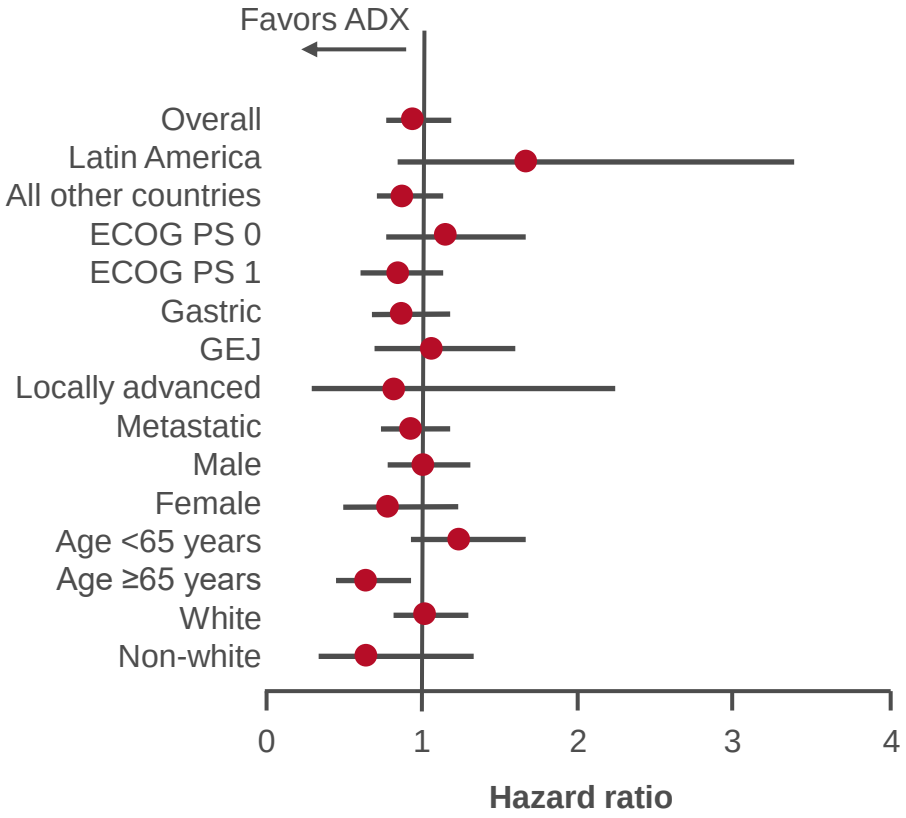
4: A phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of andecaliximab combined with mFOLFOX6 as first-line treatment in patients with advanced gastric or gastroesophageal junction adenocarcinoma (GAMMA-1) – Shah MA, et al

Key results

OS



OS by subgroup



Shah MA, et al. J Clin Oncol 2019;37(Suppl):Abstr 4

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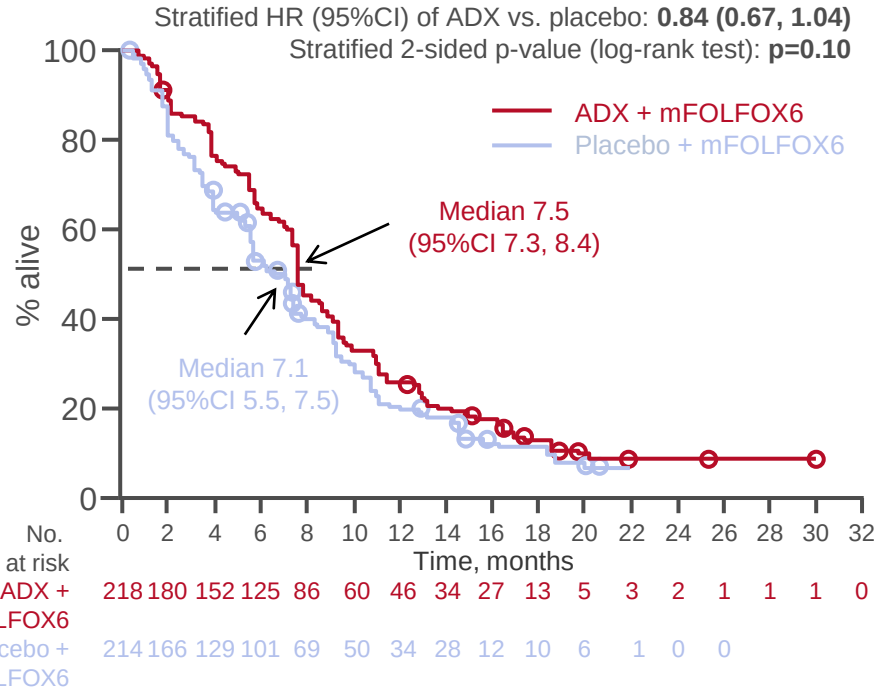
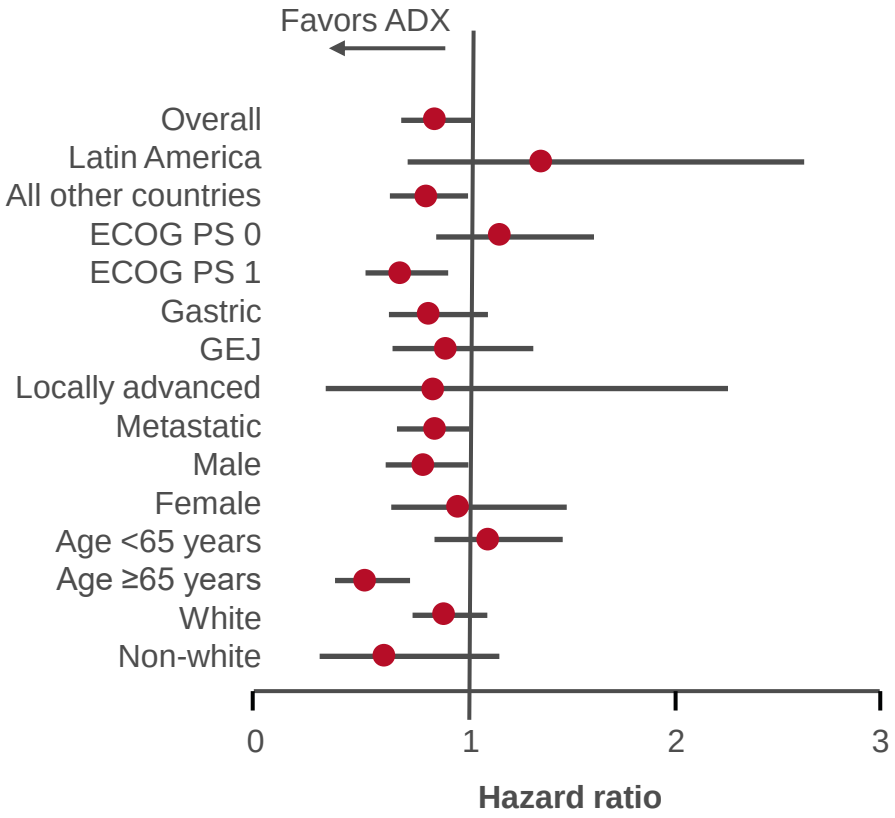
Key results (cont.)

PFS



PFS by subgroup



Shah MA, et al. J Clin Oncol 2019;37(Suppl):Abstr 4

4: A phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of andecaliximab combined with mFOLFOX6 as first-line treatment in patients with advanced gastric or gastroesophageal junction adenocarcinoma (GAMMA-1) – Shah MA, et al

Key results (cont.)

Grade ≥3 TRAEs occurring in ≥5%, %	Andecaliximab	Placebo
Neutropenia	22	27
Anemia	8	11
Fatigue	5	8
Neutrophil count decreased	7	6
Pulmonary embolism	5	8
Vomiting	6	4
Abdominal pain	5	4

Conclusions

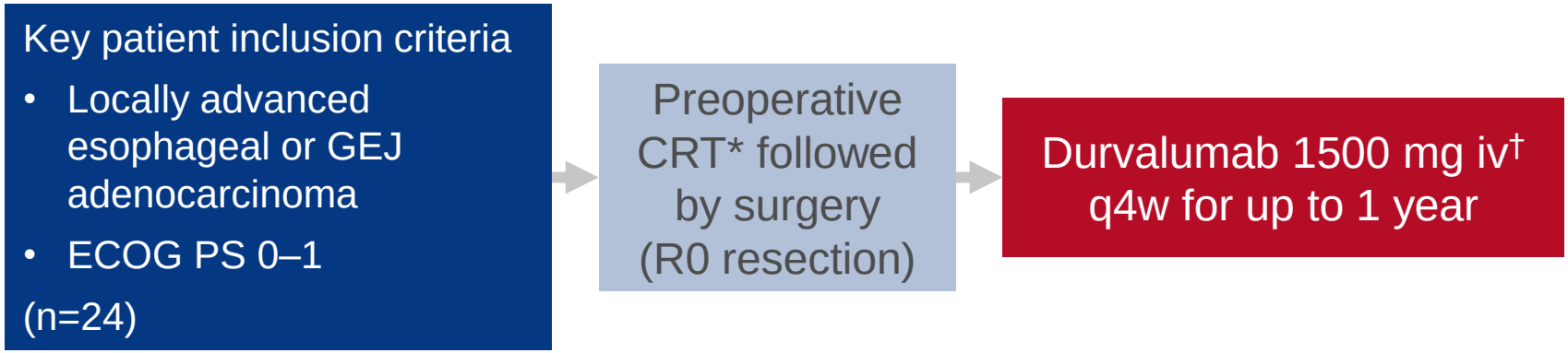
- **In treatment-naïve patients with HER2-negative gastric or GEJ adenocarcinoma, adding andecaliximab to mFOLFOX6 did not provide any improvement in survival**
- **The safety profile between the two treatment groups was similar**

Shah MA, et al. J Clin Oncol 2019;37(Suppl):Abstr 4

5: Safety and efficacy of durvalumab following trimodality therapy for locally advanced esophageal and GEJ adenocarcinoma: Early efficacy results from Big Ten Cancer Research Consortium study – Mamdani H, et al

Study objective

- To assess the efficacy and safety of durvalumab in patients with locally advanced esophageal or GEJ adenocarcinoma



PRIMARY ENDPOINT

- 1-year RFS

SECONDARY ENDPOINTS

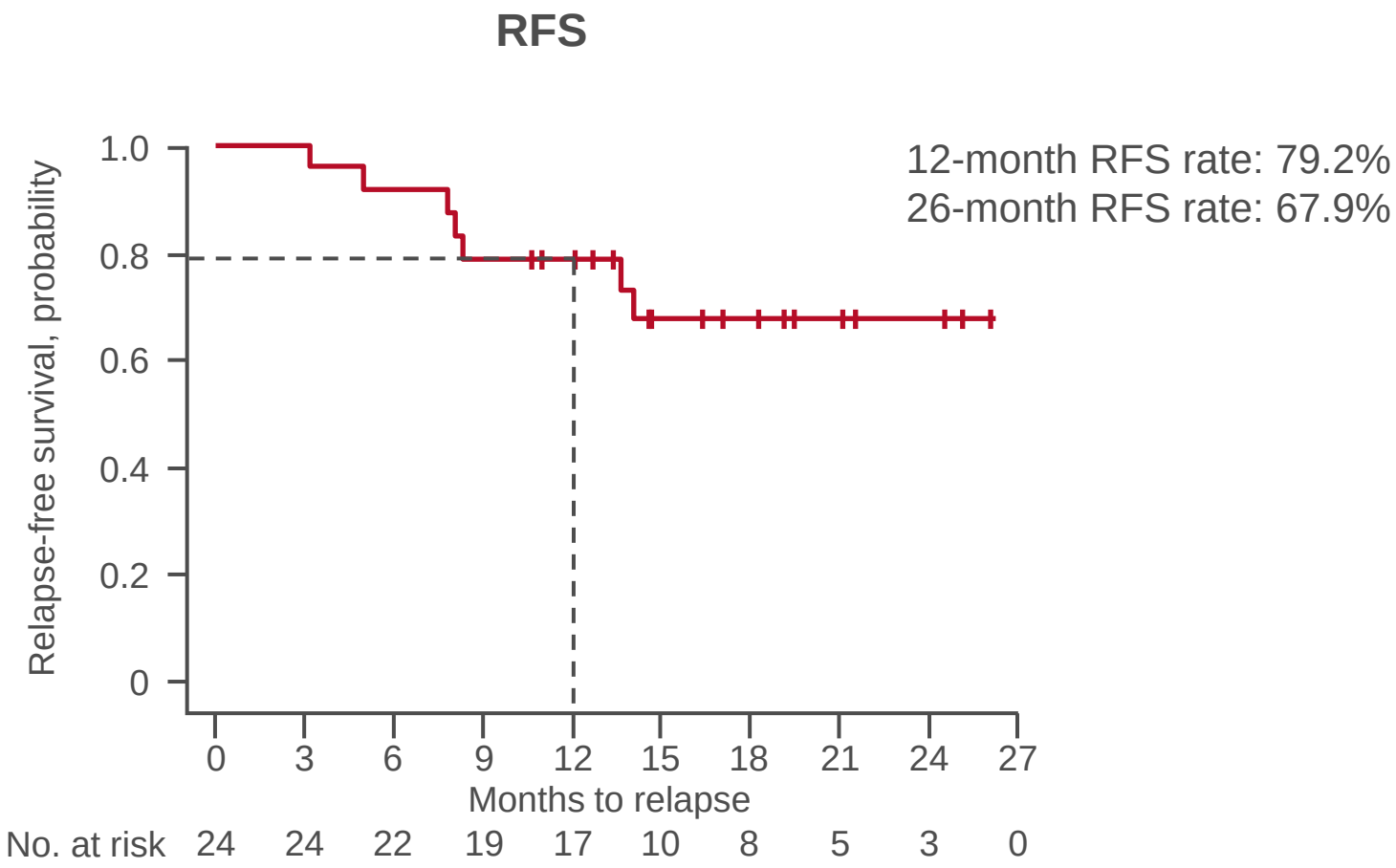
- Safety

*Carboplatin/paclitaxel or cisplatin/5FU + definitive radiation;
†durvalumab started within 1–3 months of surgery

Mamdani H, et al. J Clin Oncol 2019;37(Suppl):Abstr 5

5: Safety and efficacy of durvalumab following trimodality therapy for locally advanced esophageal and GEJ adenocarcinoma: Early efficacy results from Big Ten Cancer Research Consortium study – Mamdani H, et al

Key results



Mamdani H, et al. J Clin Oncol 2019;37(Suppl):Abstr 5

5: Safety and efficacy of durvalumab following trimodality therapy for locally advanced esophageal and GEJ adenocarcinoma: Early efficacy results from Big Ten Cancer Research Consortium study – Mamdani H, et al

Key results (cont.)

AEs occurring in ≥10%, n (%)	Grade 1	Grade 2
Fatigue	6 (25.0)	2 (8.3)
Nausea	6 (25.0)	0 (0)
Cough	3 (12.5)	2 (8.3)
Diarrhea	3 (12.5)	1 (4.2)
Pruritus	3 (12.5)	1 (4.2)
Dyspnea	1 (4.2)	2 (8.3)

- Grade 3 AEs included hypoglycemia (n=1) and hyperglycemia (n=1)
- Grade 3 TRAEs leading to discontinuation occurred in 3 patients (1 pneumonitis, 1 hepatitis, 1 colitis)

Mamdani H, et al. J Clin Oncol 2019;37(Suppl):Abstr 5

5: Safety and efficacy of durvalumab following trimodality therapy for locally advanced esophageal and GEJ adenocarcinoma: Early efficacy results from Big Ten Cancer Research Consortium study – Mamdani H, et al

Conclusions

- **In patients with locally advanced esophageal or GEJ adenocarcinoma, adjuvant durvalumab was feasible and showed encouraging efficacy data**
- **Durvalumab demonstrated a safety profile similar to previous findings**

Mamdani H, et al. J Clin Oncol 2019;37(Suppl):Abstr 5

8: Evaluation of efficacy of nivolumab by baseline factors from ATTRACTION-2 – Kang YK, et al

Study objective

- To assess factors that might contribute to early disease progression after receiving nivolumab – an exploratory analysis of ATTRACTION-2

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)

R 2:1

Nivolumab 3 mg/kg iv q2w (n=330) → PD

Placebo q2w (n=163) → PD

Stratification

- Country (Japan vs. S. Korea vs. Taiwan)
- ECOG PS (0 vs. 1)
- No. of organs with metastases (<2 vs. ≥2)

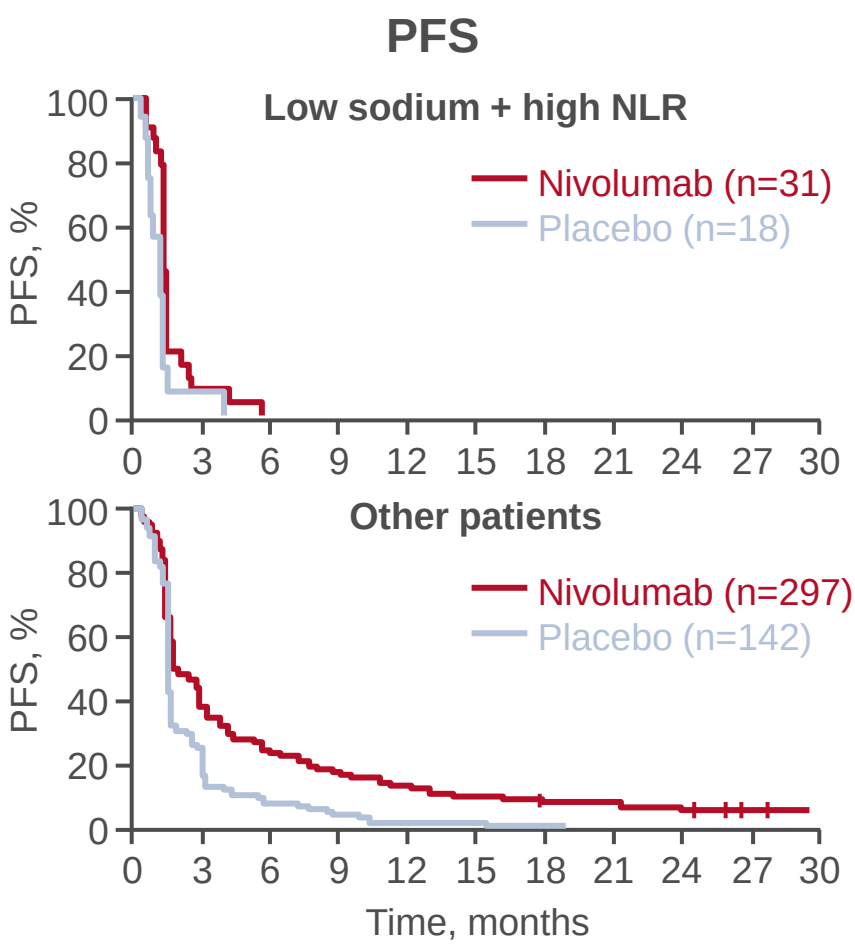
EXPLORATORY ENDPOINT

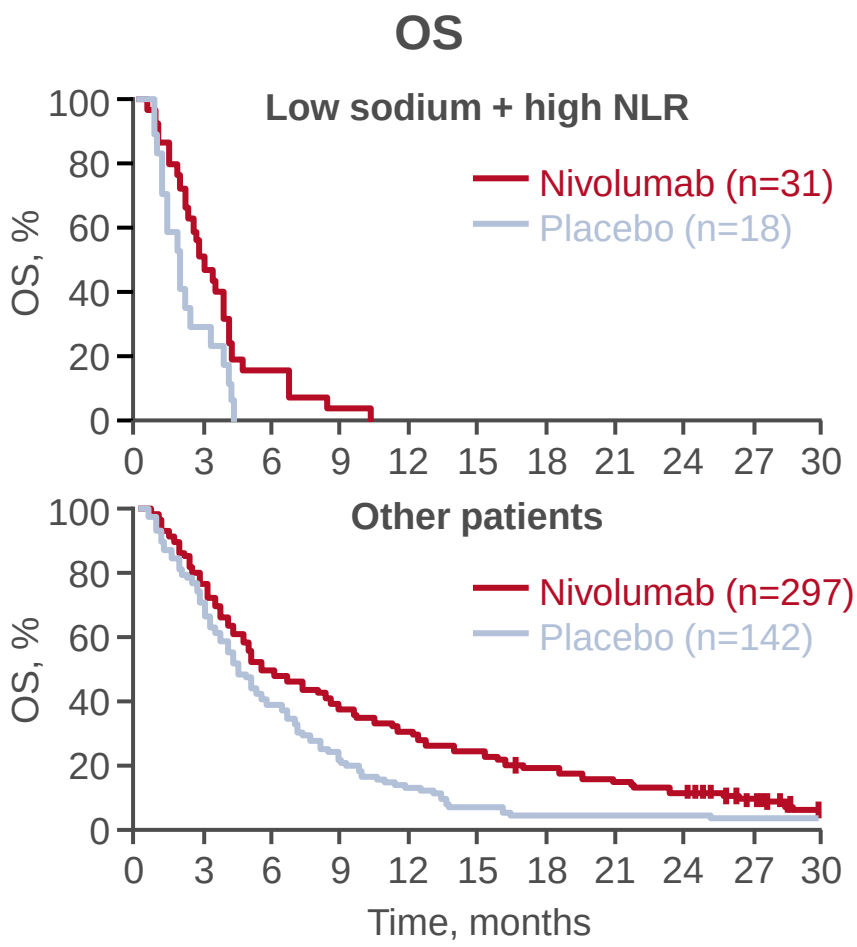
- Clinical factors for early progression/death using Bayesian additive regression trees

Kang YK, et al. J Clin Oncol 2019;37(Suppl):Abstr 8

8: Evaluation of efficacy of nivolumab by baseline factors from ATTRACTION-2 – Kang YK, et al

Key results





Kang YK, et al. J Clin Oncol 2019;37(Suppl):Abstr 8

8: Evaluation of efficacy of nivolumab by baseline factors from ATTRACTION-2 – Kang YK, et al

Key results (cont.)

- Factors found to be associated with early progression or death on nivolumab treatment included low sodium, high neutrophil-to-lymphocyte ratio (NLR), ECOG PS of 1 and no prior ramucirumab treatment
- Biomarker analysis did not find any correlation between PD-L1 expression, TMB or MSI status and the efficacy of nivolumab

Conclusions

- **In patients with advanced gastric or GEJ cancer, the efficacy of nivolumab may be reduced in those with factors suggestive of poorer overall condition such as low sodium and high NLR**
- **However, these results are exploratory and need to be verified**

Kang YK, et al. J Clin Oncol 2019;37(Suppl):Abstr 8

62: First-line pembrolizumab (P), trastuzumab (T), capecitabine (C) and oxaliplatin (O) in HER2-positive metastatic esophagogastric adenocarcinoma (mEGA) – Janjigian YY, et al

Study objective

- To assess the efficacy and safety of pembrolizumab combined with chemotherapy and trastuzumab in patients with HER2-positive metastatic esophagogastric adenocarcinoma

Key patient inclusion criteria
- Stage IV esophagogastric adenocarcinoma
- HER2 IHC 3+ or IHC 2+/ FISH >2.0 irrespective of PD-L1 status
- Treatment naive

(n=37)

→ Pembrolizumab 200 mg iv + trastuzumab 8 mg/kg 1 cycle

→ Pembrolizumab 200 mg + trastuzumab 6 mg/kg + CAPOX (oxaliplatin 130 mg/m^2 q3w + capecitabine 850 mg/m^2 D1–14) (n=24)

PRIMARY ENDPOINT

- 6-month PFS

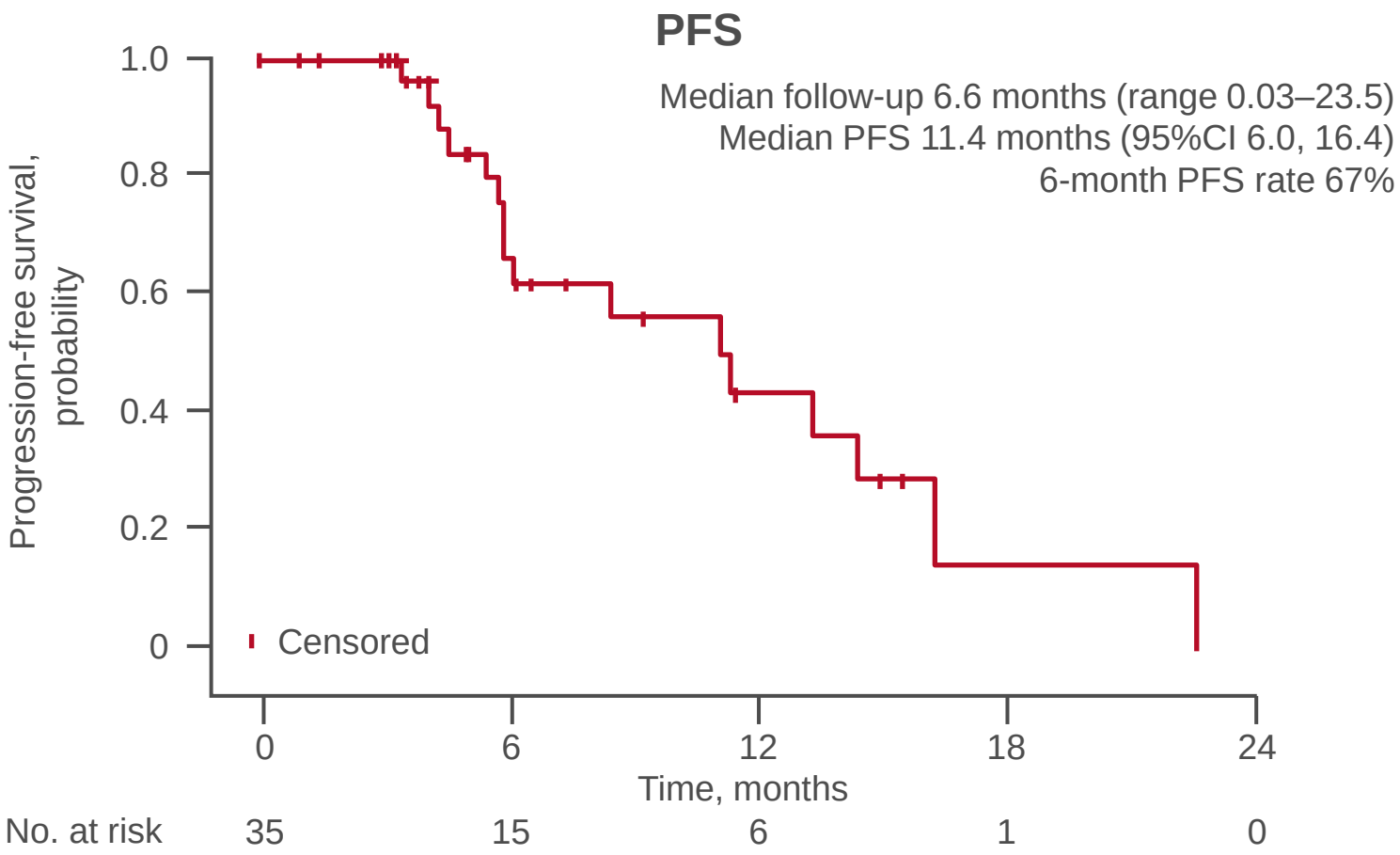
SECONDARY ENDPOINTS

- OS, ORR, DCR, safety, biomarker analysis

Janjigian YY, et al. J Clin Oncol 2019;37(Suppl):Abstr 62

62: First-line pembrolizumab (P), trastuzumab (T), capecitabine (C) and oxaliplatin (O) in HER2-positive metastatic esophagogastric adenocarcinoma (mEGA) – Janjigian YY, et al

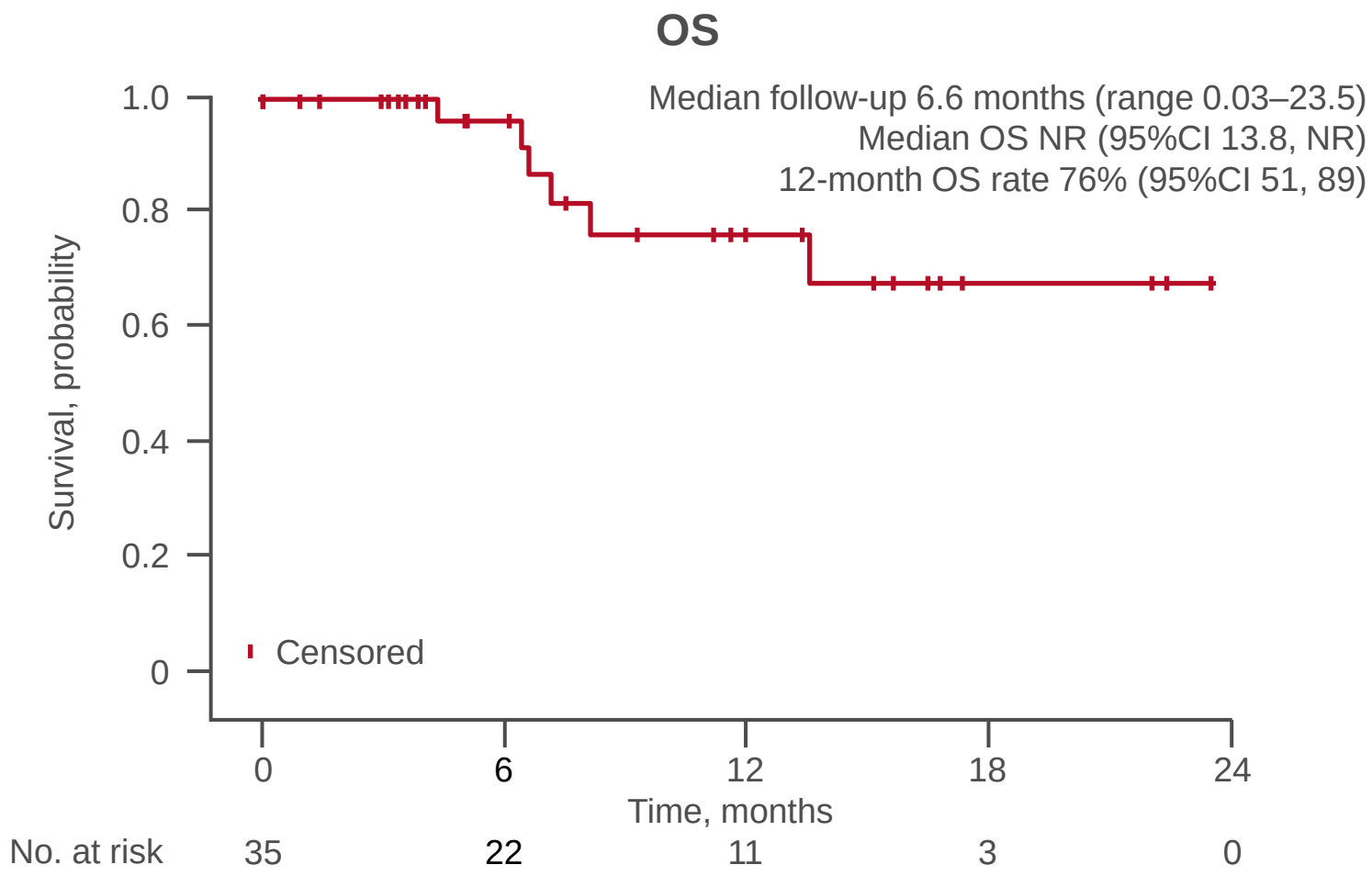
Key results



Janjigian YY, et al. J Clin Oncol 2019;37(Suppl):Abstr 62

62: First-line pembrolizumab (P), trastuzumab (T), capecitabine (C) and oxaliplatin (O) in HER2-positive metastatic esophagogastric adenocarcinoma (mEGA) – Janjigian YY, et al

Key results (cont.)



Janjigian YY, et al. J Clin Oncol 2019;37(Suppl):Abstr 62

62: First-line pembrolizumab (P), trastuzumab (T), capecitabine (C) and oxaliplatin (O) in HER2-positive metastatic esophagogastric adenocarcinoma (mEGA) – Janjigian YY, et al

Key results (cont.)

TRAEs occurring in ≥10%, n (%)	Grade 3	Grade 4
ALT/AST increased	1 (3)	
Anemia	2 (6)	
Diarrhea	1 (3)	
Dry skin/maculopapular rash	1 (3)	
Lymphocyte count decreased	3 (9)	1 (3)
Mucositis oral	1 (3)	
Nausea	2 (6)	
Immune-related		
Colitis	1 (3)	0 (0)
Interstitial nephritis	0 (0)	2 (3)
AST/ALT elevation	4 (11)	1 (3)

Conclusions

- **In patients with HER2-positive metastatic esophagogastric adenocarcinoma, pembrolizumab + trastuzumab + CAPOX provided encouraging responses and was generally well tolerated**
- **A phase 3 study (KEYNOTE-811) is ongoing**

Janjigian YY, et al. J Clin Oncol 2019;37(Suppl):Abstr 62

66: MSI-GC-01: Individual patient data (IPD) meta-analysis of microsatellite instability (MSI) and gastric cancer (GC) from four randomized clinical trials (RCTs) – Pietrantonio F, et al

Study objective

- To assess the prognostic and predictive impact of MSI in patients with gastric cancer

Methods

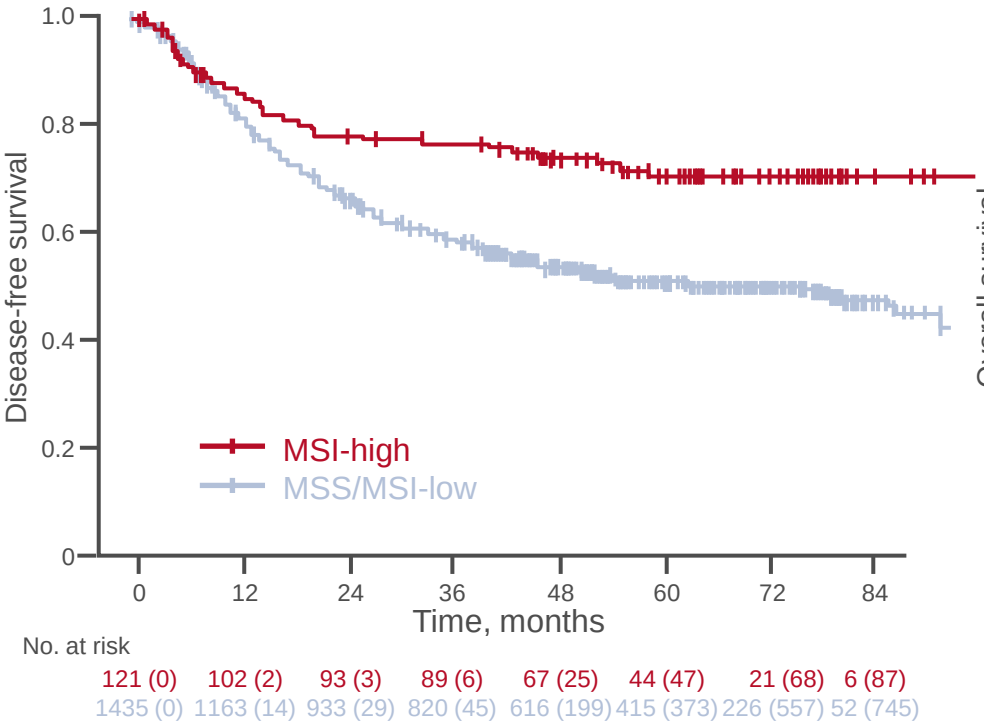
- Data for patients with resectable gastric cancer (n=1522) were pooled from 4 clinical trials – MAGIC, CLASSIC, ARTIST and ITACA-S
- The following data were collected: patient demographics (age, sex, and race), primary site (stomach vs. junctional), histotype (intestinal vs. other), T/N stage (7th TNM), treatment received (multimodal therapy vs. surgery alone) and MSI
- Univariate and multivariate associations with DFS and OS were assessed
- The predictive role of MSI according to treatment received was assessed overall and in the 2 clinical trials with a surgery alone arm (MAGIC and CLASSIC)

Pietrantonio F, et al. J Clin Oncol 2019;37(Suppl):Abstr 66

66: MSI-GC-01: Individual patient data (IPD) meta-analysis of microsatellite instability (MSI) and gastric cancer (GC) from four randomized clinical trials (RCTs) – Pietrantonio F, et al

Key results

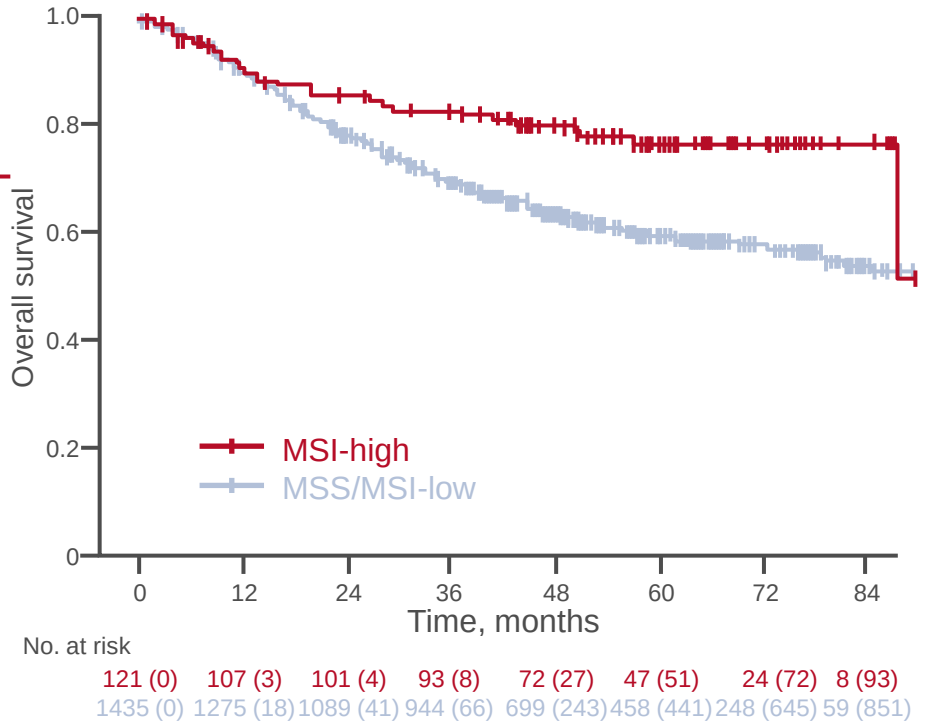
DFS



No. at risk

MSI-high	121 (0)	102 (2)	93 (3)	89 (6)	67 (25)	44 (47)	21 (68)	6 (87)
MSS/MSI-low	1435 (0)	1163 (14)	933 (29)	820 (45)	616 (199)	415 (373)	226 (557)	52 (745)

OS



No. at risk

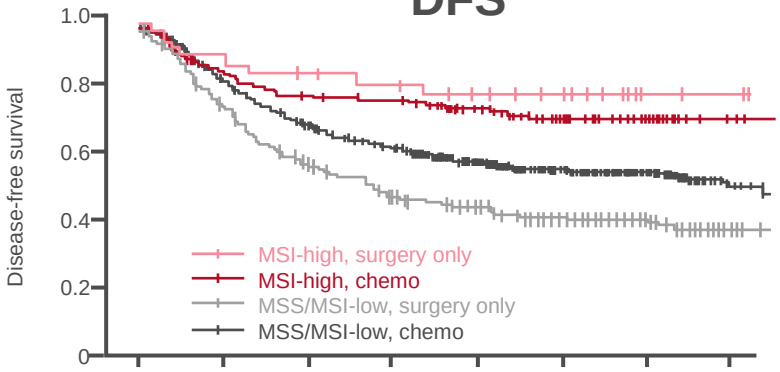
MSI-high	121 (0)	107 (3)	101 (4)	93 (8)	72 (27)	47 (51)	24 (72)	8 (93)
MSS/MSI-low	1435 (0)	1275 (18)	1089 (41)	944 (66)	699 (243)	458 (441)	248 (645)	59 (851)

Pietrantonio F, et al. J Clin Oncol 2019;37(Suppl):Abstr 66

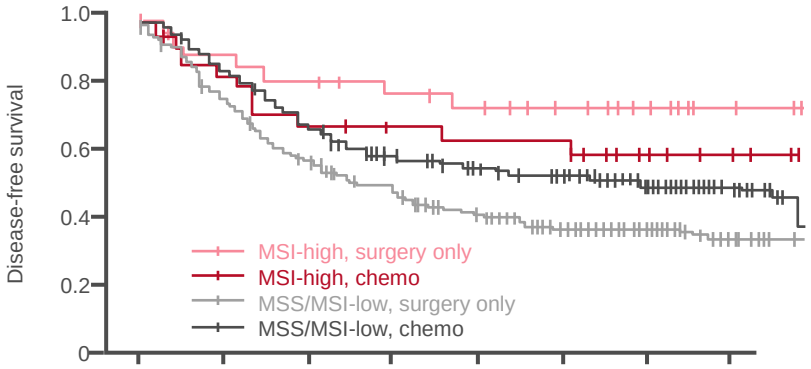
66: MSI-GC-01: Individual patient data (IPD) meta-analysis of microsatellite instability (MSI) and gastric cancer (GC) from four randomized clinical trials (RCTs) – Pietrantonio F, et al

Key results (cont.)

DFS

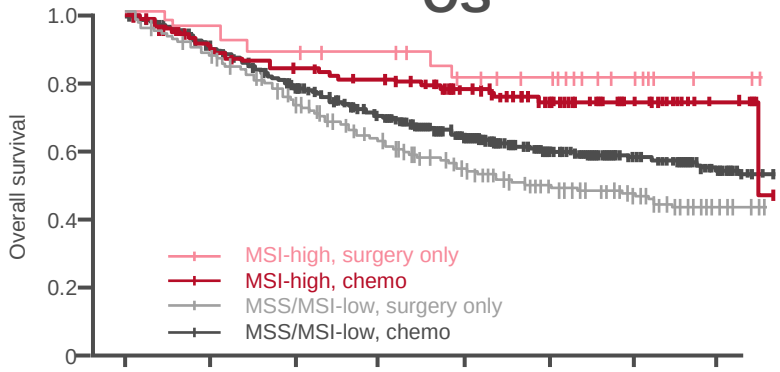


Time, months	0	12	24	36	48	60	72	84
MSI-high, surgery only	33(0)	27(2)	26(3)	23(4)	19(7)	15(12)	4(22)	1(26)
MSI-high, chemo	88(0)	75(0)	68(0)	66(2)	48(18)	29(35)	17(46)	5(61)
MSS/MSI-low, surgery only	422(0)	318(6)	238(13)	192(20)	163(34)	115(72)	68(119)	16(172)
MSS/MSI-low, chemo	1013(0)	845(8)	695(16)	628(25)	453(165)	300(301)	158(438)	36(573)

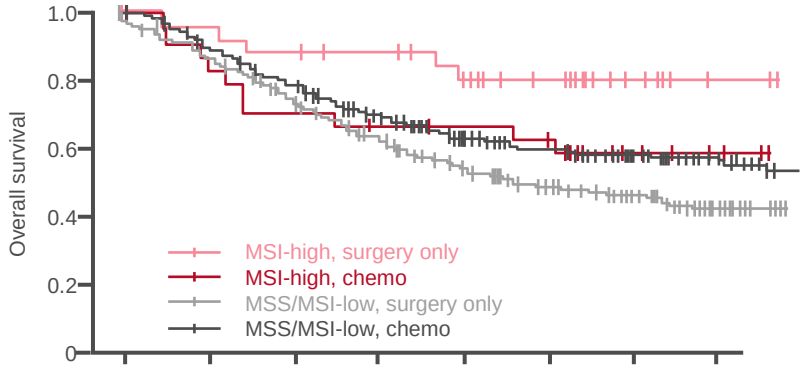


Time, months	0	12	24	36	48	60	72	84
MSI-high, surgery only	33(0)	27(2)	25(3)	23(4)	19(7)	15(12)	4(22)	1(26)
MSI-high, chemo	28(0)	23(0)	20(0)	18(2)	16(3)	12(7)	7(11)	3(18)
MSS/MSI-low, surgery only	422(0)	318(6)	238(13)	192(20)	163(34)	115(72)	68(119)	16(172)
MSS/MSI-low, chemo	428 (0)	358(5)	281(10)	252(17)	211(43)	164(83)	105(142)	31(232)

OS



	0	12	24	36	48	60	72	84
MSI-high, surgery only	33(0)	29(2)	27(3)	25(5)	20(8)	15(14)	4(24)	1(28)
MSI-high, chemo	88(0)	78(1)	74(1)	68(3)	52(19)	32(37)	20(48)	7(65)
MSS/MSI-low, surgery only	422(0)	361(7)	299(20)	245(31)	197(56)	138(101)	77(157)	18(219)
MSS/MSI-low, chemo	1013(0)	914(11)	790(21)	699(35)	502(187)	320(340)	171(488)	41(632)



	0	12	24	36	48	60	72	84
MSI-high, surgery only	33(0)	29(2)	27(3)	25(5)	20(8)	15(14)	4(24)	1(28)
MSI-high, chemo	28(0)	23(0)	21(0)	18(2)	18(2)	13(6)	8(10)	4(18)
MSS/MSI-low, surgery only	422(0)	361(7)	299(20)	245(31)	197(56)	138(101)	77(157)	18(219)
MSS/MSI-low, chemo	426(0)	377(7)	321(14)	281(26)	235(57)	177(102)	111(169)	35(263)

Pietrantonio F, et al. J Clin Oncol 2019;37(Suppl):Abstr 66

66: MSI-GC-01: Individual patient data (IPD) meta-analysis of microsatellite instability (MSI) and gastric cancer (GC) from four randomized clinical trials (RCTs) – Pietrantonio F, et al

Conclusions

- **In patients with resectable gastric cancer, MSI is an independent prognostic marker and should be considered as a stratification factor in future trials**
- **In patients with gastric cancer who are MSI-high, further investigation is required on chemotherapy omission and/or immune checkpoint blockade depending on the risk of relapse**

Pietrantonio F, et al. J Clin Oncol 2019;37(Suppl):Abstr 66

CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

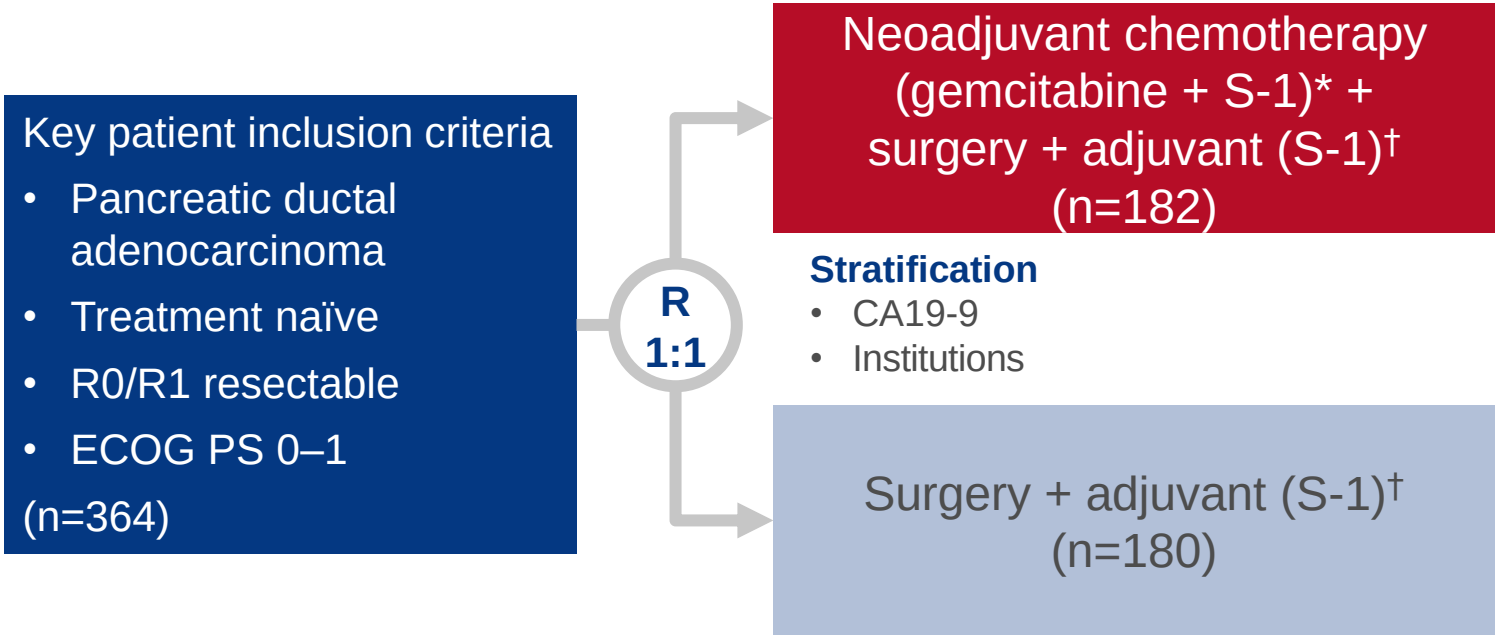
Cancers of the pancreas, small bowel and hepatobiliary tract

PANCREATIC CANCER

189: Randomized phase II/III trial of neoadjuvant chemotherapy with gemcitabine and S-1 versus upfront surgery for resectable pancreatic cancer (Prep-02/JSAP-05) – Unno M, et al

Study objective

- To assess the efficacy and safety of neoadjuvant chemotherapy compared with upfront surgery in patients with resectable pancreatic ductal adenocarcinoma



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

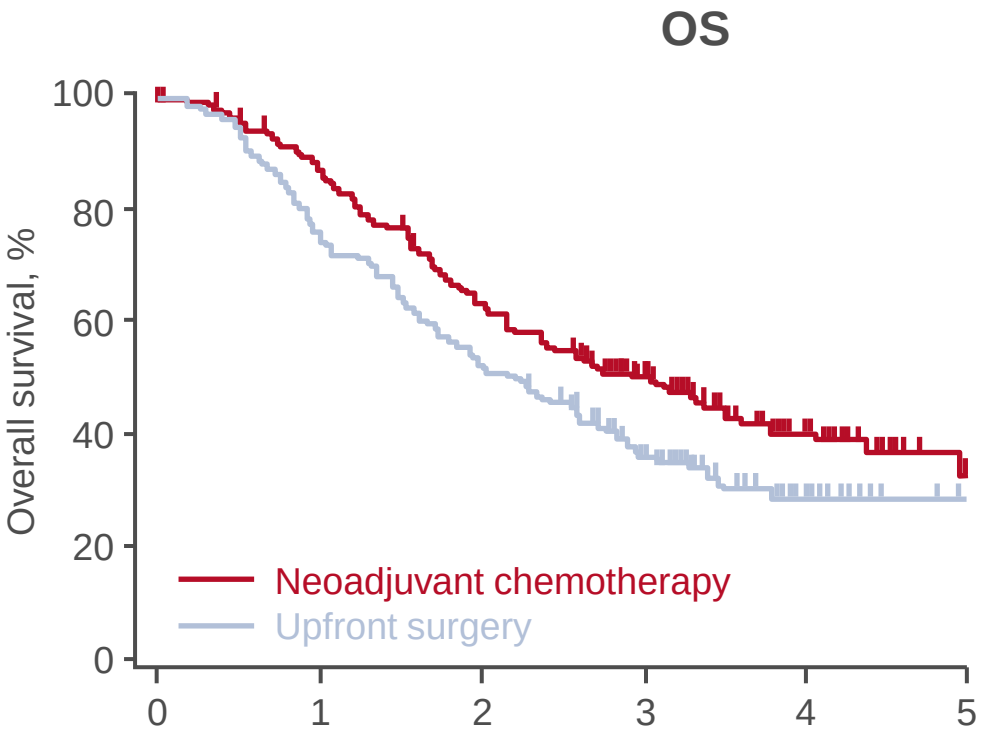
- Resection rate, RFS, safety

*Gemcitabine 1 g/m^2 D1, 8 + oral S-1 40 mg/m^2 bid D1–14 for 2 cycles; †S-1 for 6 months in patients with curative resection and fully recovered within 10 weeks of surgery

Unno M, et al. J Clin Oncol 2019;37(Suppl):Abstr 189

189: Randomized phase II/III trial of neoadjuvant chemotherapy with gemcitabine and S-1 versus upfront surgery for resectable pancreatic cancer (Prep-02/JSAP-05) – Unno M, et al

Key results



Neoadjuvant chemotherapy:
36.7 months (95%CI 28.7, 43.3)
Upfront surgery:
26.7 months (95%CI 21.0, 31.3)
HR 0.72 (95%CI 0.55, 0.94);
log-rank test p=0.015

2-year OS: 63.7% vs. 52.5%

Unno M, et al. J Clin Oncol 2019;37(Suppl):Abstr 189

189: Randomized phase II/III trial of neoadjuvant chemotherapy with gemcitabine and S-1 versus upfront surgery for resectable pancreatic cancer (Prep-02/JSAP-05) – Unno M, et al

Key results (cont.)

Recurrence, n (%)	Neoadjuvant chemotherapy (n=182)	Upfront surgery (n=180)	p-value
Local	30 (27.3)	27 (22.9)	0.54
Liver	33 (30.0)	56 (47.5)	0.01
Distant LN	18 (16.4)	28 (23.7)	0.22
Lung	20 (18.2)	16 (13.6)	0.44
Peritoneal dissemination	23 (20.9)	17 (14.4)	0.26
Others	8 (7.3)	13 (11.0)	0.46

Unno M, et al. J Clin Oncol 2019;37(Suppl):Abstr 189

189: Randomized phase II/III trial of neoadjuvant chemotherapy with gemcitabine and S-1 versus upfront surgery for resectable pancreatic cancer (Prep-02/JSAP-05) – Unno M, et al

Key results (cont.)

AEs with neoadjuvant chemotherapy, n (%)	Grade 3	Grade 4
Total	84 (48.8)	41 (23.8)
Hematologic	71 (41.3)	41 (23.8)
Leukopenia	46 (26.7)	7 (4.1)
Neutrophilia	60 (34.9)	39 (22.7)
Anemia	7 (4.1)	1 (0.6)
Thrombocytopenia	6 (3.5)	4 (2.3)
Febrile neutropenia	11 (6.4)	0
Stomatitis	10 (5.8)	0
Appetite loss	13 (7.6)	0
Skin rash	15 (8.7)	0

Conclusion

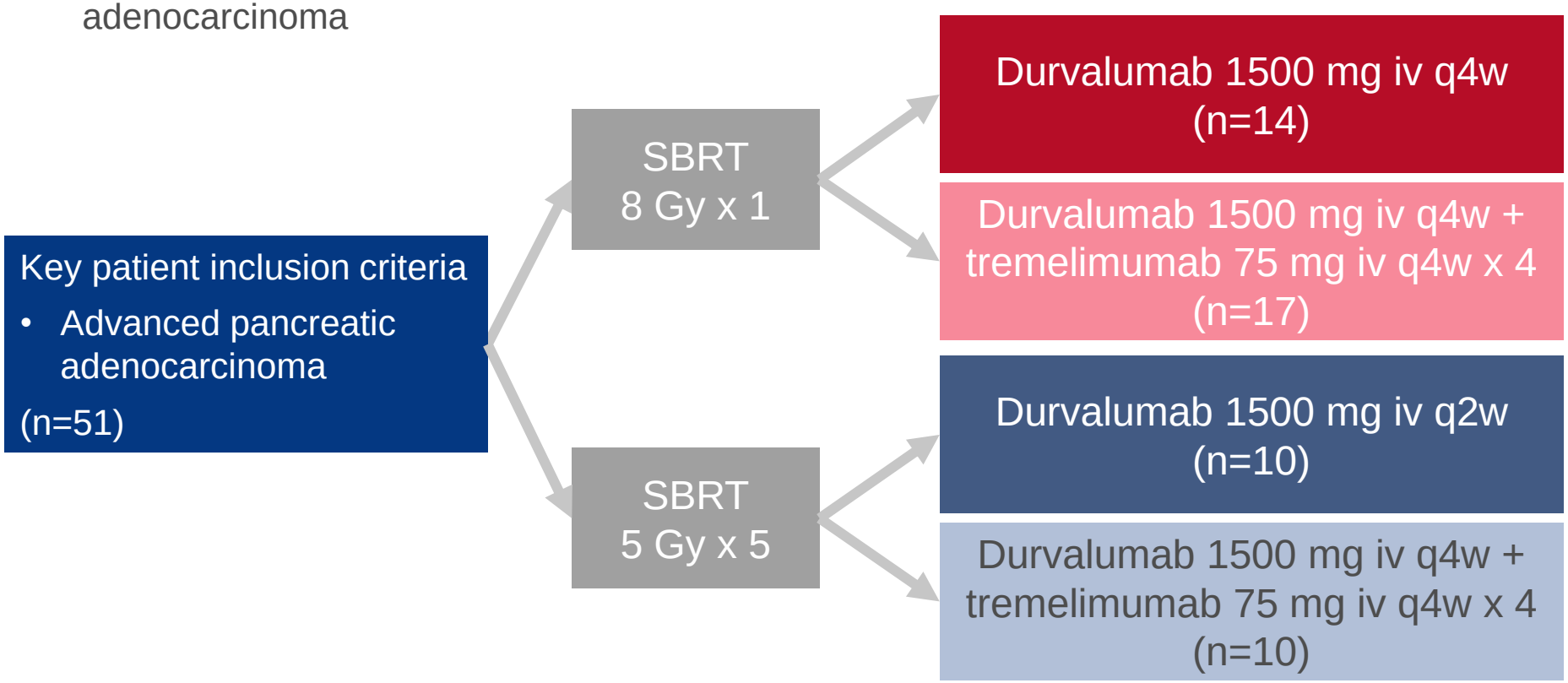
- **In patients with pancreatic ductal adenocarcinoma, neoadjuvant chemotherapy significantly improved survival over upfront surgery and may be a new SoC for these patients**

Unno M, et al. J Clin Oncol 2019;37(Suppl):Abstr 189

192: Immune checkpoint inhibition (ICI) in combination with SBRT in patients with advanced pancreatic adenocarcinoma – Brar G, et al

Study objective

- To assess the efficacy and safety of ICI + SBRT in patients with advanced pancreatic adenocarcinoma



PRIMARY ENDPOINT

- Safety

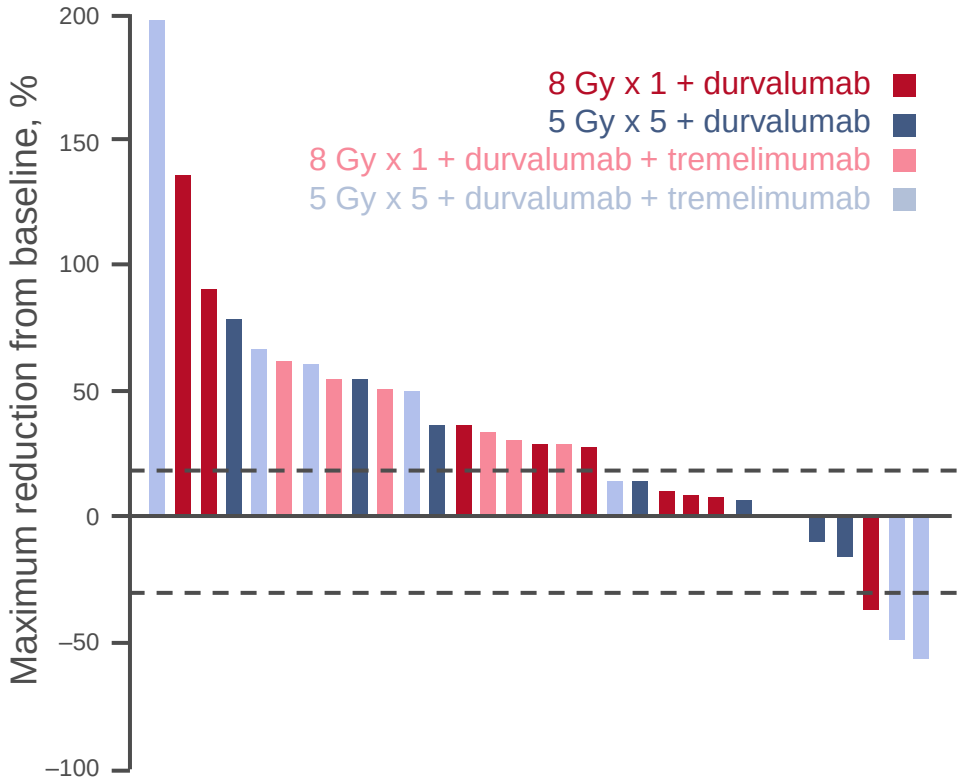
SECONDARY ENDPOINTS

- ORR, PFS, OS

Brar G, et al. J Clin Oncol 2019;37(Suppl):Abstr 192

192: Immune checkpoint inhibition (ICI) in combination with SBRT in patients with advanced pancreatic adenocarcinoma – Brar G, et al

Key results

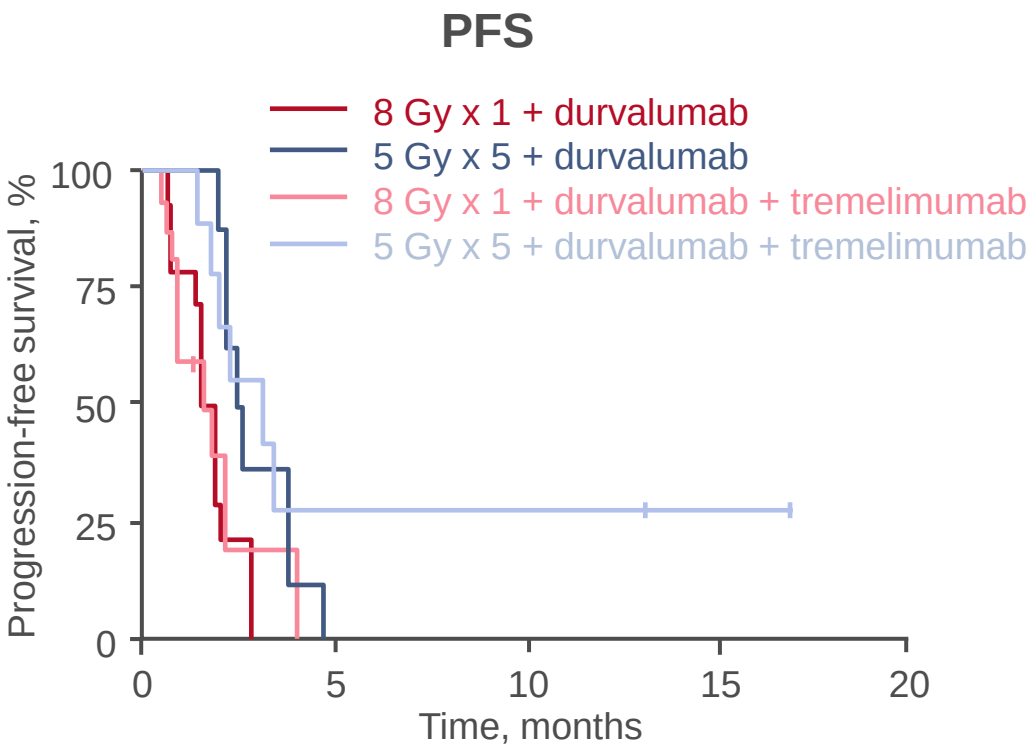


Response, n (%)	
ORR	3 (10.3)
CR	0
PR	3 (10.3)
SD	8 (27.6)
PD	18 (62.1)

Brar G, et al. J Clin Oncol 2019;37(Suppl):Abstr 192

192: Immune checkpoint inhibition (ICI) in combination with SBRT in patients with advanced pancreatic adenocarcinoma – Brar G, et al

Key results (cont.)

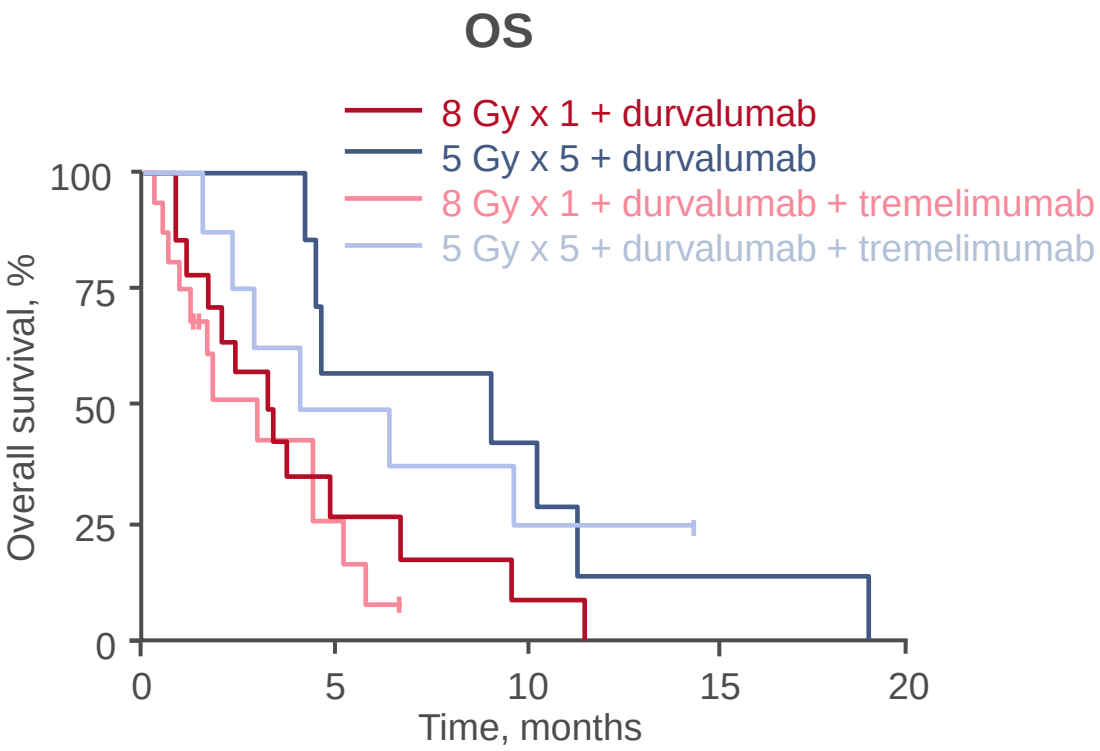


Cohort	PFS, months (95%CI)
8 Gy x 1 + durvalumab	1.7 (0.7, 2.8)
5 Gy x 5 + durvalumab	2.6 (2.1, 4.7)
8 Gy x 1 + durvalumab + tremelimumab	1.6 (0.5, 4.0)
5 Gy x 5 + durvalumab + tremelimumab	3.2 (1.5, 16.5)

Brar G, et al. J Clin Oncol 2019;37(Suppl):Abstr 192

192: Immune checkpoint inhibition (ICI) in combination with SBRT in patients with advanced pancreatic adenocarcinoma – Brar G, et al

Key results (cont.)



Cohort	OS, months (95%CI)
8 Gy x 1 + durvalumab	3.4 (0.9, 11.4)
5 Gy x 5 + durvalumab	9.1 (3.4, 18.7)
8 Gy x 1 + durvalumab + tremelimumab	3.0 (0.7, 6.6)
5 Gy x 5 + durvalumab + tremelimumab	6.4 (1.5, 17.6)

Brar G, et al. J Clin Oncol 2019;37(Suppl):Abstr 192

192: Immune checkpoint inhibition (ICI) in combination with SBRT in patients with advanced pancreatic adenocarcinoma – Brar G, et al

Key results (cont.)

- The most common grade 2 TRAEs were hypothyroidism (6.5%) and rash (3.2%) and grade 3 TRAEs were hyperthyroidism (3.2%), lymphopenia (3.2%), diarrhea (3.2%) and dysgeusia (3.2%)

Conclusion

- **In patients with advanced pancreatic adenocarcinoma, combined SBRT with ICI was generally well tolerated and provided some durable responses**

Brar G, et al. J Clin Oncol 2019;37(Suppl):Abstr 192

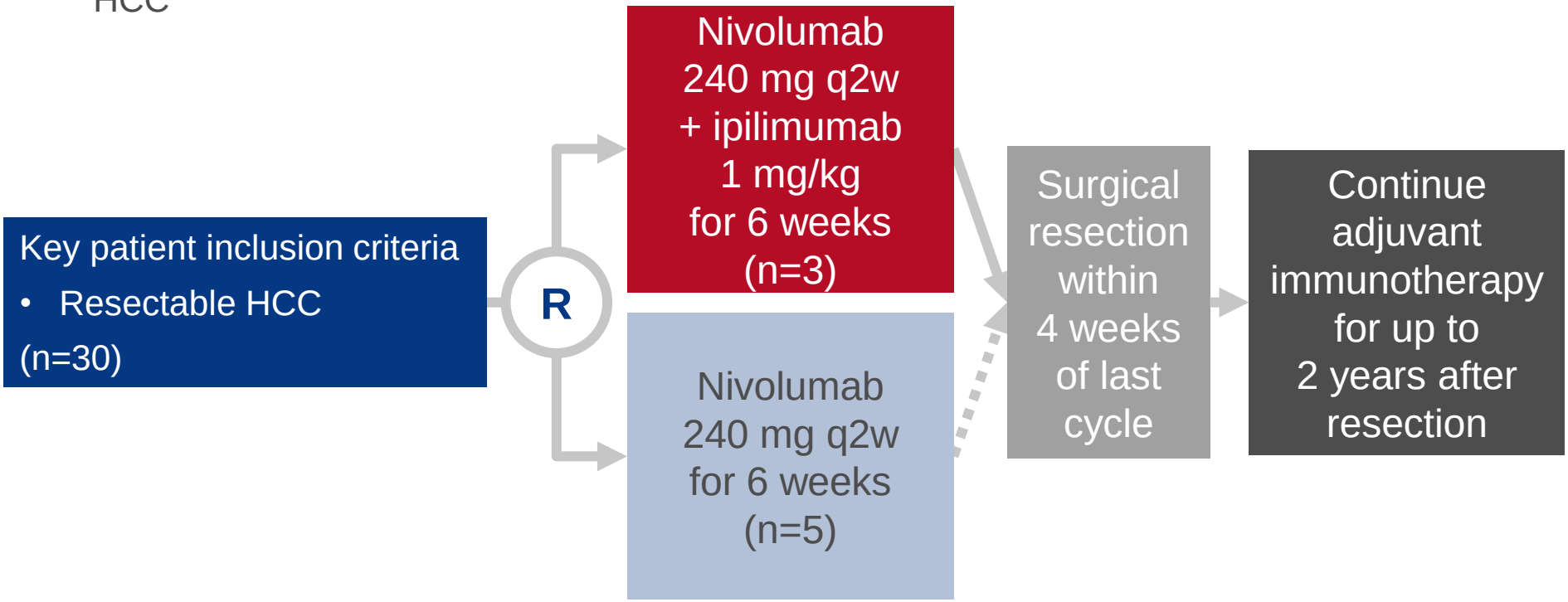
Cancers of the pancreas, small bowel and hepatobiliary tract

HEPATOCELLULAR CARCINOMA

185: Randomized, open-label, perioperative phase II study evaluating nivolumab alone versus nivolumab plus ipilimumab in patients with resectable HCC – Kaseb AO, et al

Study objective

- To assess the efficacy and safety of perioperative nivolumab + ipilimumab in patients with HCC



PRIMARY ENDPOINT

- Safety

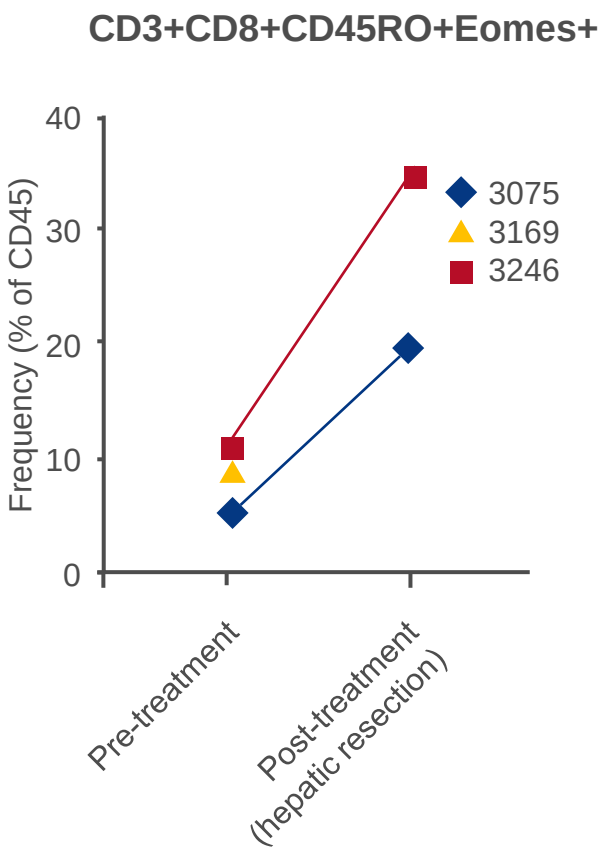
SECONDARY ENDPOINTS

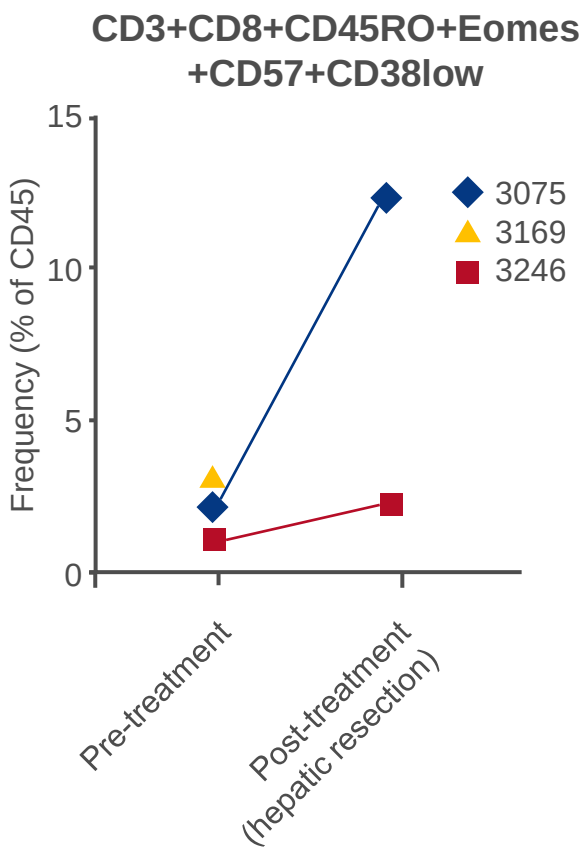
- ORR, pCR, TTP

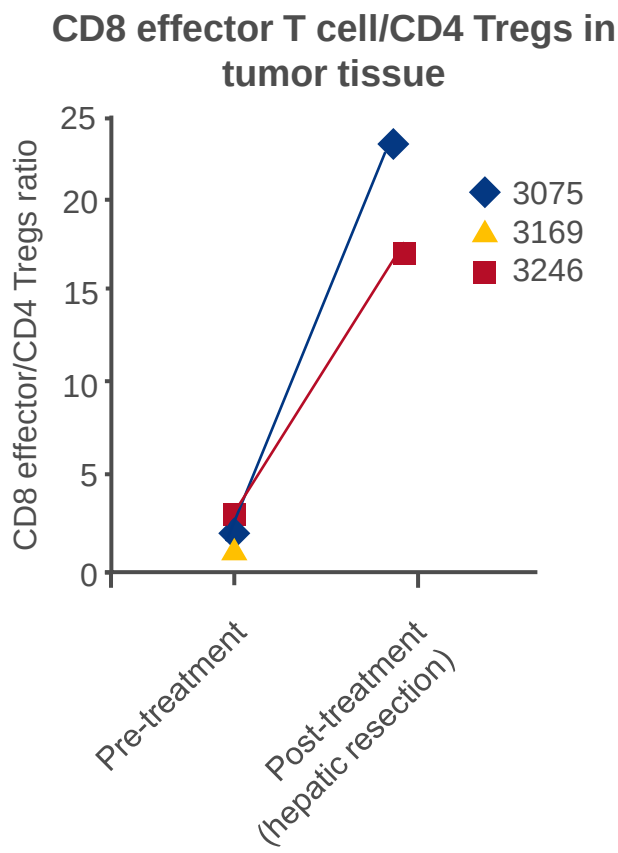
Kaseb AO, et al. J Clin Oncol 2019;37(Suppl):Abstr 185

185: Randomized, open-label, perioperative phase II study evaluating nivolumab alone versus nivolumab plus ipilimumab in patients with resectable HCC – Kaseb AO, et al

Key results





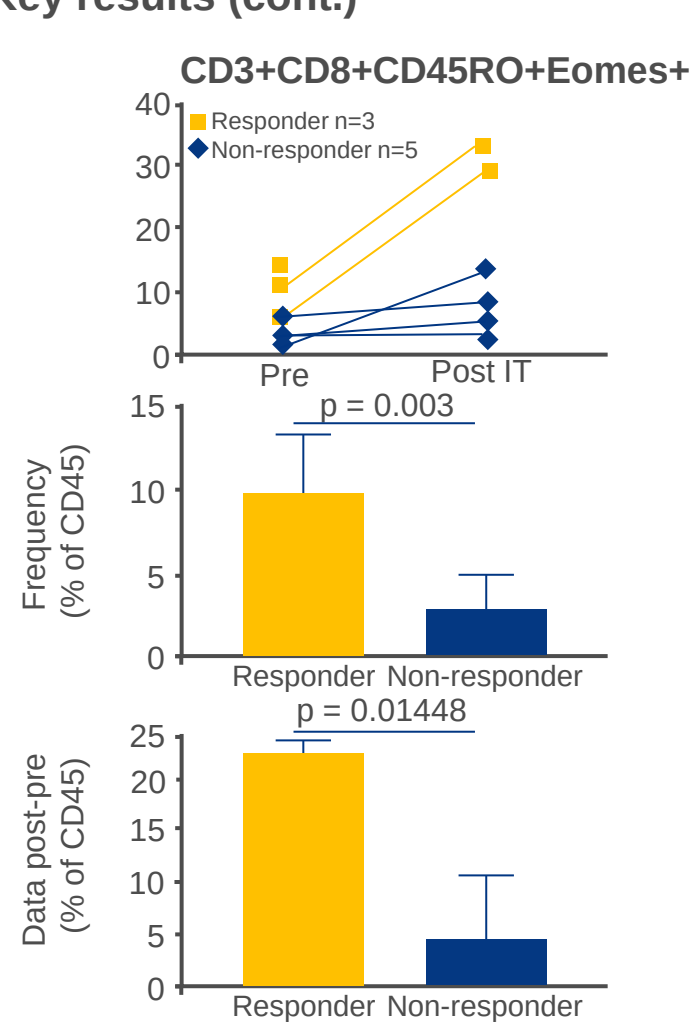


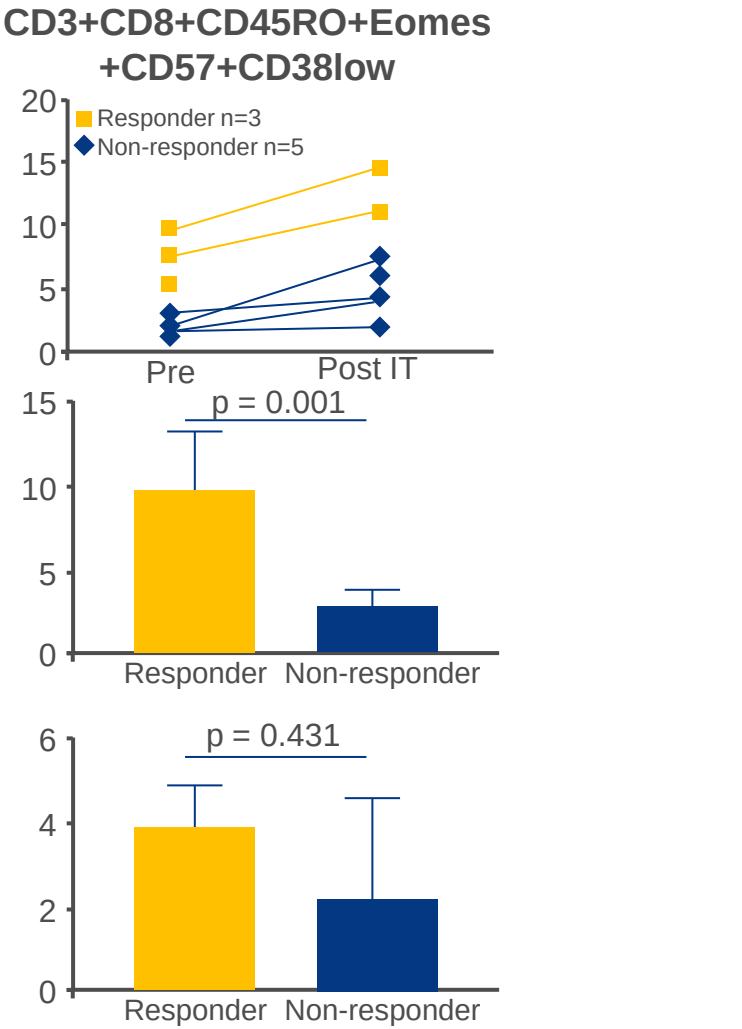
*Post therapy 'surgical' sample from 1 patient not available

Kaseb AO, et al. J Clin Oncol 2019;37(Suppl):Abstr 185

185: Randomized, open-label, perioperative phase II study evaluating nivolumab alone versus nivolumab plus ipilimumab in patients with resectable HCC – Kaseb AO, et al

Key results (cont.)





Kaseb AO, et al. J Clin Oncol 2019;37(Suppl):Abstr 185

185: Randomized, open-label, perioperative phase II study evaluating nivolumab alone versus nivolumab plus ipilimumab in patients with resectable HCC – Kaseb AO, et al

Key results (cont.)

- pCR was demonstrated in 3 of the 8 patients
- The most common grade 3 AE preoperative was ALT/AST increase in 1 patient and postoperative were colitis and amylase/lipase increase occurring in 1 patient each

Conclusion

- **In patients with resectable HCC, perioperative nivolumab + ipilimumab demonstrated encouraging responses and was generally well tolerated with no delays in surgical resection in this interim analysis**

Kaseb AO, et al. J Clin Oncol 2019;37(Suppl):Abstr 185

186: Analysis of survival and objective response (OR) in patients with hepatocellular carcinoma in a phase III study of lenvatinib (REFLECT) – Kudo M, et al

Study objective

- To assess the relationship between OR and OS in patients with HCC treated with lenvatinib or sorafenib in the REFLECT trial

Key patient inclusion criteria†

- No prior systemic therapy for unresectable HCC
- ≥1 measurable target lesion per mRECIST
- BCLC stage B or C
- Child-Pugh A
- ECOG PS ≤1

(n=954)

R 1:1

Lenvatinib 8 mg/day (BW <60 kg) or 12 mg/day (BW ≥60 kg) (n=478) → PD/ death

Stratification

- Region (Asia-Pacific vs. Western)
- MVI and/or EHS (yes vs. no)
- ECOG PS (0 vs. 1)
- BW (<60 kg vs. ≥60 kg)

Sorafenib 400 mg bid (n=476) → PD/ death

EXPLORATORY ENDPOINT

- OR and OS in responders (CR or PR) and non-responders (SD, PD or unknown/NE)

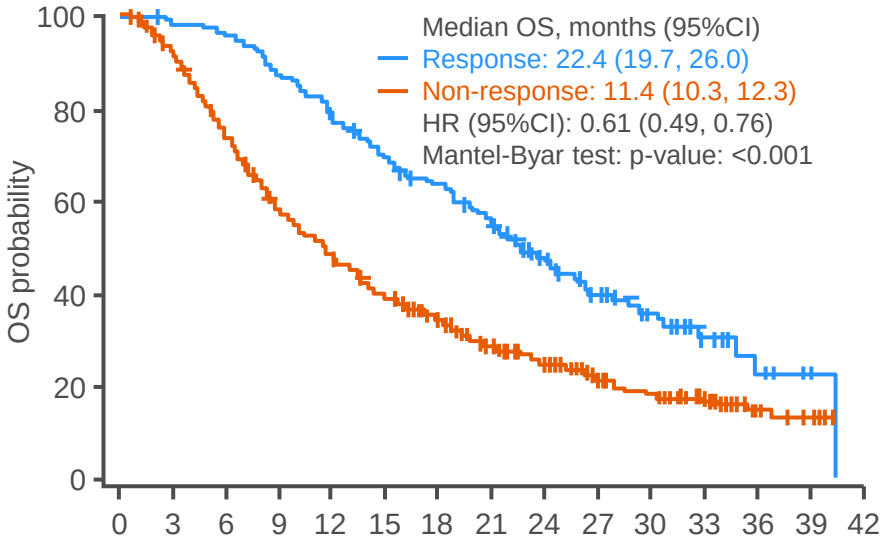
†Excluded patients with ≥50% liver occupation, clear bile duct invasion, or portal vein invasion at the main portal vein

Kudo M, et al. J Clin Oncol 2019;37(Suppl):Abstr 186

186: Analysis of survival and objective response (OR) in patients with hepatocellular carcinoma in a phase III study of lenvatinib (REFLECT) – Kudo M, et al

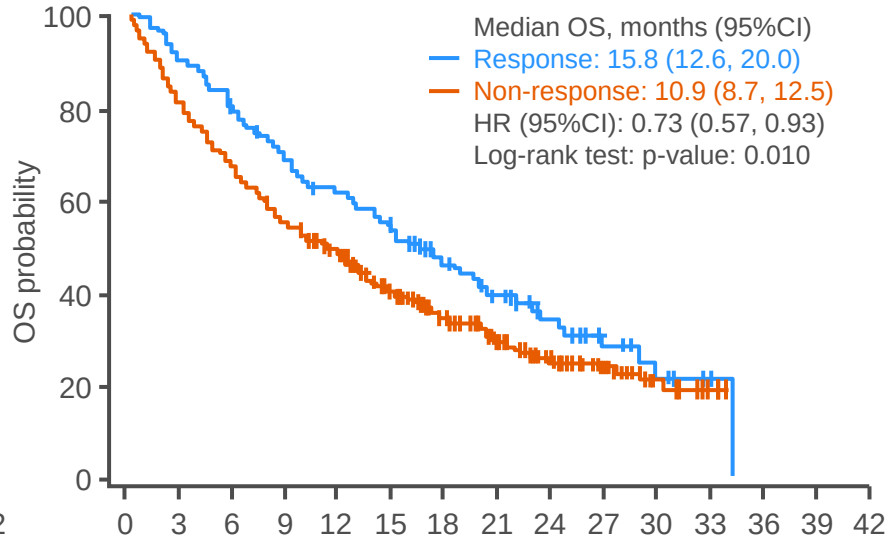
Key results

OS by OR in overall population



No. at risk														
Response	159	155	151	138	121	108	93	76	56	41	22	11	6	1	0
Non-response	795	721	571	441	362	291	241	180	129	83	51	26	10	5	0

OS by OR according to tumor response at 6 months



Response	126	113	96	84	70	57	42	31	19	10	6	1	0	0
Non-response	596	466	387	315	264	199	143	93	54	27	10	5	0	0

Kudo M, et al. J Clin Oncol 2019;37(Suppl):Abstr 186

186: Analysis of survival and objective response (OR) in patients with hepatocellular carcinoma in a phase III study of lenvatinib (REFLECT) – Kudo M, et al

Key results (cont.)

Multivariate analysis of factors associated with OS	HR (95%CI)	p-value
Macroscopic portal vein invasion (yes vs. no)	1.366 (1.141, 1.636)	0.0007
Baseline AFP (<200 vs. ≥200 mg/mL)	0.564 (0.483, 0.659)	<0.0001
No. of tumor sites at baseline (2 vs. 1)	1.400 (1.180, 1.662)	<0.0001
No. of tumor sites at baseline (≥3 vs. 1)	2.024 (1.659, 2.469)	<0.0001
Involved tumor site – liver (yes vs. no)	1.675 (1.203, 2.332)	0.0022
Etiology HBV (yes vs. no)	1.199 (1.031, 1.395)	0.0185
Prior procedure for HCC (yes vs. no)	0.844 (0.723, 0.986)	0.0323
Treatment (lenvatinib vs. sorafenib)	0.855 (0.734, 0.996)	0.0439
Objective response (yes vs. no)	0.611 (0.490, 0.762)	<0.0001

Conclusions

- **In patients with HCC, mRECIST OR was an independent predictor of OS regardless of treatment**
- **Those patients who have an OR are likely to have a longer survival**

Kudo M, et al. J Clin Oncol 2019;37(Suppl):Abstr 186

336: Combined immune checkpoint inhibition (ICI) with tremelimumab and durvalumab in patients with advanced hepatocellular carcinoma (HCC) or biliary tract carcinomas (BTC) – Floudas CS, et al

Study objective

- To assess the efficacy and safety of tremelimumab + durvalumab in patients with advanced HCC or BTC

Key patient inclusion criteria

- Advanced HCC or BTC (intrahepatic, extrahepatic, gallbladder or ampullary)
- Not amenable for resection, transplantation or ablation
- Progressed on ≥1 prior therapy*
- ECOG PS 0–2

(n=22)

→ Tremelimumab 75 mg + durvalumab 1500 mg for 4 doses → Durvalumab 1500 mg q4w → **PD/ toxicity**

PRIMARY ENDPOINT

- 6-month PFS

SECONDARY ENDPOINTS

- OS, DCR, safety

*Sorafenib for HCC and chemotherapy for BTC

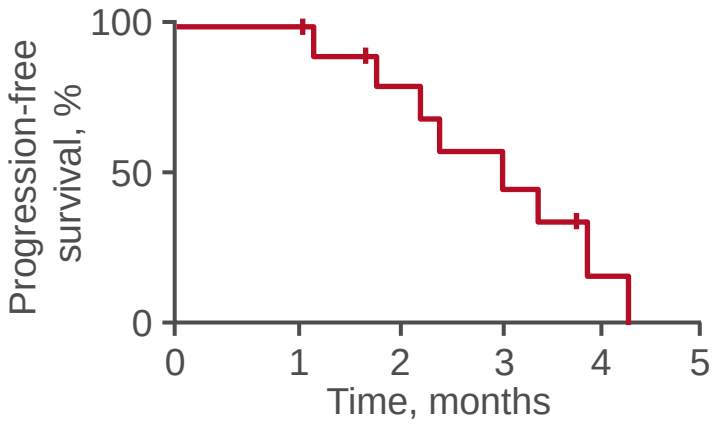
Floudas CS, et al. J Clin Oncol 2019;37(Suppl):Abstr 336

336: Combined immune checkpoint inhibition (ICI) with tremelimumab and durvalumab in patients with advanced hepatocellular carcinoma (HCC) or biliary tract carcinomas (BTC) – Floudas CS, et al

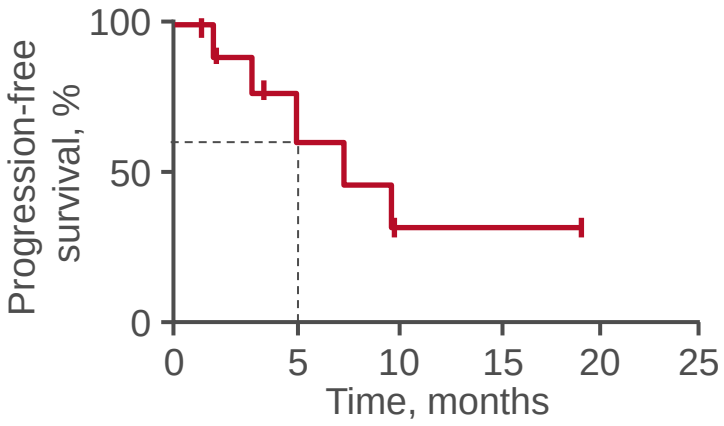
Key results

PFS

BTC: median 3.1 months (95%CI 0.8, 4.6)

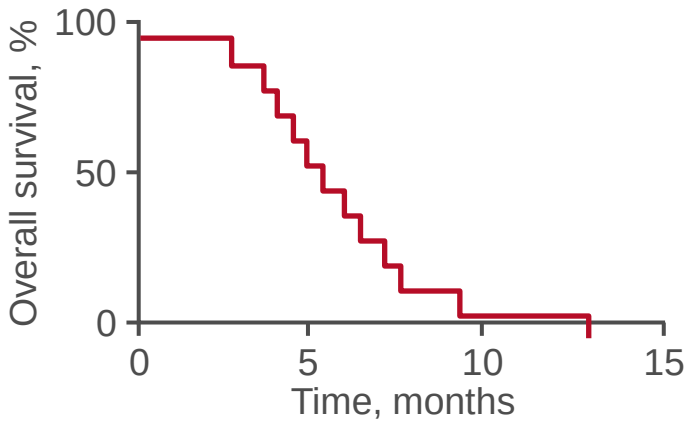


HCC: median 7.8 months (95%CI 2.6, 10.6)

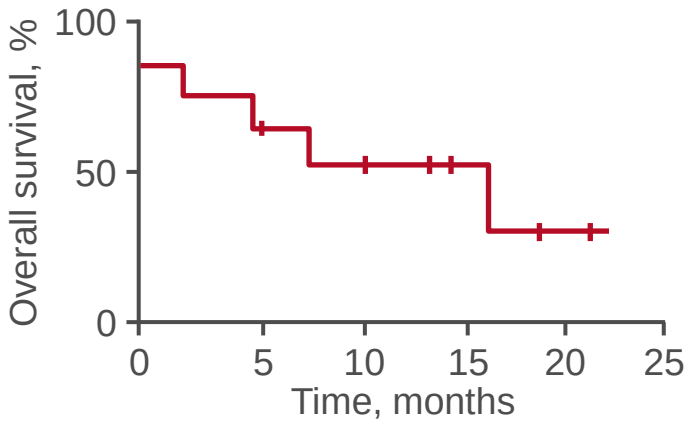


OS

BTC: median 5.45 months (95%CI 4.6, 8.3)



HCC: median 15.9 months (95%CI 7.1, 16.3)



Floudas CS, et al. J Clin Oncol 2019;37(Suppl):Abstr 336

336: Combined immune checkpoint inhibition (ICI) with tremelimumab and durvalumab in patients with advanced hepatocellular carcinoma (HCC) or biliary tract carcinomas (BTC) – Floudas CS, et al

Key results (cont.)

Response	HCC (n=10)	BTC (n=12)
BOR, n (%)		
PR	2 (20.0)	1 (8.3)
SD	5 (50.0)	5 (41.7)
PD	2 (20.0)	5 (41.7)
NA	1 (10.0)	1 (8.3)
DCR, n (%) [95%CI]	7 (70.0) [39.6, 89.2]	6 (50.0) [25.3, 74.6]

Floudas CS, et al. J Clin Oncol 2019;37(Suppl):Abstr 336

336: Combined immune checkpoint inhibition (ICI) with tremelimumab and durvalumab in patients with advanced hepatocellular carcinoma (HCC) or biliary tract carcinomas (BTC) – Floudas CS, et al

Key results (cont.)

- Grade ≥3 TRAEs included hyponatremia, lymphopenia, bullous dermatitis, hypophosphatemia, infection, oral mucositis, pain, maculopapular rash, anaphylaxis, respiratory failure, pleural effusion and dyspnea

Conclusion

- **In patients with HCC and BTC, tremelimumab + durvalumab provided encouraging activity and was generally well tolerated**

Floudas CS, et al. J Clin Oncol 2019;37(Suppl):Abstr 336

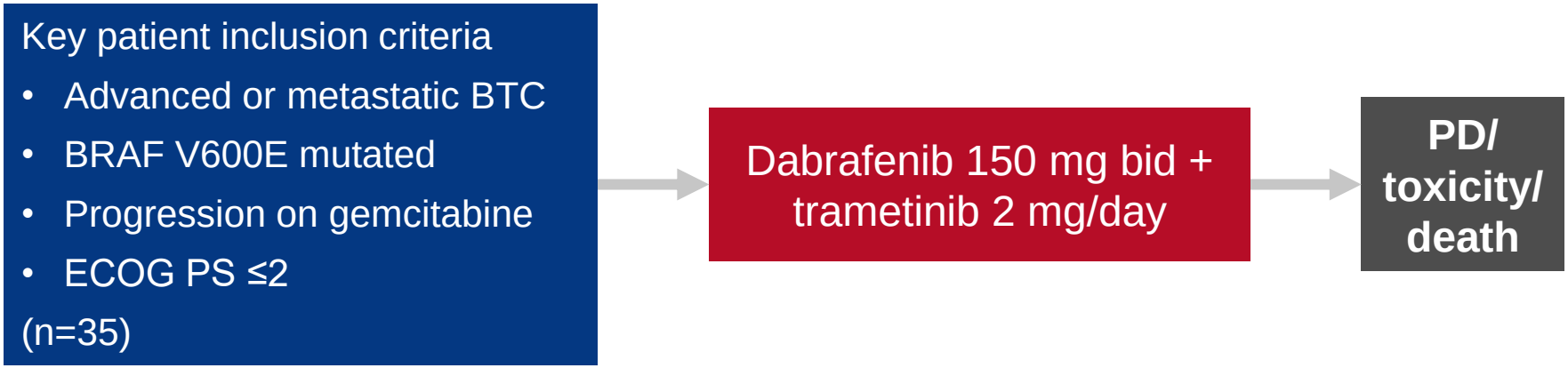
Cancers of the pancreas, small bowel and hepatobiliary tract

BILIARY TRACT CANCER

187: Efficacy and safety of dabrafenib (D) and trametinib (T) in patients (pts) with BRAF V600E-mutated biliary tract cancer (BTC): A cohort of the ROAR basket trial – Wainberg ZA, et al

Study objective

- To assess the efficacy and safety of dabrafenib (a BRAF inhibitor) + trametinib (a MEK inhibitor) in the cohort of patients with BRAF V600E-mutated BTC in the ROAR basket trial



PRIMARY ENDPOINT

- ORR (RECIST v1.1)

SECONDARY ENDPOINTS

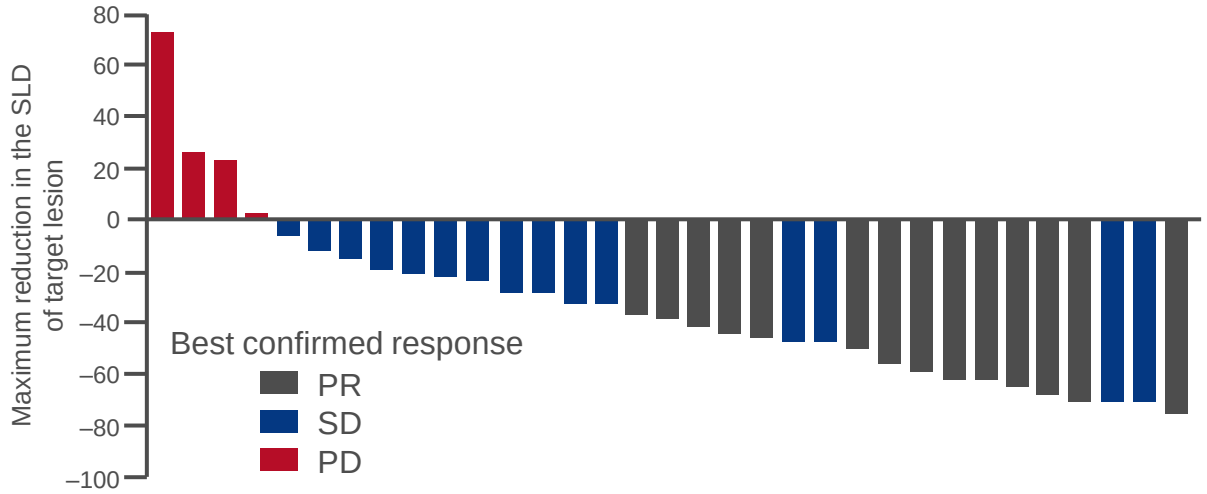
- DoR, PFS, OS, biomarkers, safety

Wainberg ZA, et al. J Clin Oncol 2019;37(Suppl):Abstr 187

187: Efficacy and safety of dabrafenib (D) and trametinib (T) in patients (pts) with BRAF V600E-mutated biliary tract cancer (BTC): A cohort of the ROAR basket trial – Wainberg ZA, et al

Key results

Response	Investigator-assessed	Independent review
BOR, n (%)		
CR	0	0
PR	14 (42)	12 (36)
SD	15 (45)	13 (39)
PD	4 (12)	4 (12)
NE/missing	0	4 (12)
ORR, n (%) [95%CI]	14 (42) [25.5, 60.8]	12 (36) [20.4, 54.9]

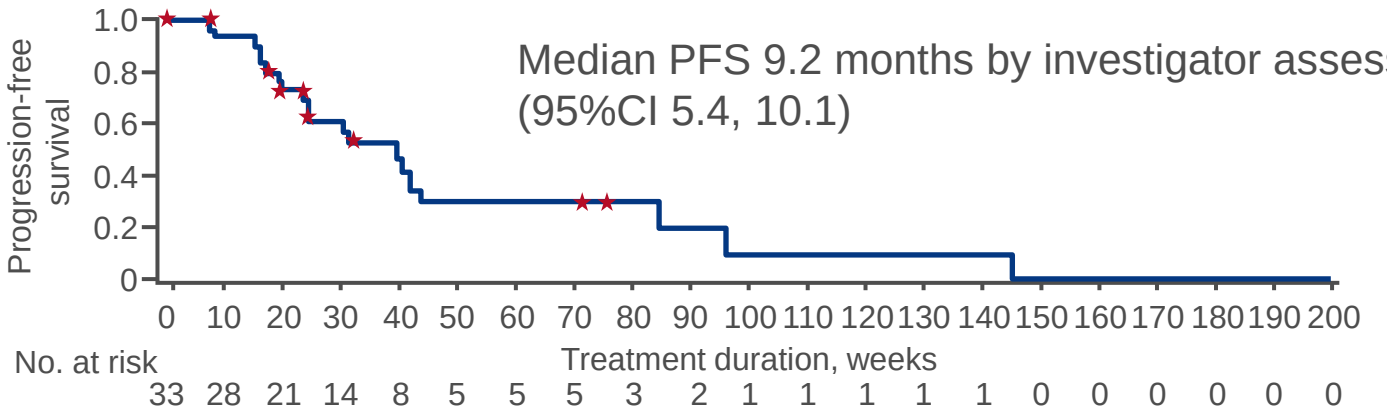


Wainberg ZA, et al. J Clin Oncol 2019;37(Suppl):Abstr 187

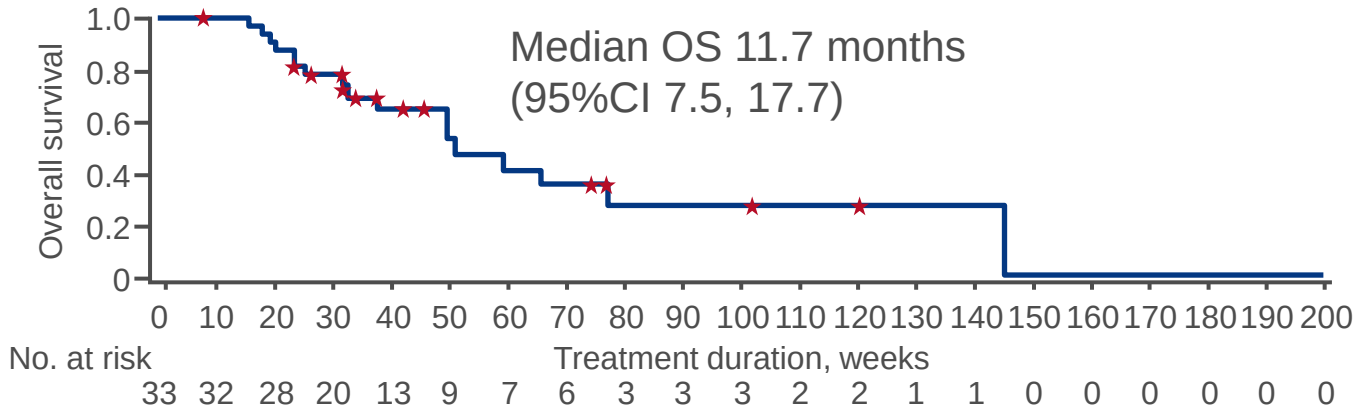
187: Efficacy and safety of dabrafenib (D) and trametinib (T) in patients (pts) with BRAF V600E-mutated biliary tract cancer (BTC): A cohort of the ROAR basket trial – Wainberg ZA, et al

Key results (cont.)

PFS



OS



Wainberg ZA, et al. J Clin Oncol 2019;37(Suppl):Abstr 187

187: Efficacy and safety of dabrafenib (D) and trametinib (T) in patients (pts) with BRAF V600E-mutated biliary tract cancer (BTC): A cohort of the ROAR basket trial – Wainberg ZA, et al

Key results (cont.)

AEs, n (%)	BTC cohort (n=35)
Any grade / grade 3–4	35 (100) / 20 (57)
TRAEs	32 (91)
Pyrexia	14 (40)
Rash	10 (29)
Nausea	8 (23)
Diarrhea	8 (23)
Fatigue	8 (23)
Chills	7 (20)
SAEs	14 (40)
Leading to dose reduction / dose interruption / discontinuation	13 (37) / 19 (54) / 1 (3)

Conclusion

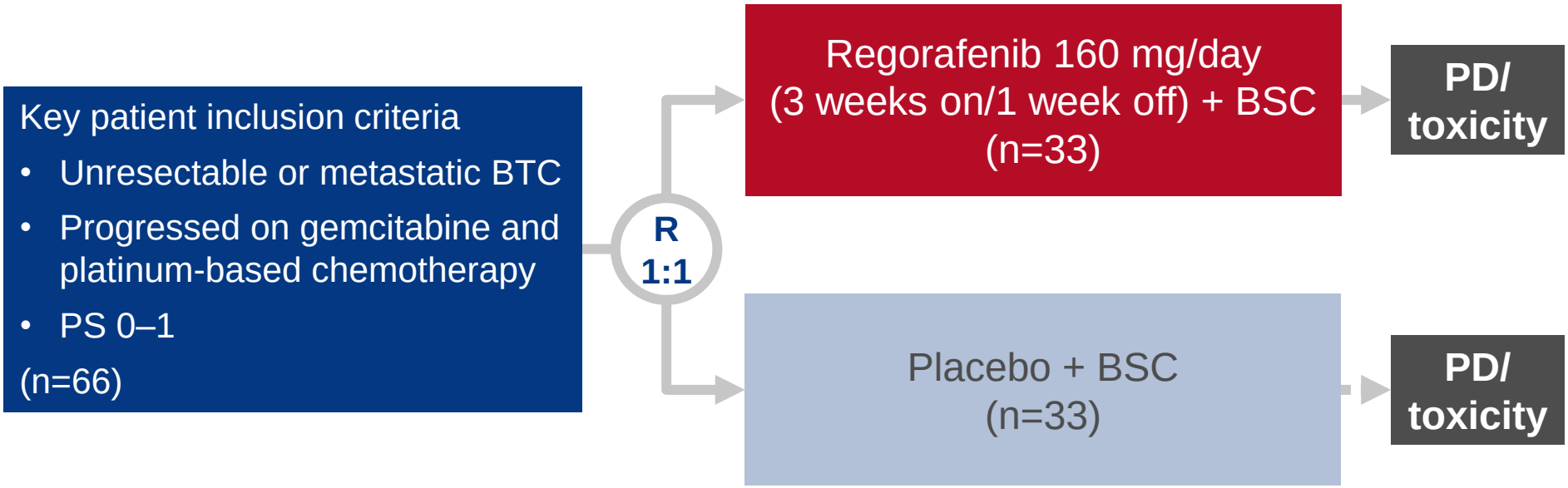
- **In patients with BRAF V600E-mutated BTC, dabrafenib + trametinib provided clinical benefit with efficacy similar to 1L gemcitabine + cisplatin**

Wainberg ZA, et al. J Clin Oncol 2019;37(Suppl):Abstr 187

345: Regorafenib after failure of gemcitabine and platinum-based chemotherapy for locally advanced (nonresectable) and metastatic biliary tumors: A randomized double-blinded placebo-controlled phase II trial – Demols A, et al

Study objective

- To assess the efficacy and safety of regorafenib + BSC in previously treated patients with unresectable or metastatic BTC



PRIMARY ENDPOINT

- PFS

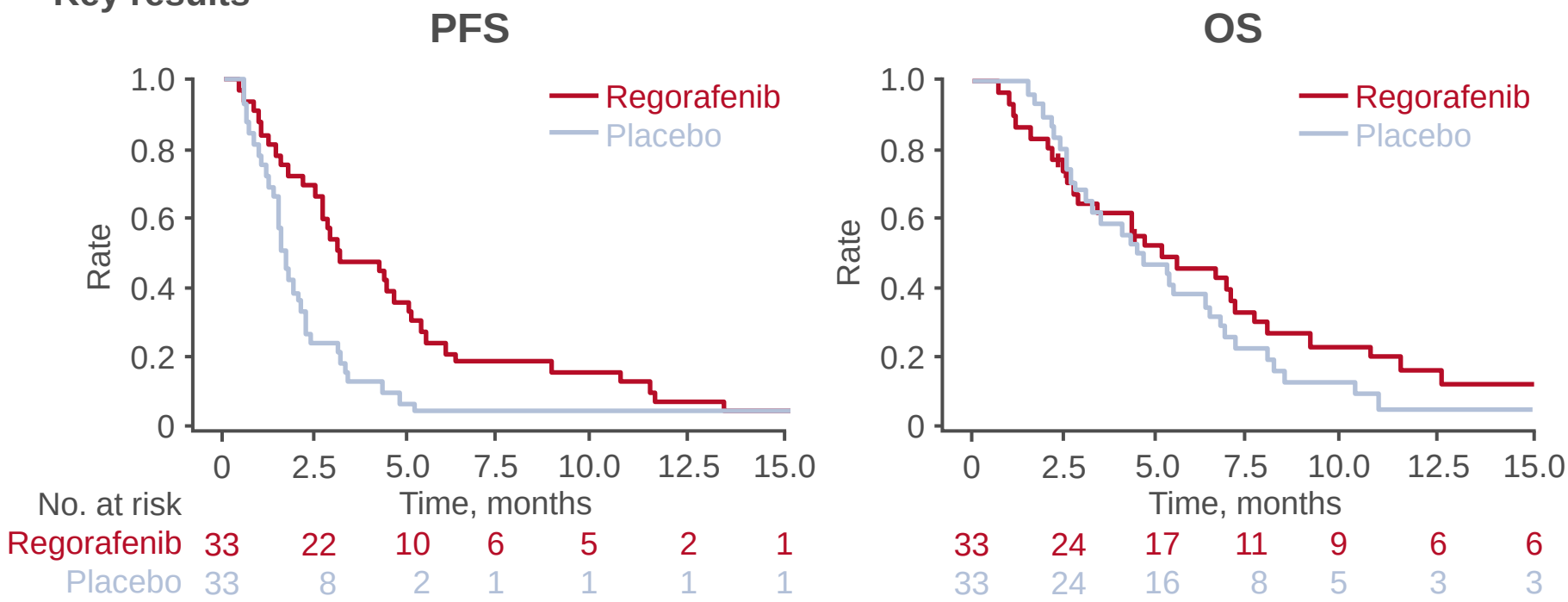
SECONDARY ENDPOINTS

- OS, ORR, safety

Demols A, et al. J Clin Oncol 2019;37(Suppl):Abstr 345

345: Regorafenib after failure of gemcitabine and platinum-based chemotherapy for locally advanced (nonresectable) and metastatic biliary tumors: A randomized double-blinded placebo-controlled phase II trial – Demols A, et al

Key results



	Regorafenib	Placebo	HR (95%CI); p-value
Median PFS, months (95%CI)	3.0 (2.3, 4.9)	1.5 (1.2, 2.0)	0.49 (0.29, 0.81); 0.005
Estimated 6-month PFS rate, % (95%CI)	21 (7, 35)	3 (0, 12)	
Median OS, months (95%CI)	5.3 (2.7, 10.5)	5.0 (3.0, 6.4)	0.76 (0.44, 1.30); 0.31
Estimated 6-month OS rate, % (95%CI)	48 (31, 65)	40 (22, 58)	
DCR, % (95%CI)	70 (51, 84)	33 (18, 52)	0.002

Demols A, et al. J Clin Oncol 2019;37(Suppl):Abstr 345

345: Regorafenib after failure of gemcitabine and platinum-based chemotherapy for locally advanced (nonresectable) and metastatic biliary tumors: A randomized double-blinded placebo-controlled phase II trial – Demols A, et al

Key results (cont.)

Grade ≥3 AEs, n	Regorafenib (n=33)	Placebo (n=33)
Nausea	2	2
Vomiting	1	0
Fatigue	6	3
Diarrhea	1	0
Hypophosphatemia	1	0
Cutaneous toxicity	2	0
Mucositis	1	0
Anorexia	1	1

Conclusions

- **In previously treated patients with unresectable or metastatic BTC, regorafenib provided significant improvement in PFS and DCR but not OS**
- **Regorafenib was generally well tolerated with no new safety signals**

Demols A, et al. J Clin Oncol 2019;37(Suppl):Abstr 345

Cancers of the pancreas, small bowel and hepatobiliary tract

NEUROENDOCRINE TUMOUR

190: Pembrolizumab treatment of advanced neuroendocrine tumors: Results from the phase II KEYNOTE-158 study – Strosberg JR, et al

Study objective

- To assess the efficacy and safety of pembrolizumab in patients with advanced neuroendocrine tumors

Key patient inclusion criteria

- Advanced neuroendocrine tumors of lung, appendix, small intestine, colon, rectum or pancreas
- Progression or intolerance to ≥1L of standard therapy
- Tumor sample for biomarker analysis
- ECOG PS 0–1

(n=107)

→ Pembrolizumab 200 mg iv q3w for up to 2 years → **PD/ toxicity/ withdrawal**

PRIMARY ENDPOINT

- ORR (RECIST v1.1)

SECONDARY ENDPOINTS

- DoR, PFS, OS, safety

Strosberg JR, et al. J Clin Oncol 2019;37(Suppl):Abstr 190

190: Pembrolizumab treatment of advanced neuroendocrine tumors: Results from the phase II KEYNOTE-158 study – Strosberg JR, et al

Key results

Response	Overall* (n=107)	PD-L1 positive (CPS ≥1) (n=17)	PD-L1 negative (n=82)
ORR, % (95%CI)	3.7 (1.0, 9.3)	0 (0, 19.5)	4.9 (1.8, 12.0)
BOR, n (%)			
CR	0	0	0
PR	4 (3.7)	0	4 (4.9)
SD	61 (57.0)	11 (64.7)	46 (56.1)
PD	33 (30.8)	6 (35.3)	23 (28.0)
NE	5 (4.7)	0	5 (6.1)
No assessment	4 (3.7)	0	4 (4.9)

*Includes 8 patients with unknown PD-L1 expression

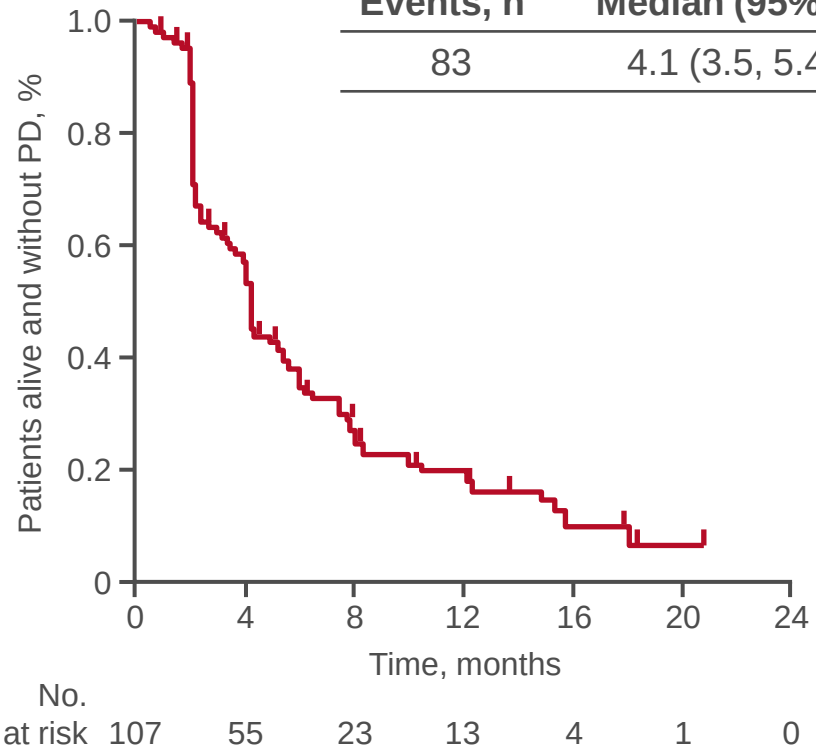
Strosberg JR, et al. J Clin Oncol 2019;37(Suppl):Abstr 190

190: Pembrolizumab treatment of advanced neuroendocrine tumors: Results from the phase II KEYNOTE-158 study – Strosberg JR, et al

Key results (cont.)

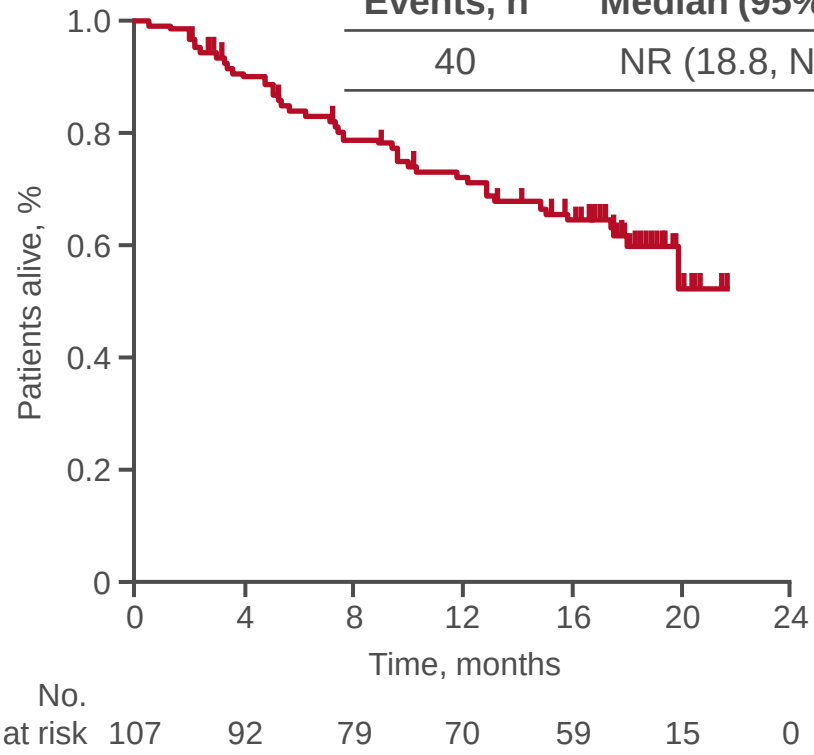
PFS

Events, n	Median (95%CI)
83	4.1 (3.5, 5.4)



OS

Events, n	Median (95%CI)
40	NR (18.8, NR)

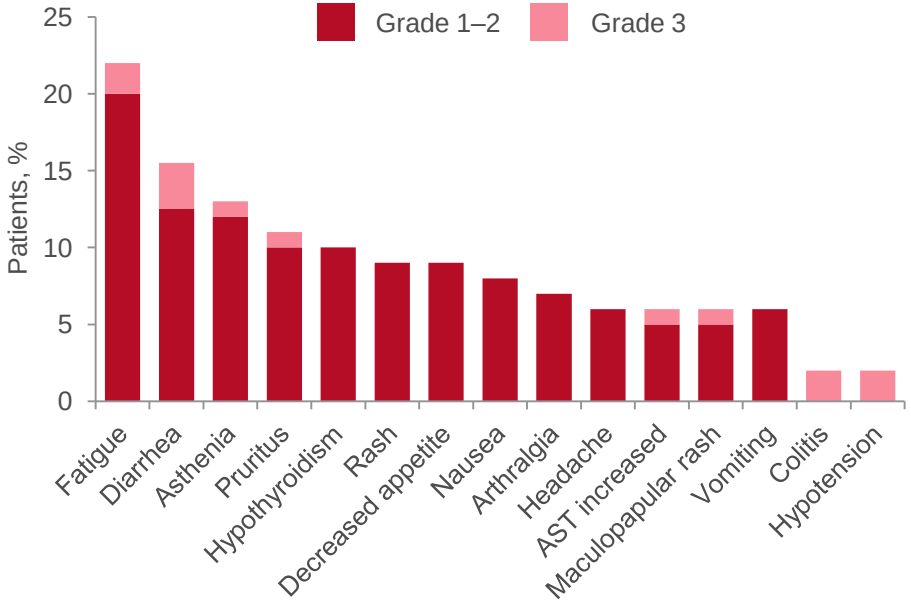


Strosberg JR, et al. J Clin Oncol 2019;37(Suppl):Abstr 190

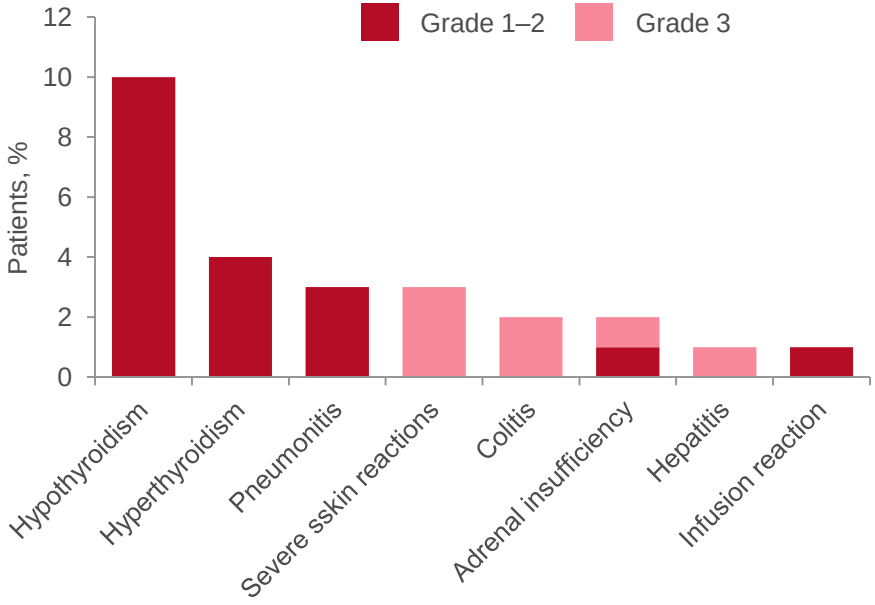
190: Pembrolizumab treatment of advanced neuroendocrine tumors: Results from the phase II KEYNOTE-158 study – Strosberg JR, et al

Key results (cont.)

TRAEs



Immune-mediated AEs



Conclusions

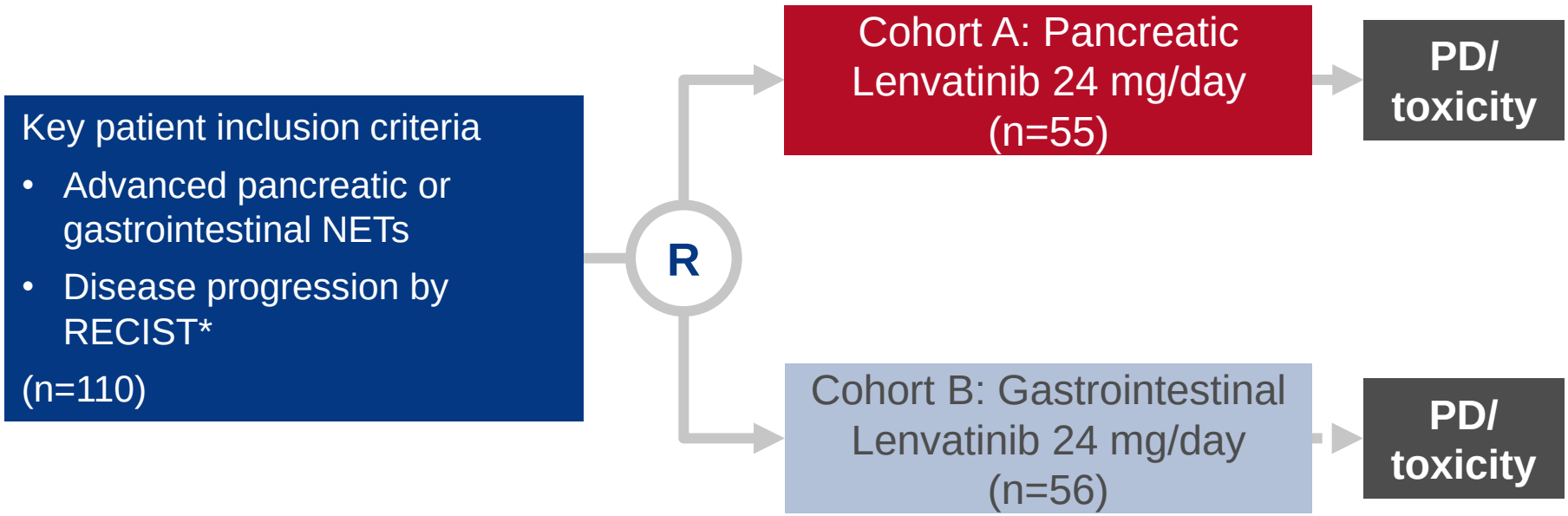
- In patients with advanced NETs, pembrolizumab demonstrated only 4 PRs although the responses were durable
- The safety profile of pembrolizumab was consistent with previous findings

Strosberg JR, et al. J Clin Oncol 2019;37(Suppl):Abstr 190

332: Progression-free survival (PFS) and subgroup analyses of lenvatinib in patients (pts) with G1/G2 advanced pancreatic (panNETs) and gastrointestinal (giNETs) neuroendocrine tumors (NETS): Updated results from the phase II TALENT trial (GETNE 1509) – Capdevila J, et al

Study objective

- To assess the efficacy and safety of lenvatinib in patients with advanced pancreatic or gastrointestinal NETs – updated results from the TALENT trial



PRIMARY ENDPOINT

- ORR (RECIST v1.1)

SECONDARY ENDPOINTS

- PFS, OS, biomarkers, safety

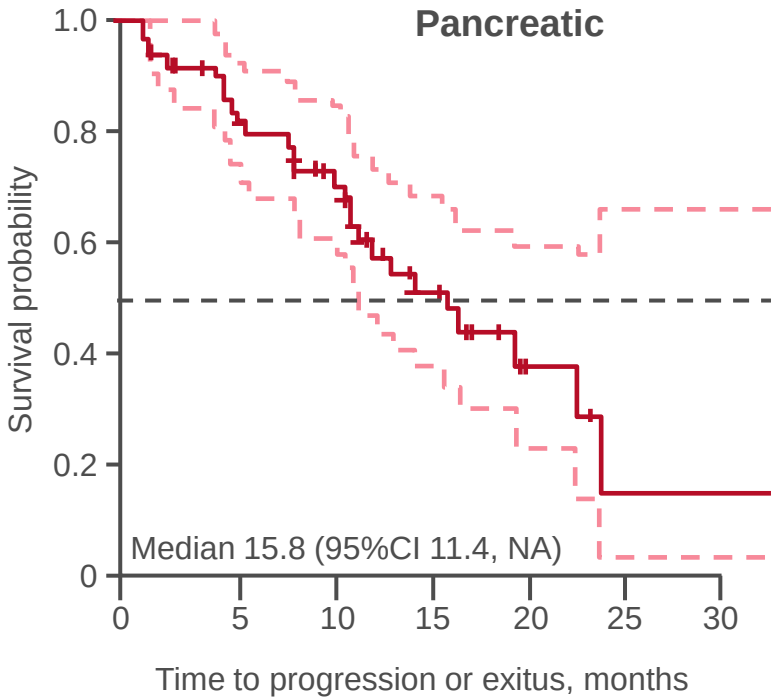
*For pancreatic NETs, PD to targeted agents was mandatory regardless of prior therapy with somatostatin analogs or chemotherapy; for gastrointestinal NETs, PD on somatostatin analogs

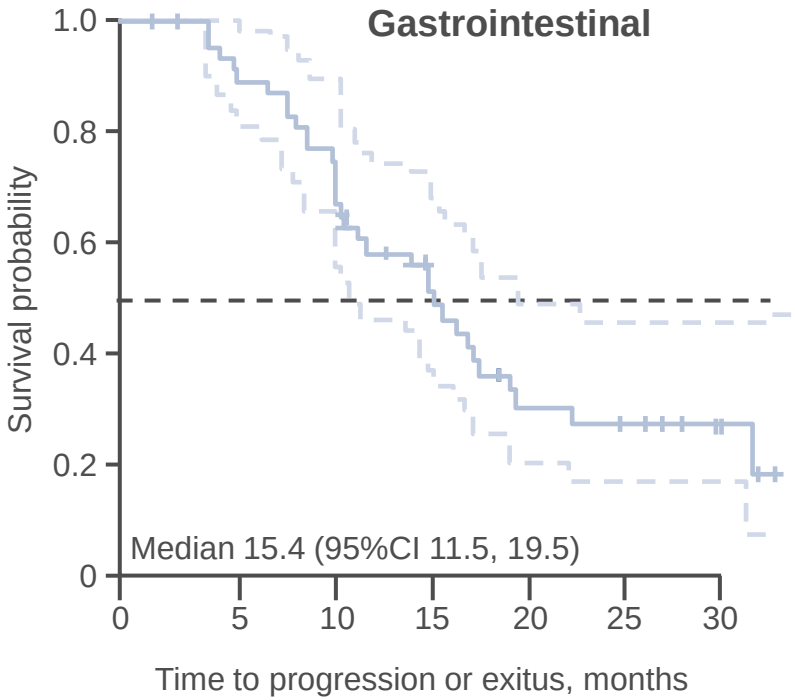
Capdevila J, et al. J Clin Oncol 2019;37(Suppl):Abstr 332

332: Progression-free survival (PFS) and subgroup analyses of lenvatinib in patients (pts) with G1/G2 advanced pancreatic (panNETs) and gastrointestinal (giNETs) neuroendocrine tumors (NETS): Updated results from the phase II TALENT trial (GETNE 1509) – Capdevila J, et al

Key results

PFS





	ORR, % (95%CI)
Pancreatic	40.4 (27.3, 54.9)
Gastrointestinal	18.5 (9.7, 31.9)

Capdevila J, et al. J Clin Oncol 2019;37(Suppl):Abstr 332

332: Progression-free survival (PFS) and subgroup analyses of lenvatinib in patients (pts) with G1/G2 advanced pancreatic (panNETs) and gastrointestinal (giNETs) neuroendocrine tumors (NETS): Updated results from the phase II TALENT trial (GETNE 1509) – Capdevila J, et al

Key results (cont.)

Grade 3/4 AEs occurring in ≥5%, n (%)	Pancreatic NETs (n=55)	Gastrointestinal NETs (n=56)
Asthenia/fatigue	4 (7.2)	11 (19.6)
Hypertension	10 (18.1)	13 (23.2)
Diarrhea	3 (5.4)	5 (8.9)
Vomiting	4 (7.2)	1 (1.8)
Abdominal pain	3 (5.4)	3 (5.3)

Conclusion

- **In patients with pancreatic or gastrointestinal NETs, lenvatinib demonstrated high ORR and encouraging PFS data**

Capdevila J, et al. J Clin Oncol 2019;37(Suppl):Abstr 332

CANCERS OF THE COLON, RECTUM AND ANUS

480: A randomized, double-blinded, placebo-controlled multicentre phase II trial of adjuvant immunotherapy with tecemotide (L-BLP25) after R0/R1 hepatic colorectal cancer metastasectomy (LICC): Final results – Schimanski CC, et al

Study objective

- To assess the efficacy and safety of tecemotide (an antigen-specific cancer vaccine targeting MUC1) in patients with liver metastases limited to CRC

Key patient inclusion criteria

- Stage IV CRC limited to liver metastases
- Resection (R0/R1) of all liver metastases
- Metastasectomy with any neoadjuvant therapy
- ECOG PS 0–1

(n=121)

R 2:1

Tecemotide* 930 µg weekly x8 sc followed by 6-week maintenance for up to 2 years (n=79) → PD

Placebo* (n=42) → PD

CO-PRIMARY ENDPOINTS

- RFS, 3-year OS

SECONDARY ENDPOINTS

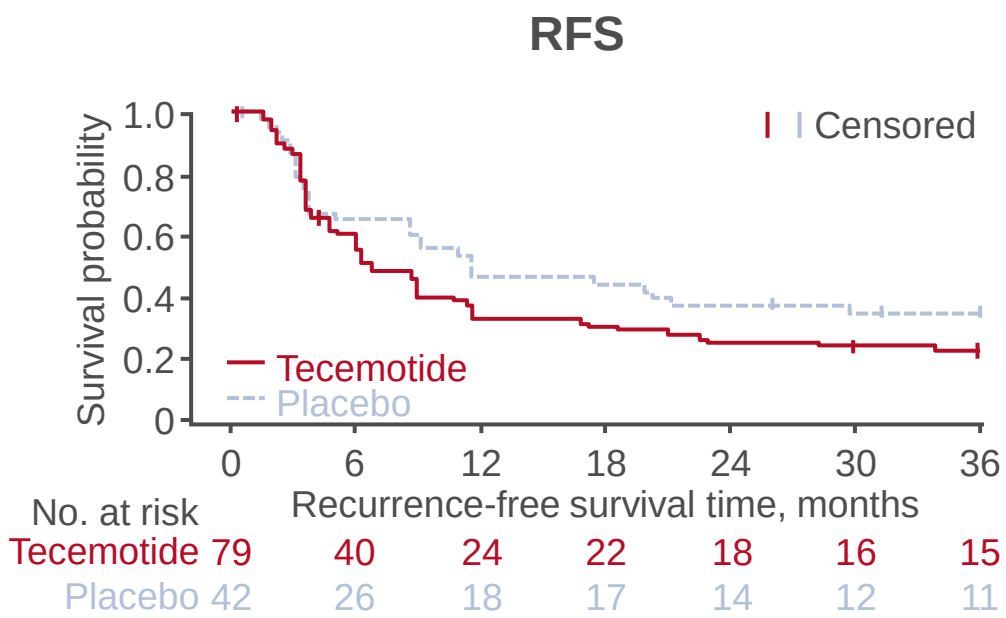
- RFS and OS by MUC1 expression, safety

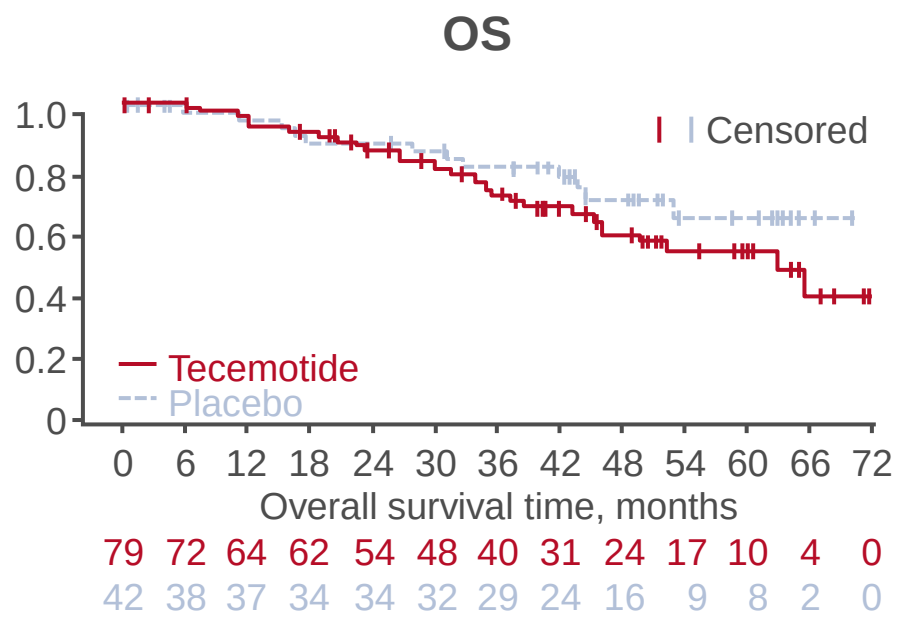
*Three days prior to tecemotide or placebo, cyclophosphamide 300 mg/m^2 or matching saline was given IV, respectively

Schimanski CC, et al. J Clin Oncol 2019;37(Suppl):Abstr 480

480: A randomized, double-blinded, placebo-controlled multicentre phase II trial of adjuvant immunotherapy with tecemotide (L-BLP25) after R0/R1 hepatic colorectal cancer metastasectomy (LICC): Final results – Schimanski CC, et al

Key results





Outcome	Tecemotide (n=79)	Placebo (n=42)	p-value
Median RFS, months (90%CI)	6.1 (5.8, 8.8)	11.4 (5.0, 20.3)	0.1754
Median OS, months (90%CI)	62.8 (45.1, NR)	NA (53.6, NR)	0.2141

Schimanski CC, et al. J Clin Oncol 2019;37(Suppl):Abstr 480

480: A randomized, double-blinded, placebo-controlled multicentre phase II trial of adjuvant immunotherapy with tecemotide (L-BLP25) after R0/R1 hepatic colorectal cancer metastasectomy (LICC): Final results – Schimanski CC, et al

Key results (cont.)

Grade 3/4 AEs occurring in ≥2 patients, n (%)	Tecemotide (n=79)	Placebo (n=42)
Diarrhea	2 (2.5)	2 (4.8)
Back pain	2 (2.5)	-
Anemia	2 (2.5)	-
Cholestasis	1 (1.3)	2 (4.8)
Ileus	2 (2.5)	-
Jaundice cholestatic	2 (2.5)	-
Blood uric acid increased	2 (2.5)	-

Conclusion

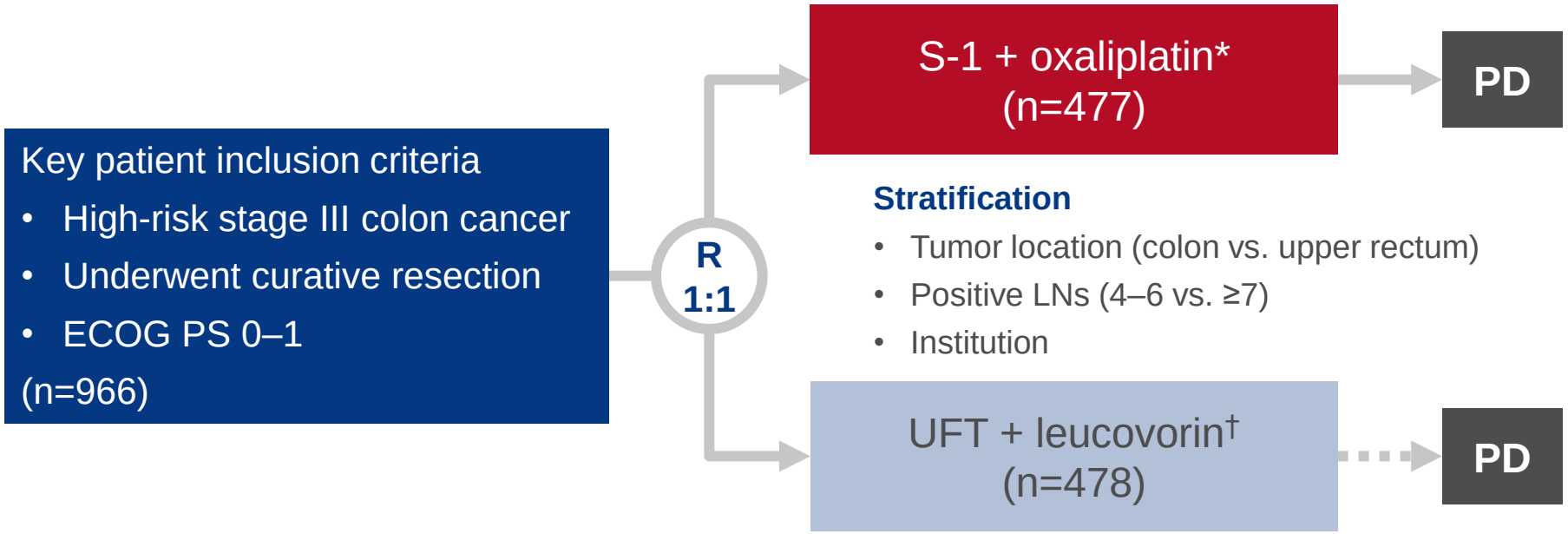
- **In patients with hepatic CRC metastasectomy, tecemotide did not provide any benefit in survival over placebo**

Schimanski CC, et al. J Clin Oncol 2019;37(Suppl):Abstr 480

484: A randomized phase III trial of S-1/oxaliplatin (SOX) versus UFT/leucovorin as adjuvant chemotherapy for high-risk stage III colon cancer: The ACTS-CC 02 trial – Takahashi T, et al

Study objective

- To assess the efficacy and safety of S-1 + oxaliplatin (SOX) compared with UFT + leucovorin in patients with high-risk stage III colon cancer



PRIMARY ENDPOINT

- DFS

SECONDARY ENDPOINTS

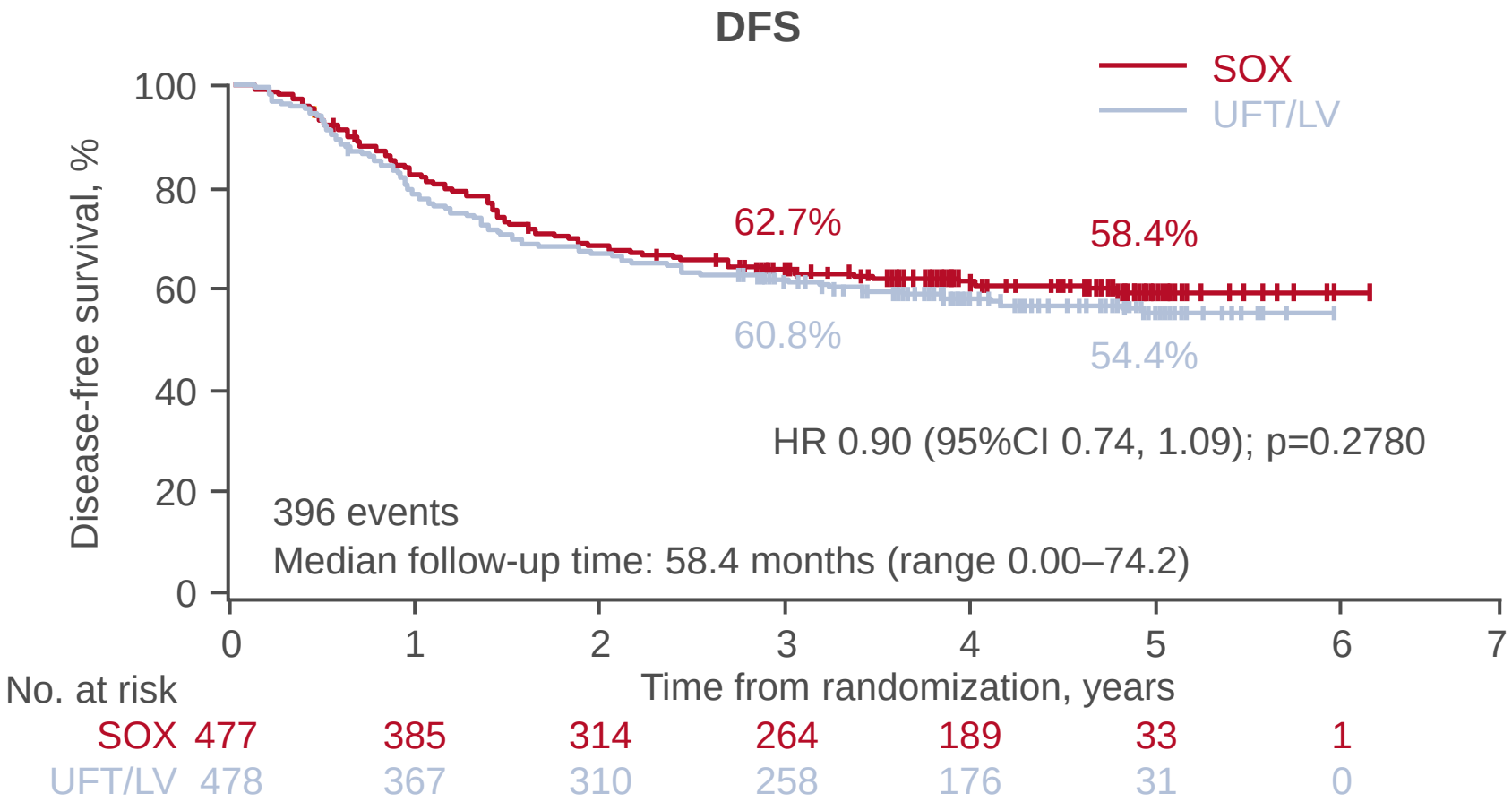
- RFS, OS, safety

*S-1 80–120 mg/day according to BSA D1–14 + oxaliplatin 100 mg/m^2 q3w for 8 course; †UFT 300–600 mg/day according to BSA + leucovorin 75 mg/day D1–28 every 35 days for 5 courses

Takahashi T, et al. J Clin Oncol 2019;37(Suppl):Abstr 484

484: A randomized phase III trial of S-1/oxaliplatin (SOX) versus UFT/leucovorin as adjuvant chemotherapy for high-risk stage III colon cancer: The ACTS-CC 02 trial – Takahashi T, et al

Key results



Takahashi T, et al. J Clin Oncol 2019;37(Suppl):Abstr 484

484: A randomized phase III trial of S-1/oxaliplatin (SOX) versus UFT/leucovorin as adjuvant chemotherapy for high-risk stage III colon cancer: The ACTS-CC 02 trial – Takahashi T, et al

Key results (cont.)

Grade ≥3 AEs occurring in ≥2%, n (%)	SOX (n=459)	UFT + leucovorin (n=472)
Neutropenia	79 (17.2)	7 (1.5)
Thrombocytopenia	13 (2.8)	3 (0.6)
AST	3 (0.7)	10 (2.1)
ALT	4 (0.9)	14 (3.0)
Nausea	9 (2.0)	4 (0.8)
Diarrhea	25 (5.4)	38 (8.1)
Anorexia	16 (3.5)	11 (2.3)
Peripheral sensory neuropathy	21 (4.6)	1 (0.2)

Conclusion

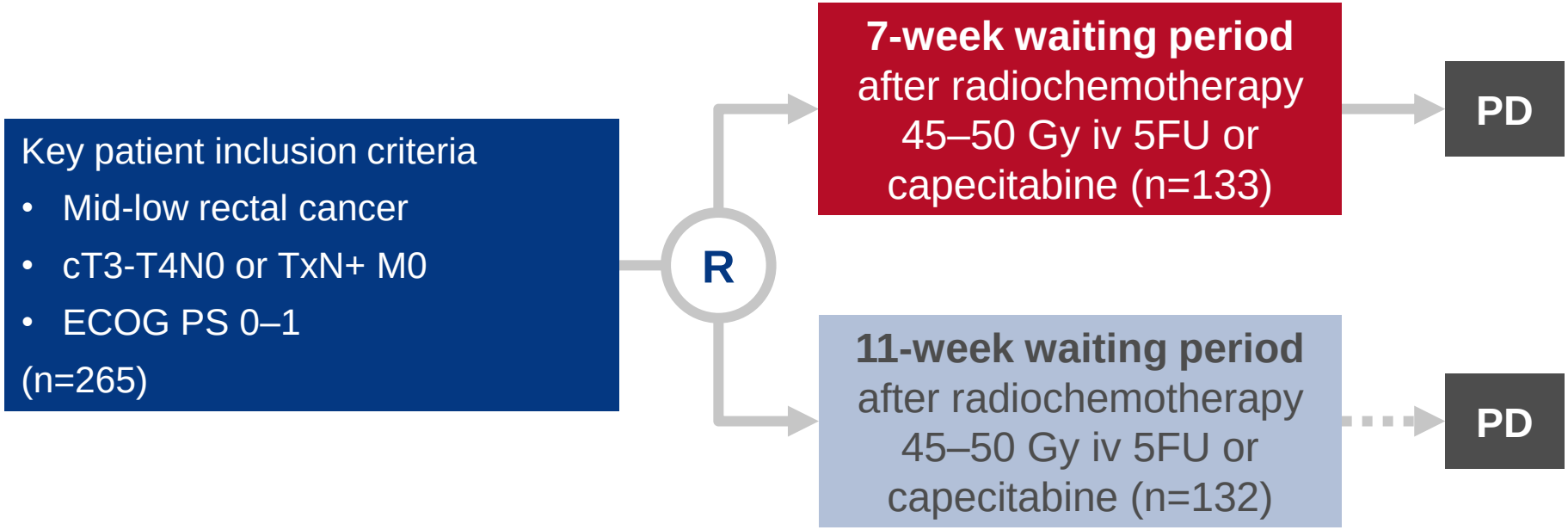
- **In patients with high-risk stage III colon cancer, SOX was not superior to UFT + leucovorin, although in more advanced disease (stage IIIC, N2b) SOX may be effective**

Takahashi T, et al. J Clin Oncol 2019;37(Suppl):Abstr 484

483: Does a longer waiting period after neoadjuvant radiochemotherapy improve the oncological prognosis of rectal cancer? Three-year follow-up results of the GRECCAR-6 randomized multicentre trial – Lefevre JH, et al

Study objective

- To assess whether a long waiting period between radiochemotherapy and resection in patients with rectal cancer impacts the rate of cPR (ypT0N0) in the GRECCAR6 trial



PRIMARY ENDPOINT

- Pathologic complete response (ypT0N0) rate

SECONDARY ENDPOINTS

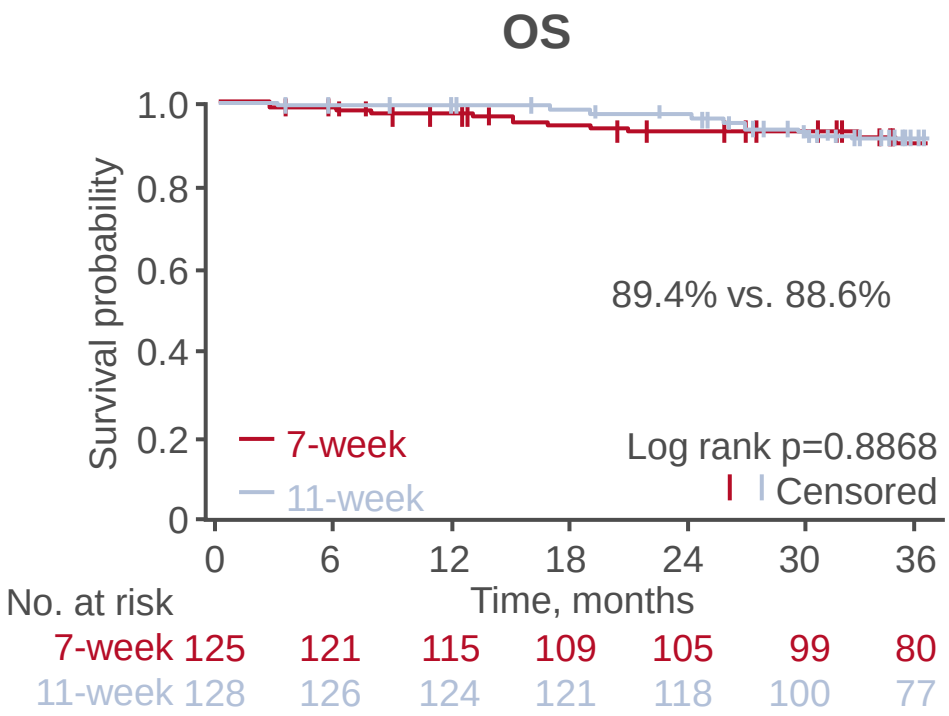
- OS, DFS, rate of recurrence

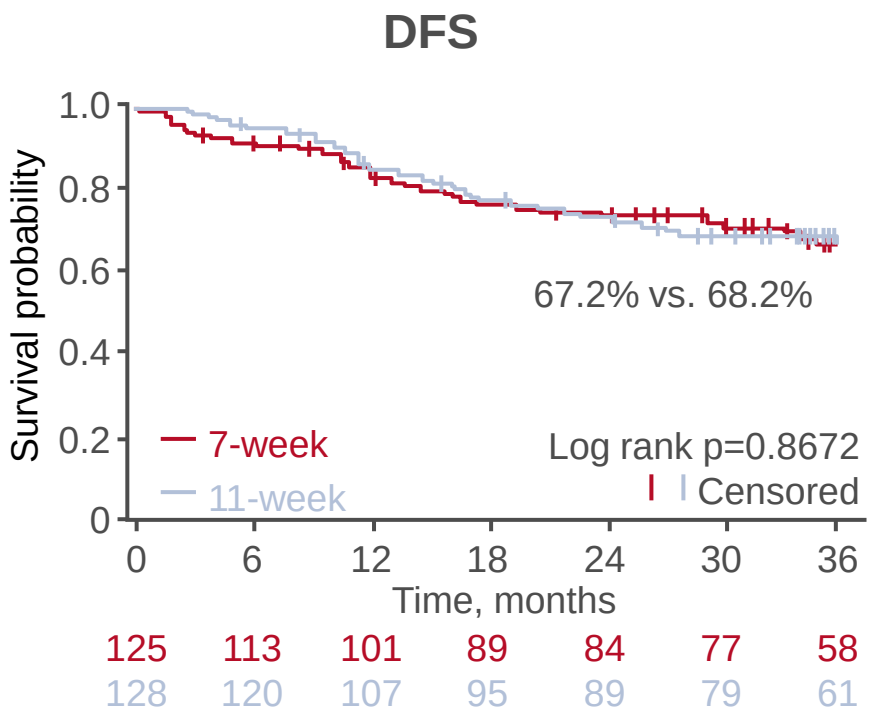
Lefevre JH, et al. J Clin Oncol 2019;37(Suppl):Abstr 483

483: Does a longer waiting period after neoadjuvant radiochemotherapy improve the oncological prognosis of rectal cancer? Three-year follow-up results of the GRECCAR-6 randomized multicentre trial – Lefevre JH, et al

Key results

- The pathologic complete response (ypT0N0) rate was 15% and 17.4% in the 7- and 11-week groups, respectively (p=0.5983)





Lefevre JH, et al. J Clin Oncol 2019;37(Suppl):Abstr 483

483: Does a longer waiting period after neoadjuvant radiochemotherapy improve the oncological prognosis of rectal cancer? Three-year follow-up results of the GRECCAR-6 randomized multicentre trial – Lefevre JH, et al

Key results (cont.)

Outcomes at 3 years, %	7-week	11-week	p-value
Metastatic recurrence	24.3	25.4	0.8589
Local recurrence	8.6	9.7	0.5780
In patients achieving ypT0N0 (n=43)			
OS	89	95	0.2597
Metastatic recurrence	5	29	0.0045
Local recurrence	11	0	0.0357

Conclusions

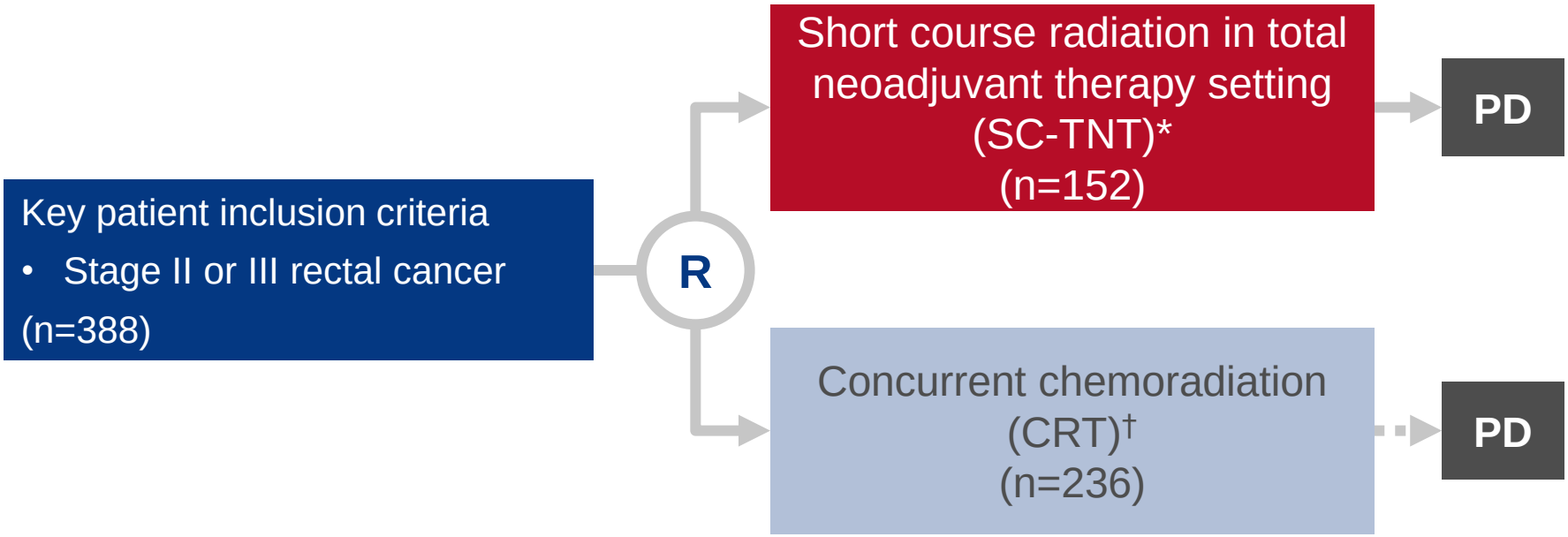
- **In patients with rectal cancer, there was no difference on pathologic complete response rate or survival and recurrence between a 7- or 11-week waiting period after neoadjuvant radiochemotherapy**
- **It is suggested that surgery should be performed around 7–8 weeks after radiochemotherapy in the absence of a rectal sparing strategy**

Lefevre JH, et al. J Clin Oncol 2019;37(Suppl):Abstr 483

486: Total neoadjuvant therapy with short course radiation compared to concurrent chemoradiation in rectal cancer – Chapman W Jr, et al

Study objective

- To assess whether short course radiation in the total neoadjuvant therapy setting impacts outcomes as compared with concurrent chemoradiation



ENDPOINTS

- Downstaging by pCR and neoadjuvant rectal (NAR) score, DFS

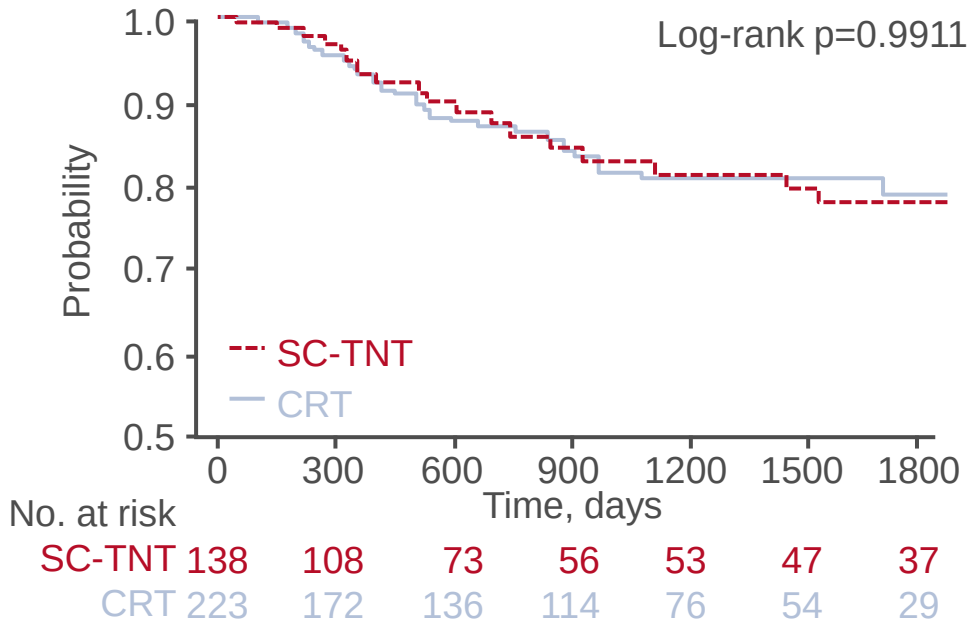
*25–35 Gy 5 fractions followed by CAPOX or FOLFOX;
†50–55 Gy 25–28 fractions with concurrent 5FU or capecitabine

Chapman W Jr, et al. J Clin Oncol 2019;37(Suppl):Abstr 486

486: Total neoadjuvant therapy with short course radiation compared to concurrent chemoradiation in rectal cancer – Chapman W Jr, et al

Key results

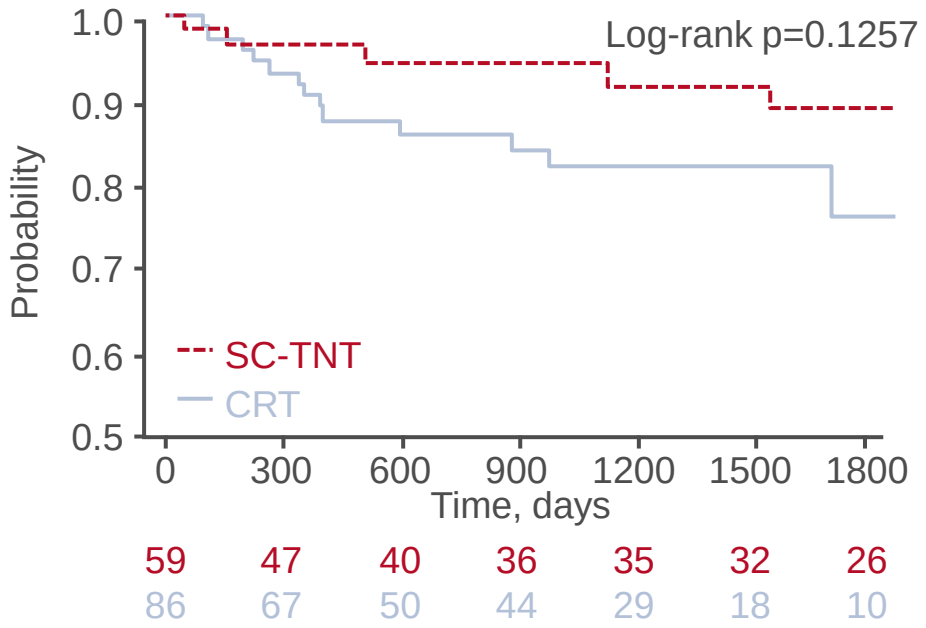
DFS in total population



No. at risk

SC-TNT	138	108	73	56	53	47	37
CRT	223	172	136	114	76	54	29

DFS in PROSPECT eligible subgroup



SC-TNT	59	47	40	36	35	32	26
CRT	86	67	50	44	29	18	10

Chapman W Jr, et al. J Clin Oncol 2019;37(Suppl):Abstr 486

486: Total neoadjuvant therapy with short course radiation compared to concurrent chemoradiation in rectal cancer – Chapman W Jr, et al

Key results (cont.)

Outcomes, %	Short course radiation	Concurrent chemoradiation	p-value
Downstaging			
pCR	38 (25)	45 (19)	0.16
NAR <8	55 (36)	65 (28)	0.07
Any recurrence	21 (14.9)	32 (14.3)	0.87

Conclusion

- **In patients with rectal cancer, the use of short course radiation demonstrated comparable effectiveness as concurrent chemoradiation with similar DFS although short course radiation may provide better downstaging**

Chapman W Jr, et al. J Clin Oncol 2019;37(Suppl):Abstr 486