GI SLIDE DECK 2017

Selected abstracts from:

ESMO 2017 CONGRESS

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esdo european society of digestive oncology

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Letter from ESDO

DEAR COLLEAGUES

It is my 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 2017. This slide set specifically focuses on the **ESMO 2017 Congress** and is available in English, French 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 that 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,

Eric Van Cutsem
Wolff Schmiegel
Phillippe Rougier
Thomas Seufferlein

(ESDO Governing Board)

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european society of digestive oncology

ESDO Medical Oncology Slide Deck
Editors 2017

COLORECTAL CANCERS



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PANCREATIC CANCER AND HEPATOBILIARY TUMOURS


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GASTRO-OESOPHAGEAL AND NEUROENDOCRINE TUMOURS


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BIOMARKERS


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esdo

Glossary

1/2/3L	first-/second-/third-line
5FU	5-fluorouracil
AE	adverse event
AFP	alpha-fetoprotein
ALP	alkaline phosphatase
ANG	angiopoietin
ASNS	asparagine synthetase
BEV	bevacizumab
bid	twice daily
BOR	best overall response
BSC	best supportive care
CAPOX	capecitabine-oxaliplatin
CBR	clinical benefit rate
CD4/8/16	cluster of differentiation 4/8/16
CI	confidence interval
CIMP	CpG island methylator phenotype
CIV	continuous intravenous infusion
CMS	consensus molecular subtype
CR	complete response
(m)CRC	(metastatic) colorectal cancer
CRT	chemoradiotherapy
CT	chemotherapy
ctDNA	circulating DNA
D	day
DCR	disease control rate
DFS	disease-free survival
DLL4	delta-like ligand 4
dMMR	DNA mismatch repair deficient
DoR	duration of response
dsRNA	double-stranded RNA
ECF	epirubicin + cisplatin + 5FU
ECX	epirubicin + cisplatin + capecitabine
ECOG	Eastern Cooperative Oncology Group
EHS	extrahepatic spread
EORTC	European Organisation for Research and Treatment of Cancer
FGF	fibroblast growth factor
FFPE	formalin fixed paraffin-embedded
FLOT	docetaxel + 5FU + leucovorin + oxaliplatin
FOLFIRI	5-fluorouracil + irinotecan + folinic acid
mFOLFIRINOX	leucovorin + 5-fluorouracil + irinotecan + oxaliplatin
mFOLFOX	leucovorin + 5-fluorouracil + oxaliplatin
FOLFOX	5-fluorouracil + oxaliplatin
FP	fluoropyrimidine
GEJ	gastro-oesophageal junction
GI	gastrointestinal
HCC	hepatocellular carcinoma
HMIE	hybrid minimally invasive oesophagectomy
HR	hazard ratio
HV	hepatitis virus
IFN	interferon
IHC	immunohistochemistry
IRI	irinotecan
ITT	intent-to-treat
IV	intravenous
mAb	monoclonal antibody
MSI-H	microsatellite instability-high
MUT	mutant
MVI	macroscopic vascular invasion
nab	nanoparticle albumin–bound
NE	not evaluable
NK	natural killer
NYHA	New York Heart Association
OE	open oesophagectomy
OR	odds ratio
ORR	overall/objective response rate
(m)OS	(median) overall survival
PCR	polymerase chain reaction
PD	progressive disease
PD-L1	programmed death-ligand 1
PK	pharmacokinetics
(m)PFS	(median) progression-free survival
PPS	post-progression survival
PR	partial response
PS	performance status
q(2/3/4)w	every (2/3/4) week(s)
qd	once daily
QLQ-C30	quality of life questionnaire C30
QLQ-HCC18	quality of life questionnaire for hepatocellular carcinoma 18
QoL	quality of life
R	randomized
RCT	randomized controlled trial
RECIST	Response Evaluation Criteria In Solid Tumors
RFS	relapse-free survival
RT	radiotherapy
S-1	tegafur + gimeracil + oteracil
SAR	survival after recurrence
SD	stable disease
SIRT	selective internal radiotherapy
SoC	standard of care
SUV_{max}	maximum standardized uptake value
TFS	(median)time to failure of strategy
TR(S)AE	treatment-related (serious) adverse event
TRG	tumour regression grade
TTF	time to treatment failure
TTR	time to response
VEGF	vascular endothelial growth factor
WHO	World Health Organization
wk	week
WT	wild type

Contents

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CANCERS OF THE OESOPHAGUS AND STOMACH

LBA27_PR: Docetaxel, oxaliplatin, and fluorouracil/leucovorin (FLOT) for resectable esophagogastric cancer: updated results from multicenter, randomized phase 3 FLOT4-AIO trial (German Gastric Group at AIO) – Al-Batran S-E, et al

Study objective

- To provide updated efficacy and safety data from the phase 3 FLOT4-AIO study in patients with oesogastric cancer

Key patient inclusion criteria

- Gastric cancer or adenocarcinoma of the GEJ type I–III
- Medically and technically operable
- cT2-4/cN-any/cM0 or cT-any/cN+/cM0

(n=716)

R 1:1

FLOT* x 4, resection, then FLOT* x 4 (n=356) → PD

Stratification

- ECOG PS (0 or 1 vs. 2)
- Primary location (GEJ type I vs. type II/III vs. stomach)
- Age (<60 vs. 60–69 vs. ≥70 years)
- Nodal status (cN+ vs. cN-)

ECF/ECX† x 3, resection, then ECF/ECX† x 3 (n=360) → PD

PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

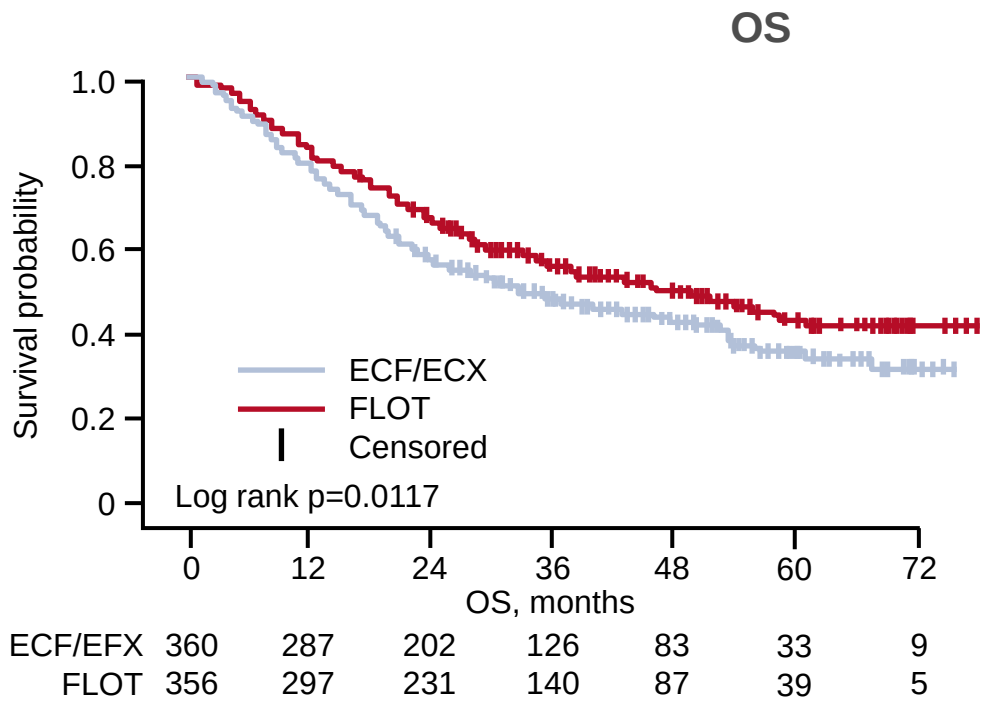
- PFS, safety

*Docetaxel 50 mg/m^2 D1 + 5FU 2600 mg/m^2 D1 + leucovorin 200 mg/m^2 D1 + oxaliplatin 85 mg/m^2 D1 q2w; †Epirubicin 50 mg/m^2 D1 + cisplatin 60 mg/m^2 D1 + 5FU 200 mg/m^2 (or capecitabine 1250 mg/m^2 po divided into two doses D1–21) q3w

Al-Batran S-E, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA27_PR

LBA27_PR: Docetaxel, oxaliplatin, and fluorouracil/leucovorin (FLOT) for resectable esophagogastric cancer: updated results from multicenter, randomized phase 3 FLOT4-AIO trial (German Gastric Group at AIO) – Al-Batran S-E, et al

Key results



	ECF/ECX	FLOT
mOS, months (95%CI)	35 (27, 46)	50 (38, NE)
HR (95%CI)	0.77 (0.63, 0.94)	
Log-rank p-value	0.012	

OS rate*, %	ECF/ECX	FLOT
2-year	59	68
3-year	48	57
5-year	36	45

Median follow-up for surviving patients: 43 months in both arms

*Projected OS rates

Al-Batran S-E, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA27_PR

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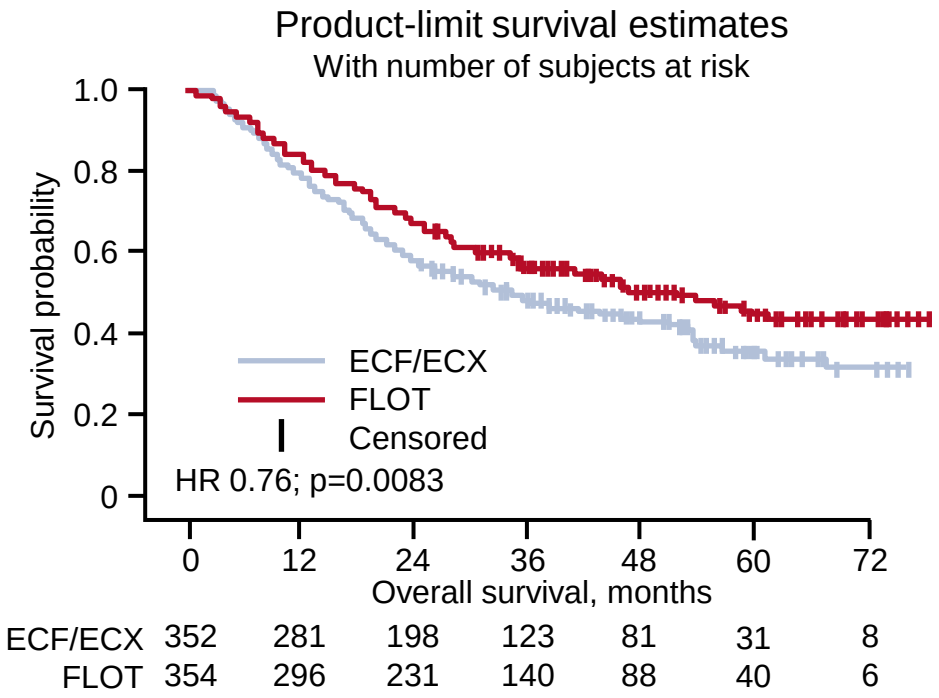
Key results (cont.)

OS in PP population* (predefined analysis)



*Eligible patients who received at least one cycle of CT, analysed as treated

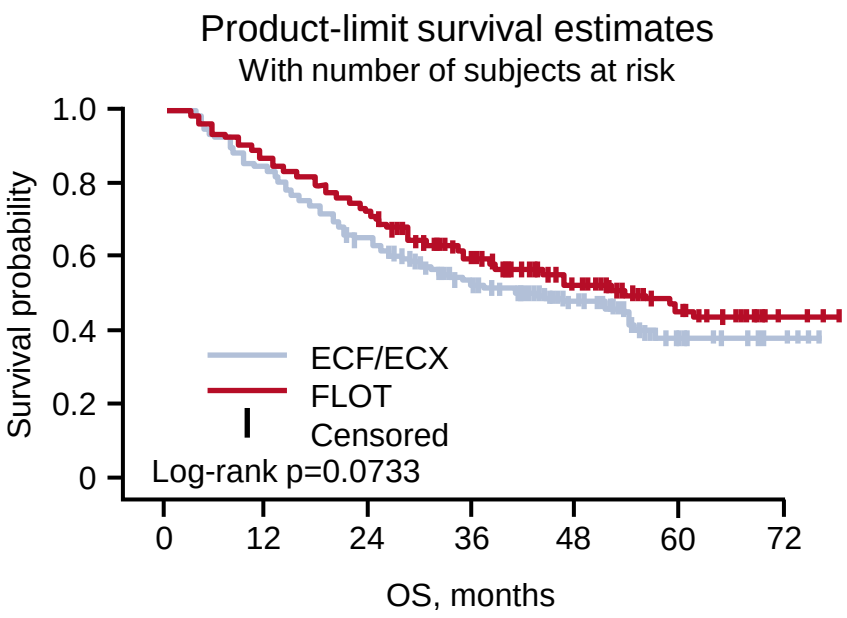
Al-Batran S-E, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA27_PR

LBA27_PR: Docetaxel, oxaliplatin, and fluorouracil/leucovorin (FLOT) for resectable esophagogastric cancer: updated results from multicenter, randomized phase 3 FLOT4-AIO trial (German Gastric Group at AIO) – Al-Batran S-E, et al

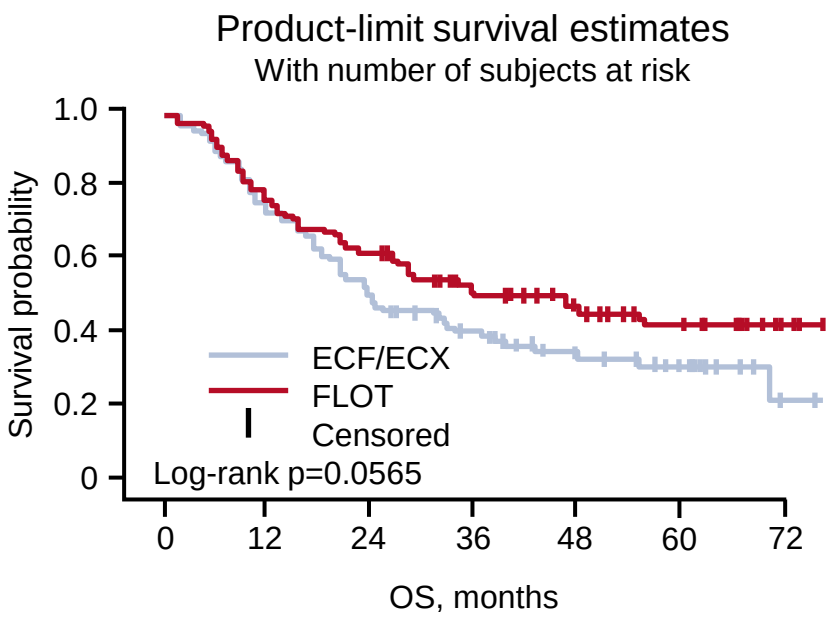
Key results (cont.)

Efficacy by histology: signet cell tumours derive pronounced benefit

OS with ECF/ECX vs. FLOT in patients with no signet cells



OS with ECF/ECX vs. FLOT in patients with signet cells



Al-Batran S-E, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA27_PR

LBA27_PR: Docetaxel, oxaliplatin, and fluorouracil/leucovorin (FLOT) for resectable esophagogastric cancer: updated results from multicenter, randomized phase 3 FLOT4-AIO trial (German Gastric Group at AIO) – Al-Batran S-E, et al

Conclusions

- **In patients with oesogastric cancer, compared with ECF/ECX, FLOT increased rates of curative surgery and prolonged PFS and OS**
- **FLOT demonstrated a consistent relative effect across all subgroups and sensitivity analyses**
- **In perioperative treatment of patients with oesogastric cancer, FLOT may be considered as a new standard of care**

Al-Batran S-E, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA27_PR

615O_PR: Hybrid minimally invasive vs. open esophagectomy for patients with esophageal cancer: Long-term outcomes of a multicenter, open-label, randomized phase III controlled trial, the MIRO trial – Mariette C, et al

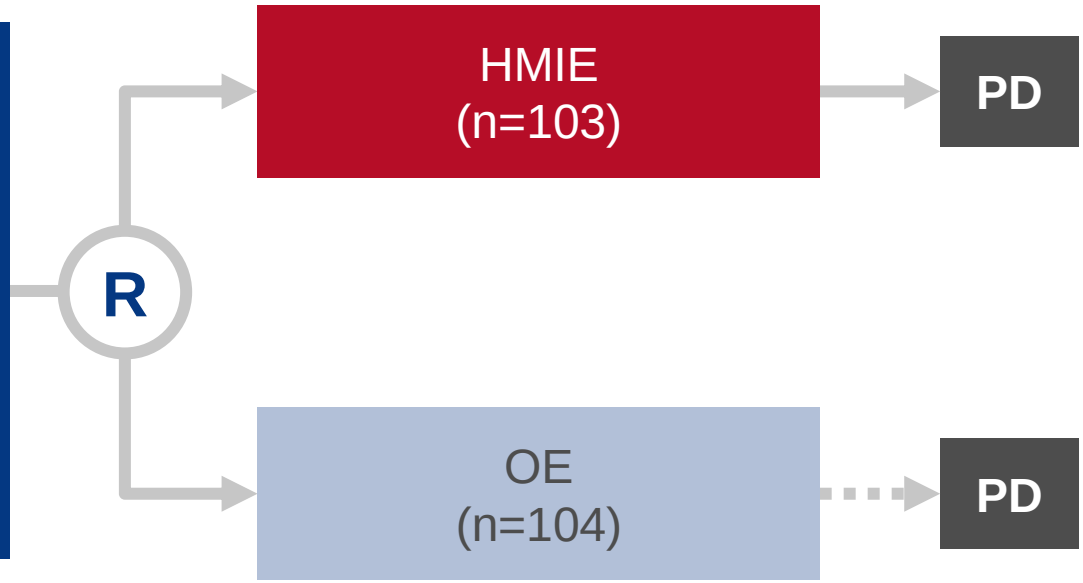
Study objective

- To investigate whether HMIE reduces morbidity compared with OE in patients with resectable oesophageal cancer

Key patient inclusion criteria

- Resectable cancers of the middle or lower third of the oesophagus
- Eligible for Ivor-Lewis procedure after standard pre-operative work-up

(n=207)



PRIMARY ENDPOINT

- 30-day grade II–IV postoperative morbidity

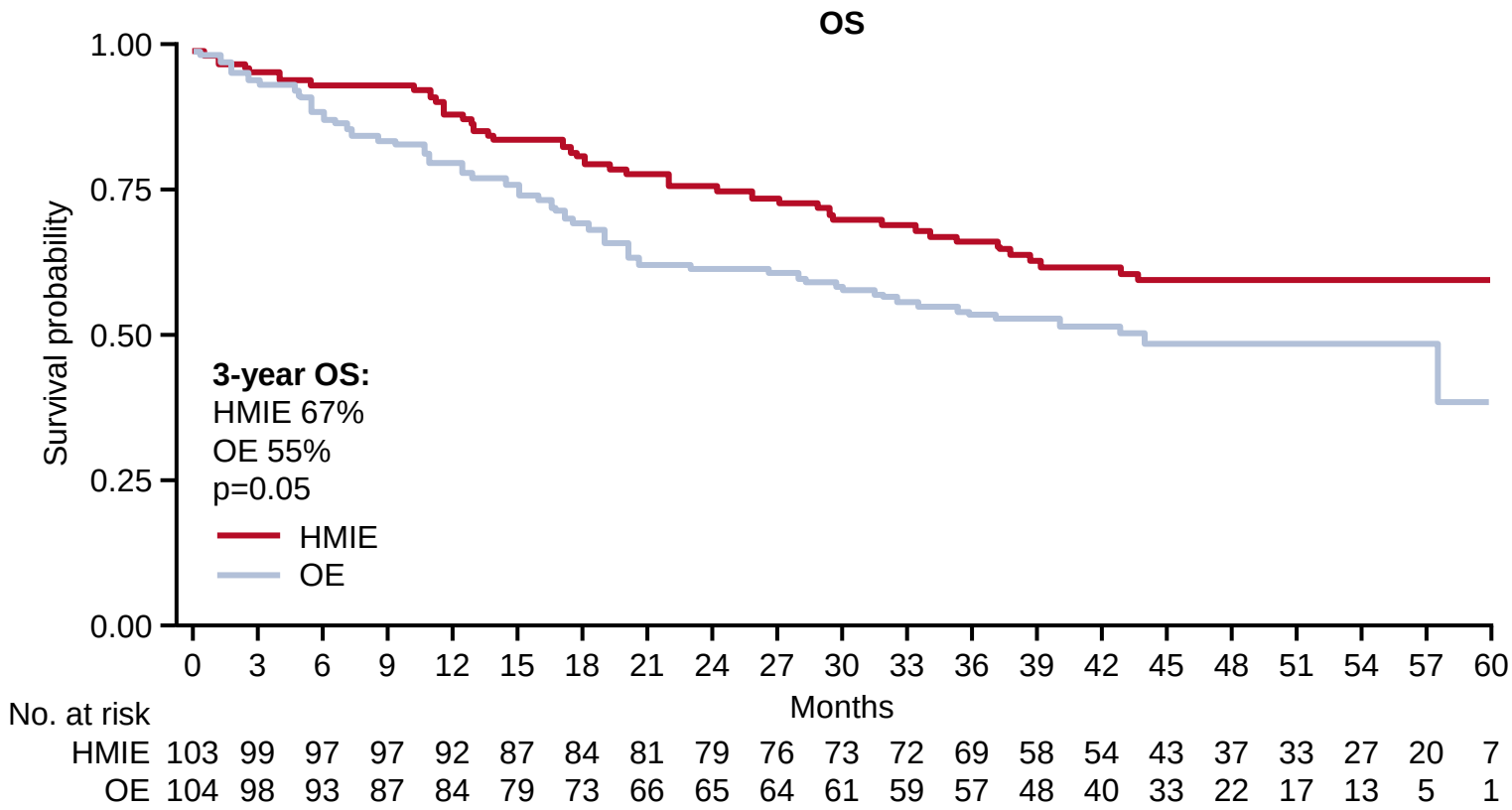
SECONDARY ENDPOINTS

- 30-day postoperative mortality, OS, DFS

Mariette C, et al. Ann Oncol 2017;28(Suppl 5):Abstr 615O_PR

615O_PR: Hybrid minimally invasive vs. open esophagectomy for patients with esophageal cancer: Long-term outcomes of a multicenter, open-label, randomized phase III controlled trial, the MIRO trial – Mariette C, et al

Key results



	HMIO (n=103)	OE (n=104)	OR (95%CI); p-value
30-day pre- and post-operative morbidity grade II–IV, n (%)	37 (35.9)	67 (64.4)	0.31 (0.18, 0.55); <0.0001

Mariette C, et al. Ann Oncol 2017;28(Suppl 5):Abstr 615O_PR

615O_PR: Hybrid minimally invasive vs. open esophagectomy for patients with esophageal cancer: Long-term outcomes of a multicenter, open-label, randomized phase III controlled trial, the MIRO trial – Mariette C, et al

Key results (cont.)

Grade II–IV complications at 30 days	HMIE, n=102	OE, n=103
Mortality, n (%)	1 (1.0)	2 (1.9)
Medical morbidity, n (%)	20 (19.6)	41 (39.8)
Major pulmonary complications*, n (%)	**18 (17.7)**	**31 (30.1)**
Surgical morbidity	15 (14.7)	21 (20.4)
Anastomotic leakage	8 (7.8)	5 (4.9)
Plasty necrosis	2 (2.0)	3 (2.9)
Median length of hospital stay, days (range)	14 (7–95)	14 (3–218)

Conclusions

- **HMIE is an oncologically sound procedure and reduces the incidence of major morbidity, specifically pulmonary, vs. OE in patients with oesophageal cancer**
- **Suggests that improvements in surgery might improve per se the prognosis of patients with oesophageal cancer**

*p=0.037

Mariette C, et al. Ann Oncol 2017;28(Suppl 5):Abstr 615O_PR

616O: Pertuzumab (P) + trastuzumab (H) + chemotherapy (CT) for HER2-positive metastatic gastric or gastro-oesophageal junction cancer (mGC/GEJC): Final analysis of a phase III study (JACOB) – Tabernero J, et al

Study objective

- To assess the efficacy and safety of adding pertuzumab to trastuzumab + CT in patients with HER2$^+$ metastatic gastric or GEJ cancer

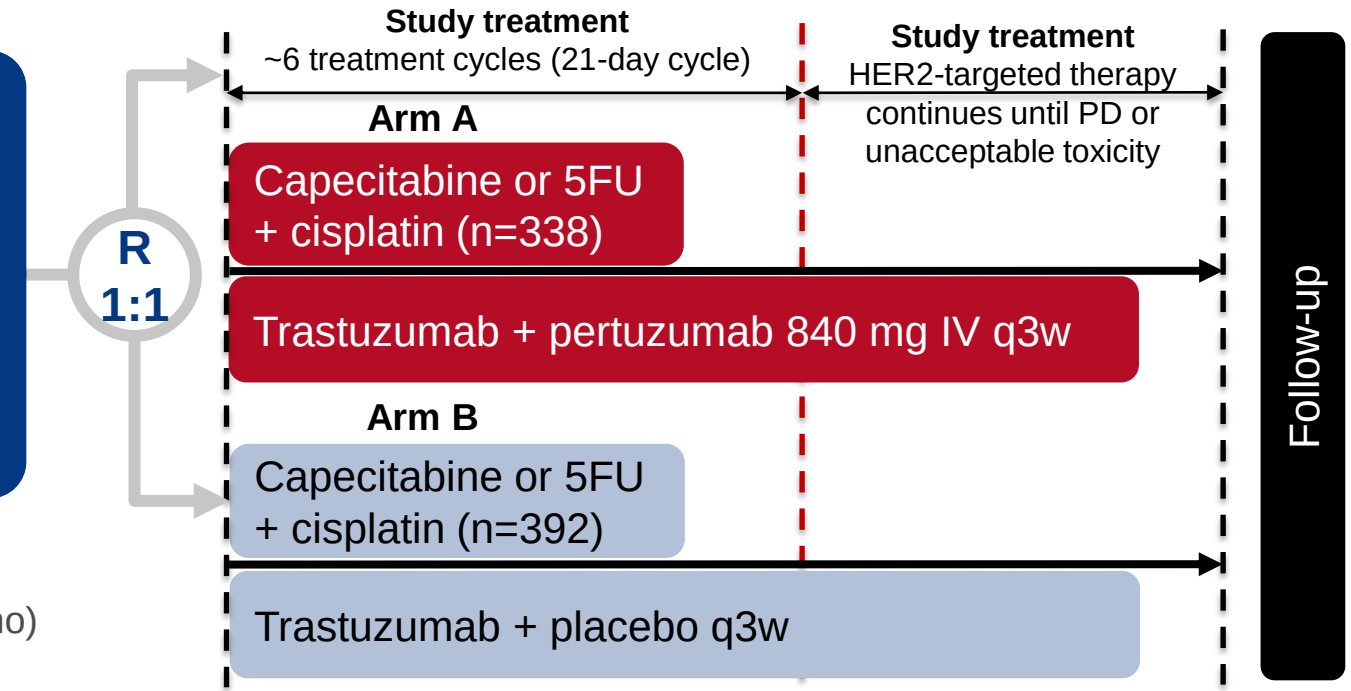
Key patient inclusion criteria

- 1L HER2$^+$ metastatic gastric or GEJ cancer
- ECOG PS 0 or 1

(n=780)

Stratification

- Geographical region
- Prior gastrectomy (yes/no)
- IHC 3$^+$ vs. IHC 2$^+$ /ISH$^+$



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

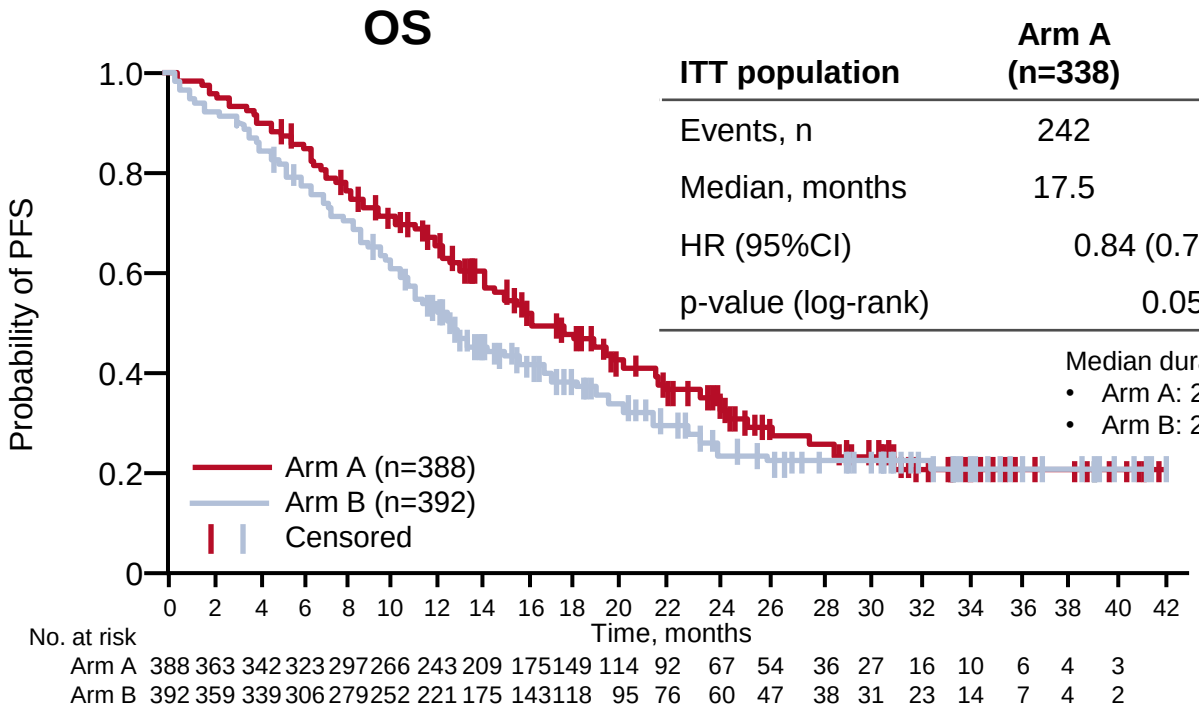
- PFS, ORR, DoR, CBR, safety, PK, QoL

Tabernero J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 616O

616O: Pertuzumab (P) + trastuzumab (H) + chemotherapy (CT) for HER2-positive metastatic gastric or gastro-oesophageal junction cancer (mGC/GEJC): Final analysis of a phase III study (JACOB) – Tabernero J, et al

Key results

- OS not statistically significant: 16% reduction in risk of death; 3.3-month increase in mOS



ITT population	Arm A (n=338)	Arm B (n=392)
Events, n	242	262
Median, months	17.5	14.2
HR (95%CI)	0.84 (0.71, 1.00)	
p-value (log-rank)	0.0565	

Median duration of survival follow-up
- Arm A: 24.4 months (min–max 22.3–26.1)
- Arm B: 25.0 months (min–max 22.3–28.9)

	Arm A (n=388)	Arm B (n=392)	HR (95%CI)
mPFS, months	8.5	7.0	0.73 (0.62, 0.86)

Tabernero J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 616O

616O: Pertuzumab (P) + trastuzumab (H) + chemotherapy (CT) for HER2-positive metastatic gastric or gastro-oesophageal junction cancer (mGC/GEJC): Final analysis of a phase III study (JACOB) – Tabernero J, et al

Key results (cont.)

ORR in patients with measurable disease at baseline	Arm A (n=351)	Arm B (n=352)
Objective response, %	56.7	48.3
Difference, % (95%CI)	8.4 (0.9, 15.9)	
Median duration of objective response, months (95%CI)	10.2 (8.4, 10.7)	8.4 (6.8, 10.7)

Conclusions

- The JACOB study did not meet the primary endpoint of OS
  - A treatment effect trend with pertuzumab + trastuzumab + CT was observed
- OS was generally consistent in the subgroups*
- Key secondary endpoints of PFS and ORR showed similar trends, but statistical significance could not be concluded due to hierarchical testing
- Safety was comparable between treatment arms, apart from diarrhoea*
  - Diarrhoea incidence increased with pertuzumab; however, there were no pertuzumab discontinuations due to diarrhoea

*Data not shown

Tabernero J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 616O

617O: A phase 3 study of nivolumab (Nivo) in previously treated advanced gastric or gastroesophageal junction (G/GEJ) cancer: Updated results and subset analysis by PD-L1 expression (ATTRACTION-02) – Boku N, et al

Study objective

- To investigate the efficacy and safety of nivolumab vs. placebo in patients with previously treated advanced gastric 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)

R 2:1

Nivolumab 3 mg/kg IV q2w (n=330) → PD

Stratification

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

Placebo q2w (n=163) → PD

PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

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

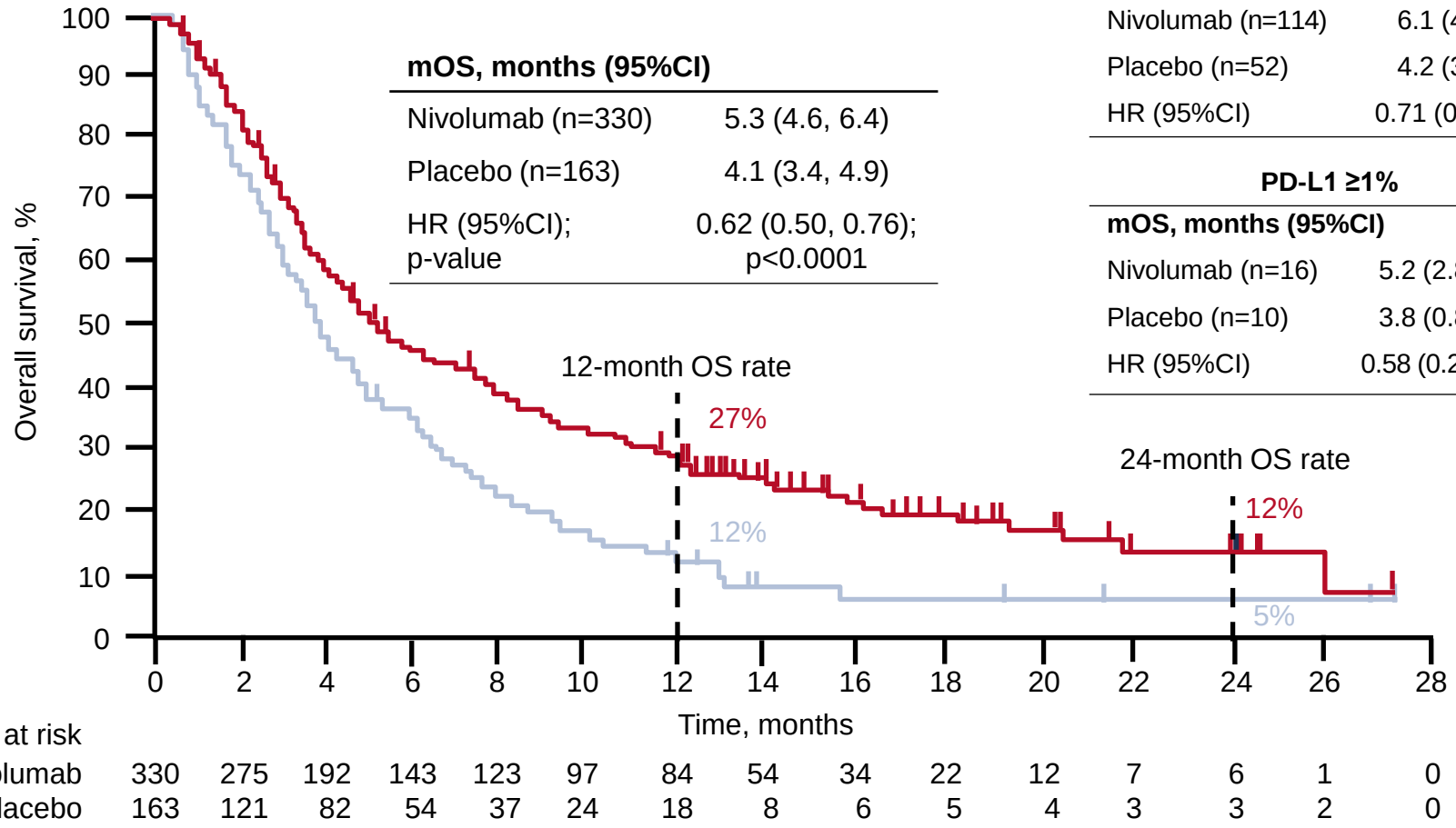
Boku N, et al. Ann Oncol 2017;28(Suppl 5):Abstr 617O

617O: A phase 3 study of nivolumab (Nivo) in previously treated advanced gastric or gastroesophageal junction (G/GEJ) cancer: Updated results and subset analysis by PD-L1 expression (ATTRACTION-02) – Boku N, et al

Key results

OS

mOS, months (95%CI)	
Nivolumab (n=330)	5.3 (4.6, 6.4)
Placebo (n=163)	4.1 (3.4, 4.9)
HR (95%CI); p-value	0.62 (0.50, 0.76); p<0.0001



PD-L1 <1%	
mOS, months (95%CI)	
Nivolumab (n=114)	6.1 (4.8, 8.6)
Placebo (n=52)	4.2 (3.0, 6.9)
HR (95%CI)	0.71 (0.50, 1.01)

PD-L1 ≥1%	
mOS, months (95%CI)	
Nivolumab (n=16)	5.2 (2.8, 9.4)
Placebo (n=10)	3.8 (0.8, 5.0)
HR (95%CI)	0.58 (0.24, 1.38)

*Time from first dose to data cut-off for surviving patients

Boku N, et al. Ann Oncol 2017;28(Suppl 5):Abstr 617O

617O: A phase 3 study of nivolumab (Nivo) in previously treated advanced gastric or gastroesophageal junction (G/GEJ) cancer: Updated results and subset analysis by PD-L1 expression (ATTRACTION-02) – Boku N, et al

Key results (cont.)

	Nivolumab (n=268)	Placebo (n=131)	p-value
ORR, n (%) [95%CI]	31 (12) [8, 16]	0 (0) [0, 2.8]	<0.0001
BOR, n (%)			
CR	0	0	-
PR	31 (12)	0	-
SD	77 (29)	33 (25)	-
PD	124 (46)	79 (60)	-
NE	36 (13)	19 (15)	-
DCR, n (%) [95%CI]	108 (40) [34.4, 46.4]	33 (25) [18.0, 33.5]	0.0036

Conclusions

- In patients with previously treated advanced gastric cancer, nivolumab provided a significant survival advantage vs. placebo regardless of PD-L1 expression
- The safety profile of nivolumab was manageable and similar to previous reports*
- Additional studies are ongoing to assess nivolumab as a 1L therapy and in non-Asian patients

*Data not shown

Boku N, et al. Ann Oncol 2017;28(Suppl 5):Abstr 617O

LBA28_PR: KEYNOTE-059 update: Efficacy and safety of pembrolizumab alone or in combination with chemotherapy in patients with advanced gastric or gastroesophageal (G/GEJ) cancer – Wainberg ZA, et al

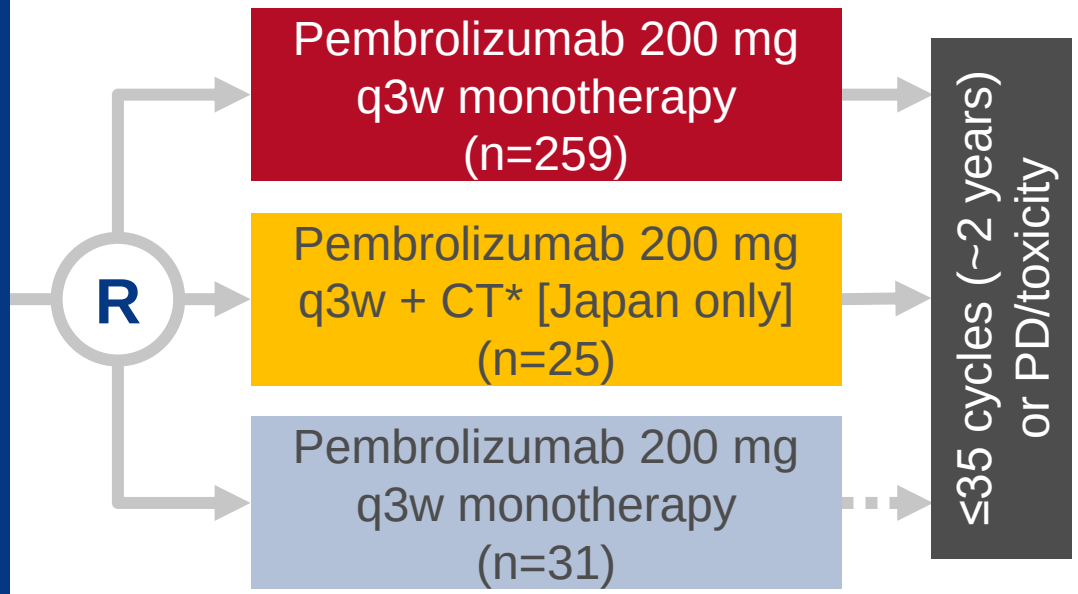
Study objective

- To evaluate the efficacy and safety of pembrolizumab alone or in combination with CT in patients with advanced gastric cancer

Key patient inclusion criteria

- Recurrent or metastatic gastric or GEJ adenocarcinoma
- **Cohort 1:** ≥2 prior lines of CT; PD-L1 positive or negative
- **Cohort 2:** No prior therapy; PD-L1 positive or negative
- **Cohort 3:** No prior therapy; PD-L1-positive

(n=315)



PRIMARY ENDPOINTS

- Safety (all), ORR (cohorts 1 + 3)

SECONDARY ENDPOINTS

- ORR (cohort 2), DCR, PFS, OS

*Cisplatin 80 mg/m^2 D1 + 5FU 800 mg/m^2 D1–5 q3w or capecitabine 1000 mg/m^2 bid

Wainberg ZA, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA28_PR

LBA28_PR: KEYNOTE-059 update: Efficacy and safety of pembrolizumab alone or in combination with chemotherapy in patients with advanced gastric or gastroesophageal (G/GEJ) cancer – Wainberg ZA, et al

Key results

Cohort 1	All (n=259)	PD-L1 positive (n=148)	PD-L1 negative (n=109)
ORR, % (95%CI)	12 (8, 17)	16 (11, 23)	6 (3, 13)
DCR, % (95%CI)	27 (22, 33)	34 (26, 42)	19 (12, 28)
mPFS, months (95%CI)	2.0 (2.0, 2.1)	2.1 (2.0, 2.1)	2.0 (1.9, 2.0)
mOS, months (95%CI)	5.5 (4.2, 6.5)	5.8 (4.4, 7.8)	4.6 (3.2, 6.5)

Cohort 2	All (n=25)	PD-L1 positive (n=15)	PD-L1 negative (n=8)
ORR, % (95%CI)	60 (39, 79)	73 (45, 92)	38 (9, 76)
DCR, % (95%CI)	80 (59, 93)	80 (52, 96)	75 (35, 97)
mPFS, months (95%CI)	6.6 (5.9, 10.6)	-	-
mOS, months (95%CI)	13.8 (8.6, NR)	-	-

Cohort 3	All (n=31)
ORR, % (95%CI)	26 (12, 45)
DCR, % (95%CI)	36 (19, 55)
mPFS, months (95%CI)	3.3 (2.0, 6.0)
mOS, months (95%CI)	20.7 (9.2, 20.7)

Wainberg ZA, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA28_PR

LBA28_PR: KEYNOTE-059 update: Efficacy and safety of pembrolizumab alone or in combination with chemotherapy in patients with advanced gastric or gastroesophageal (G/GEJ) cancer – Wainberg ZA, et al

Key results (cont.)

TRAEs, n (%)	Cohort 1 (n=259)	Cohort 2 (n=25)	Cohort 3 (n=31)
Any	159 (61)	25 (100)	24 (77)
Grades ≥3	46 (18)	19 (76)	7 (23)
Anaemia	7 (3) [grade 3]	2 (8)	-
Fatigue	6 (2) [grade 3]	2 (8)	-
Dehydration	3 (1) [grade 3]	-	-
Neutropenia	-	6 (24)	-
Stomatitis	-	5 (20)	-
Decreased platelet count	-	2 (8)	-
Decreased appetite	-	2 (8)	-
Serious	29 (11)	-	-
Led to discontinuation	7 (3)	3 (12)	0 (0)
Led to death	2 (1)	0 (0)	1 (3)

Conclusions

- **In patients with advanced gastric cancer, pembrolizumab continues to demonstrate promising anti-tumour activity:**
  - **As monotherapy in patients with PD after ≥2 prior lines of CT**
  - **In combination with CT in previously untreated patients**
  - **As monotherapy in previously untreated patients with PD-L1–positive tumours**
- **Responses were higher in patients with PD-L1–positive tumours in cohorts 1 and 2**
- **Safety was manageable and consistent with that of previous reports**

Wainberg ZA, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA28_PR

626PD: A randomized phase III trial comparing 4 courses and 8 courses of S-1 adjuvant chemotherapy for p-stage II gastric cancer: JCOG1104 (OPAS-1) – Yoshikawa T, et al

Study objective

- To evaluate the efficacy of 6 vs. 12 months of S-1 adjuvant CT in patients with stage II gastric cancer

Key patient inclusion criteria

- Histologically proven adenocarcinoma of the stomach – stage II (excl. T1N2-3 and T3N0)
- R0 resection
- Surgery by laparotomy (or laparoscopic approach for stage I)
- ECOG PS 0–1

(n=528)

R

Arm A: 8 courses* (1 year)
S-1 80 mg/m^2 (n=262)

Stratification

- Stage (IIA/IIB)
- Age (<70/≥70 years)
- Surgery (open bursectomy/open non-bursectomy/laparoscopic surgery)
- Institution

Arm B: 4 courses* (6 months)
S-1 80 mg/m^2 (n=266)

PRIMARY ENDPOINT(S)

- RFS

SECONDARY ENDPOINTS

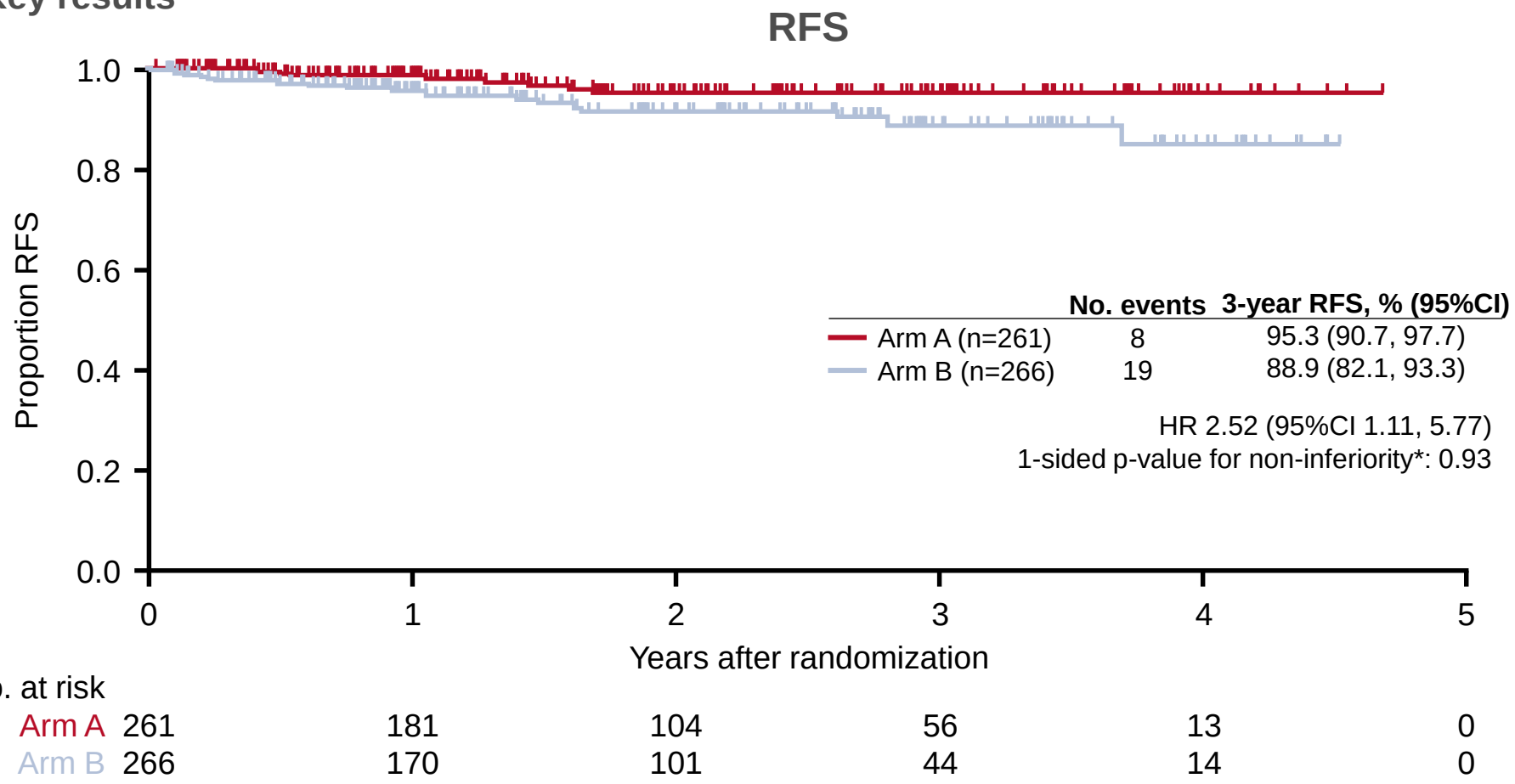
- OS, TTF, safety, proportion of the treatment continuation at each time point

*1 course = 4-weeks on, 2-weeks off

Yoshikawa T, et al. Ann Oncol 2017;28(Suppl 5):Abstr 626PD

626PD: A randomized phase III trial comparing 4 courses and 8 courses of S-1 adjuvant chemotherapy for p-stage II gastric cancer: JCOG1104 (OPAS-1) – Yoshikawa T, et al

Key results

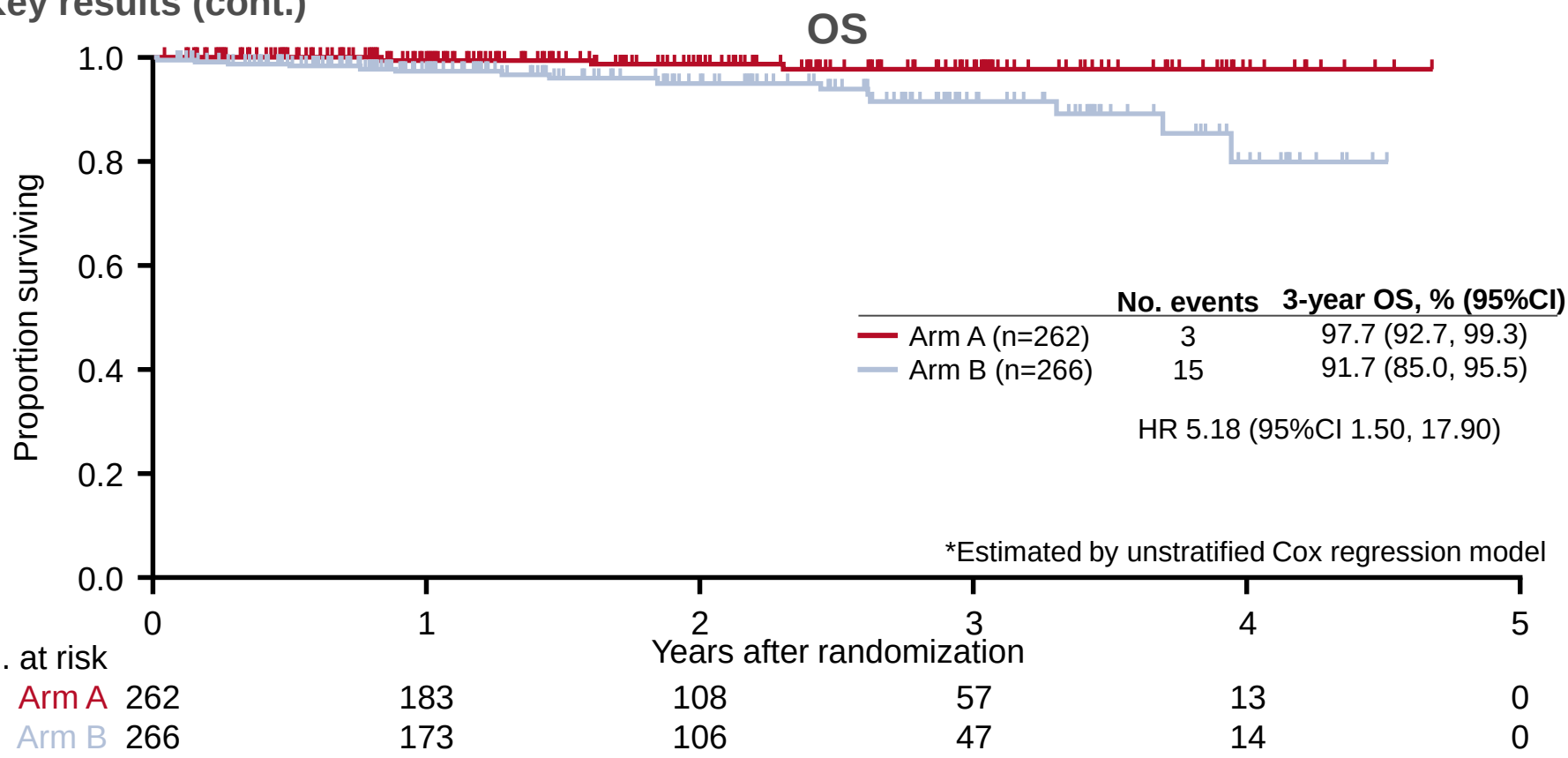


*Estimated by stratified Cox regression model according to p-stage

Yoshikawa T, et al. Ann Oncol 2017;28(Suppl 5):Abstr 626PD

626PD: A randomized phase III trial comparing 4 courses and 8 courses of S-1 adjuvant chemotherapy for p-stage II gastric cancer: JCOG1104 (OPAS-1) – Yoshikawa T, et al

Key results (cont.)



Conclusion

- **In patients with pathological stage II gastric cancer, it is possible to continue postoperative S-1 adjuvant CT for up to 1 year**

Yoshikawa T, et al. Ann Oncol 2017;28(Suppl 5):Abstr 626PD

CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

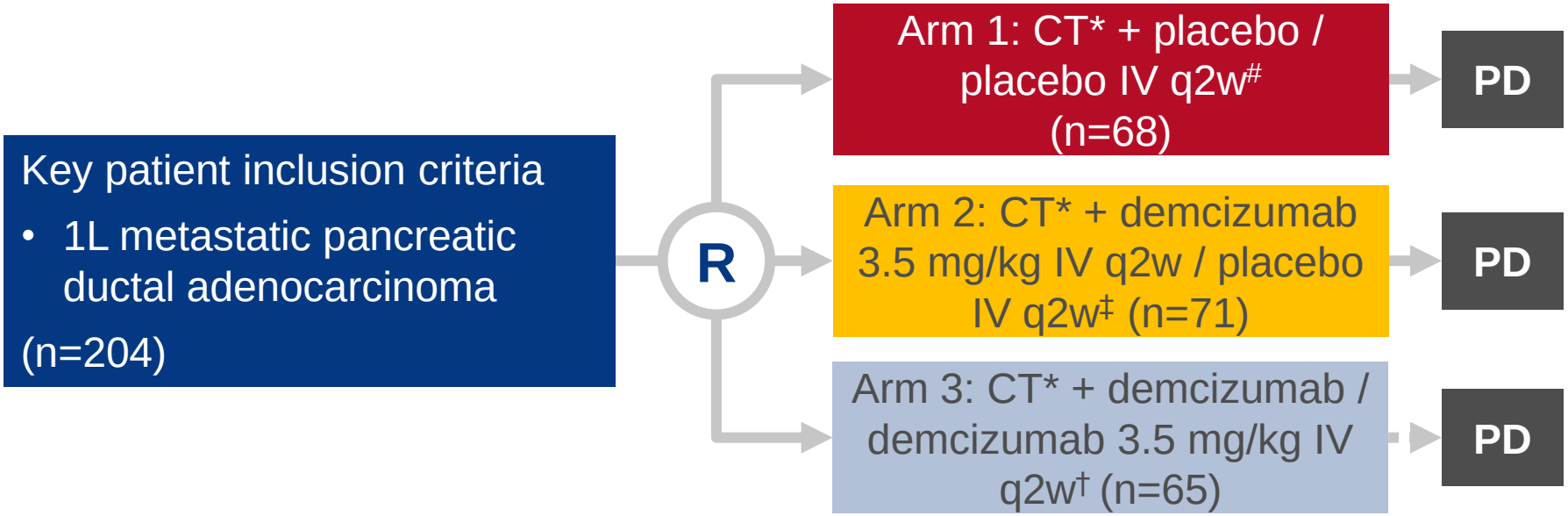
Cancers of the pancreas, small bowel and hepatobiliary tract

PANCREATIC CANCER

620PD: YOSEMITE: A 3 arm double-blind randomized phase 2 study of gemcitabine, paclitaxel protein-bound particles for injectable suspension, and placebo (GAP) versus gemcitabine, paclitaxel protein-bound particles for injectable suspension and either 1 or 2 truncated courses of demcizumab (GAD) – Cubillo Gracian A, et al

Study objective

- To evaluate efficacy and safety with 1L CT + demcizumab (a humanized, anti-DLL4 antibody) vs. placebo in patients with metastatic pancreatic cancer



PRIMARY ENDPOINT(S)

- PFS

SECONDARY ENDPOINTS

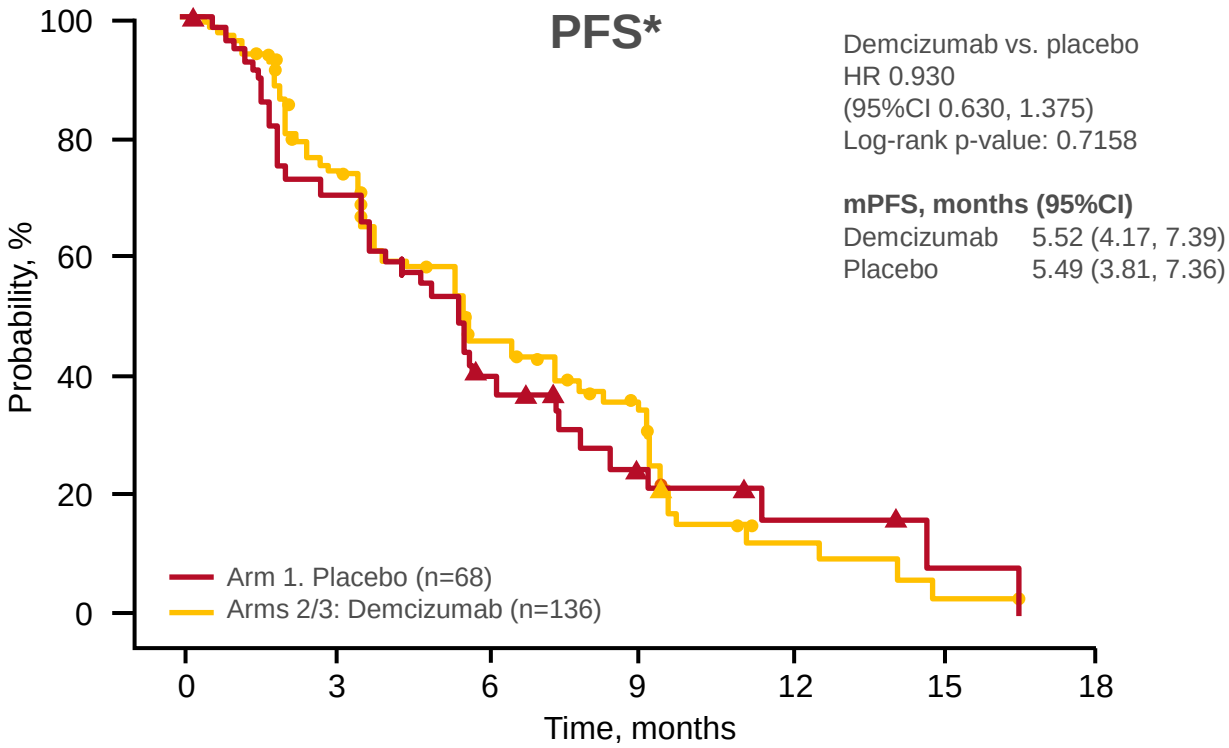
- Response, survival, safety

*Nab-paclitaxel 125 mg/m^2 IV D1, 8, 15 per 28-D cycle + gemcitabine 1000 mg/m^2 IV D1, 8, 15 per 28-D cycle; †CT + placebo x3, CT x3, CT + placebo x3, then CT; ‡CT + demcizumab x3, CT x3, CT + placebo x3, then CT; #CT + demcizumab x3, CT x3, CT + demcizumab x3, then CT

Cubillo Gracian A, et al. Ann Oncol 2017;28(Suppl 5):Abstr 620PD

620PD: YOSEMITE: A 3 arm double-blind randomized phase 2 study of gemcitabine, paclitaxel protein-bound particles for injectable suspension, and placebo (GAP) versus gemcitabine, paclitaxel protein-bound particles for injectable suspension and either 1 or 2 truncated courses of demcizumab (GAD) – Cubillo Gracian A, et al

Key results



OS*	Arm 1: Placebo	Arms 2/3: Demcizumab
Median, months (95%CI)	NR (8.97, NR)	13.2 (9.79, 16.53)
HR† (95%CI); p-value	1.018 (0.616, 1.683); 0.9443	

*The primary efficacy analyses compared Arm 1 vs. Arms 2 + 3 combined; †Demcizumab vs. placebo

Cubillo Gracian A, et al. Ann Oncol 2017;28(Suppl 5):Abstr 620PD

620PD: YOSEMITE: A 3 arm double-blind randomized phase 2 study of gemcitabine, paclitaxel protein-bound particles for injectable suspension, and placebo (GAP) versus gemcitabine, paclitaxel protein-bound particles for injectable suspension and either 1 or 2 truncated courses of demcizumab (GAD) – Cubillo Gracian A, et al

Key results (cont.)

BOR* (RECIST)	Arm 1: Placebo (n=68)	Arms 2/3: Demcizumab (n=136)	p-value
CR, n	0	1	-
PR, n	28	44	-
SD, n	20	56	-
PD, n	14	19	-
Response rate†, n (%)	28 (41.2%)	45 (33.1%)	0.2815
Clinical benefit‡, n (%)	48 (70.6%)	101 (74.3%)	0.5023

Conclusions

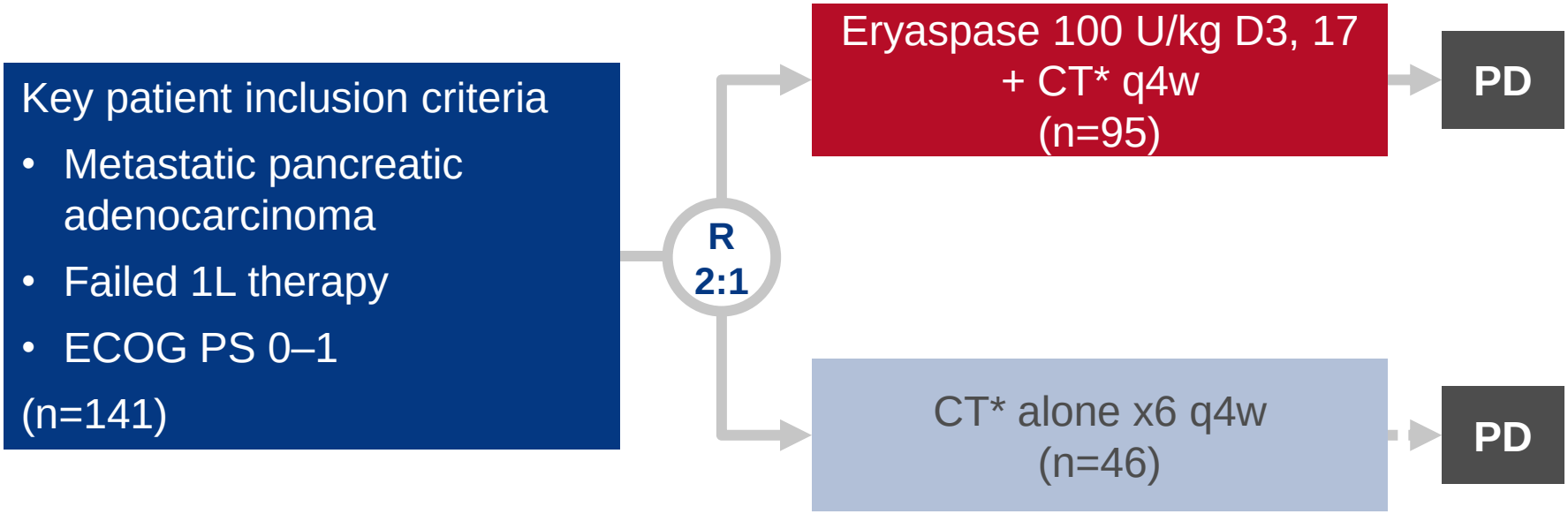
- PFS, ORR and OS were similar between Arm 1 vs. Arms 2/3 combined
- PFS, ORR and OS were also similar between each individual treatment arm
- The incidence of grade ≥3 heart failure and pulmonary hypertension were low and similar in all 3 treatment arms
- The incidence of grade ≥3 bleeding was higher in the demcizumab arms#

*The primary efficacy analyses compared Arm 1 vs. Arms 2 + 3 combined; †CR + PR; ‡CR + PR + SD; #Data not shown Cubillo Gracian A, et al. Ann Oncol 2017;28(Suppl 5):Abstr 620PD

621PD: A Phase 2b of eryaspase in combination with gemcitabine or FOLFOX as second-line therapy in patients with metastatic pancreatic adenocarcinoma (NCT02195180) – Hammel P, et al

Study objective

- To evaluate 2L eryaspase + CT in patients with metastatic pancreatic cancer



PRIMARY ENDPOINT(S)

- OS + PFS (asparagine synthetase [ASNS] 0/1^{+}): positive study if HR <0.85 irrespective of significance

SECONDARY ENDPOINTS

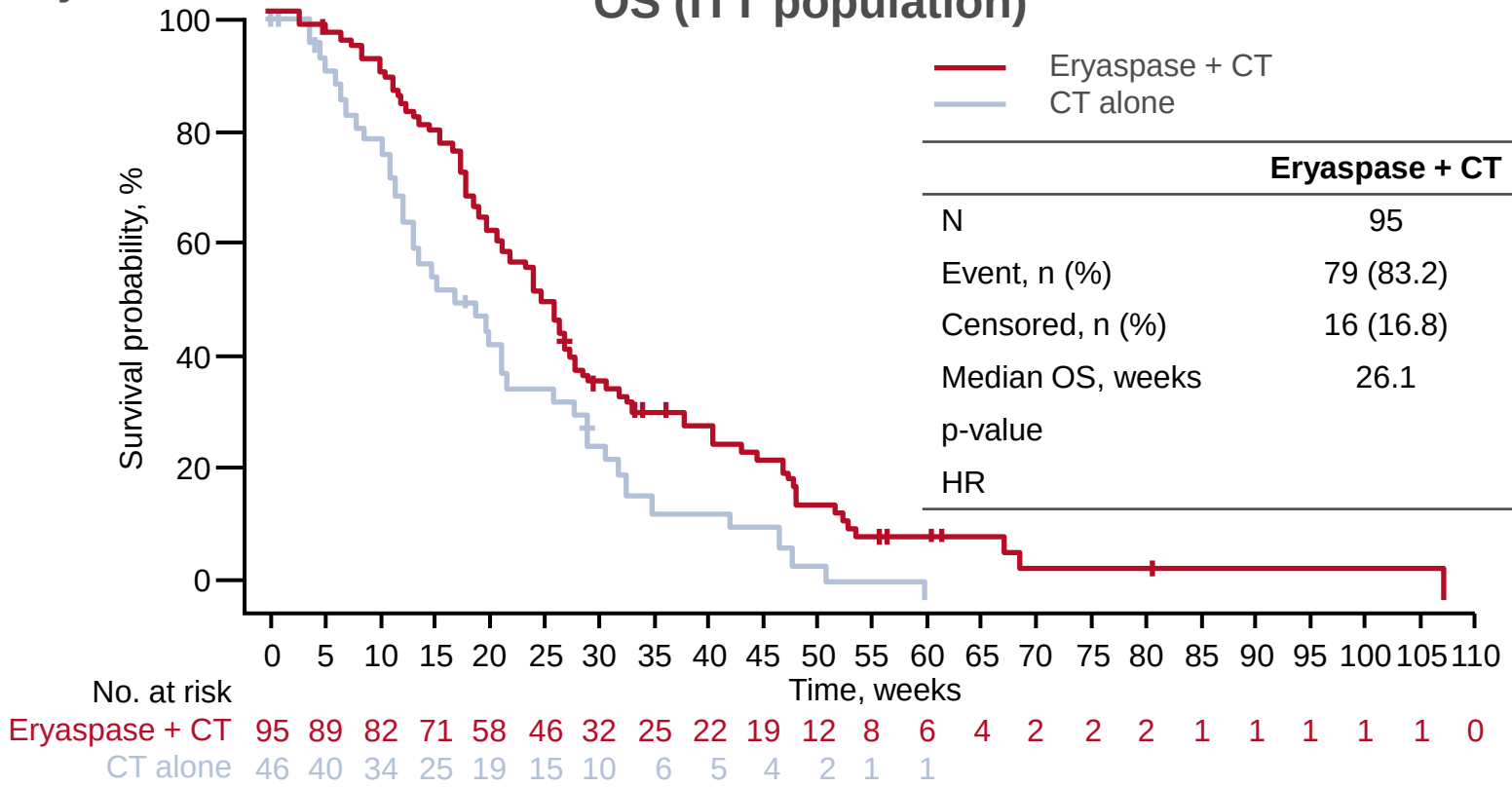
- OS + PFS in key treatment populations
- ORR, safety, QoL

*Gemcitabine 1000 mg/m^2 30 min IV D1, 8, 15 or mFOLFOX6 (oxaliplatin 85 mg/m^2 IV D1, 15 + leucovorin 200 mg/m^2 IV D1,15 + 5FU 400 mg/m^2 IV + 5FU 2400 mg/m^2 D1, 15 CIV D1, 2 and D15, 16)

Hammel P, et al. Ann Oncol 2017;28(Suppl 5):Abstr 621PD

621PD: A Phase 2b of eryaspase in combination with gemcitabine or FOLFOX as second-line therapy in patients with metastatic pancreatic adenocarcinoma (NCT02195180) – Hammel P, et al

Key results



	Eryaspase + CT	CT alone
N	95	46
Event, n (%)	79 (83.2)	40 (87.0)
Censored, n (%)	16 (16.8)	6 (13.0)
Median OS, weeks	26.1	19.0
p-value		0.0094
HR		0.597

mOS, weeks (95%CI)	Eryaspase + CT	CT alone	HR; p-value
ASNS 0/1^{+}	27.0 (22.3, 31.1)	21.7 (13.0, 31.0)	0.65 (0.40, 1.05); 0.0766
ASNS 2^{+}/3^{+}	21.0 (14.9, 29.4)	11.9 (6.9, 19.7)	0.45 (0.22, 0.95); 0.0361

Hammel P, et al. Ann Oncol 2017;28(Suppl 5):Abstr 621PD

621PD: A Phase 2b of eryaspase in combination with gemcitabine or FOLFOX as second-line therapy in patients with metastatic pancreatic adenocarcinoma (NCT02195180) – Hammel P, et al

Key results (cont.)

	Eryaspase + CT (n=95)	CT alone (n=46)	HR; p-value
mPFS, weeks (95%CI)	8.6 (7.6, 14.6)	7.0 (6.1, 7.6)	0.59 (0.40, 0.89); 0.011
24-week PFS, %	16.9	5.8	-
ORR, n (%) [95%CI]	11 (11.6) [5.9, 19.8]	3 (6.5) [1.4, 17.9]	-
DCR, n (%) [95%CI]	45 (47.4) [37.0, 57.9]	11 (23.9) [12.6, 38.8]	-

Conclusions

- **Eryaspase + CT led to a trend of improved OS + PFS* in patients with metastatic pancreatic cancer whose tumours had low expression of ASNS (ASNS 0/1^{+})**
- **OS and PFS were prolonged in the ITT population and improvement in DCR was observed for the combination of eryaspase + CT**
- **The safety* profile of eryaspase + CT was comparable with the known safety profile of each CT used**
- **A global phase 3 study is currently being planned**

*Data not shown

Hammel P, et al. Ann Oncol 2017;28(Suppl 5):Abstr 621PD

622PD: nab-Paclitaxel (nab-P) plus gemcitabine (G) for patients (Pts) with locally advanced pancreatic cancer (LAPC): Interim efficacy and safety results from the Phase 2 LAPACT Trial – Philip PA, et al

Study objective

- To evaluate the efficacy and safety of 1L nab-paclitaxel + gemcitabine in patients with unresectable locally advanced pancreatic cancer

Key patient inclusion criteria

- Previously untreated, unresectable locally advanced pancreatic cancer

(n=107)

→

Induction phase: Nab-paclitaxel* + gemcitabine†

→

Investigator's choice:

- Nab-paclitaxel + gemcitabine
- CRT
- Surgical resection

PRIMARY ENDPOINT(S)

- TTF

SECONDARY ENDPOINTS

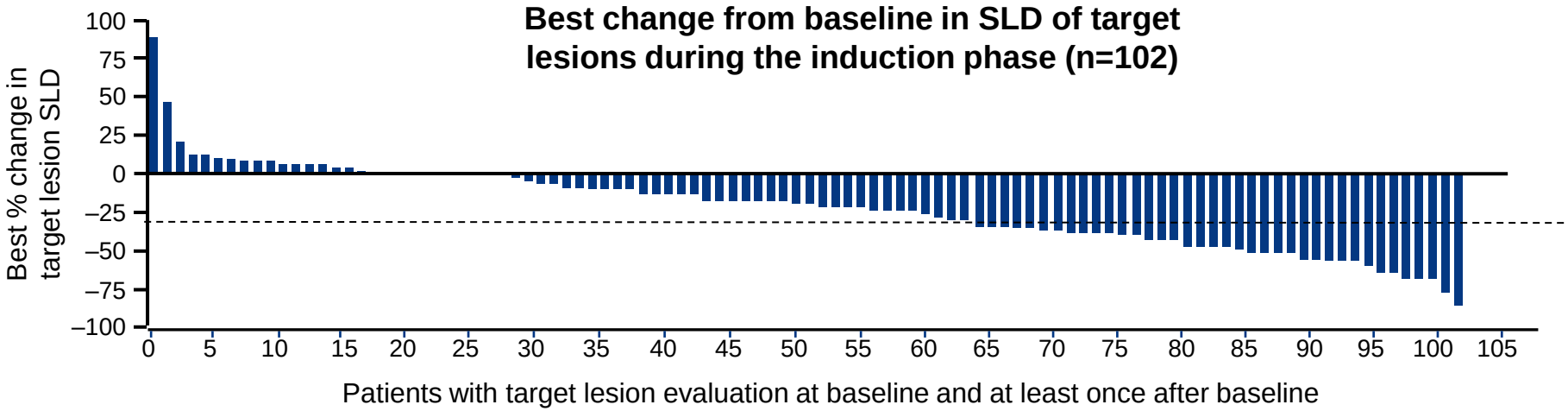
- DCR, ORR, PFS, OS, safety, QoL

*125 mg/m^2 q3/4w ≤6 cycles; †1000 mg/m^2 q3/4w ≤6 cycles

Philip PA, et al. Ann Oncol 2017;28(Suppl 5):Abstr 622PD

622PD: nab-Paclitaxel (nab-P) plus gemcitabine (G) for patients (Pts) with locally advanced pancreatic cancer (LAPC): Interim efficacy and safety results from the Phase 2 LAPACT Trial – Philip PA, et al

Key results



Best response by RECIST v1.1 for induction phase	Nab-paclitaxel + gemcitabine (n=107)
CR, n (%)	0
PR, n (%)	36 (33.6)
SD, n (%)	61 (57.0)
DCR, n (% [95%CI]) SD ≥16 weeks + CR + PR SD ≥24 weeks + CR + PR	 83 (77.6 [70.3, 83.5]) 71 (66.4 [58.5, 73.4])
PD	5 (4.7)
NE or no post-baseline value	5 (4.7)

Philip PA, et al. Ann Oncol 2017;28(Suppl 5):Abstr 622PD

622PD: nab-Paclitaxel (nab-P) plus gemcitabine (G) for patients (Pts) with locally advanced pancreatic cancer (LAPC): Interim efficacy and safety results from the Phase 2 LAPACT Trial – Philip PA, et al

Key results (cont.)

	Nab-paclitaxel + gemcitabine, n=106	
TRAEs in ≥5% patients, n (%)	All grades	Grade ≥3
Patients with ≥1 AE	105 (99.1)	85 (80.2)
Neutropenia	61 (57.5)	43 (40.6)
Anaemia	50 (47.2)	12 (11.3)
Fatigue	53 (50.0)	11 (10.4)
Asthenia	37 (34.9)	8 (7.5)
Hyperglycaemia	12 (11.3)	7 (6.6)
Thrombocytopenia	44 (41.5)	7 (6.6)
ALT increased	20 (18.9)	6 (5.7)

Conclusions

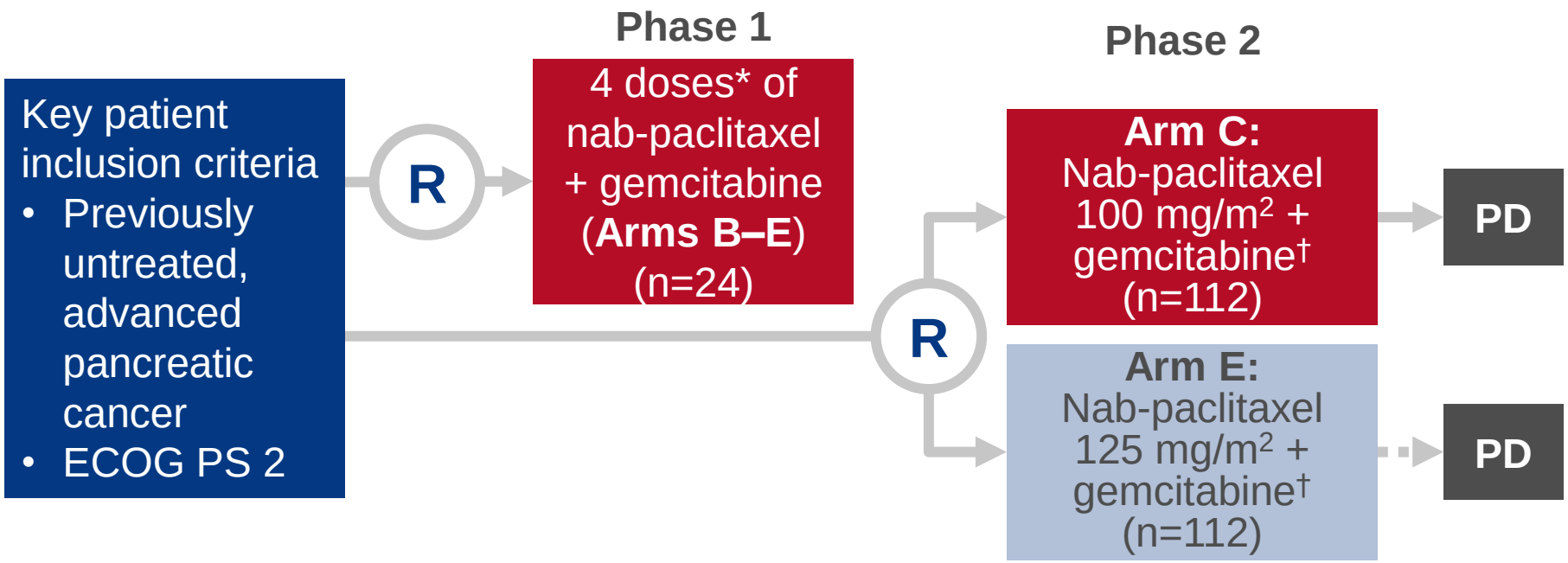
- **The DCR was promising and indicative of anti-tumour activity in patients with locally advanced pancreatic cancer treated with nab-paclitaxel + gemcitabine**
- **All patients were unresectable at baseline, yet 15% were resectable after the induction phase and all of these patients underwent R0 or R1 resection**
- **Nab-paclitaxel + gemcitabine had a tolerable safety profile**

Philip PA, et al. Ann Oncol 2017;28(Suppl 5):Abstr 622PD

623PD: A phase I and randomized phase II trial to evaluate the efficacy and safety of nab-paclitaxel (nab-P) in combination with gemcitabine (G) for the treatment of patients with ECOG 2 advanced pancreatic cancer (PDAC) – Hidalgo M, et al

Study objective

- To select a tolerable dose of 1L nab-paclitaxel + gemcitabine (phase 1) and to evaluate its efficacy (phase 2) in patients with advanced pancreatic cancer



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

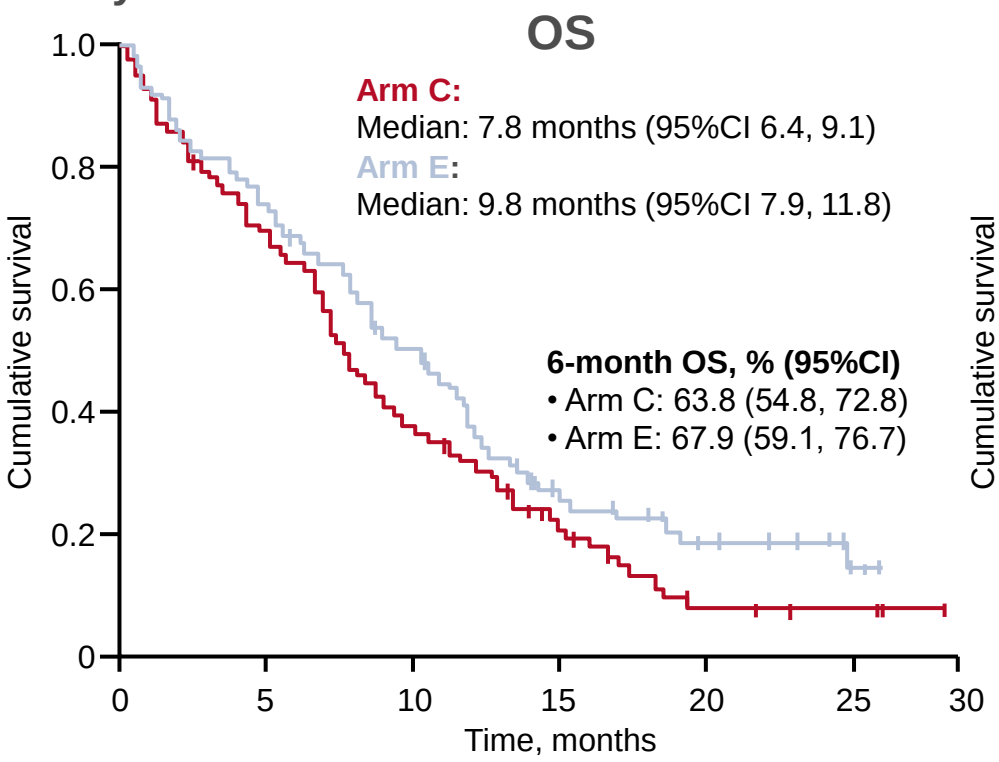
- PFS, ORR, safety

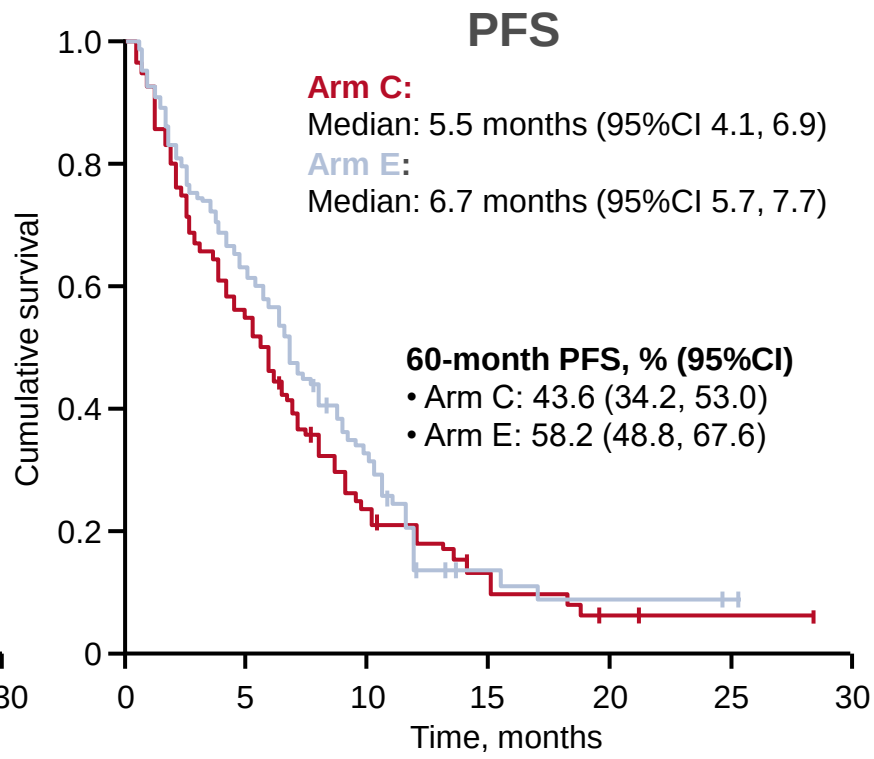
*Gemcitabine 1000 mg/m^2 + nab-paclitaxel 150 mg/m^2 (**Arm B**) or 125 mg/m^2 (**Arm D**) weeks 1, 3/4, or gemcitabine 1000 mg/m^2 + nab-paclitaxel 100 mg/m^2 (**Arm C**) or 125 mg/m^2 (**Arm E**) weeks 1, 2, 3/4; †1000 mg/m^2 IV weeks 1, 2, 3/4

Hidalgo M, et al. Ann Oncol 2017;28(Suppl 5):Abstr 623PD

623PD: A phase I and randomized phase II trial to evaluate the efficacy and safety of nab-paclitaxel (nab-P) in combination with gemcitabine (G) for the treatment of patients with ECOG 2 advanced pancreatic cancer (PDAC) – Hidalgo M, et al

Key results





% (95%CI)	Arm C	Arm E
ORR	20.7 (13.2, 28.3)	22.7 (14.9, 30.6)
Clinical benefit rate	64.9 (56.0, 73.7)	71.8 (63.4, 80.2)

Hidalgo M, et al. Ann Oncol 2017;28(Suppl 5):Abstr 623PD

623PD: A phase I and randomized phase II trial to evaluate the efficacy and safety of nab-paclitaxel (nab-P) in combination with gemcitabine (G) for the treatment of patients with ECOG 2 advanced pancreatic cancer (PDAC) – Hidalgo M, et al

Key results (cont.)

Most common TRAEs grade ≥3, n (%)	Arm C (n=111)	Arm E (n=110)
Neutropenia	36 (32.4)	33 (30.0)
Asthenia	16 (14.4)	17 (15.5)
Leukopenia	14 (12.6)	8 (7.3)
Anaemia	13 (11.7)	8 (7.3)
Neurotoxicity	13 (11.7)	20 (18.2)
Thrombocytopenia	8 (7.2)	12 (10.9)
Transaminases increased	7 (6.3)	5 (4.5)
Febrile neutropenia	4 (3.6)	4 (3.6)
Diarrhoea	2 (1.8)	7 (6.4)

Conclusions

- **In patients with advanced pancreatic cancer receiving nab-paclitaxel + gemcitabine, OS, PFS and response rate were acceptable**
- **Both doses of nab-paclitaxel were well tolerated**

Hidalgo M, et al. Ann Oncol 2017;28(Suppl 5):Abstr 623PD

1733PD: New promising combination therapy of a mitochondrial metabolism inhibitor with mFOLFIRINOX in pancreatic cancer – Alistar AT, et al

Study objective

- To determine the efficacy, safety and maximum tolerated dose of CPI-613* when used in combination with mFOLFIRINOX in patients with pancreatic cancer

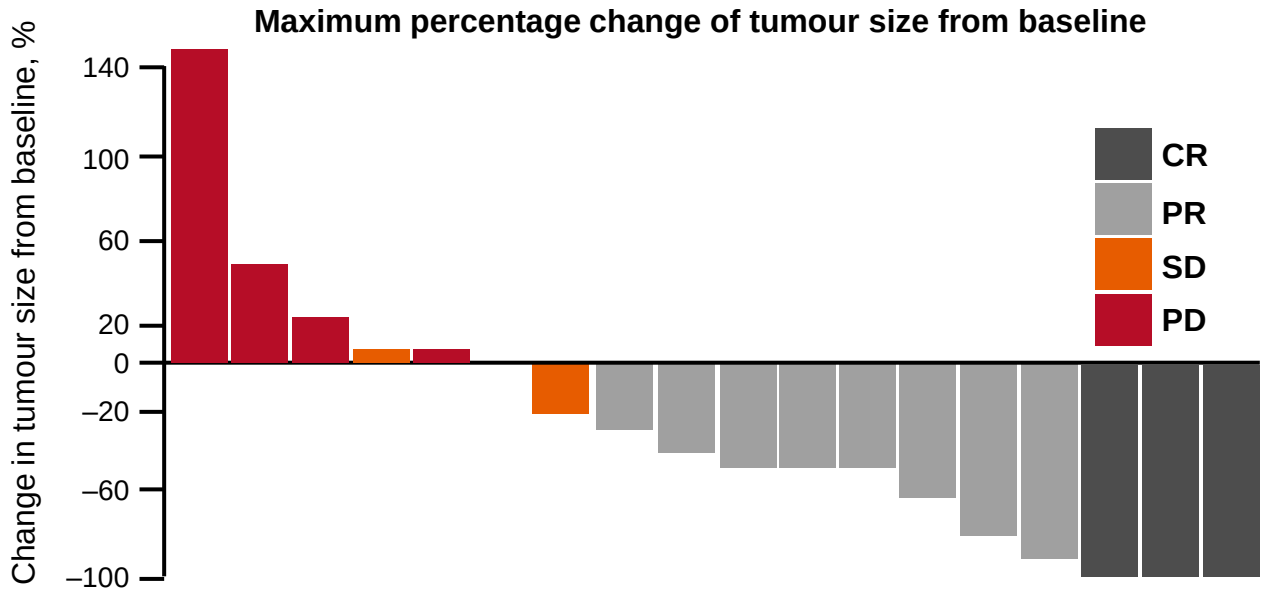
*A first in class non-redox active lipoate derivative

Alistar AT, et al. Ann Oncol 2017;28(Suppl 5):Abstr 1733PD

1733PD: New promising combination therapy of a mitochondrial metabolism inhibitor with mFOLFIRINOX in pancreatic cancer – Alistar AT, et al

Key results

- The maximum tolerated dose was 500 mg/m^2 and 18 patients were treated at this dose



	CPI-613 + mFOLFIRINOX
mOS, months	20.1
mPFS, months	10.4
ORR, %	61

Alistar AT, et al. Ann Oncol 2017;28(Suppl 5):Abstr 1733PD

1733PD: New promising combination therapy of a mitochondrial metabolism inhibitor with mFOLFIRINOX in pancreatic cancer – Alistar AT, et al

Key results (cont.)

AEs in ≥5 of patients, n	Grade 3	Grade 4	Grade 5
Diarrhoea	5	0	0
Hyperglycaemia	9	1	0
Hypokalaemia	5	1	0
Lymphocytes count decreased	5	0	0
Peripheral sensory neuropathy	5	0	0

Conclusions

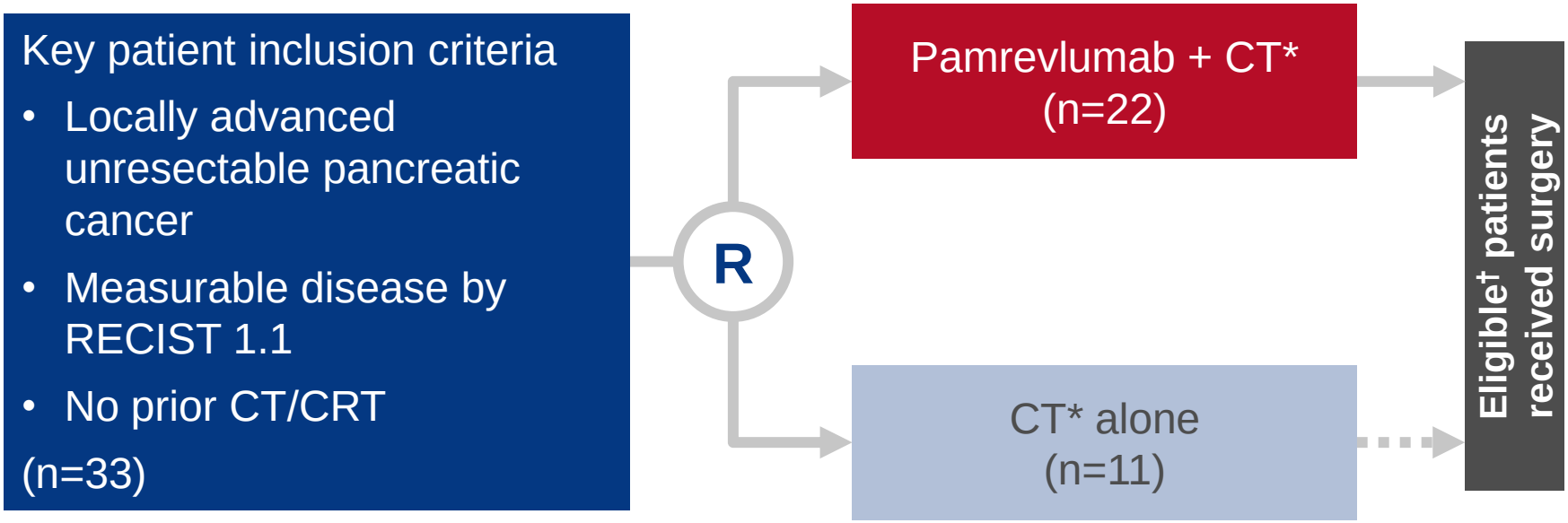
- **The treatment combination of CPI-613 + mFOLFIRINOX was feasible and well-tolerated in patients with stage IV pancreatic cancer**
- **A randomized phase 3 study of CPI613 + FOLFIRINOX will open in 2018**

Alistar AT, et al. Ann Oncol 2017;28(Suppl 5):Abstr 1733PD

1734PD: Anti-CTGF human recombinant monoclonal antibody pamrevlumab increases resectability and resection rate when combined with gemcitabine/Nab-paclitaxel in the treatment of locally advanced pancreatic cancer patients – Carrier E, et al

Study objective

- To evaluate the efficacy and safety of 1L neoadjuvant pamrevlumab (anti-connective tissue growth factor antibody) + CT in patients with locally advanced pancreatic cancer



PRIMARY ENDPOINT

- Safety

SECONDARY ENDPOINTS

- Proportion of patients eligible for resection, PFS, OS, tumour response

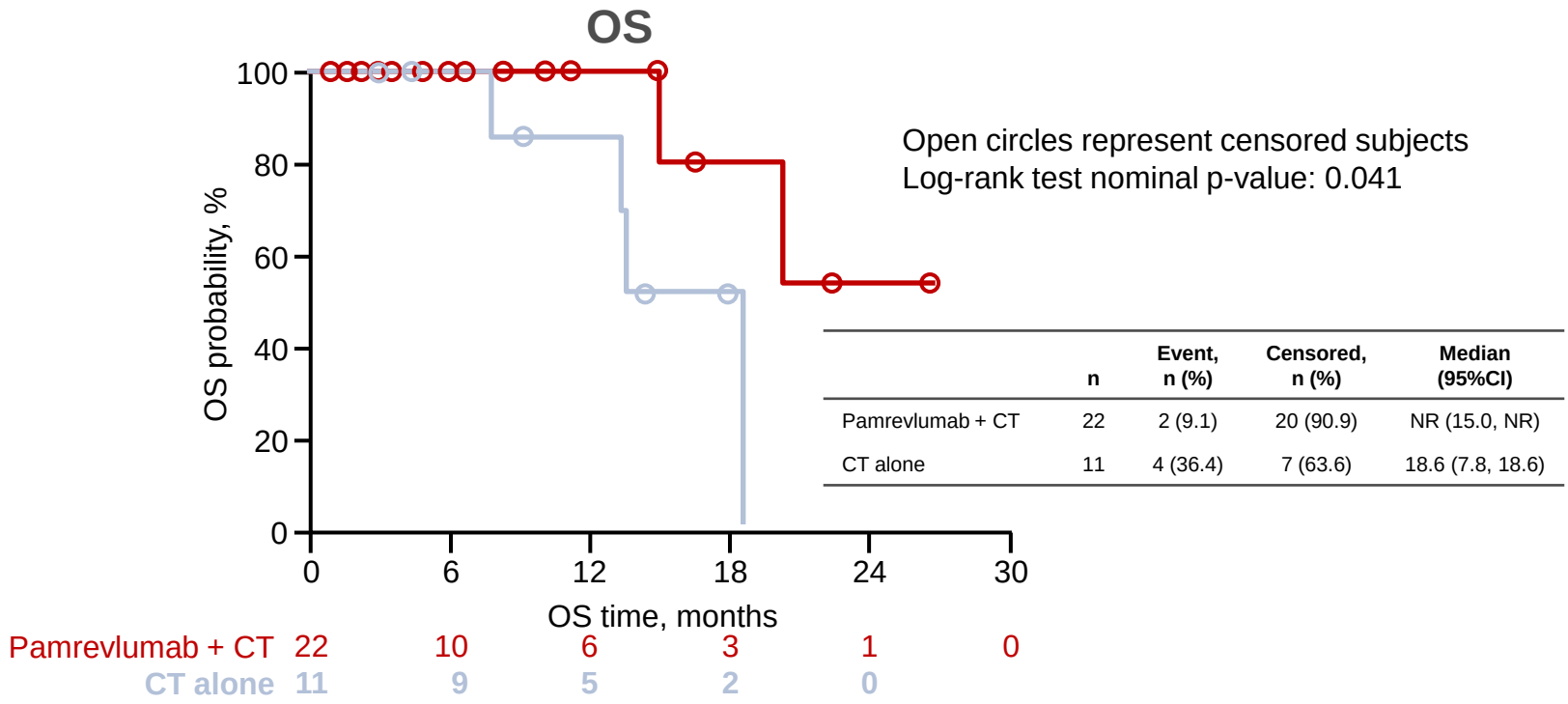
*Gemcitabine + nab-paclitaxel q4w x6 cycles; †CA19.9 decreases of ≥50%, PET SUV_{max} decreases of ≥30%, RECIST (PR or CR), or NCCN resectable/borderline-resectable criteria

Carrier E, et al. Ann Oncol 2017;28(Suppl 5):Abstr 1734PD

1734PD: Anti-CTGF human recombinant monoclonal antibody pamrevlumab increases resectability and resection rate when combined with gemcitabine/Nab-paclitaxel in the treatment of locally advanced pancreatic cancer patients – Carrier E, et al

Key results

	Eligible for surgical exploration	R0 resection	R1 resection	Resection not achieved
Pamrevlumab + CT	7	3	1	3
CT alone	1	1	0	0



	n	Event, n (%)	Censored, n (%)	Median (95%CI)
Pamrevlumab + CT	22	2 (9.1)	20 (90.9)	NR (15.0, NR)
CT alone	11	4 (36.4)	7 (63.6)	18.6 (7.8, 18.6)

Carrier E, et al. Ann Oncol 2017;28(Suppl 5):Abstr 1734PD

1734PD: Anti-CTGF human recombinant monoclonal antibody pamrevlumab increases resectability and resection rate when combined with gemcitabine/Nab-paclitaxel in the treatment of locally advanced pancreatic cancer patients – Carrier E, et al

Key results (cont.)

Treatment-emergent SAEs of interest, n (%)	Pamrevlumab + CT (n=22)	CT alone (n=11)
Any	7 (31.8)	4 (36.4)
Haematological		
Haemolytic uremic syndrome	1 (4.5)	0
Lymphadenopathy	1 (4.5)	0
GI / hepatobiliary		
Cholangitis	0	2 (18.2)
Hyperbilirubinaemia	0	1 (9.1)
Nausea	1 (4.5)	0
Pancreatitis	1 (4.5)	0
Vomiting	1 (4.5)	0

Conclusions

- **In patients with locally advanced pancreatic cancer, pamrevlumab + CT was associated with increased eligibility for surgery, increased resection rates and a positive trend in OS vs. CT alone**
- **No new safety signals were identified**

Carrier E, et al. Ann Oncol 2017;28(Suppl 5):Abstr 1734PD

Cancers of the pancreas, small bowel and hepatobiliary tract

HEPATOCELLULAR CARCINOMA

LBA30: Analysis of serum biomarkers (BM) in patients (pts) from a phase 3 study of lenvatinib (LEN) vs sorafenib (SOR) as first-line treatment for unresectable hepatocellular carcinoma (uHCC) – Finn RS, et al

Study objective

- To assess the impact of biomarkers* in patients with unresectable HCC treated with 1L lenvatinib vs. sorafenib

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

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

PRIMARY ENDPOINT(S)

- OS

SECONDARY ENDPOINTS

- PFS, TTP, ORR

*Serum samples were analysed for VEGF, FGF + ANG2 using ELISA and gene expression profiling was performed on tissue samples; †Excluded patients with ≥50% liver occupation, clear bile duct invasion, or portal vein invasion at the main portal vein

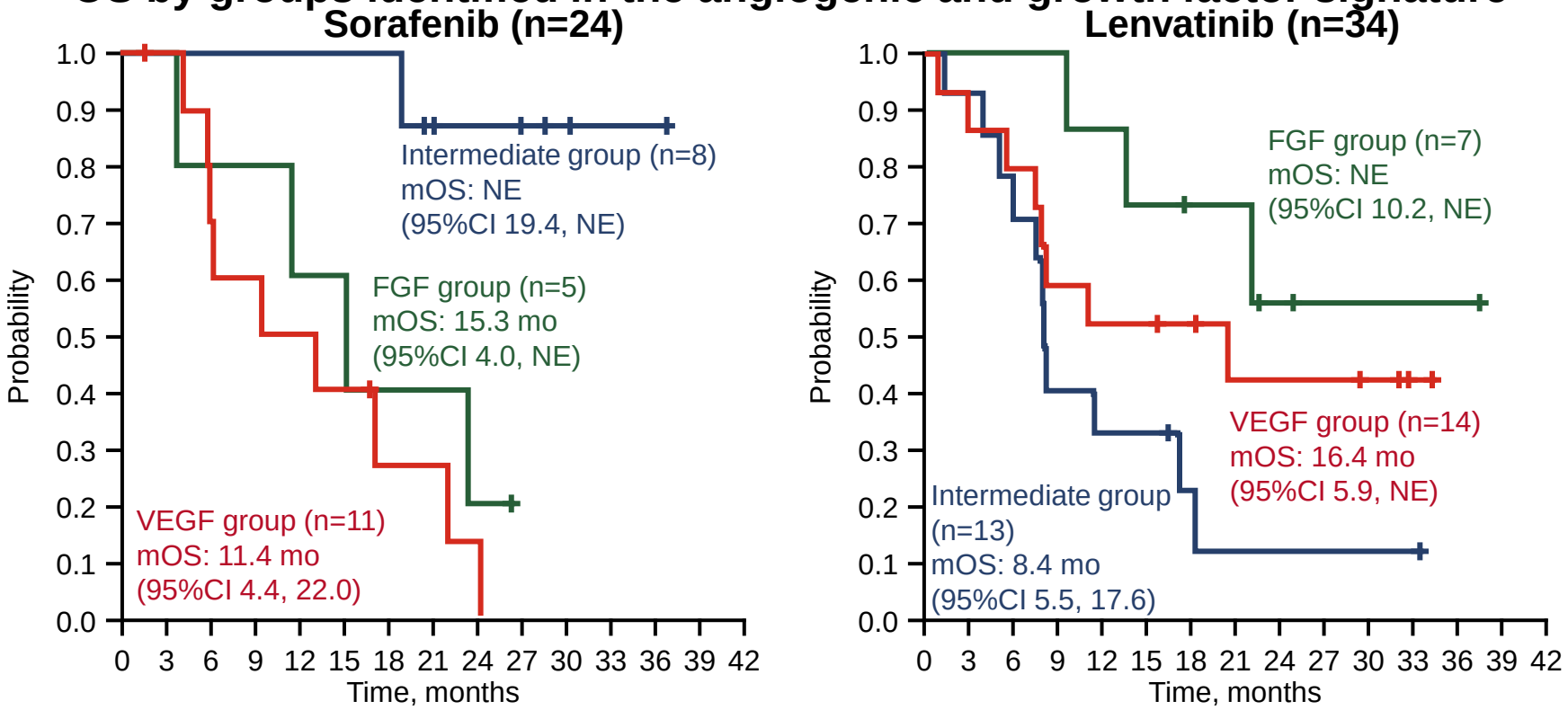
Finn RS, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA30

LBA30: Analysis of serum biomarkers (BM) in patients (pts) from a phase 3 study of lenvatinib (LEN) vs sorafenib (SOR) as first-line treatment for unresectable hepatocellular carcinoma (uHCC) – Finn RS, et al

Key results

ITT population	Lenvatinib	Sorafenib	HR (95%CI)
mOS, months (95%CI)	13.6 (12.1, 14.9)	12.3 (10.4, 13.9)	0.92 (0.79, 1.06)

OS by groups identified in the angiogenic and growth factor signature*



*A cluster analysis using expression levels of 36 genes involved in VEGF, FGF and angiopoietin signalling identified 3 groups: (1) VEGF enriched, (2) FGF enriched , (3) FGF/VEGF intermediate

Finn RS, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA30

LBA30: Analysis of serum biomarkers (BM) in patients (pts) from a phase 3 study of lenvatinib (LEN) vs sorafenib (SOR) as first-line treatment for unresectable hepatocellular carcinoma (uHCC) – Finn RS, et al

Conclusions

- This is the first phase 3 study to meet its primary endpoint in the last 10 years as 1L in patients with unresectable HCC
- There were key differences in target engagement between lenvatinib and sorafenib observed in the serum biomarker analyses
- For both sorafenib and lenvatinib, VEGF, ANG2* and FGF21 maybe potential prognostic factors
- In the lenvatinib arm, improvement in OS was seen in a group enriched for higher expression of VEGF and FGF genes
- Comparison between lenvatinib and sorafenib groups is not possible owing to the small number of patients who contributed samples for analysis and the results should be considered as hypothesis generating

*Data not shown

Finn RS, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA30

618O: Health-related quality of Life (HRQOL) and disease symptoms in patients with unresectable hepatocellular carcinoma (HCC) treated with lenvatinib (LEN) or sorafenib (SOR) – Vogel A

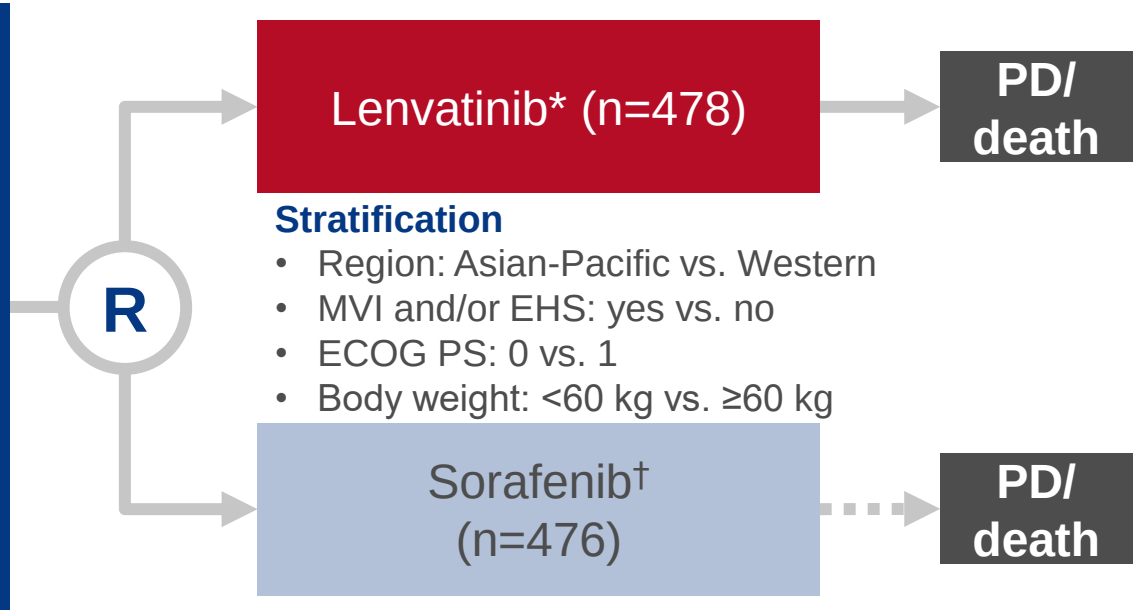
Study objective

- To compare HRQoL with lenvatinib vs. sorafenib in patients with unresectable HCC

Key patient inclusion criteria

- Unresectable HCC
- No prior systemic therapy
- ≥1 measurable target lesion
- BCLC stage B or C
- Child-Pugh class A
- ECOG PS≤ 1

(n=954)



PRIMARY ENDPOINT(S)

- OS

SECONDARY ENDPOINTS

- PFS, TTP, ORR, HRQoL, PK

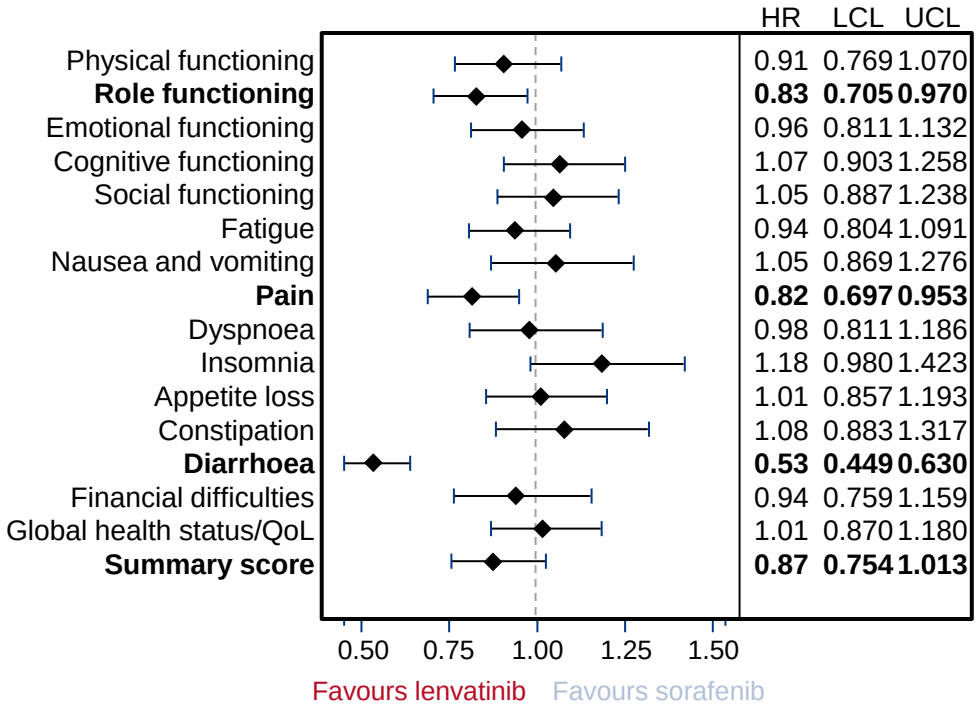
*8 mg/day (body weight <60 kg) or 12 mg/day (body weight ≥60 kg); †400 mg bid

Vogel A, et al. Ann Oncol 2017;28(Suppl 5):Abstr 6180

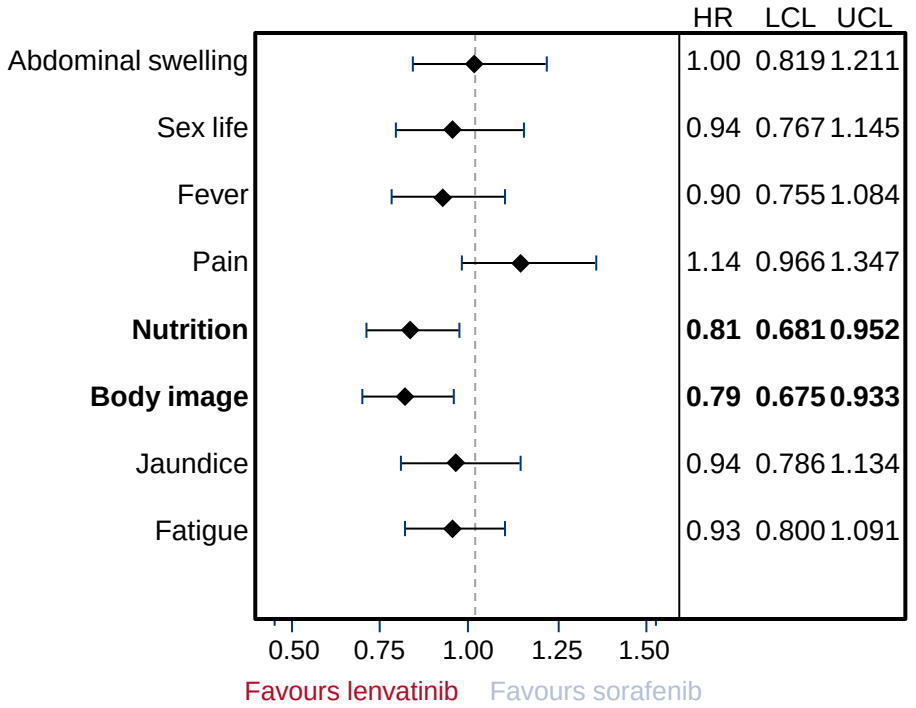
618O: Health-related quality of Life (HRQOL) and disease symptoms in patients with unresectable hepatocellular carcinoma (HCC) treated with lenvatinib (LEN) or sorafenib (SOR) – Vogel A

Key results

EORTC QLQ-C30



EORTC QLQ-HCC18



Vogel A, et al. Ann Oncol 2017;28(Suppl 5):Abstr 6180

618O: Health-related quality of Life (HRQOL) and disease symptoms in patients with unresectable hepatocellular carcinoma (HCC) treated with lenvatinib (LEN) or sorafenib (SOR) – Vogel A

Conclusions

- **In patients with unresectable HCC, HRQoL declined during treatment with either lenvatinib or sorafenib and was generally similar between the groups**
- **Clinically meaningful delays in role function deterioration, general cancer pain, diarrhoea, nutrition and body image were observed in those receiving lenvatinib compared with sorafenib**
  - **There were no significant improvements in HRQoL with sorafenib vs. lenvatinib**
- **The efficacy benefits of lenvatinib compared with sorafenib were not at the cost of decreased QoL**

Vogel A, et al. Ann Oncol 2017;28(Suppl 5):Abstr 6180

619O: JET-HCC: A phase 3 randomized, double-blind, placebo-controlled study of tivantinib as a second-line therapy in patients with c-Met high hepatocellular carcinoma – Kobayashi I, et al

Study objective

- To evaluate the efficacy and safety of tivantinib* vs. placebo as 2L therapy in Japanese patients with HCC and high c-Met expression

Key patient inclusion criteria

- c-Met high† HCC
- Refractory/intolerant to one systemic therapy including sorafenib
- Child Pugh A
- ≥1 measurable lesion
- ECOG PS ≤ 1

(n=195)

R 2:1

Tivantinib 120 mg bid (n=134) → PD

Stratification

- Vascular invasion (yes/no)
- ECOG PS (0/1)

Placebo (n=61) → PD

PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

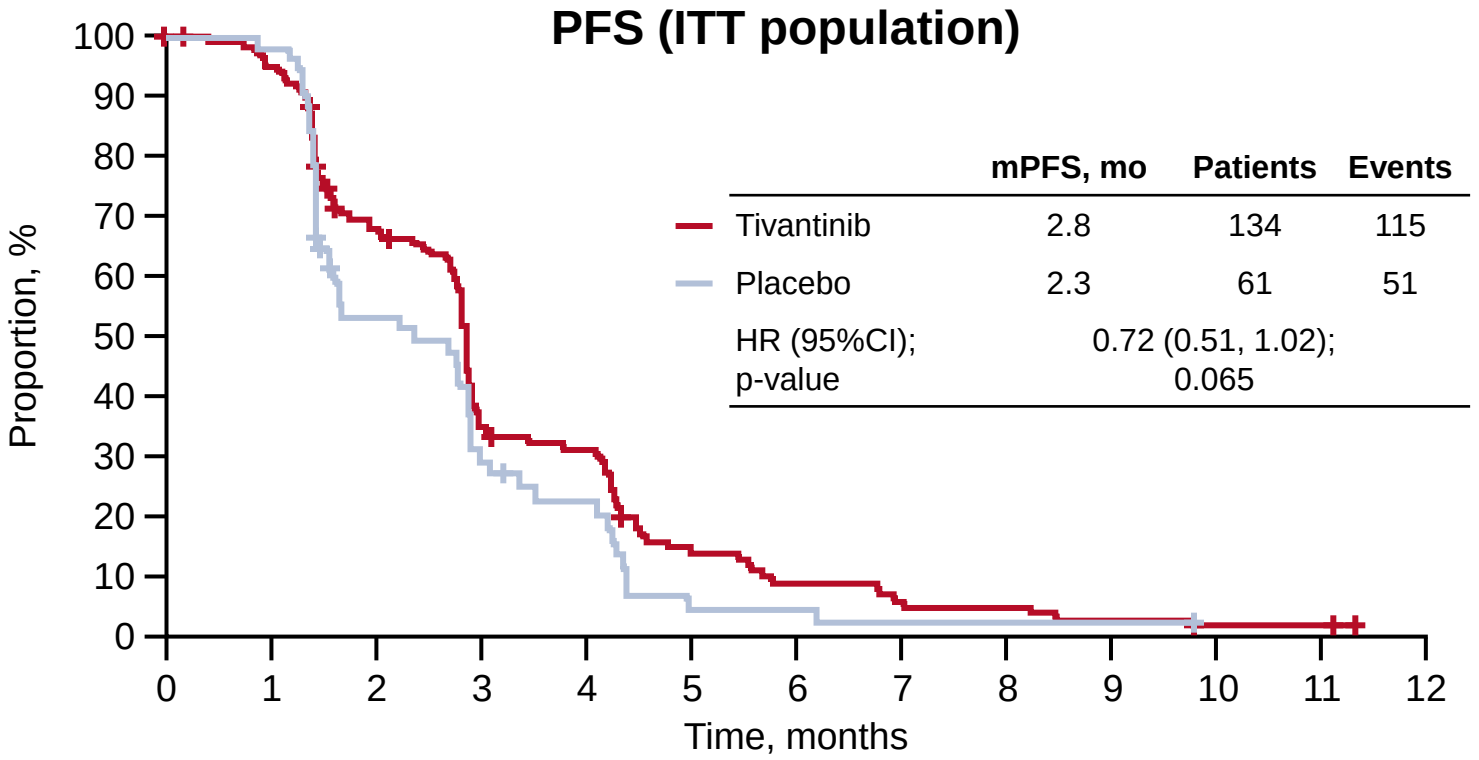
- OS, ORR, DCR, safety

*A small molecule inhibitor of c-Met; †Defined as ≥2+ in ≥50% of tumour cells, by IHC

Kobayashi I, et al. Ann Oncol 2017;28(Suppl 5):Abstr 619O

619O: JET-HCC: A phase 3 randomized, double-blind, placebo-controlled study of tivantinib as a second-line therapy in patients with c-Met high hepatocellular carcinoma – Kobayashi I, et al

Key results



n (%) [95%CI]	Tivantinib (n=134)	Placebo (n=61)	Difference, % (95%CI)
ORR	1 (0.7) [0.0, 4.1]	1 (1.6) [0.0, 8.8]	-0.9 (-4.4, 2.6)
DCR	83 (61.9) [53.2, 70.2]	34 (55.7) [42.4, 68.5]	6.2 (-8.7, 21.1)

Kobayashi I, et al. Ann Oncol 2017;28(Suppl 5):Abstr 619O

619O: JET-HCC: A phase 3 randomized, double-blind, placebo-controlled study of tivantinib as a second-line therapy in patients with c-Met high hepatocellular carcinoma – Kobayashi I, et al

Key results (cont.)

	Tivantinib (n=133)		Placebo (n=61)	
Most frequent TEAEs, n (%)	All grades	Grade 3–4	All grades	Grade 3–4
Neutropenia	59 (44.4)	42 (31.6)	4 (6.6)	1 (1.6)
Febrile neutropenia	8* (6.0)	8* (6.0)	0 (0)	0 (0)
WBC count decreased	50 (37.6)	33 (24.8)	0 (0)	0 (0)
Anaemia	45 (33.8)	19 (14.3)	5 (8.2)	1 (1.6)
Alopecia	23 (17.3)	0 (0)	2 (3.3)	0 (0)
Decreased appetite	23 (17.3)	3 (2.3)	9 (14.8)	2 (3.3)
Pyrexia	22 (16.5)	1 (0.8)	5 (8.2)	0 (0)
Malaise	20 (15.0)	0 (0)	7 (11.5)	0 (0)
Lymphocyte count decreased	18 (13.5)	10 (7.5)	1 (1.6)	0 (0)

Conclusions

- **Tivantinib 120 mg bid did not show a significant benefit as a 2L therapy for c-MET high HCC in Japanese patients**
- **Neutropenia was the most frequent TEAE, and it was mostly manageable**
- **Overall tolerability was consistent with previous safety findings**

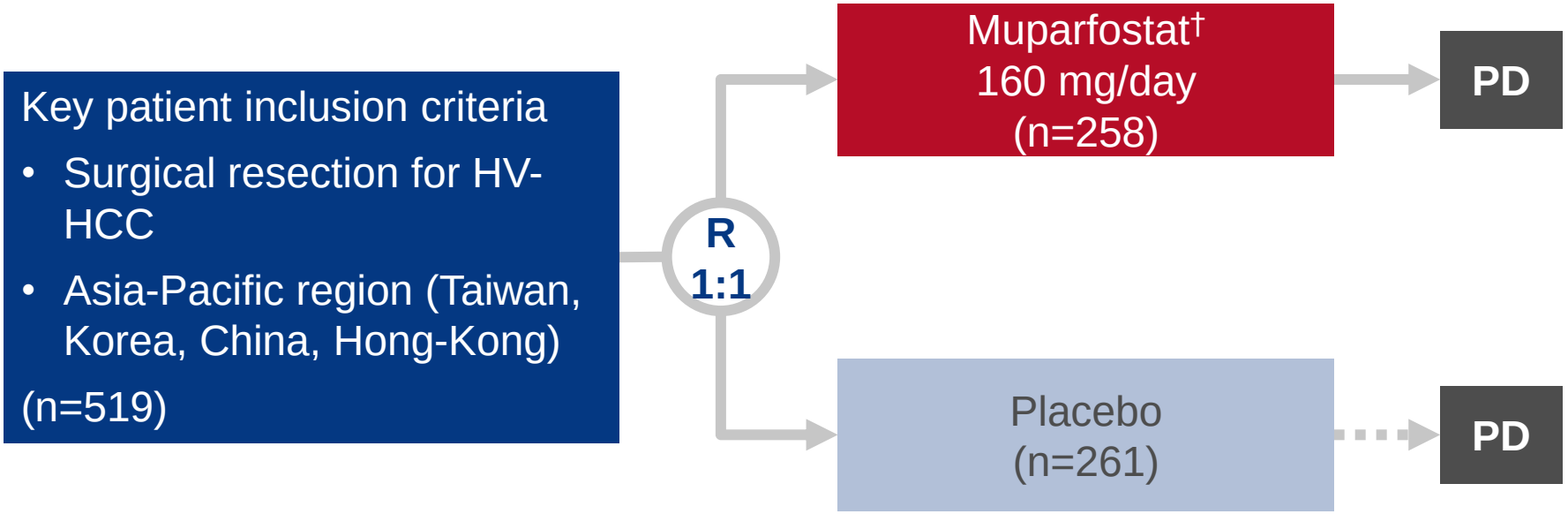
*One patient died due to sepsis following febrile neutropenia

Kobayashi I, et al. Ann Oncol 2017;28(Suppl 5):Abstr 619O

624PD: A phase III trial of muparfostat (PI-88) as adjuvant therapy in patients with hepatitis virus related hepatocellular carcinoma (HV-HCC) after resection – Chen P, et al

Study objective

- To investigate the efficacy and safety of muparfostat* as adjuvant therapy in patients with HV-HCC receiving surgical resection



PRIMARY ENDPOINT(S)

- DFS

SECONDARY ENDPOINTS

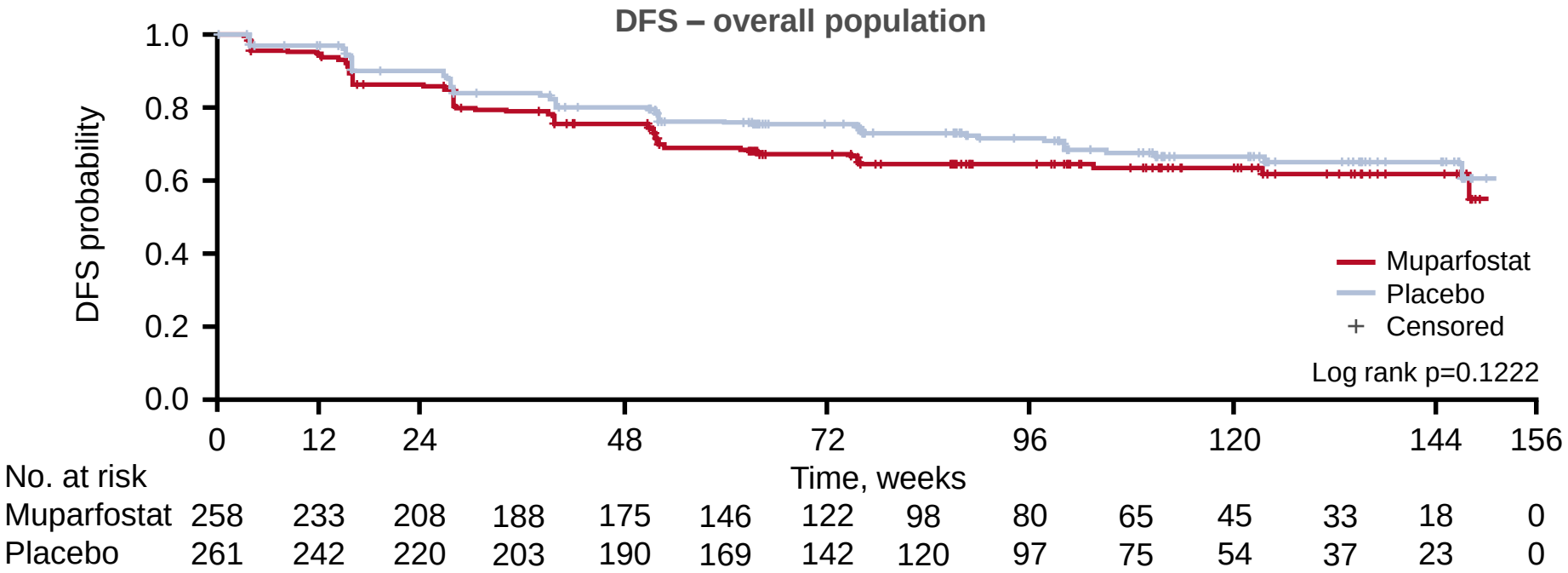
- OS, TTR, safety

*An oligosaccharides-mimicking heparan sulphate that antagonizes angiogenic growth factors and blocks heparanase; †4-days on/3-days off, 3-weeks on/1-week off

Chen P, et al. Ann Oncol 2017;28(Suppl 5):Abstr 624PD

624PD: A phase III trial of muparfostat (PI-88) as adjuvant therapy in patients with hepatitis virus related hepatocellular carcinoma (HV-HCC) after resection – Chen P, et al

Key results

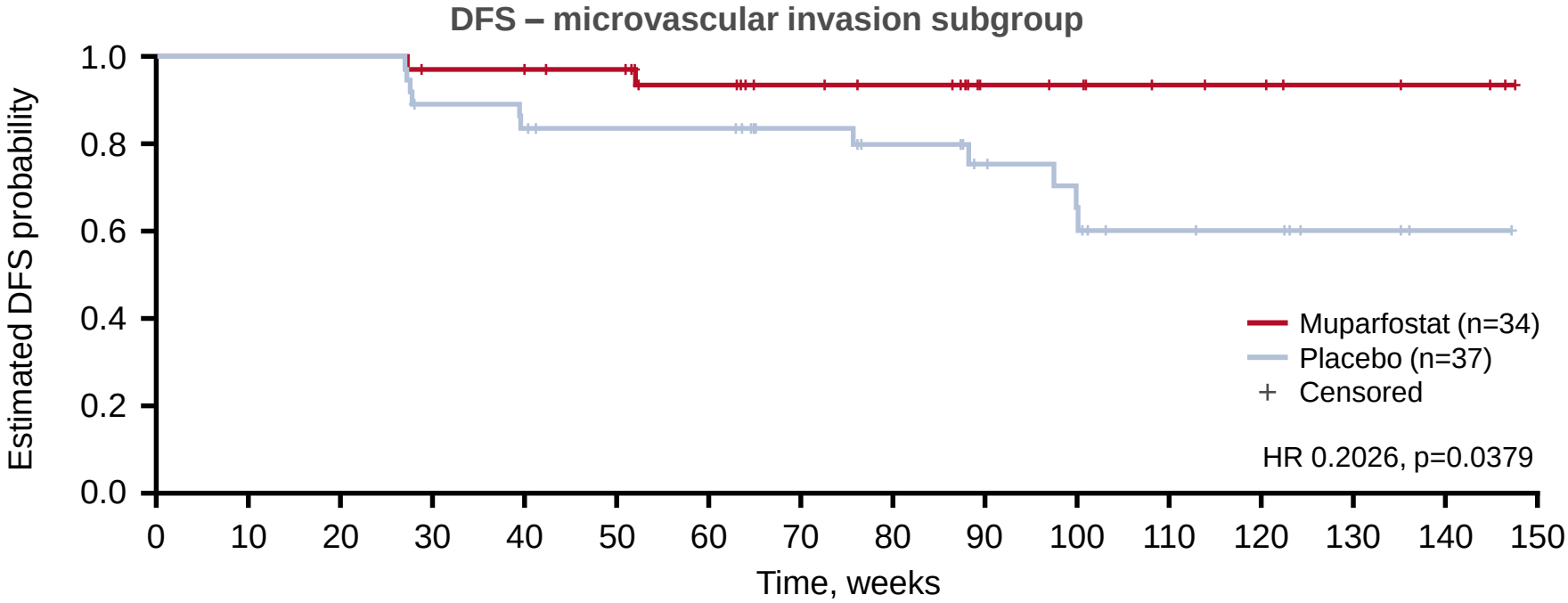


HCC tumour vascular invasion subtype	Muparfostat (n=261)	Placebo (n=258)	Total (n=519)
Macro, n (%)	22 (8.4)	18 (7.0)	40 (7.7)
Micro, n (%)	**105 (40.2)**	**106 (41.1)**	**211 (40.7)**
Absent, n (%)	134 (51.3)	134 (51.9)	268 (51.6)

Chen P, et al. Ann Oncol 2017;28(Suppl 5):Abstr 624PD

624PD: A phase III trial of muparfostat (PI-88) as adjuvant therapy in patients with hepatitis virus related hepatocellular carcinoma (HV-HCC) after resection – Chen P, et al

Key results (cont.)



Conclusions

- Adjuvant muparfostat did not improve DFS overall in patients with HV-HCC receiving surgical resection, but DFS was prolonged in the microvascular-invasion subgroup
- The results suggest that muparfostat as a single therapy or in combination with other anti-cancer agents could be assessed in future HCC adjuvant therapy trials

Chen P, et al. Ann Oncol 2017;28(Suppl 5):Abstr 624PD

Cancers of the pancreas, small bowel and hepatobiliary tract

BILIARY TRACT CANCER

LBA29: Adjuvant GEMOX for biliary tract cancer: updated relapse-free survival and first overall survival results of the randomized PRODIGE 12-ACCORD 18 (UNICANCER GI) phase III trial – Edeline J, et al

Study objective

- To assess the efficacy and safety of adjuvant GEMOX in patients with biliary tract cancer

Key patient inclusion criteria

- Biliary tract cancer (ICC/ECC/GBC)
- R0 or R1 surgery
- ECOG PS 0–2
- Adequate liver function
- Randomization within 3 months of surgery

(n=194)

R 1:1

GEMOX* 85 q2w 12 cycles (n=95) → PD

Stratification

- Tumour site
- R0 vs. R1
- N0 vs. N+ vs. NX
- Centres

Surveillance† only: ACE, CA 19.9 + CT scans (n=99) → PD

PRIMARY ENDPOINTS

- RFS, QoL

SECONDARY ENDPOINTS

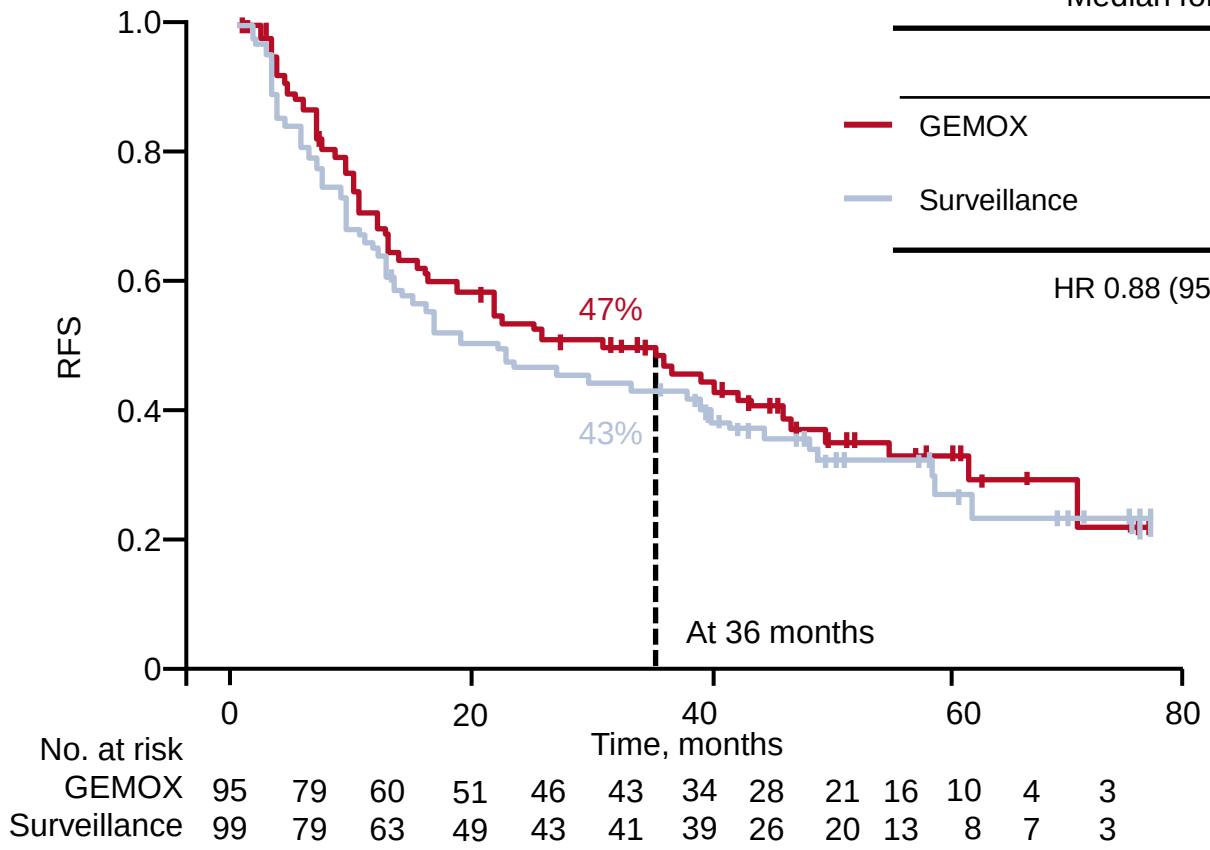
- OS, DFS, toxicity, translation research

*Gemcitabine 1000 mg/m^2 D1; oxaliplatin 85 mg/m^2 D2;
†every 3 months for 2 years then every 6 months for 3 years

Edeline J, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA29

LBA29: Adjuvant GEMOX for biliary tract cancer: updated relapse-free survival and first overall survival results of the randomized PRODIGE 12-ACCORD 18 (UNICANCER GI) phase III trial – Edeline J, et al

Key results



Median follow-up: 46.5 months

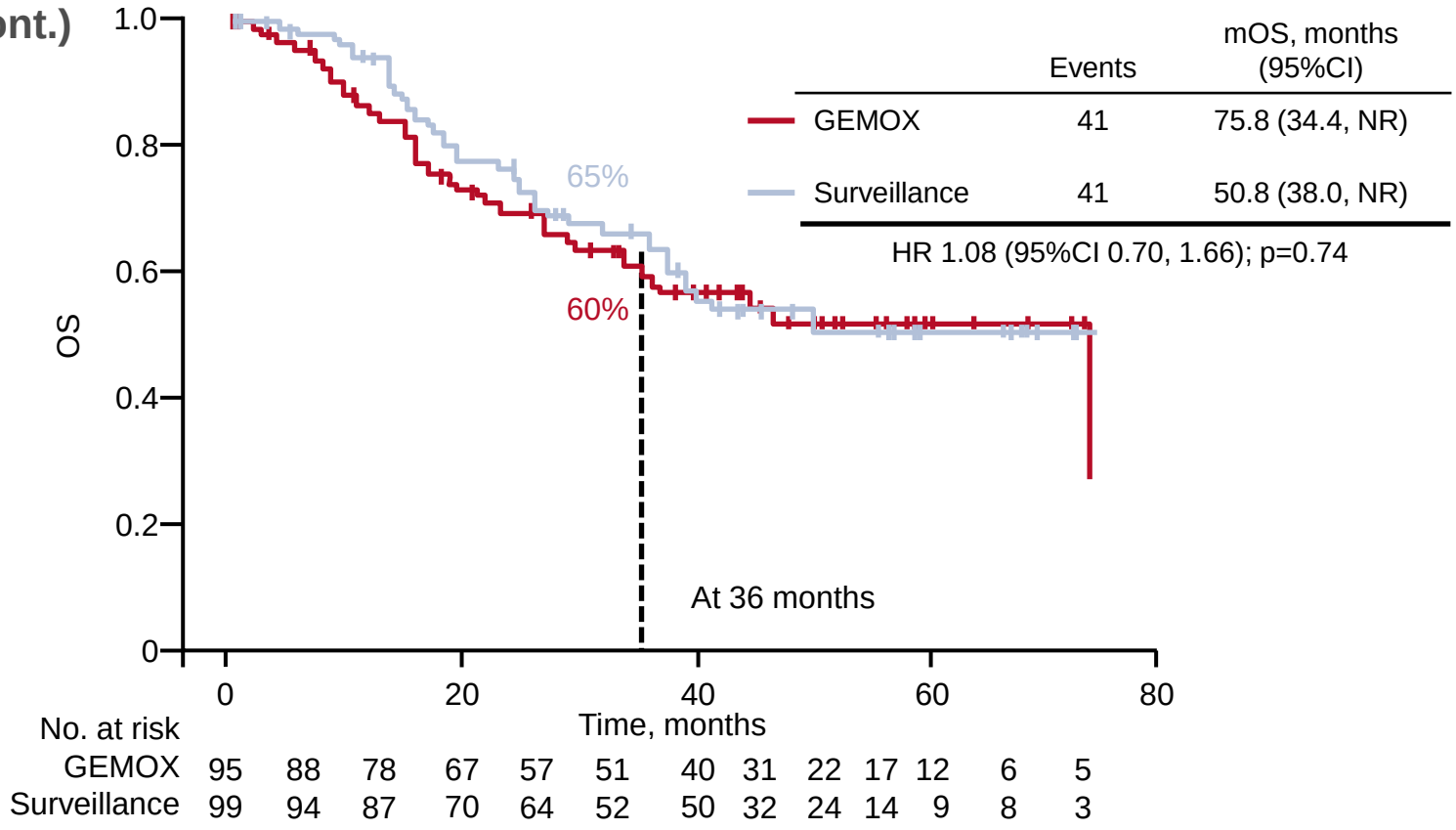
	mRFS, months (95%CI)
GEMOX	30.4 (15.4, 43.0)
Surveillance	18.5 (12.6, 38.2)

HR 0.88 (95%CI 0.62, 1.25); p=0.47

Edeline J, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA29

LBA29: Adjuvant GEMOX for biliary tract cancer: updated relapse-free survival and first overall survival results of the randomized PRODIGE 12-ACCORD 18 (UNICANCER GI) phase III trial – Edeline J, et al

Key results (cont.)



Conclusion

- **In patients with biliary tract cancer, there was no benefit of GEMOX vs. surveillance, therefore, GEMOX CT is not recommended in the adjuvant setting**

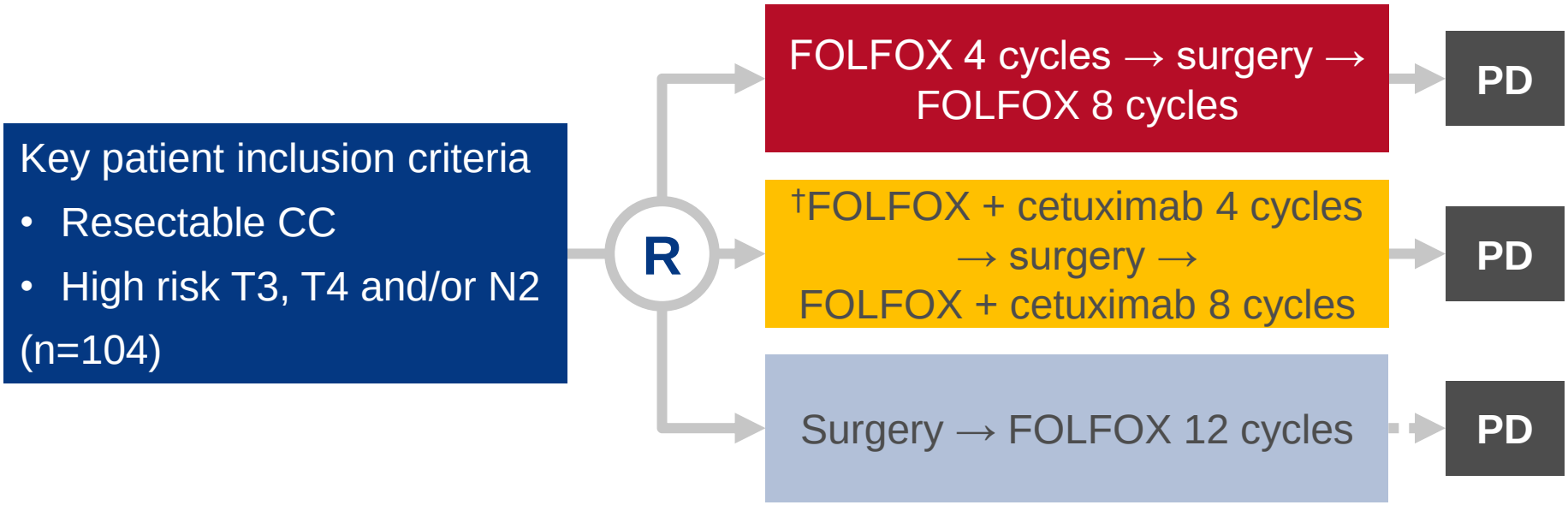
Edeline J, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA29

CANCERS OF THE COLON, RECTUM AND ANUS

476O: Neoadjuvant FOLFOX 4 versus FOLFOX 4 plus cetuximab versus immediate surgery for high-risk stage II and III colon cancers: A phase II multicentre randomised controlled trial (PRODIGE 22) – Karoui M, et al

Study objective

- To assess efficacy and safety with neoadjuvant FOLFOX4 or FOLFOX4 + cetuximab vs. adjuvant FOLFOX4 after colectomy in patients with high risk colon cancer



PRIMARY ENDPOINT(S)

- Tumour regression grade (TRG)

SECONDARY ENDPOINTS

- Toxicity, primary tumour complications, postoperative morbidity, quality of surgery, radiological staging, 3-year DFS, QoL

†In RAS WT patients only

Karoui M, et al. Ann Oncol 2017;28(Suppl 5):Abstr 476O

476O: Neoadjuvant FOLFOX 4 versus FOLFOX 4 plus cetuximab versus immediate surgery for high-risk stage II and III colon cancers: A phase II multicentre randomised controlled trial (PRODIGE 22) – Karoui M, et al

Key results

Tumour response, n (%)	FOLFOX (n=52)	Surgery (n=52)	p-value
TRG 1	4 (8)	0	0.118
TRG 2	19 (36)	4 (8)	-
TRG 3	25 (48)	45 (86)	-
N/A	4 (8)	3 (6)	-
Significant tumour regression (TRG 1 + 2)	23 (44)	4 (8)	<0.001

TRG 1, no viable cancer cells/single cells or small groups of cancer cells; TRG2, residual cancer outgrown by fibrosis; TRG 3, significant fibrosis outgrown by cancer/no fibrosis with extensive residual cancer

Karoui M, et al. Ann Oncol 2017;28(Suppl 5):Abstr 476O

476O: Neoadjuvant FOLFOX 4 versus FOLFOX 4 plus cetuximab versus immediate surgery for high-risk stage II and III colon cancers: A phase II multicentre randomised controlled trial (PRODIGE 22) – Karoui M, et al

Key results (cont.)

Radiological staging	FOLFOX (n=48)	Surgery (n=51)	p-value
Stage, n (%)			0.019
I	4 (8)	0	
II	25 (52)	20 (39)	
III	19 (40)	31 (61)	
pT4 and/or N2, n (%)	18 (38)	30 (59)	0.033
Vascular emboli, lymphatic and/or perinervous invasion, n (%)	9 (19)	25 (49)	0.001
Harvested LN, mean (±SD)	26.6 (11.3)	25.2 (11.2)	0.529
Positive LN, mean (±SD)	1.65 (2.9)	2.5 (3.9)	0.215

Conclusions

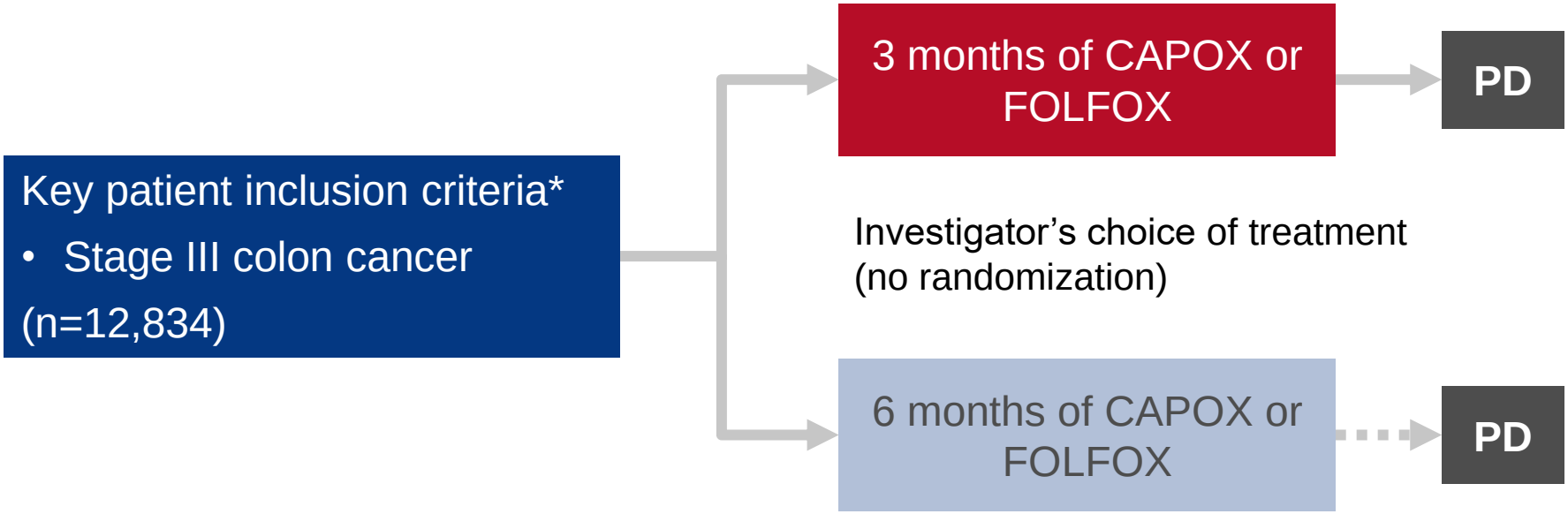
- **In patients with locally advanced colon cancer, neoadjuvant FOLFOX was well tolerated in a perioperative setting**
- **Neoadjuvant FOLFOX compared with upfront surgery did not increase surgical morbidity, was not associated with TRG1, but was associated with significant tumour regression**
- **3-year DFS and 5-year OS are being assesses in phase 3 studies**

Karoui M, et al. Ann Oncol 2017;28(Suppl 5):Abstr 476O

LBA21_PR: Prospective pooled analysis of six Phase III trials investigating duration of adjuvant oxaliplatin-based therapy (3 vs 6 months) for patients with stage III colon cancer: updated results of IDEA (International Duration Evaluation of Adjuvant chemotherapy) – Grothey A, et al

Study objective

- To assess the efficacy and safety of 3 vs. 6 months of FOLFOX or CAPOX in patients with stage III colon cancer



PRIMARY ENDPOINT

- DFS

SECONDARY ENDPOINTS

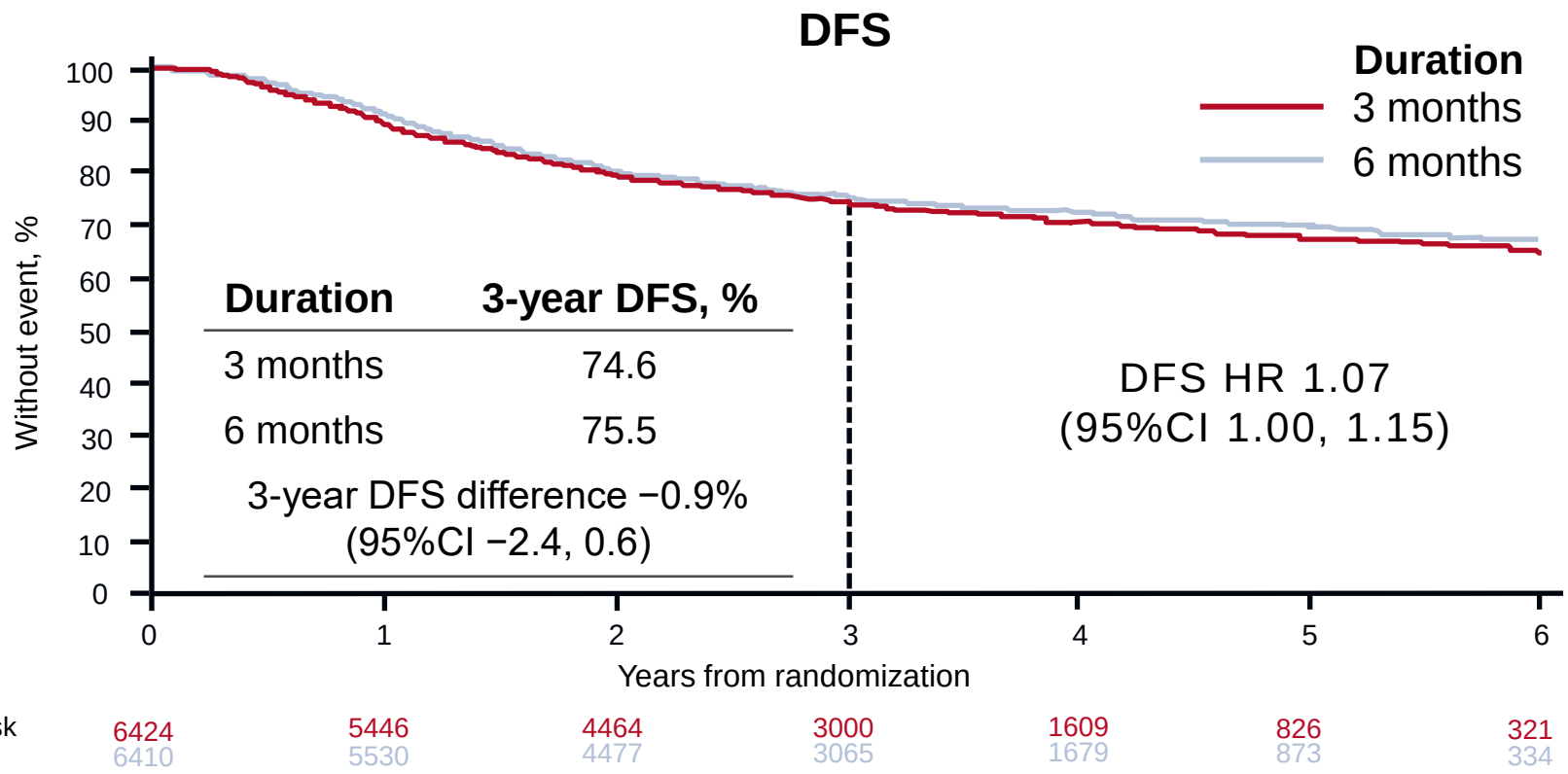
- Safety

*Includes data from six phase 3 studies: SCOT, TOSCA, Alliance/SWOG 80702, IDEA France, ACHIEVE and HORG

Grothey A, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA21_PR

LBA21_PR: Prospective pooled analysis of six Phase III trials investigating duration of adjuvant oxaliplatin-based therapy (3 vs 6 months) for patients with stage III colon cancer: updated results of IDEA (International Duration Evaluation of Adjuvant chemotherapy) – Grothey A, et al

Key results



Grothey A, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA21_PR

LBA21_PR: Prospective pooled analysis of six Phase III trials investigating duration of adjuvant oxaliplatin-based therapy (3 vs 6 months) for patients with stage III colon cancer: updated results of IDEA (International Duration Evaluation of Adjuvant chemotherapy) – Grothey A, et al

Key results (cont.)

3-yr DFS rate (%) and HR by regimen and risk group		Regimen								
		CAPOX			FOLFOX			CAPOX/FOLFOX combined		
		3-yr DFS, % (95%CI)		HR (95%CI)	3-yr DFS, % (95%CI)		HR (95%CI)	3-yr DFS, % (95%CI)		HR (95%CI)
		3 months	6 months		3 months	6 months		3 months	6 months	
Risk group	Low-risk (T1–3 N1) ~60%	85.0 (83.1, 86.9)	83.1 (81.1, 85.2)	0.85 (0.71, 1.01)	81.9 (80.2, 83.6)	83.5 (81.9, 85.1)	1.10 (0.96, 1.26)	83.1 (81.8, 84.4)	83.3 (82.1, 84.6)	1.01 (0.90, 1.12)
	High-risk (T4 and / or N2) ~40%	64.1 (61.3, 67.1)	64.0 (61.2, 67.0)	1.02 (0.89, 1.17)	61.5 (58.9, 64.1)	64.7 (62.2, 67.3)	1.20 (1.07, 1.35)	62.7 (60.8, 64.4)	64.4 (62.6, 66.4)	1.12 (1.03, 1.23)
	Risk groups combined	75.9 (74.2, 77.6)	74.8 (73.1, 76.6)	0.95 (0.85, 1.06)	73.6 (72.2, 75.1)	76.0 (74.6, 77.5)	1.16 (1.06, 1.26)	p-value interaction test: Regimen: 0.0061 Risk group: 0.11		

Non-inferior **Not proven** **Inferior**

Grothey A, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA21_PR

LBA21_PR: Prospective pooled analysis of six Phase III trials investigating duration of adjuvant oxaliplatin-based therapy (3 vs 6 months) for patients with stage III colon cancer: updated results of IDEA (International Duration Evaluation of Adjuvant chemotherapy) – Grothey A, et al

Key results (cont.)

IDEA recommendations

		Regimen	
		CAPOX	FOLFOX
Risk group	Low-risk (T1–3 N1) ~60%	3 months	(3)–6 months
	High-risk (T4 and/or N2) ~40%	(3)–6 months	6 months

Grothey A, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA21_PR

LBA21_PR: Prospective pooled analysis of six Phase III trials investigating duration of adjuvant oxaliplatin-based therapy (3 vs 6 months) for patients with stage III colon cancer: updated results of IDEA (International Duration Evaluation of Adjuvant chemotherapy) – Grothey A, et al

Results (cont.)

	FOLFOX			CAPOX		
AEs, %	3-month arm	6-month arm	p-value[1]	3-month arm	6-month arm	p-value[1]
Overall						
Grade 2	32	32	<0.0001	41	48	<0.0001
Grade 3/4	38	57		24	37	
Neurotoxicity						
Grade 2	14	32	<0.0001	12	36	<0.0001
Grade 3/4	3	16		3	9	
Diarrhoea						
Grade 2	11	13	<0.0001	10	13	0.0117
Grade 3/4	5	7		7	9	

Conclusions

- The IDEA results can be used as a framework for discussions on risks and benefits of individualised adjuvant therapy approaches
- A remarkable reduction in (neuro)toxicity was noted with shorter duration of therapy
- Treatment with CAPOX for 3 months was as good as 6 months, particularly in the low-risk population
- Treatment with FOLFOX for 6 months provided additional benefit in terms of DFS, particularly in the high-risk population

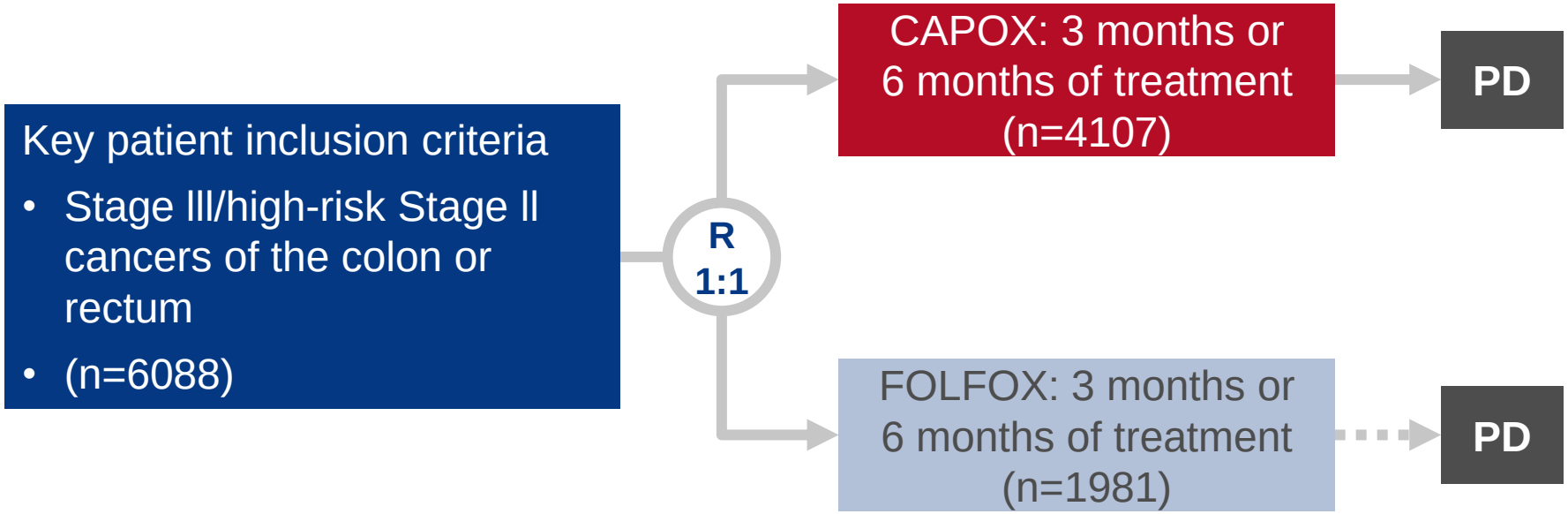
*AEs only collected on first 617 patients enrolled to SCOT trial; †Chi-squared test for trend, total of 19 grade 5 events

Grothey A, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA21_PR

LBA22: Updated results of the SCOT study; An international phase III randomised (1:1) non-inferiority trial comparing 3 versus 6 months of oxaliplatin based adjuvant chemotherapy for colorectal cancer – Iveson T, et al

Study objective

- To assess the effect of treatment duration on DFS by CT regimen (CAPOX or FOLFOX) and risk group in patients with colon/rectum cancer



PRIMARY ENDPOINT

- DFS

SECONDARY ENDPOINTS

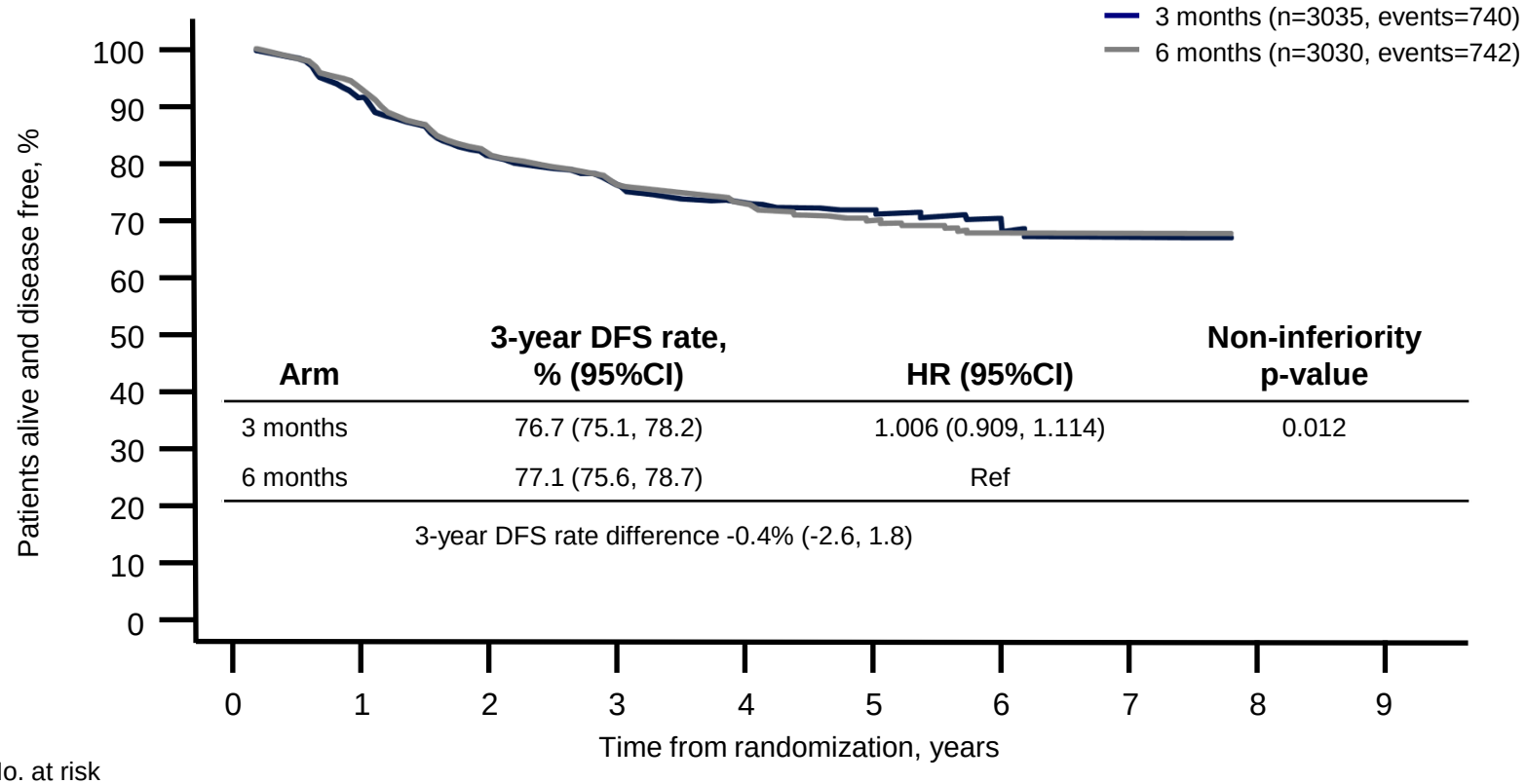
- DFS by disease risk group and regimen duration

Iveson T, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA22

LBA22: Updated results of the SCOT study; An international phase III randomised (1:1) non-inferiority trial comparing 3 versus 6 months of oxaliplatin based adjuvant chemotherapy for colorectal cancer – Iveson T, et al

Key results

DFS overall population



Arm	3-year DFS rate, % (95%CI)	HR (95%CI)	Non-inferiority p-value
3 months	76.7 (75.1, 78.2)	1.006 (0.909, 1.114)	0.012
6 months	77.1 (75.6, 78.7)	Ref	

3-year DFS rate difference -0.4% (-2.6, 1.8)

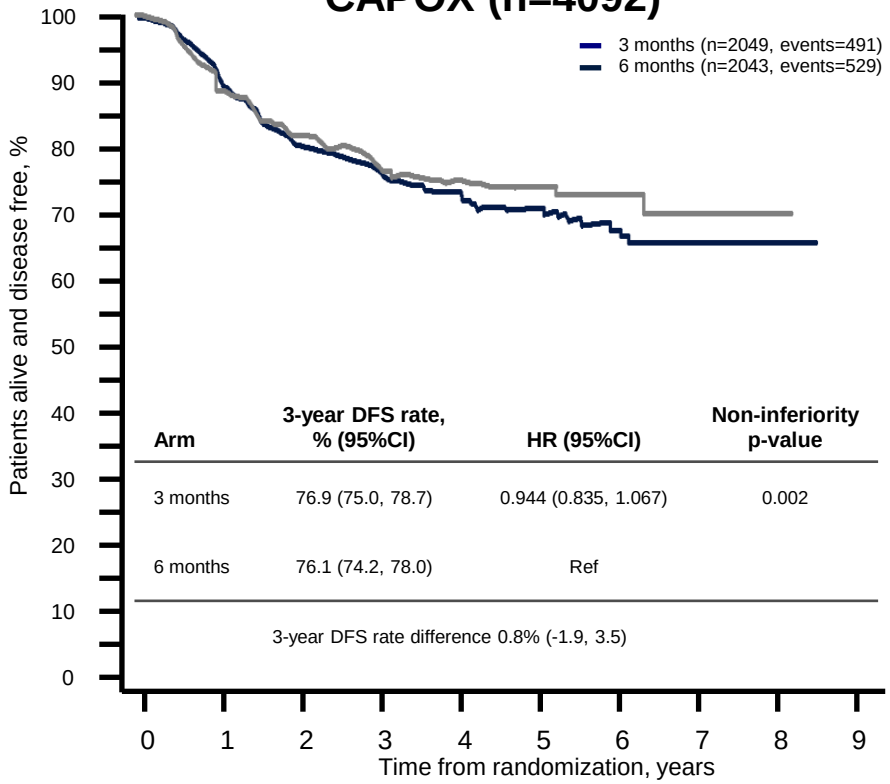
Iveson T, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA22

LBA22: Updated results of the SCOT study; An international phase III randomised (1:1) non-inferiority trial comparing 3 versus 6 months of oxaliplatin based adjuvant chemotherapy for colorectal cancer – Iveson T, et al

Key results (cont.)

DFS by regimen

CAPOX (n=4092)



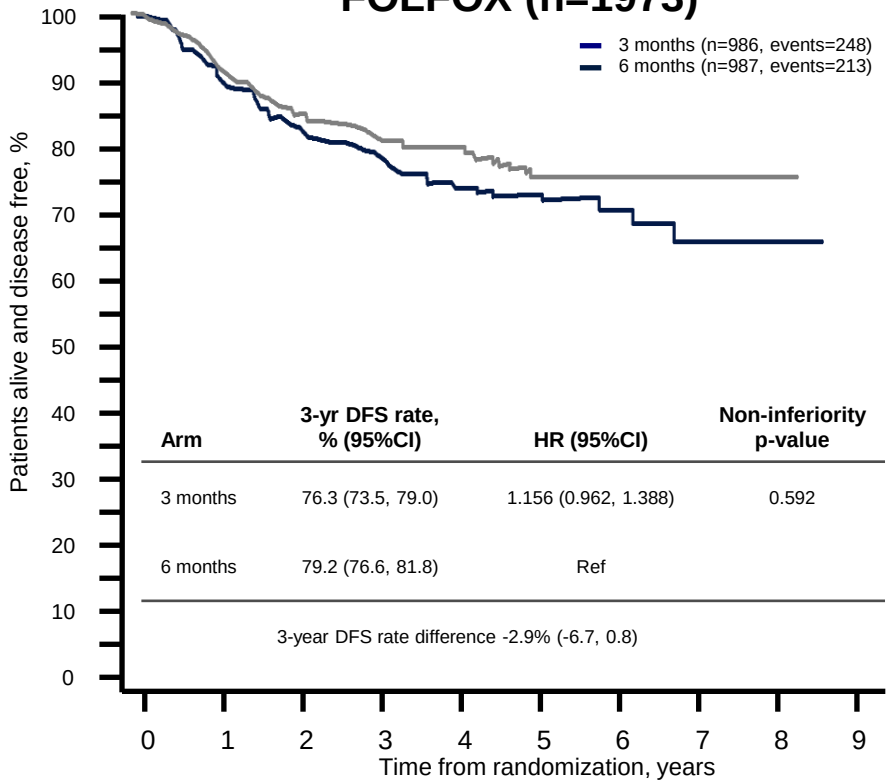
Arm	3-year DFS rate, % (95%CI)	HR (95%CI)	Non-inferiority p-value
3 months	76.9 (75.0, 78.7)	0.944 (0.835, 1.067)	0.002
6 months	76.1 (74.2, 78.0)	Ref	

3-year DFS rate difference 0.8% (-1.9, 3.5)

No. at risk

3 months:	2049	1795	1578	1014	482	236	66	14	1	0
6 months:	2043	1810	1544	1024	517	238	71	18	3	0

FOLFOX (n=1973)



Arm	3-yr DFS rate, % (95%CI)	HR (95%CI)	Non-inferiority p-value
3 months	76.3 (73.5, 79.0)	1.156 (0.962, 1.388)	0.592
6 months	79.2 (76.6, 81.8)	Ref	

3-year DFS rate difference -2.9% (-6.7, 0.8)

No. at risk

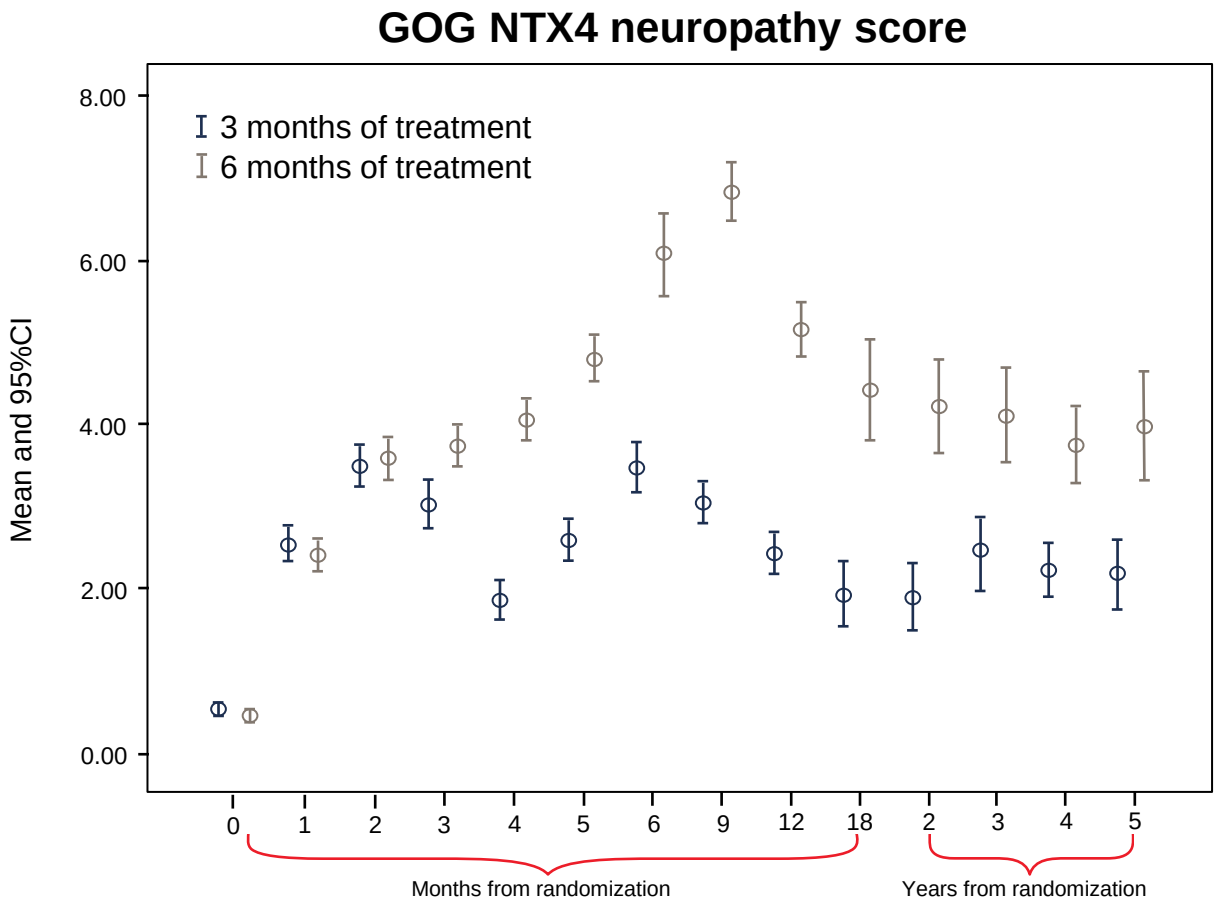
3 months:	986	886	751	486	223	103	36	10	2	0
6 months:	987	887	773	516	240	108	42	10	1	0

Iveson T, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA22

LBA22: Updated results of the SCOT study; An international phase III randomised (1:1) non-inferiority trial comparing 3 versus 6 months of oxaliplatin based adjuvant chemotherapy for colorectal cancer – Iveson T, et al

Key results (cont.)

Neuropathy measured over time by treatment duration



Iveson T, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA22

LBA22: Updated results of the SCOT study; An international phase III randomised (1:1) non-inferiority trial comparing 3 versus 6 months of oxaliplatin based adjuvant chemotherapy for colorectal cancer – Iveson T, et al

Conclusions

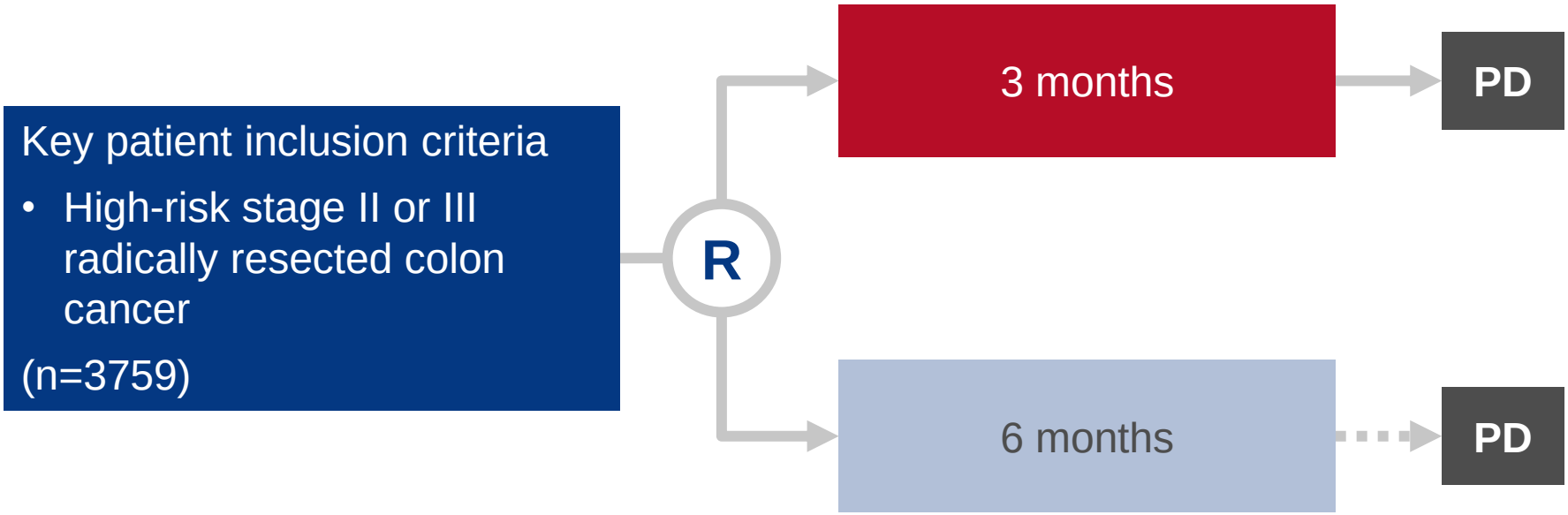
- **The SCOT trial met its non-inferiority target for 3 months of adjuvant CT**
- **The duration of adjuvant CT is dependent on regimen with 3 months sufficient for CAPOX but 6 months may be required for FOLFOX**
- **Treatment for 6 months provided small additional benefit in DFS benefit but was associated with considerable long-lasting toxicity**
- **It is important to consider patient choice**

Iveson T, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA22

LBA23: FOLFOX4/XELOX in stage II–III colon cancer: Efficacy and safety results of the Italian Three Or Six Colon Adjuvant (TOSCA) trial – Labianca R, et al

Study objective

- To compare 3 vs. 6 month treatment duration in patients with high risk stage II or III colon cancer receiving FOLFOX4 or CAPOX



PRIMARY ENDPOINT

- RFS

SECONDARY ENDPOINTS

- OS, safety

Labianca R, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA23

LBA23: FOLFOX4/XELOX in stage II–III colon cancer: Efficacy and safety results of the Italian Three Or Six Colon Adjuvant (TOSCA) trial – Labianca R, et al

Key results

3-year RFS	3 months, %	6 months, %	HR* (95%CI)	Difference* (95%CI)
Overall population	81.1	83.0	1.14 (0.99, 1.32)	−1.9 (−4.8, 1.0)
Stage II	85.5	91.2	1.41 (1.05, 1.89)	−5.7 (−9.7, −1.7)
Stage III	78.8	78.7	1.07 (0.91, 1.26)	0.1 (−3.4, 3.6)
FOLFOX	80.4	83.3	1.23 (1.03, 1.46)	−2.9 (−6.2, 0.4)
CAPOX	82.5	82.5	0.98 (0.77, 1.26)	0.0 (−4.5, 4.5)

*3 vs. 6 months

Labianca R, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA23

LBA23: FOLFOX4/XELOX in stage II–III colon cancer: Efficacy and safety results of the Italian Three Or Six Colon Adjuvant (TOSCA) trial – Labianca R, et al

Key results (cont.)

	Grade 1–2, %		Grade 2–3, %		
AEs	3 months	6 months	3 months	6 months	p-value*
Neurological	37.0	41.0	9.0†	31.0†	<0.0001
Febrile neutropenia	1.7	3.5	1.4	2.7	<0.0001
Thrombocytopenia	33.0	47.0	1.6	2.1	<0.0001
Diarrhoea	29.0	35.0	5.1	6.4	<0.0001
Allergic reactions	3.4	6.4	0.5	2.0	<0.0001

Conclusions

- **In patients with high risk stage II or III colon cancer, 3 months of oxaliplatin-based adjuvant treatment was not shown to be as efficacious as 6 months**
- **Nevertheless, because the absolute difference in RFS between the two treatment durations is small and clinically not meaningful, the decision to complete the whole 6-month program should be individualised based on toxicity and patient attitude**

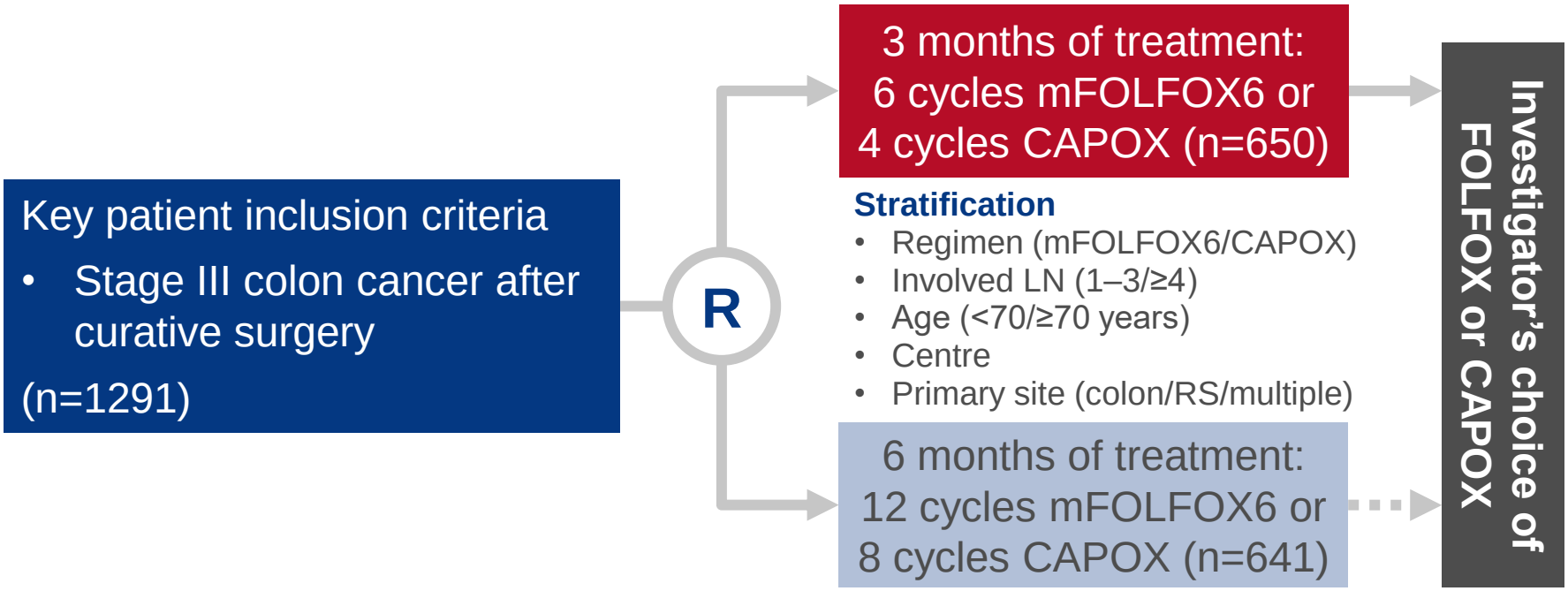
*Chi-squared test for trend; †Clinically relevant neurological toxicity (grade 2, 3 and 4)

Labianca R, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA23

LBA24: Efficacy of 3 versus 6 months of oxaliplatin-based adjuvant chemotherapy for stage III colon cancer: Results from phase III ACHIEVE trial as part of the International Duration Evaluation of Adjuvant therapy (IDEA) collaboration – Yoshino T, et al

Study objective

- To assess the efficacy of 3 vs. 6 months of oxaliplatin-based adjuvant CT for stage III colon cancer



PRIMARY ENDPOINT

- DFS

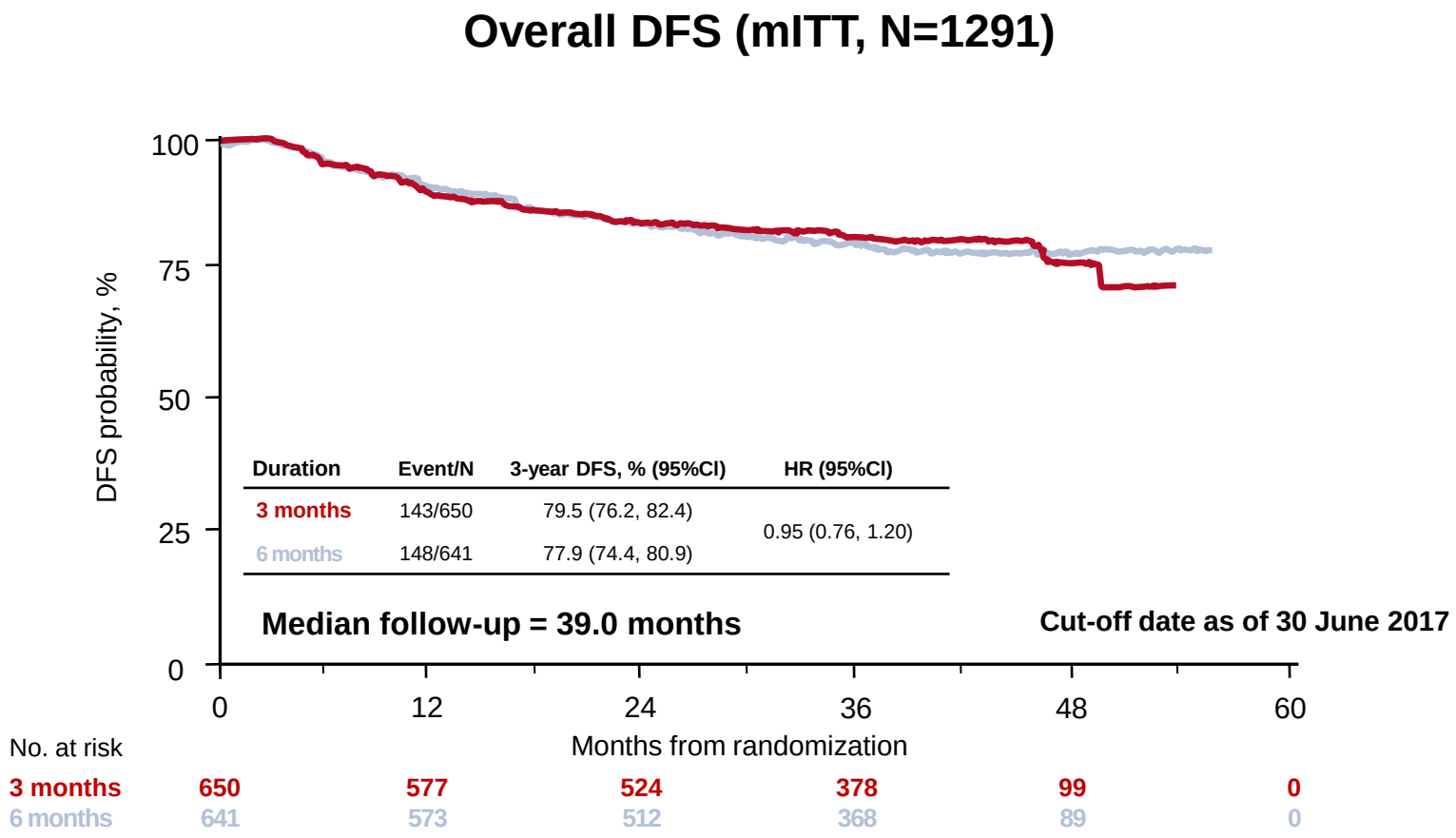
SECONDARY ENDPOINTS

- OS, TTF, compliance, toxicity

Yoshino T, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA24

LBA24: Efficacy of 3 versus 6 months of oxaliplatin-based adjuvant chemotherapy for stage III colon cancer: Results from phase III ACHIEVE trial as part of the International Duration Evaluation of Adjuvant therapy (IDEA) collaboration – Yoshino T, et al

Key results

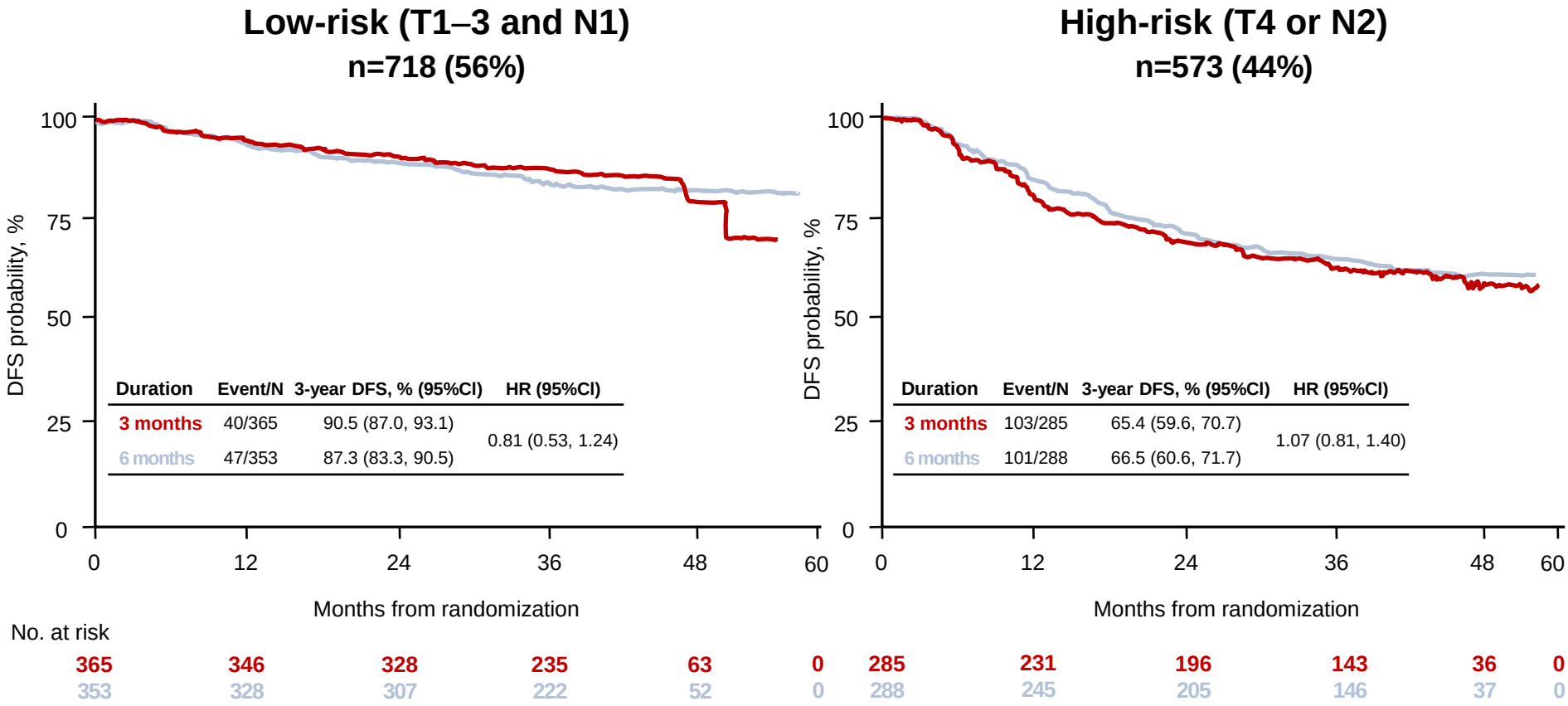


Yoshino T, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA24

LBA24: Efficacy of 3 versus 6 months of oxaliplatin-based adjuvant chemotherapy for stage III colon cancer: Results from phase III ACHIEVE trial as part of the International Duration Evaluation of Adjuvant therapy (IDEA) collaboration – Yoshino T, et al

Key results (cont.)

DFS by risk (T and N stage)

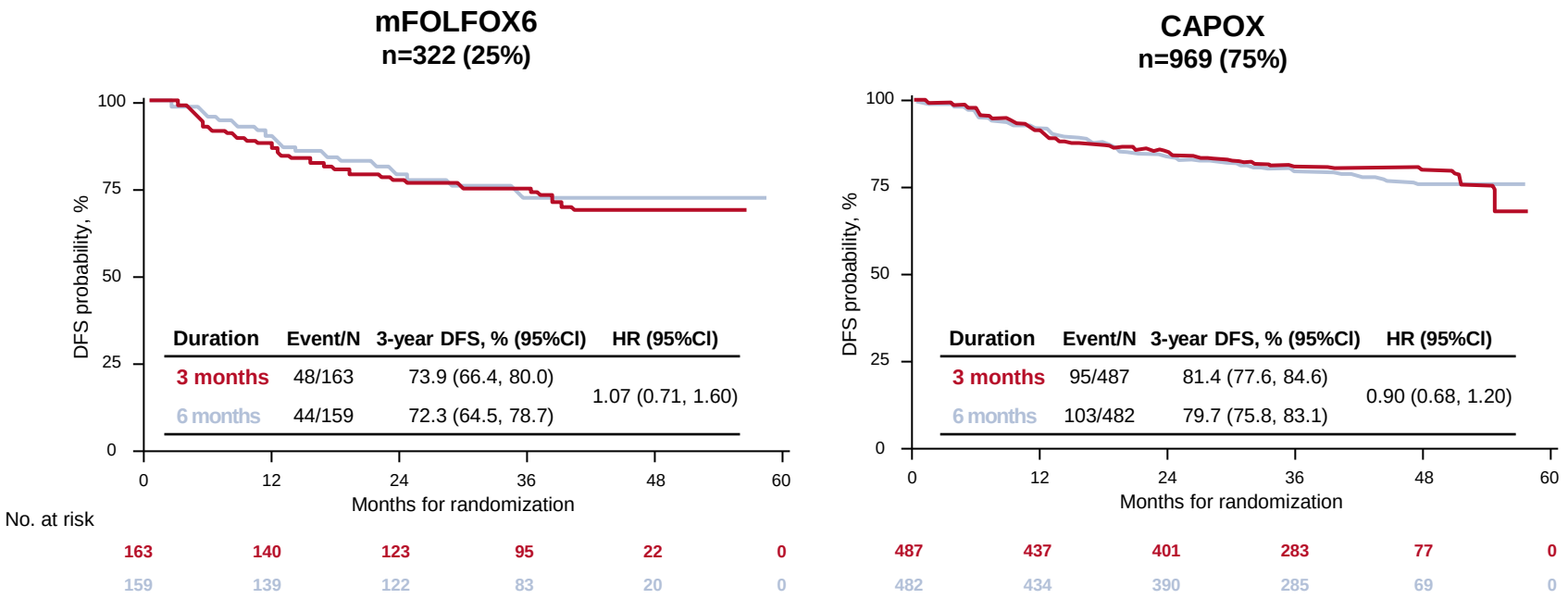


Yoshino T, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA24

LBA24: Efficacy of 3 versus 6 months of oxaliplatin-based adjuvant chemotherapy for stage III colon cancer: Results from phase III ACHIEVE trial as part of the International Duration Evaluation of Adjuvant therapy (IDEA) collaboration – Yoshino T, et al

Key results (cont.)

DFS by regimen



Yoshino T, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA24

LBA24: Efficacy of 3 versus 6 months of oxaliplatin-based adjuvant chemotherapy for stage III colon cancer: Results from phase III ACHIEVE trial as part of the International Duration Evaluation of Adjuvant therapy (IDEA) collaboration – Yoshino T, et al

Conclusions

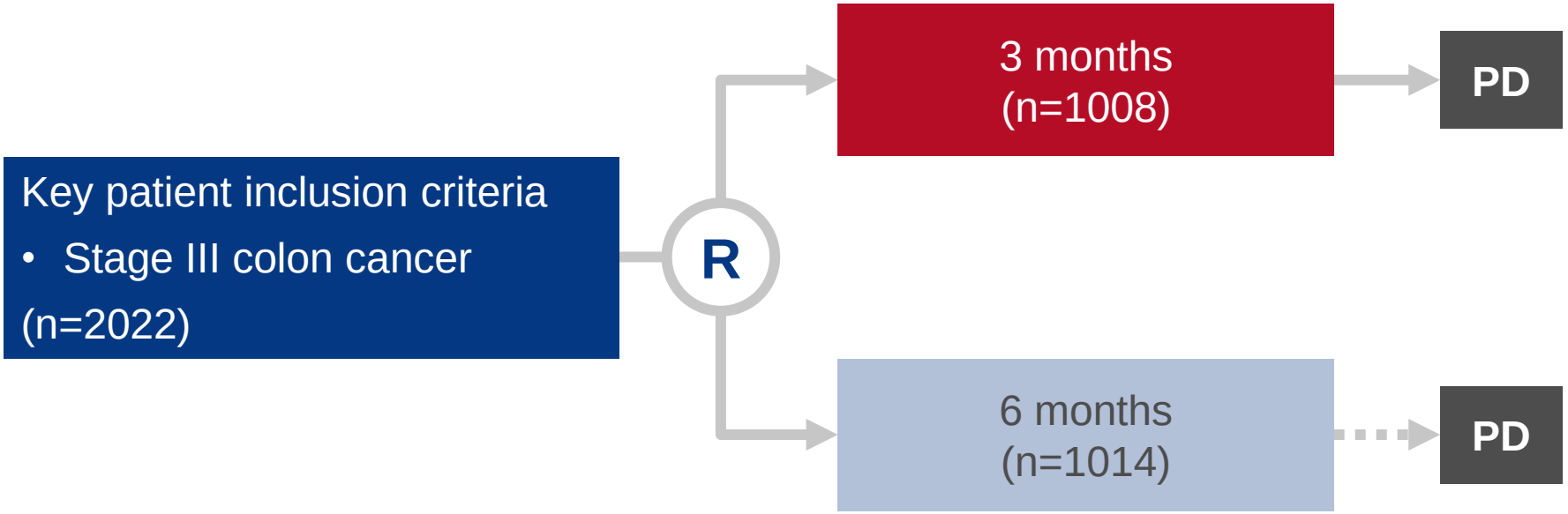
- ACHIEVE was the only one of the six IDEA trials in Asia
- The data for relative benefits of 3 months over 6 months according to risk and regimen were consistent with those of the other IDEA trials
- Treatment for 3 months is sufficient for those with low-risk cancers with CAPOX being more comfortable, while for those with high-risk cancers treatment for 6 months may be required

Yoshino T, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA24

473O: Three versus six months' adjuvant oxaliplatin-based chemotherapy for patients with stage III colon cancer: Per-protocol, subgroups and long-lasting neuropathy results – Taieb J, et al

Study objective

- To compare DFS with 3 vs. 6 months of treatment with FOLFOX or CAPOX in patients with stage III colon cancer



PRIMARY ENDPOINT(S)

- DFS

SECONDARY ENDPOINTS

- Safety

Taieb J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 473O

473O: Three versus six months' adjuvant oxaliplatin-based chemotherapy for patients with stage III colon cancer: Per-protocol, subgroups and long-lasting neuropathy results – Taieb J, et al

Key results

DFS	3-month arm, % (95%CI)	6-month arm, % (95%CI)	HR (95%CI)	p-value
mITT* population	72 (69, 75)	76 (73, 78)	1.24 (1.05, 1.46)	0.01
mPP† population	72 (69, 75)	78 (75, 80)	1.36 (1.14, 1.63)	0.0007
T1–3, N1	80 (76, 83)	83 (79, 85)	1.15 (0.91, 1.47)	-
T4 and/or N2	59 (54, 64)	65 (60, 70)	1.38 (1.10, 1.73)	-
FOLFOX (90% of patients)	72 (69, 75)	76 (73, 78)	1.24 (1.05, 1.46)	-
CAPOX (10% patients)	72 (63, 80)	71 (60, 79)	0.97 (0.59, 1.59)	-

*Received treatment; †Received ≥2.5 months (3-month arm) or ≥5 months (6-month arm) of treatment

Taieb J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 473O

473O: Three versus six months' adjuvant oxaliplatin-based chemotherapy for patients with stage III colon cancer: Per-protocol, subgroups and long-lasting neuropathy results – Taieb J, et al

Conclusions

- **In patients with stage III colon cancer, 6 months adjuvant CT is superior to 3 months**
- **In FOLFOX treated patients:**
  - **T4 and/or N2: 6 months adjuvant CT is superior to 3 months**
    - **If mFOLFOX6 is chosen, patients should be treated for 6 months**
  - **T1-3 N1: no significant difference between 3 vs. 6 months**
    - **Duration needs to be balanced with toxicities and 3 months is possible**
- **Data for CAPOX are limited owing to small number of patients**

Taieb J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 473O

485PD: Randomized phase III study of adjuvant chemotherapy with S-1 versus capecitabine in patients with stage III colorectal cancer: Updated results of Japan Clinical Oncology Group study (JCOG0910) – Hamaguchi T, et al

Study objective

- To investigate whether adjuvant S-1 was superior to adjuvant capecitabine in terms of DFS in patients with stage III CRC

Key patient inclusion criteria

- Stage III CRC (except for lower rectal cancer [Rb])
- R0 with D2/3 lymph node dissection
- ECOG PS 0–1
- No prior CT/RT

(n=1,564)

R

Capecitabine* (n=782) → PD

Stratification

- Tumour location : Colon vs. rectum
- Lymph node metastasis : n<3 vs. 4<n
- Surgery: conventional vs. non-touch isolation
- Institution

S-1† (n=782) → PD

PRIMARY ENDPOINT

- DFS

SECONDARY ENDPOINTS

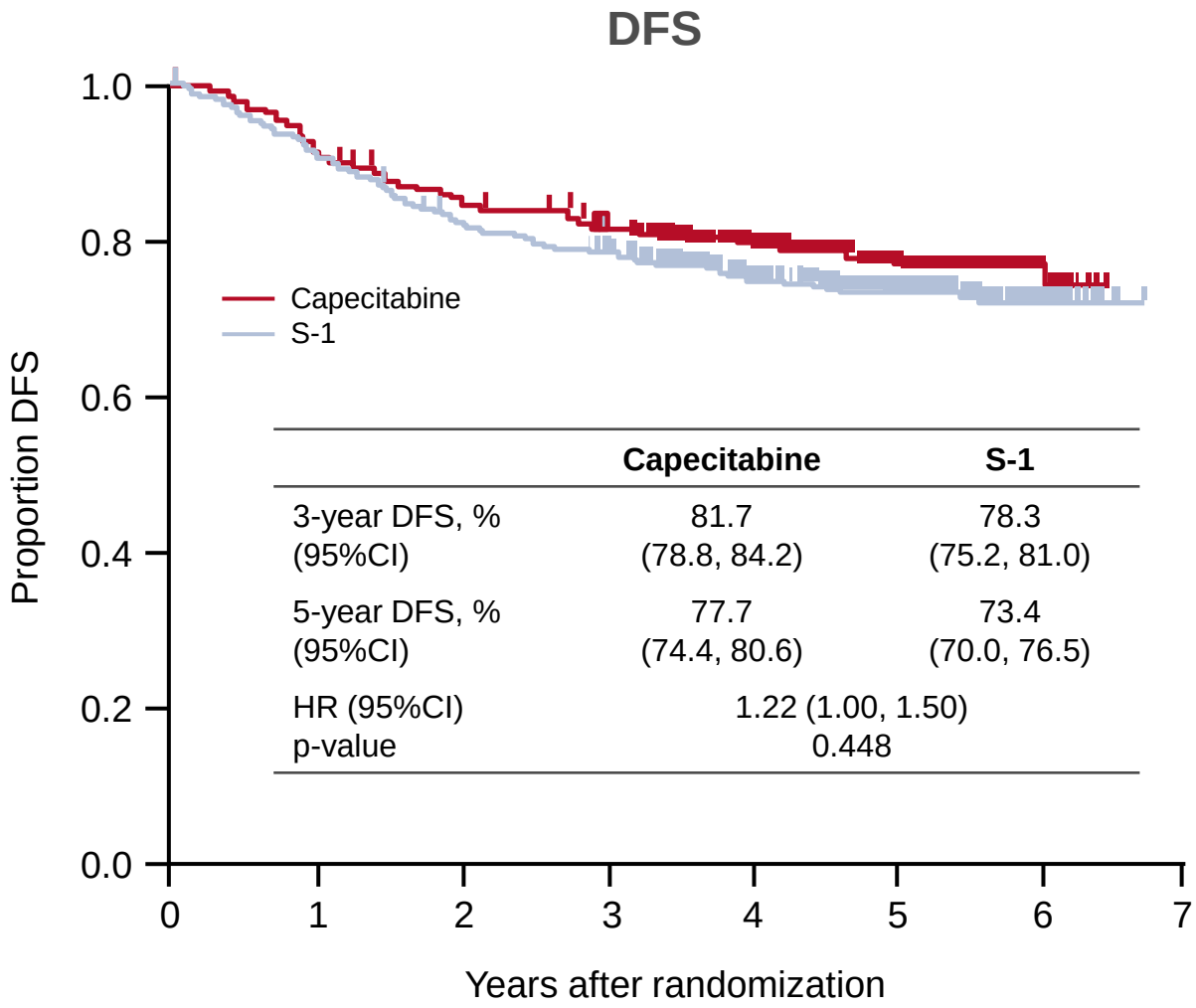
- OS, RFS, safety

*1,250 mg/m^2 bid D1–14, q3w;
†40 mg/m^2 bid D1–28, q6w

Hamaguchi T, et al. Ann Oncol 2017;28(Suppl 5):Abstr 485PD

485PD: Randomized phase III study of adjuvant chemotherapy with S-1 versus capecitabine in patients with stage III colorectal cancer: Updated results of Japan Clinical Oncology Group study (JCOG0910) – Hamaguchi T, et al

Key results



	Capecitabine	S-1
3-year DFS, % (95%CI)	81.7 (78.8, 84.2)	78.3 (75.2, 81.0)
5-year DFS, % (95%CI)	77.7 (74.4, 80.6)	73.4 (70.0, 76.5)
HR (95%CI) p-value	1.22 (1.00, 1.50) 0.448	

Hamaguchi T, et al. Ann Oncol 2017;28(Suppl 5):Abstr 485PD

485PD: Randomized phase III study of adjuvant chemotherapy with S-1 versus capecitabine in patients with stage III colorectal cancer: Updated results of Japan Clinical Oncology Group study (JCOG0910) – Hamaguchi T, et al

Key results (cont.)

	Capecitabine (n=782)	S1 (n=782)
3-year RFS, % (95%CI)	84.6 (81.9, 87.0)	81.5 (78.6, 84.1)
5-year RFS, % (95%CI)	81.9 (78.9, 84.6)	78.9 (75.8, 81.6)
HR (95%CI)	1.21 (0.96, 1.53)	
3-year OS, % (95%CI)	96.3 (94.7, 97.4)	95.4 (93.6, 96.6)
5-year OS, % (95%CI)	92.4 (90.0, 94.2)	90.9 (88.3, 92.9)
HR (95%CI)	1.18 (0.83, 1.68)	

Conclusions

- **S-1 was not demonstrated to be non-inferior to capecitabine in terms of DFS in patients with stage III CRC**
- **In patients with stage III colorectal cancer, adjuvant capecitabine remains the standard treatment while adjuvant S-1 should not be considered**

Hamaguchi T, et al. Ann Oncol 2017;28(Suppl 5):Abstr 485PD

480O: Prognostic value of methylator phenotype in stage III colon cancer treated with oxaliplatin-based adjuvant chemotherapy – Gallois C, et al

Study objective

- To evaluate the methylator phenotype (CIMP^{+}) in stage III colon cancer and its the prognostic and predictive value for the efficacy of cetuximab

Data source

- Data from 1,907 tumour DNA samples (FFPE) from patients included in the PETACC-8 trial

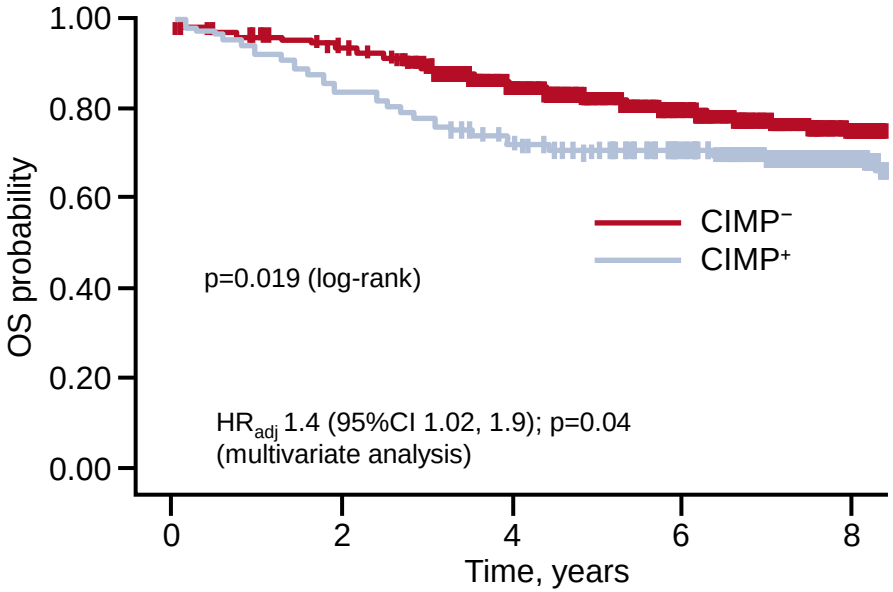
Analysis of DNA methylation

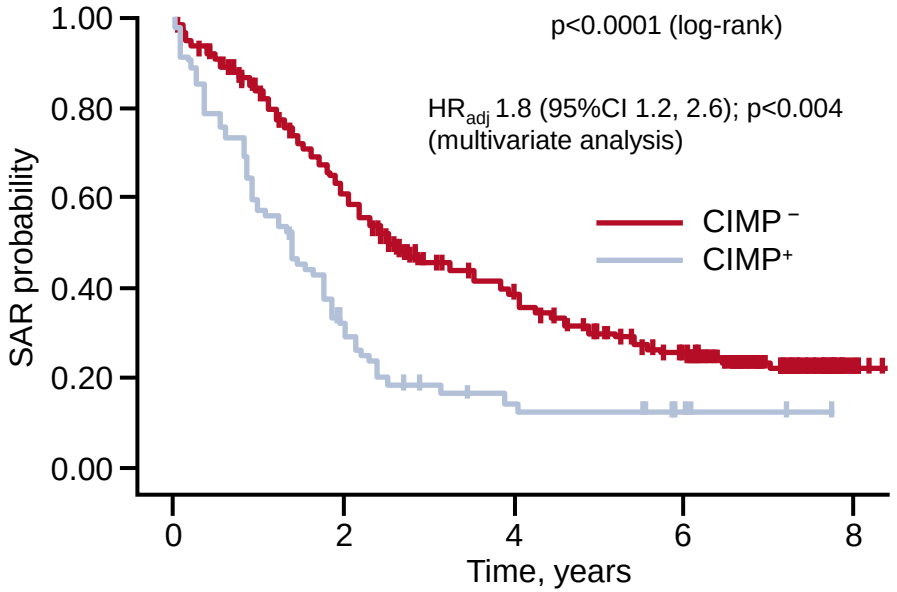
- Panel of 5 genes: *IGF2*, *CACNA1G*, *RUNX3*, *NEUROG1* and *SOCS1*
  - CIMP+ = methylation of ≥3 of 5 marker genes
- Step 1 – multiplex PCR for *IGF2/CACNA1G/NEUROG1*
- Step 2 (if 1/2 genes characterized in Step 1) – analysis of *RUNX3* and *SOCS1*

Gallois C, et al. Ann Oncol 2017;28(Suppl 5):Abstr 480O

480O: Prognostic value of methylator phenotype in stage III colon cancer treated with oxaliplatin-based adjuvant chemotherapy – Gallois C, et al

Key results





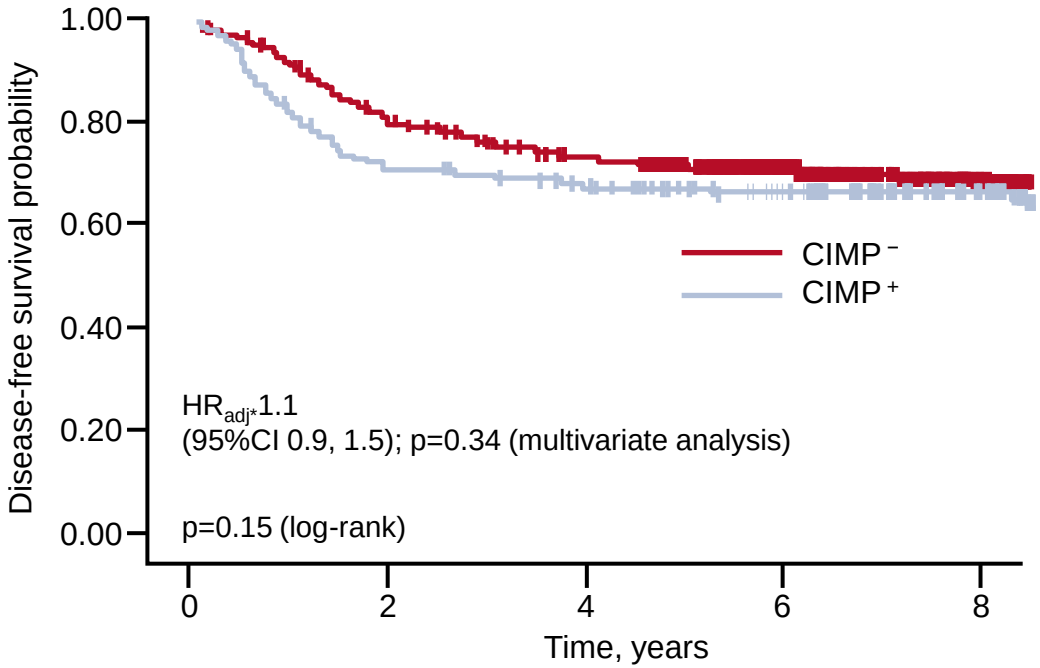
	CIMP⁻ vs. CIMP⁺	MSS tumours (n=1560)	MSI tumours (n=172)
OS	HR_{adj}	1.4	2.8
	95%CI	1.0, 2.0	0.9, 8.2
	p-value (multivariate)	0.049	0.06
	p-value (log-rank)	<0.0001	0.85
SAR	HR_{adj}	2	2.3
	95%CI	1.3, 2.9	0.5, 9.7
	p-value (multivariate)	<0.001	0.26
	p-value (log-rank)	<0.0001	0.91

SAR, survival after recurrence

Gallois C, et al. Ann Oncol 2017;28(Suppl 5):Abstr 480O

480O: Prognostic value of methylator phenotype in stage III colon cancer treated with oxaliplatin-based adjuvant chemotherapy – Gallois C, et al

Key results (cont.)



Conclusions

- **The method of methylation analysis is fast, easy to interpret, effective and reliable**
- **Methylator phenotype (CIMP $^{+}$) is associated with poor prognosis – this maybe a new prognostic biomarker for SAR and OS of stage III colon cancer**

Gallois C, et al. Ann Oncol 2017;28(Suppl 5):Abstr 480O

481PD: Sidedness influences prognosis in stage III but not in stage II colon cancer patients receiving an adjuvant therapy: A GISCAD analysis from three randomized trials including 5234 patients – Cascinu S, et al

Study objective

- To assess the prognostic effect of sidedness in patients with stage II/III colon cancer receiving adjuvant therapy, using data from three large RCTs*

Data from 3 RCTs* of patients with stage II/III colon cancer:

- 5FU vs. control (n=821)
- 5FU vs. systemic 5FU (n=990)
- FOLFOX vs. XELOX (n=3513)

(n=5324)

→

Data were analysed according to tumour sidedness†:

- Right
- Transverse
- Left

ENDPOINTS

- DFS, post-progression survival (PPS), OS (overall and in each trial)

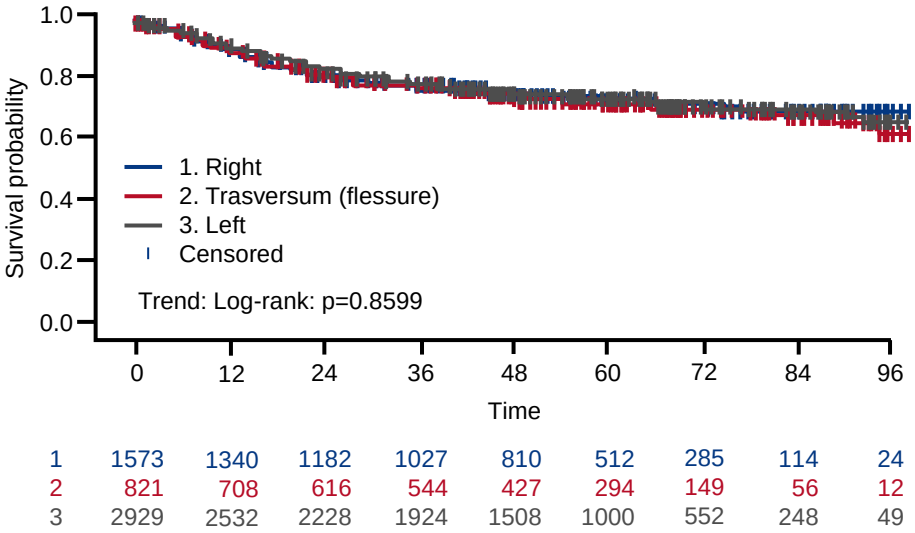
*SITAC-1, SMAC and TOSCA; †right-sided was considered caecum to hepatic flexure, left-sided splenic flexure to rectum and transverse hepatic to splenic flexure

Cascinu S, et al. Ann Oncol 2017;28(Suppl 5):Abstr 481PD

481PD: Sidedness influences prognosis in stage III but not in stage II colon cancer patients receiving an adjuvant therapy: A GISCAD analysis from three randomized trials including 5234 patients – Cascinu S, et al

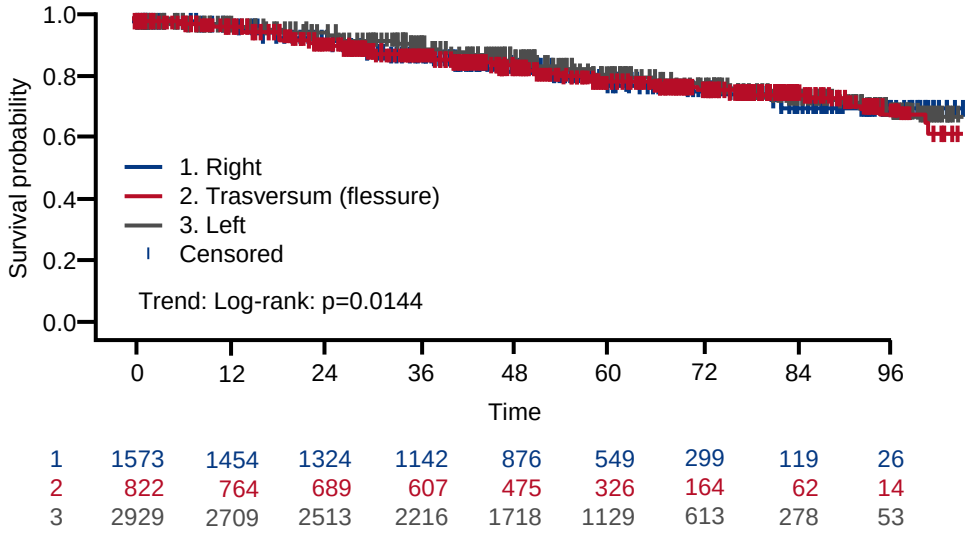
Key results

DFS by site



1	1573	1340	1182	1027	810	512	285	114	24
2	821	708	616	544	427	294	149	56	12
3	2929	2532	2228	1924	1508	1000	552	248	49

OS by site

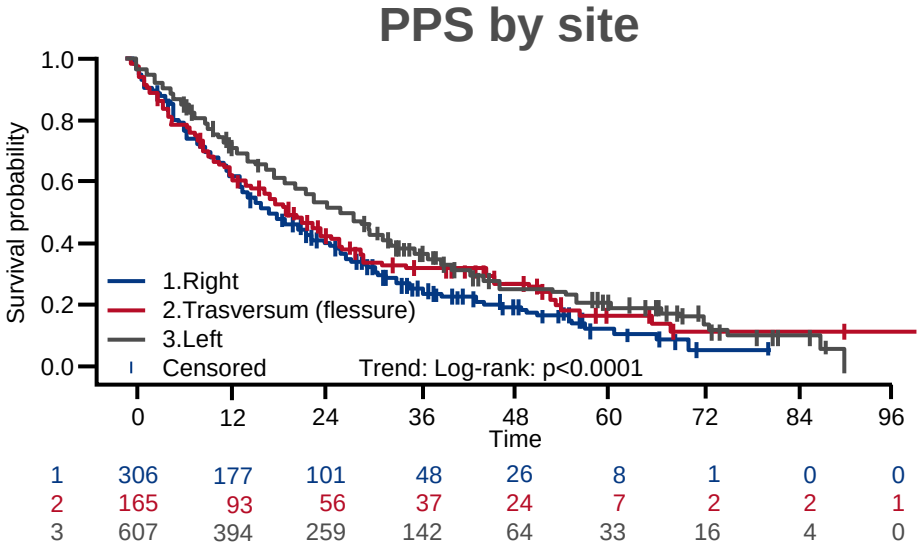


1	1573	1454	1324	1142	876	549	299	119	26
2	822	764	689	607	475	326	164	62	14
3	2929	2709	2513	2216	1718	1129	613	278	53

Cascinu S, et al. Ann Oncol 2017;28(Suppl 5):Abstr 481PD

481PD: Sidedness influences prognosis in stage III but not in stage II colon cancer patients receiving an adjuvant therapy: A GISCAD analysis from three randomized trials including 5234 patients – Cascinu S, et al

Key results (cont.)



	DFS	PPS	OS
All	L=R	L>R*	L>R*
Stage III	L>R*	L>R*	L>R*
Stage II	L<R*	L≥R†	L=R

Conclusions

- In patients with stage II/III colon cancer, greater improvements in PPS and OS were seen in left vs. right tumours
  - This may be due to the fact that left tumours have fewer KRAS/BRAF mutations, enabling more treatments with anti-EGFR agents
- Transverse primary tumours showed a prognosis halfway between right and left primary tumours, but appeared clinically more similar to right than left tumours

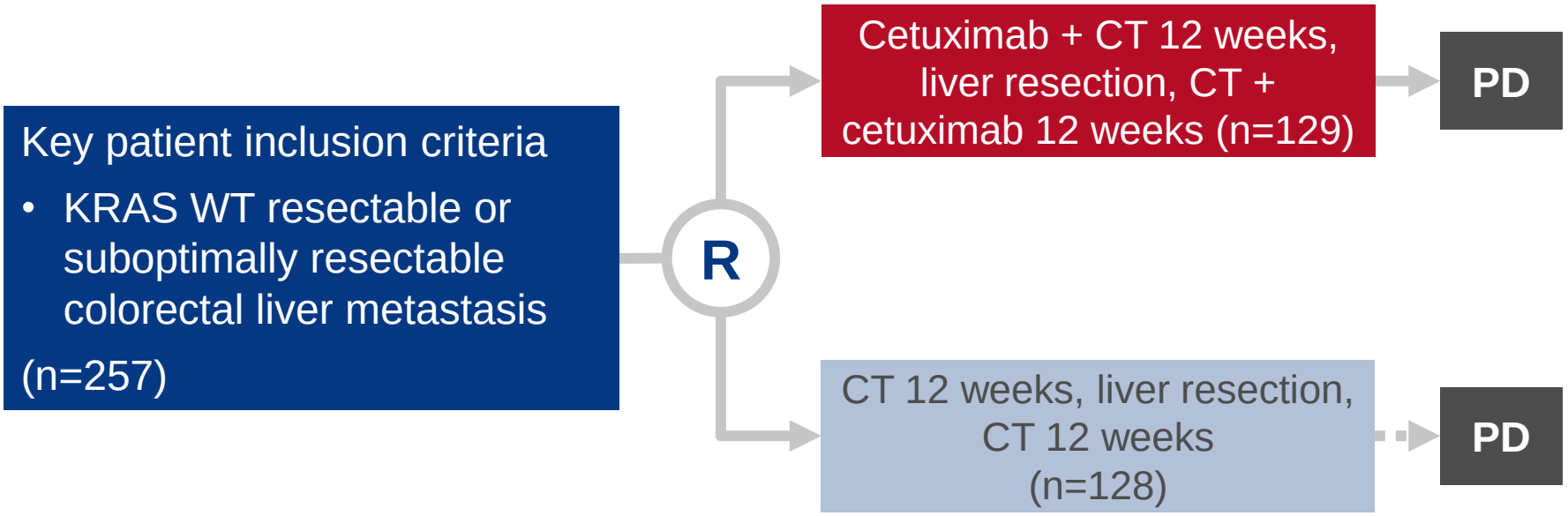
*Statistically significant; †Trend towards an advantage

Cascinu S, et al. Ann Oncol 2017;28(Suppl 5):Abstr 481PD

483PD: Perioperative chemotherapy with or without cetuximab in patients (pts) with resectable colorectal liver metastasis (CRLM): Mature analysis of overall survival (OS) in the New EPOC randomised controlled trial – Bridgewater J, et al

Study objective

- To compare survival with perioperative CT + cetuximab vs. perioperative CT alone in patients with resectable colorectal liver metastasis



PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

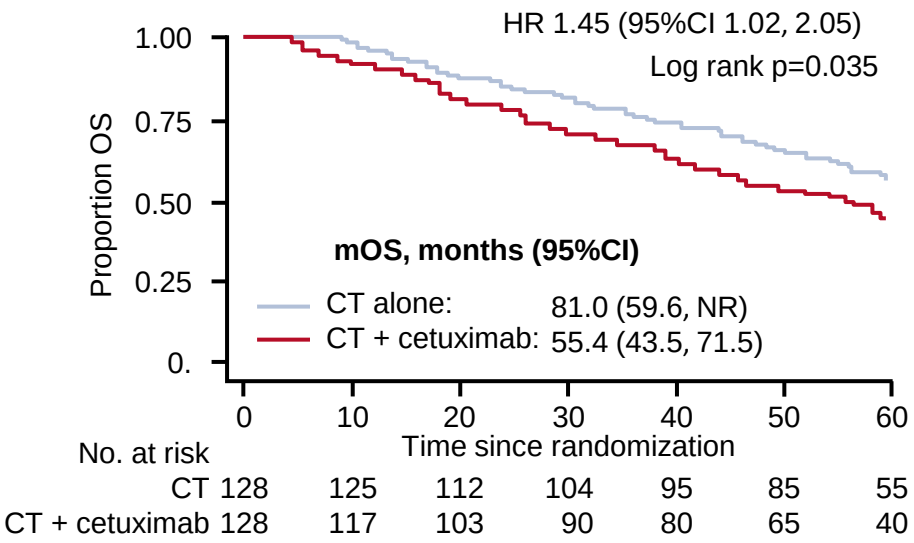
- OS, toxicity

Bridgewater J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 483PD

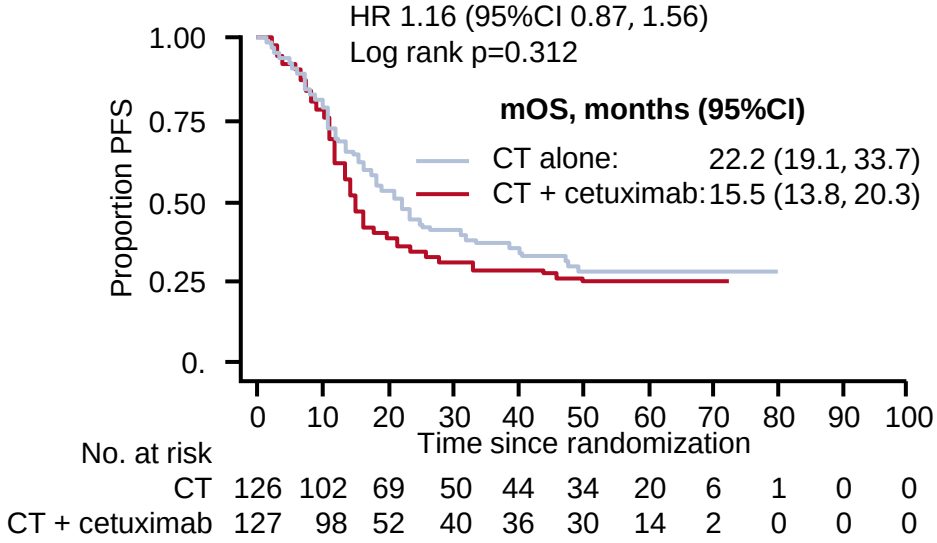
483PD: Perioperative chemotherapy with or without cetuximab in patients (pts) with resectable colorectal liver metastasis (CRLM): Mature analysis of overall survival (OS) in the New EPOC randomised controlled trial – Bridgewater J, et al

Key results

OS



PFS



Post-progression survival	CT + cetuximab	CT alone
Median, months (95%CI)	23.5 (15.9, 22.1)	35.4 (25.0, 44.8)
HR (95%CI); p-value	1.60 (1.10, 2.33); 0.014	

Bridgewater J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 483PD

483PD: Perioperative chemotherapy with or without cetuximab in patients (pts) with resectable colorectal liver metastasis (CRLM): Mature analysis of overall survival (OS) in the New EPOC randomised controlled trial – Bridgewater J, et al

Key results (cont.)

OS, months (95%CI)	CT + cetuximab	CT alone
OS by presence of prognostic markers*		
No	45.8 (28.2, 71.5)	NR (78.9, NR)
Yes	58.3 (45.0, NR)	59.2 (44.4, NR)
OS by preoperative response		
CR/PR	60.7 (48.0, NR)	81.1 (65.7, NR)
SD/PD	34.5 (19.4, 58.2)	79.9 (50.2, NR)

Conclusions

- **In patients with resectable colorectal liver metastasis, OS and PFS was shorter with perioperative CT + cetuximab vs. perioperative CT alone**
- **These improvements were primarily in those patients with conventionally favourable prognostic features**
- **OS was not improved in patients responding to CT by RECIST vs. non-responders, suggesting that any benefit of systemic treatment was through elimination of micro-metastatic disease rather than by downsizing of radiologically evaluable disease**

*≥4 metastases, N2 primary tumour, poorly differentiated primary tumour

Bridgewater J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 483PD

LBA26: FOXFIRE-SIRFLOX-FOXFIRE Global prospective randomised studies of first-line selective internal radiotherapy (SIRT) in patients with liver metastases from colorectal cancer: RAS mutation and tumour site analysis – Wasan H, et al

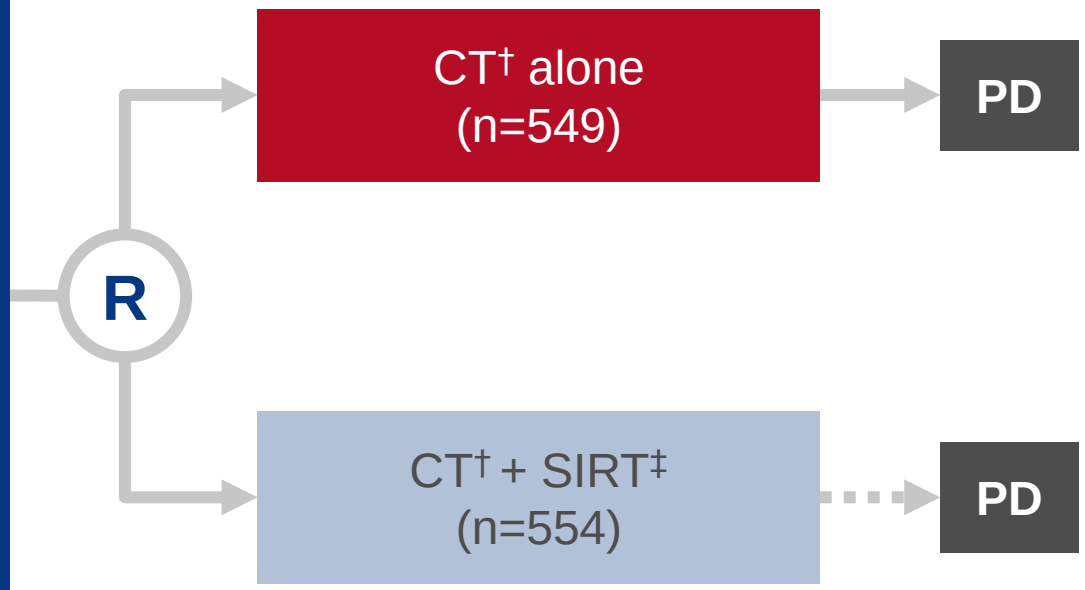
Study objective

- To evaluate the impact of KRAS mutation status and primary tumour site on OS in patients with CRLM receiving 1L CT ± SIRT, utilising data from three RCTs*

Key patient inclusion criteria

- mCRC with liver metastases; not resectable or ablatable
- Eligible for 1L systemic CT
- WHO PS 0–1
- Permitted to have primary tumours in situ and/or limited extrahepatic metastases

(n=1103)



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

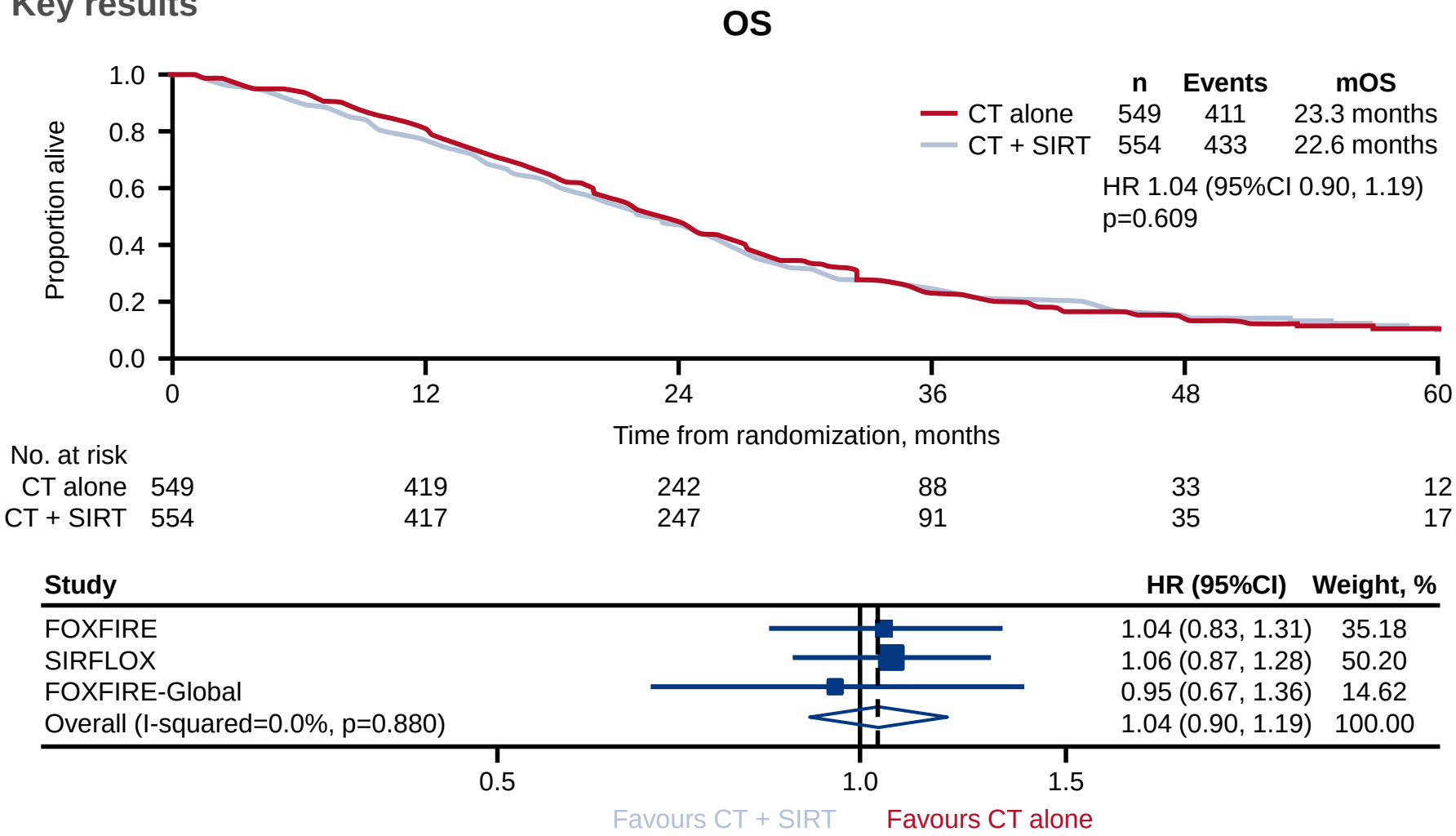
- ORR, PFS, liver-PFS, safety

*FOXFIRE, SIRFLOX and FOXFIRE-Global; †mFOLFOX6 or OxMdG ± bevacizumab or cetuximab at the investigators' discretion; ‡Single SIRT treatment with CT in cycle 1 or 2

Wasan H, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA26

LBA26: FOXFIRE-SIRFLOX-FOXFIRE Global prospective randomised studies of first-line selective internal radiotherapy (SIRT) in patients with liver metastases from colorectal cancer: RAS mutation and tumour site analysis – Wasan H, et al

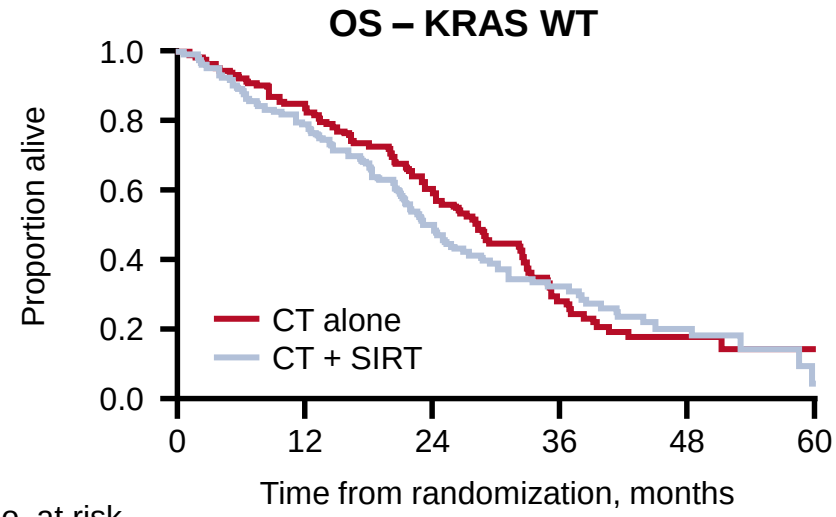
Key results

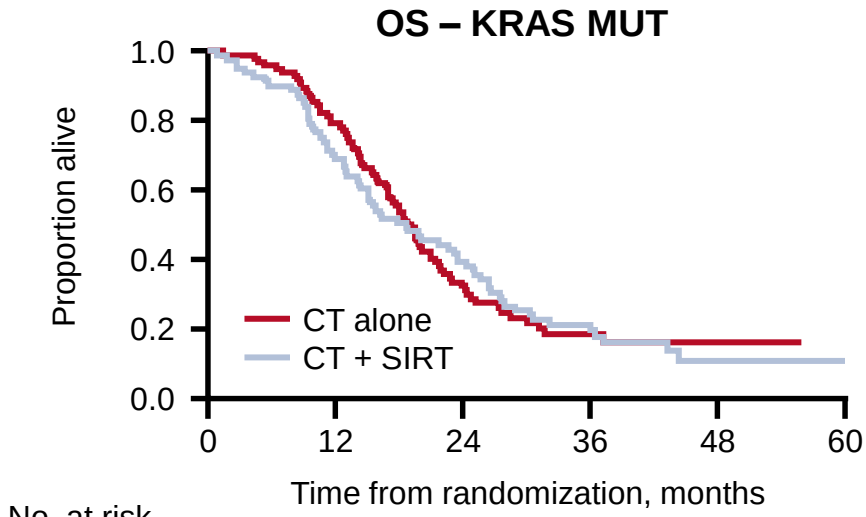


Wasan H, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA26

LBA26: FOXFIRE-SIRFLOX-FOXFIRE Global prospective randomised studies of first-line selective internal radiotherapy (SIRT) in patients with liver metastases from colorectal cancer: RAS mutation and tumour site analysis – Wasan H, et al

Key results (cont.)





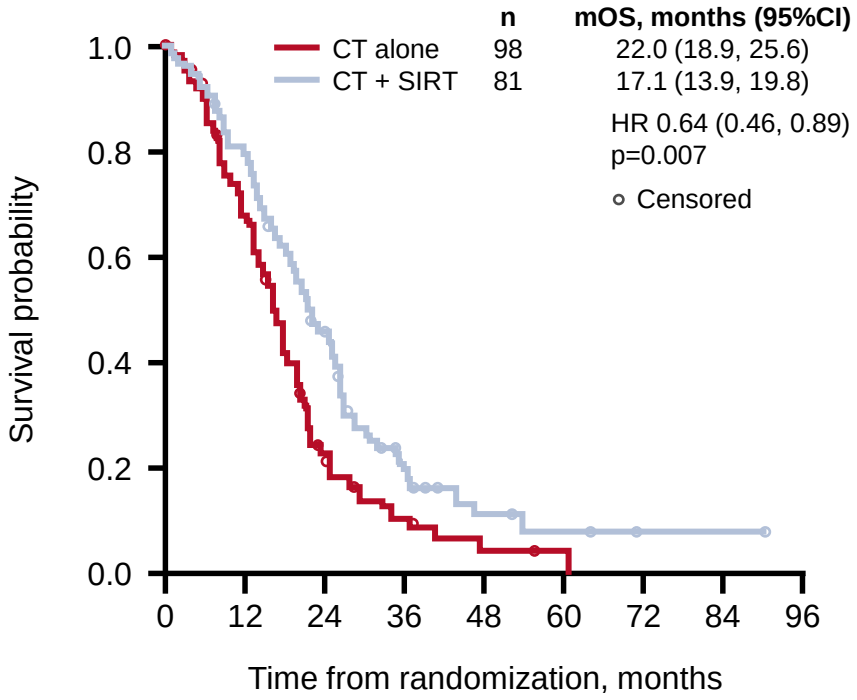
	KRAS WT		KRAS MUT		KRAS status unknown	
	CT (n=142)	CT + SIRT (n=137)	CT (n=100)	CT + SIRT (n=82)	CT (n=307)	CT + SIRT (n=335)
mOS (95%CI)	28.3 (24.3, 32.5)	24.2 (21.0, 27.5)	19.1 (16.9, 21.3)	18.7 (14.4, 23.4)	23.1 (21.0, 25.0)	22.6 (20.2, 25.1)

Wasan H, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA26

LBA26: FOXFIRE-SIRFLOX-FOXFIRE Global prospective randomised studies of first-line selective internal radiotherapy (SIRT) in patients with liver metastases from colorectal cancer: RAS mutation and tumour site analysis – Wasan H, et al

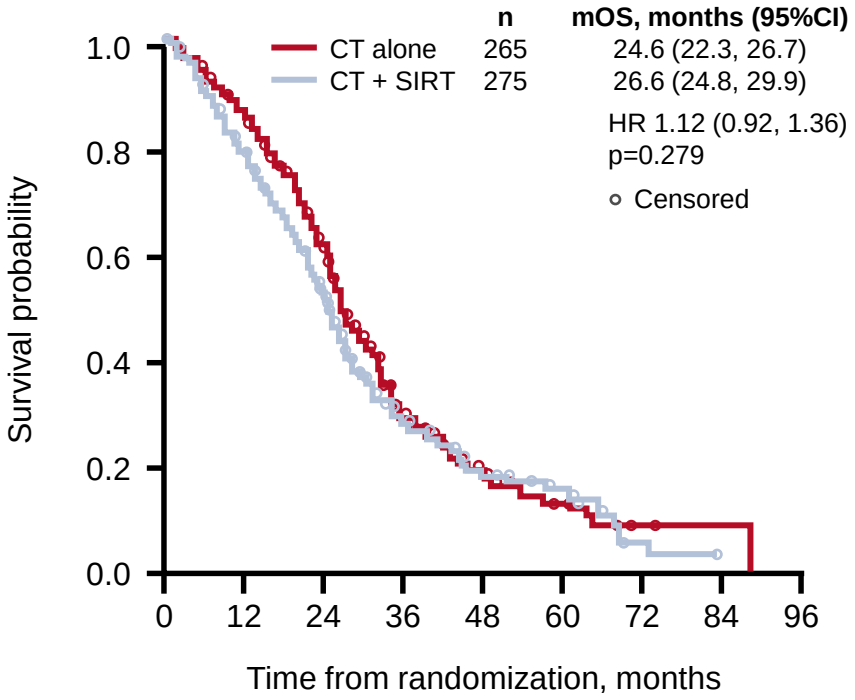
Key results (cont.)

OS* – Right-sided primary tumours



No. at risk									
CT alone	80	50	15	6	2	1	0		
CT + SIRT	98	78	43	14	5	3	1	1	0

OS* – left-sided primary tumours



No. at risk									
CT alone	275	222	150	54	22	7	2	1	0
CT + SIRT	265	199	130	47	20	12	2	0	

*Based on data from the SIRFLOX and FOXFIRE-Global studies only

Wasan H, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA26

LBA26: FOXFIRE-SIRFLOX-FOXFIRE Global prospective randomised studies of first-line selective internal radiotherapy (SIRT) in patients with liver metastases from colorectal cancer: RAS mutation and tumour site analysis – Wasan H, et al

Key results (cont.)

Grade ≥3 AEs, %	CT	CT + SIRT	p-value
Any	66.5	74.0	0.009
Haematological	28.9	45.6	-
Neutropenia	24.2	36.7	-

Conclusions

- The addition of SIRT to 1L CT did not improve OS for patients with CRLM vs. CT alone, regardless of KRAS status
- However, significantly higher tumour response rates were achieved with SIRT
- The addition of SIRT to 1L CT was associated with a significant improvements in OS vs. CT alone for patients with right-sided but not left-sided primary tumours
  - These data suggest that the primary tumour site but not KRAS status may predict for potential treatment interaction with SIRT
  - This analysis may support a side-based approach to patient selection for SIRT

Wasan H, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA26

367PD: Early FDG-PET response correlates with dose and clinical efficacy in patients with microsatellite stable (MSS) metastatic CRC (mCRC) treated with the CEA-CD3 T-cell bispecific antibody plus atezolizumab – Sandoval F, et al

Study objective

- To investigate early pharmacodynamic responses with CEA-TCB* in combination with atezolizumab using FDG-PET imaging, in patients with MSS mCRC

Key patient inclusion criteria

- mCRC with CEA^{+} solid tumours
- ≥1 tumour lesion able to be biopsied
- PD or intolerant of standard CT
- ECOG PS 0–1

(n=25)

→ CEA-TCB 5–300 mg IV qw + atezolizumab 1200 mg q3w → **PD**

PRIMARY ENDPOINTS

- Safety/tolerability

SECONDARY ENDPOINTS

- Anti-tumour activity, ORR, DoR, DCR, PFS, pharmacodynamics

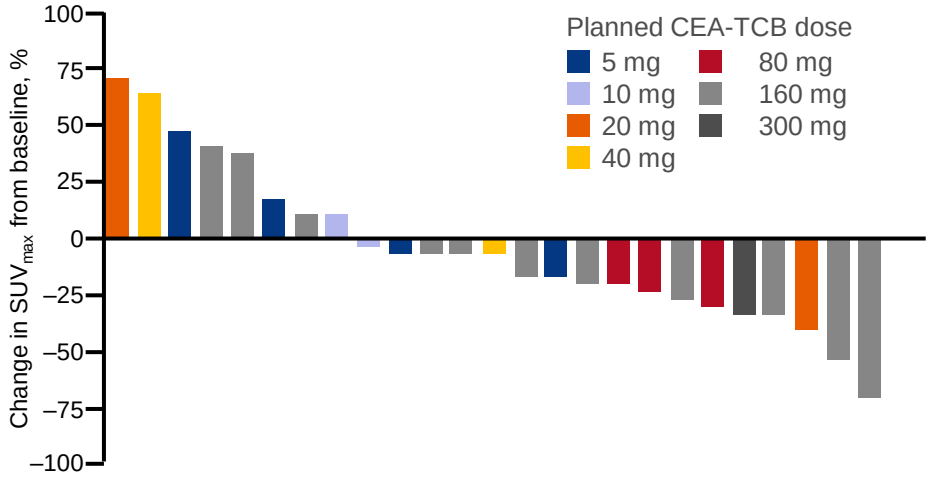
*A novel T-cell bispecific antibody targeting CEA on tumour cells and CD3 on T cells

Sandoval F, et al. Ann Oncol 2017;28(Suppl 5):Abstr 367PD

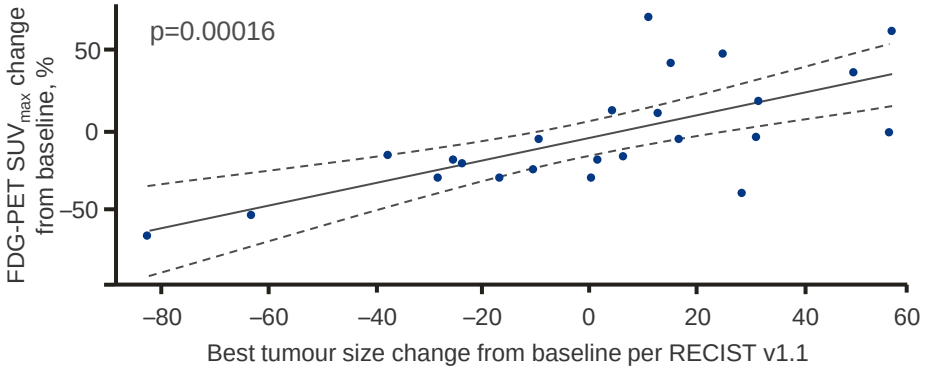
367PD: Early FDG-PET response correlates with dose and clinical efficacy in patients with microsatellite stable (MSS) metastatic CRC (mCRC) treated with the CEA-CD3 T-cell bispecific antibody plus atezolizumab – Sandoval F, et al

Key results

Change from baseline in FDG-PET SUV_{max} by CEA-TCB dose



Correlation between change in FDG-PET SUV_{max} and best tumour size change from baseline

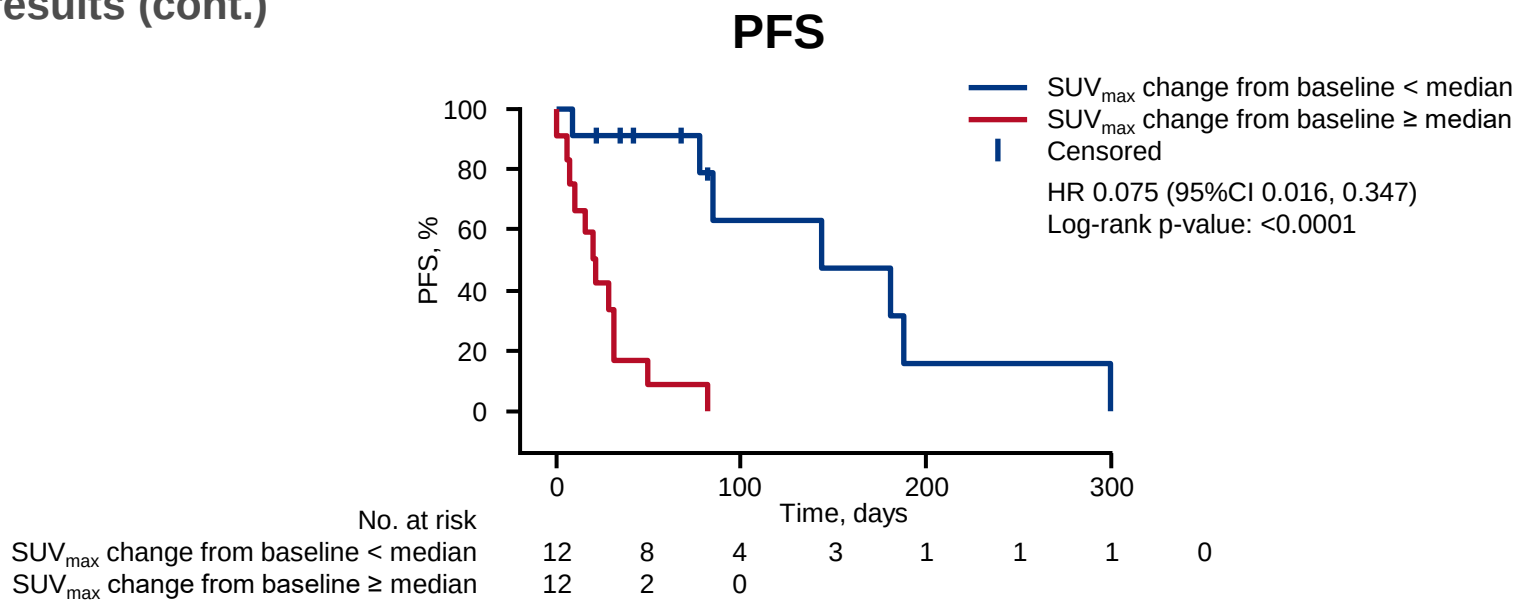


FDG-PET response	All patients (n=25)	Patients treated <80 mg qw CEA-TCB (n=10)	Patients treated ≥80 mg qw CEA-TCB (n=15)
PD	15	9	6
PR	9	1	8
SD	1	-	1

Sandoval F, et al. Ann Oncol 2017;28(Suppl 5):Abstr 367PD

367PD: Early FDG-PET response correlates with dose and clinical efficacy in patients with microsatellite stable (MSS) metastatic CRC (mCRC) treated with the CEA-CD3 T-cell bispecific antibody plus atezolizumab – Sandoval F, et al

Key results (cont.)



Conclusions

- In patients with MSS mCRC, SUV_{max} reductions after CEA-TCB + atezolizumab treatment correlated with higher doses of CEA-TCB
- Reduction in SUV_{max} appeared to correlate with improved tumour shrinkage + PFS
- Early on-treatment changes in FDG-PET may serve as a pharmacodynamic biomarker related to treatment efficacy and could potentially guide dose selection

Sandoval F, et al. Ann Oncol 2017;28(Suppl 5):Abstr 367PD

475O: mFOLFOXIRI + panitumumab versus FOLFOXIRI as first-line treatment in patients with RAS wild-type metastatic colorectal cancer m(CRC): A randomized phase II VOLFI trial of the AIO (AIO-KRK0109) – Geissler M, et al

Study objective

- To compare the efficacy and safety of 1L treatment with mFOLFOXIRI + panitumumab vs. FOLFOXIRI in patients with RAS WT mCRC

Key patient inclusion criteria

- Unresectable mCRC; 1L
- WT RAS
- ECOG PS 0–1

(n=96)

R 2:1

mFOLFOXIRI* q2w + panitumumab† (n=63) → PD

FOLFOXIRI‡ q2w (n=33) → PD

Stratification

- **Cohort 1**: inoperable or unresectable
- **Cohort 2**: chance of secondary resection

PRIMARY ENDPOINT

- ORR

SECONDARY ENDPOINTS

- Secondary resection rate, time to relapse, PFS, OS; pathological response, toxicity, QoL

*IRI 150 mg/m^2, oxaliplatin 85 mg/m^2 + LV 200 mg/m^2 + 5FU 3000 mg/m^2 CIV; †6 mg/kg q2w; ‡oxaliplatin 85 mg/m^2 + IRI 165 mg/m^2, 5FU 3200mg/m^2 cont. 48 h, LV 200 mg/m^2

Geissler M, et al. Ann Oncol 2017;28(Suppl 5):Abstr 475O

475O: mFOLFOXIRI + panitumumab versus FOLFOXIRI as first-line treatment in patients with RAS wild-type metastatic colorectal cancer m(CRC): A randomized phase II VOLFI trial of the AIO (AIO-KRK0109) – Geissler M, et al

Key results

	mFOLFOXIRI + panitumumab	FOLFOXIRI
ORR, % (95%CI)	85.7 (74.6, 93.3)	60.6 (42.1, 77.1)
OR (95%CI); p-value	3.90 (1.44, 10.52); 0.0096	
ORR left-sided, %	90.6	68.0
OR (95%CI); p-value	4.518 (1.29, 15.71); 0.0210	
ORR right-sided	60.0	37.5
OR (95%CI); p-value	2.500 (0.37, 16.88); 0.6372	
ORR super WT*, %	86.0	64.7
OR (95%CI); p-value	3.364 (0.90, 12.54); 0.0806	
ORR BRAF mutation, %	71.4	22.2
OR (95%CI); p-value	8.750 (0.9, 84.80) 0.1262	
mPFS, months (95%CI)	10.5 (8.7, 12.5)	10.8 (8.7, 11.5)
HR (95%CI); p-value	1.107 (0.69, 1.75); 0.6634	

*RAS + all BRAF

Geissler M, et al. Ann Oncol 2017;28(Suppl 5):Abstr 475O

475O: mFOLFOXIRI + panitumumab versus FOLFOXIRI as first-line treatment in patients with RAS wild-type metastatic colorectal cancer m(CRC): A randomized phase II VOLFI trial of the AIO (AIO-KRK0109) – Geissler M, et al

Key results (cont.)

SAEs of interest, n (%)	mFOLFOXIRI + panitumumab	FOLFOXIRI	p-value
≥1 treatment-related SAE	26 (40.6)	6 (18.2)	0.0393
≥1 treatment-related SAE grade 3–5	21 (32.8)	4 (12.1)	0.0297
Haematological grade 3–5	1 (1.6)	2 (6.1)	0.2662
GI grade 3–5	16 (25)	1 (3)	0.0093

Conclusions

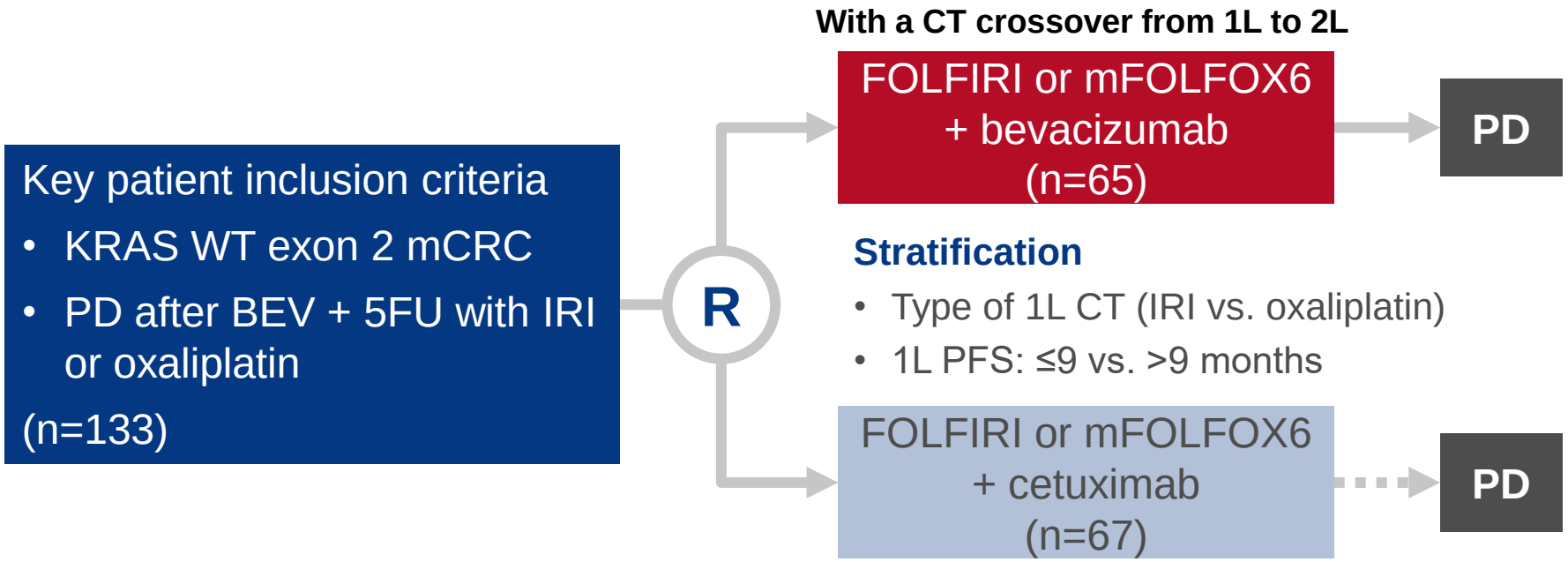
- **In patients with RAS WT mCRC, compared with FOLFOXIRI, 1L treatment with mFOLFOXIRI + panitumumab achieved significantly higher ORR**
- **High response rates were observed in left/right sided and BRAF-mutated mCRC for mFOLFOXIRI + panitumumab**
- **There was no difference in PFS between treatment groups**
- **mFOLFOXIRI + panitumumab had relevant haematological and GI toxicity that were manageable and it is recommended for patients with ECOG PS 0–1 only**

Geissler M, et al. Ann Oncol 2017;28(Suppl 5):Abstr 475O

477O: Bevacizumab (Bev) or cetuximab (Cet) plus chemotherapy after progression with bevacizumab plus chemotherapy in patients with wild-type (WT) KRAS metastatic colorectal cancer (mCRC): Final analysis of a French randomized, multicenter, phase II study (PRODIGE 18) – Bennouna J, et al

Study objective

- To evaluate PFS at 4 months with bevacizumab + CT vs. cetuximab + CT after PD with BEV + 5FU in patients with KRAS WT mCRC



PRIMARY ENDPOINT(S)

- 4-month PFS rate

SECONDARY ENDPOINTS

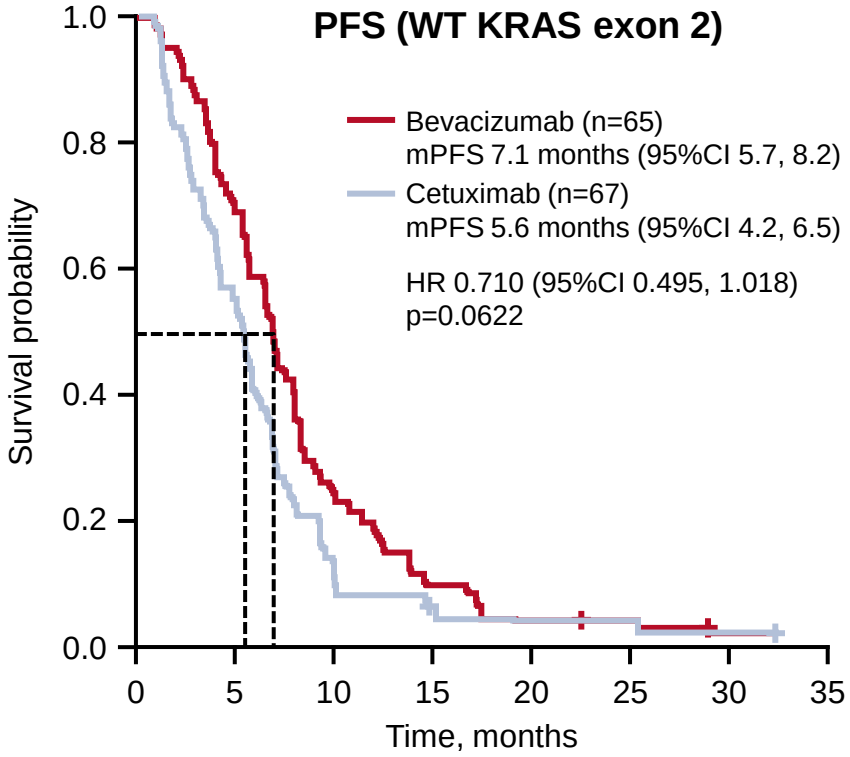
- ORR, OS, PFS, OS from start of 1L therapy, safety, QoL

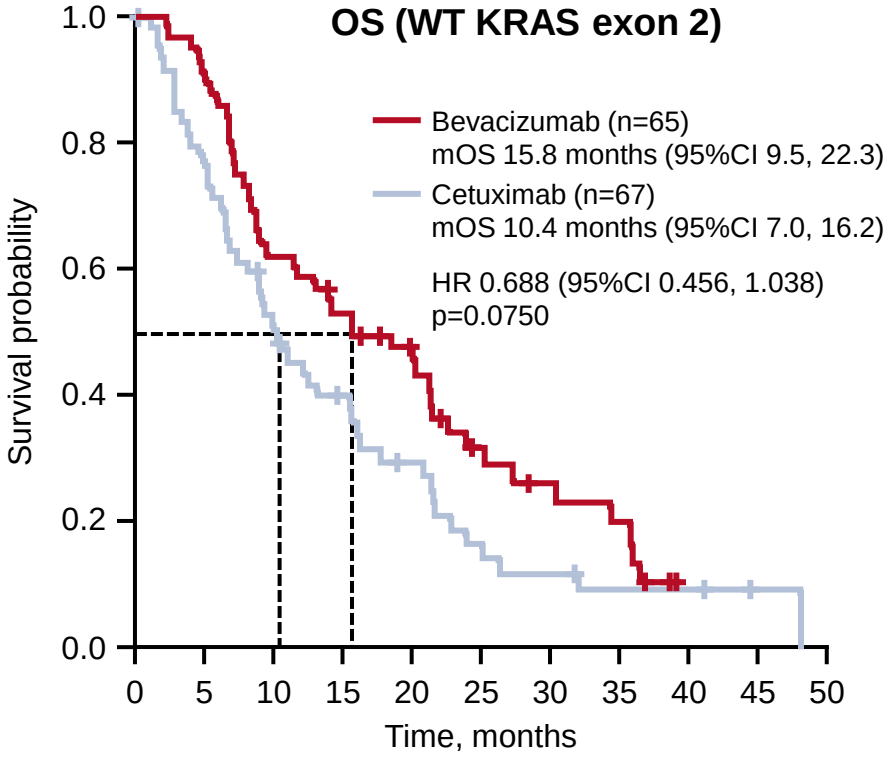
Bennouna J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 477O

477O: Bevacizumab (Bev) or cetuximab (Cet) plus chemotherapy after progression with bevacizumab plus chemotherapy in patients with wild-type (WT) KRAS metastatic colorectal cancer (mCRC): Final analysis of a French randomized, multicenter, phase II study (PRODIGE 18) – Bennouna J, et al

Key results

4-month PFS rate, % (95%CI)	Bevacizumab + CT	Cetuximab + CT
WT KRAS exon 2	80.3 (68.0, 88.3)	66.6 (53.6, 76.8)
WT KRAS + NRAS exon 2,3,4	88.8 (71.2, 94.3)	65.7 (48.5, 78.5)
WT KRAS + NRAS exon 2,3,4 + WT BRAF	90.9 (74.4, 97.0)	68.6 (50.5, 81.2)





Bennouna J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 477O

477O: Bevacizumab (Bev) or cetuximab (Cet) plus chemotherapy after progression with bevacizumab plus chemotherapy in patients with wild-type (WT) KRAS metastatic colorectal cancer (mCRC): Final analysis of a French randomized, multicenter, phase II study (PRODIGE 18) – Bennouna J, et al

Key results (cont.)

AEs in ≤60% of patients, %	Bevacizumab + CT		Cetuximab + CT	
	Any grade	Grade 3–4	Any grade	Grade 3–4
Anaemia	66.1	4.6	68.6	13.4
Neutropenia	61.5	18.4	52.2	14.9
Thrombocytopenia	61.5	18.4	52.2	14.9
Fatigue	83.1	10.8	74.6	10.4
Diarrhoea	64.6	7.7	37.3	8.9
Skin disorders	38.4	-	85.1	19.4

Conclusions

- PRODIGE 18 demonstrated efficacy data that was in line with that seen in subgroup analysis of the FIRE-3, SPIRITT and COMETS studies
- Results from these studies indicate that anti-EGFR antibodies only exhibit a modest activity in 2L after bevacizumab
- Data from the FIRE-3 study suggest that an anti-EGFR antibody + CT could be the first choice of treatment followed at progression with bevacizumab + a CT switch
- There is now a growing body of evidence that anti-EGFR antibodies, panitumumab or cetuximab, should be considered in 3L after bevacizumab beyond the first progression according to the TML strategy, if bevacizumab is used in 1L

Bennouna J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 477O

484PD: Analysis of tumor PD-L1 expression and biomarkers in relation to clinical activity in patients (pts) with deficient DNA mismatch repair (dMMR)/high microsatellite instability (MSI-H) metastatic colorectal cancer (mCRC) treated with nivolumab (NIVO) + ipilimumab (IPI): CheckMate 142 – André T, et al

Study objective

- To evaluate PD-L1 expression and biomarkers in patients with dMMR/MSI-H mCRC receiving nivolumab + ipilimumab

Key patient inclusion criteria

- Histologically confirmed metastatic/recurrent CRC
- dMMR/MSI-H
- ≥1 prior line of therapy

(n=158)

→ *Nivolumab 3 mg/kg + ipilimumab 1 mg/kg (n=84) → PD

PRIMARY ENDPOINT

- ORR (investigator assessment)

SECONDARY ENDPOINTS

- ORR (blinded independent central review), PFS, OS, safety

*Nivolumab + ipilimumab q3w ×4 doses followed by nivolumab q2w

André T, et al. Ann Oncol 2017;28(Suppl 5):Abstr 848PD

484PD: Analysis of tumor PD-L1 expression and biomarkers in relation to clinical activity in patients (pts) with deficient DNA mismatch repair (dMMR)/high microsatellite instability (MSI-H) metastatic colorectal cancer (mCRC) treated with nivolumab (NIVO) + ipilimumab (IPI): CheckMate 142 – André T, et al

Key results

	Nivolumab + ipilimumab (n=84)	
Patients, n (%) [95%CI]	**ORR**	**DCR**
Tumour PD-L1 expression		
≥1% (n=16)	9 (56) [29.9, 80.3]	12 (75) [47.6, 92.7]
<1% (n=50)	27 (54) [39.3, 68.2]	39 (78) [64.0, 88.5]
Unknown (n=18)	10 (56) [30.8, 78.5]	15 (83) [58.6, 96.4]
Mutation status		
BRAF mutant (n=21)	10 (48) [25.7, 70.2]	16 (76) [52.8, 91.8]
KRAS mutant (n=30)	19 (63) [43.9, 80.1]	26 (87) [69.3, 96.3]
BRAF/KRAS WT (n=22)	13 (59) [36.4, 79.3]	17 (77) [54.6, 92.2]
Unknown (n=11)	4 (36) [10.9, 69.2]	7 (64) [30.8, 89.1]
Clinical history of Lynch syndrome		
Yes (n=27)	20 (74) [53.7, 88.9]	22 (81) [61.9, 93.7]
No (n=25)	12 (48) [27.8, 68.7]	19 (76) [54.9, 90.6]
Unknown (n=32)	14 (44) [26.4, 62.3]	25 (78) [60.0, 90.7]

André T, et al. Ann Oncol 2017;28(Suppl 5):Abstr 848PD

484PD: Analysis of tumor PD-L1 expression and biomarkers in relation to clinical activity in patients (pts) with deficient DNA mismatch repair (dMMR)/high microsatellite instability (MSI-H) metastatic colorectal cancer (mCRC) treated with nivolumab (NIVO) + ipilimumab (IPI): CheckMate 142 – André T, et al

Key results (cont.)

TRAEs reported in ≥15% of patients, n (%)	Nivolumab + ipilimumab (n=84)	
	Any Grade	Grade 3–4
Diarrhoea	20 (24)	1 (1)
Fatigue	14 (17)	1 (1)
ALT increase	14 (17)	8 (10)
Pyrexia	13 (15)	0
Pruritus	13 (15)	2 (2)

Conclusions

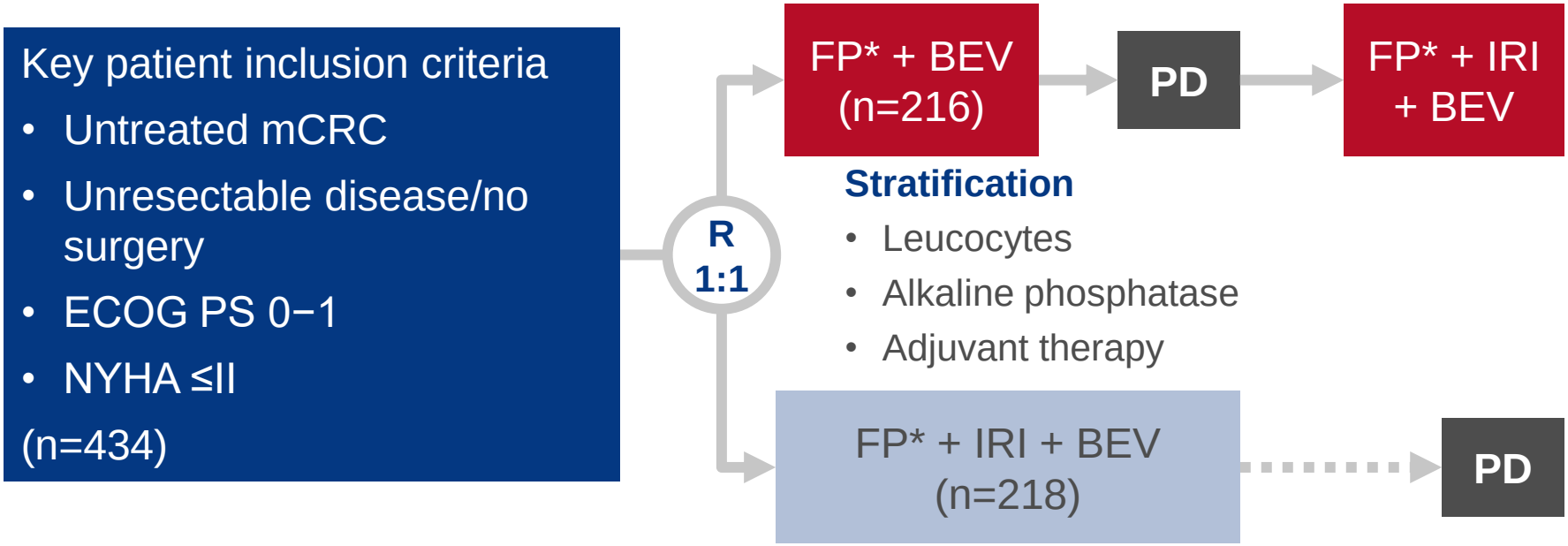
- **In patients with dMMR/MSI-H mCRC, nivolumab + ipilimumab demonstrated clinical responses across all biomarker groups assessed and were regardless of PD-L1 tumour expression, BRAF or KRAS mutations or a clinical history of Lynch syndrome**
- **The safety profile of nivolumab + ipilimumab was manageable**
- **These results support the use of dMMR/MSI-H status to identify patients who may respond to nivolumab-based therapy**

André T, et al. Ann Oncol 2017;28(Suppl 5):Abstr 848PD

486O:Sequential first-line therapy of metastatic colorectal cancer (mCRC) starting with fluoropyrimidine (FP) plus bevacizumab (BEV) vs. initial FP plus irinotecan (IRI) and BEV: German AIO KRK0110 (ML22011)- study – Modest DP, et al

Study objective

- To assess the efficacy and safety of initial FP + BEV vs. FP + IRI + BEV in mCRC



PRIMARY ENDPOINT(S)

- TFS

SECONDARY ENDPOINTS

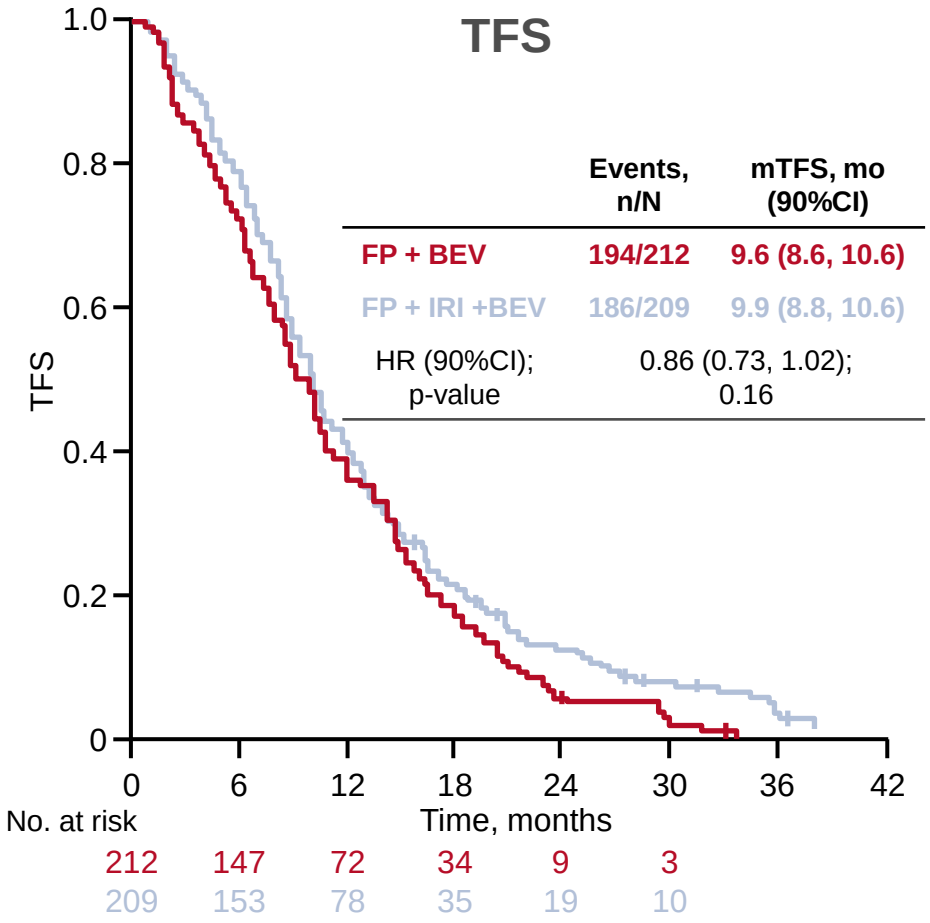
- ORR, PFS-1, OS, efficacy in molecular subgroups, QoL, safety

*Restricted to capecitabine from 2010–2013, investigators choice 2013–2016

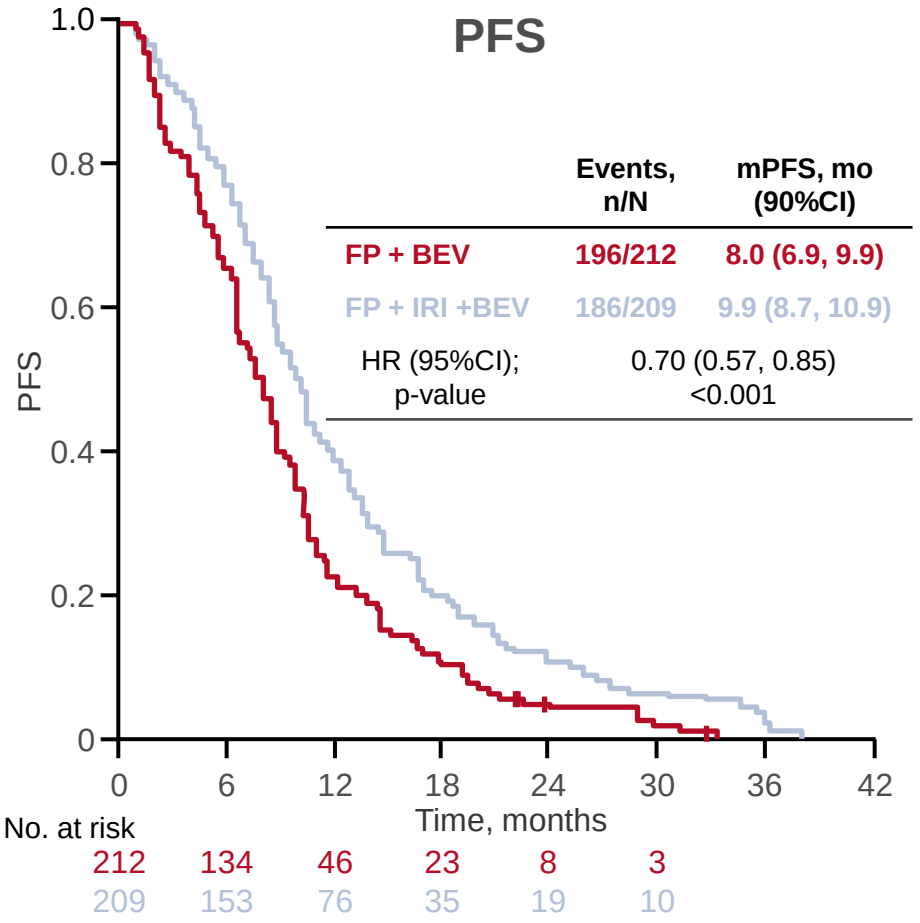
Modest DP, et al. Ann Oncol 2017;28(Suppl 5):Abstr 486O

486O:Sequential first-line therapy of metastatic colorectal cancer (mCRC) starting with fluoropyrimidine (FP) plus bevacizumab (BEV) vs. initial FP plus irinotecan (IRI) and BEV: German AIO KRK0110 (ML22011)- study – Modest DP, et al

Key results



	Events, n/N	mTFS, mo (90%CI)
FP + BEV	194/212	9.6 (8.6, 10.6)
FP + IRI +BEV	186/209	9.9 (8.8, 10.6)
HR (90%CI); p-value	0.86 (0.73, 1.02); 0.16	



	Events, n/N	mPFS, mo (90%CI)
FP + BEV	196/212	8.0 (6.9, 9.9)
FP + IRI +BEV	186/209	9.9 (8.7, 10.9)
HR (95%CI); p-value	0.70 (0.57, 0.85) <0.001	

Modest DP, et al. Ann Oncol 2017;28(Suppl 5):Abstr 486O

486O:Sequential first-line therapy of metastatic colorectal cancer (mCRC) starting with fluoropyrimidine (FP) plus bevacizumab (BEV) vs. initial FP plus irinotecan (IRI) and BEV: German AIO KRK0110 (ML22011)- study – Modest DP, et al

Key results (cont.)

		FP + BEV (n=212)	FP + IRI + BEV (n=209)	p-value
Response rate, %	FAS*	36.8	53.6	0.005
	RAS/BRAF WT	44.3	65.8	0.01
	RAS MUT	33.0	46.4	0.08
	BRAF MUT	25.0	30.0	0.79
TFS, HR (90%CI)	FAS	0.86 (0.73, 1.02)		
	RAS/BRAF WT	0.61 (0.46, 0.82)		
	RAS MUT	1.09 (0.81, 1.46)		
	BRAF MUT	1.62 (0.76, 3.47)		
OS, months	Median (95%CI)	21.9 (20.2, 25.0)	23.5 (20.9, 27.9)	
	HR (95%CI)	0.84 (0.66, 1.06)		0.14

Conclusions

- **In patients with mCRC, sequential escalation of therapy was only feasible in a minority and should only be considered for fit patients who are RAS MUT**
- **In fit patients with RAS/BRAF WT mCRC, initial FP + BEV for intensive combination regimens should not be considered**
- **In patients with RAS MUT mCRC, outcomes were not substantially improved with 1L combination CT and the numbers are too small for patients with BRAF MUT mCRC to draw any conclusions**

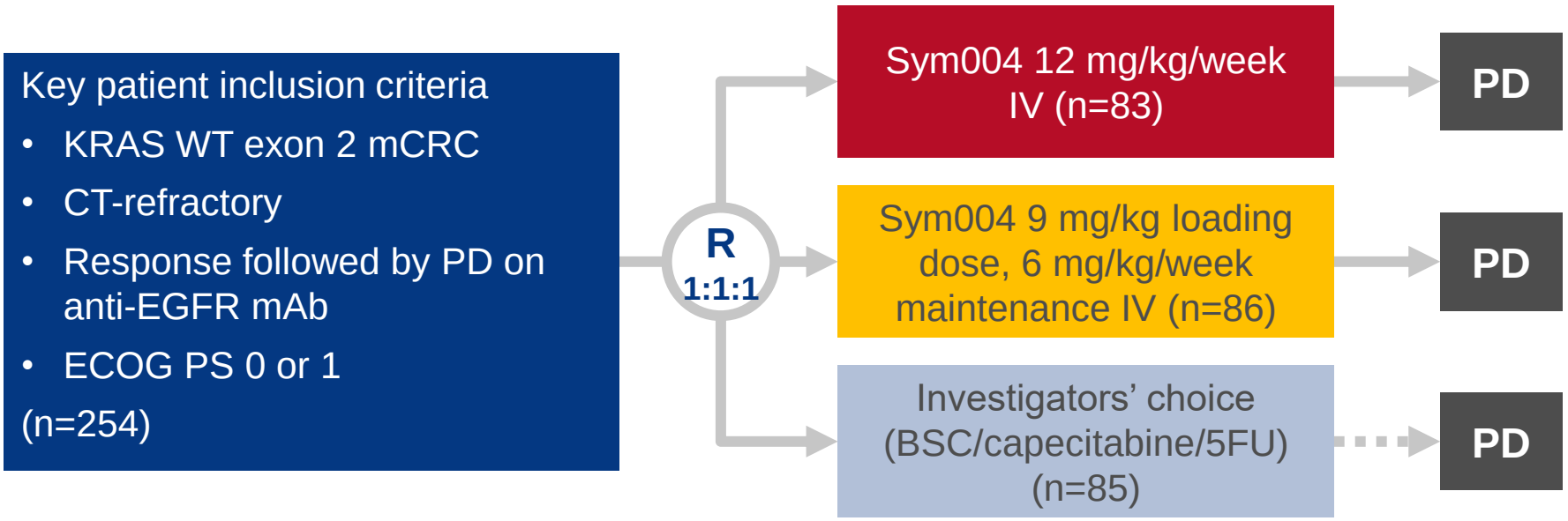
*Activation of the Fas receptor (a death receptor belonging to the tumour necrosis factor superfamily) mediates apoptosis

Modest DP, et al. Ann Oncol 2017;28(Suppl 5):Abstr 486O

478O: Efficacy and safety of Sym004 in refractory metastatic colorectal cancer with acquired resistance to anti-EGFR therapy: Results of a randomized phase II study (RP2S) – Taberno J, et al

Study objective

- To assess the efficacy and safety of Sym004* in refractory mCRC with acquired resistance to anti-EGFR therapy



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, ORR, DCR, safety

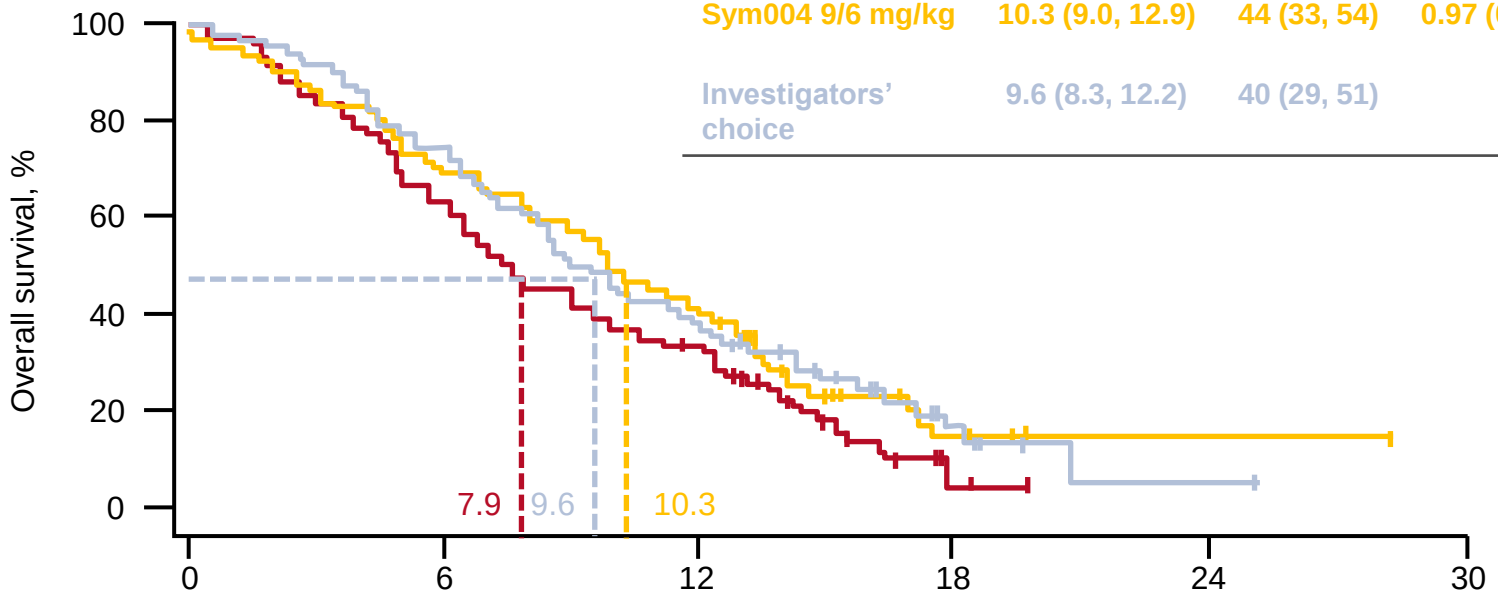
*A mixture of two non-overlapping anti-EGFR mAbs

Taberno J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 478O

478O: Efficacy and safety of Sym004 in refractory metastatic colorectal cancer with acquired resistance to anti-EGFR therapy: Results of a randomized phase II study (RP2S) – Taberno J, et al

Key results

	mOS, mo (95%CI)	1 year OS, %	HR* (95%CI)
Sym004 12 mg/kg	7.9 (6.5, 9.9)	37 (26, 47)	1.31 (0.92, 1.86)
Sym004 9/6 mg/kg	10.3 (9.0, 12.9)	44 (33, 54)	0.97 (0.68, 1.40)
Investigators' choice	9.6 (8.3, 12.2)	40 (29, 51)	-



No. at risk					
Sym004 12 mg/kg	83	53	29	2	1
Sym004 9/6 mg/kg	86	60	36	5	1
Investigators' choice	85	55	29	6	

*vs. investigators' choice

Taberno J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 478O

478O: Efficacy and safety of Sym004 in refractory metastatic colorectal cancer with acquired resistance to anti-EGFR therapy: Results of a randomized phase II study (RP2S) – Taberno J, et al

Key results (cont.)

	Sym004 12 mg/kg (n=83)	Sym004 9/6 mg/kg (n=86)	Investigators' choice (n=85)
Response rate, n (%)			
CR	-	-	1 (1.4)
PR	11 (14.1)	8 (9.6)	1 (1.4)
SD	40 (51.3)	47 (56.6)	37 (52.9)
PD	27 (34.6)	28 (33.7)	31 (44.3)
NE	5	3	15
mPFS, months (95%CI)	2.8 (1.8, 3.2)	2.7 (2.6, 3.3)	2.6 (1.4, 3.1)
HR (vs. INV choice) (95%CI)	1.08 (0.77, 1.50)	0.98 (0.71, 1.35)	
PFS at 6 months, % (95%CI)	14 (7, 22)	21 (13, 31)	23 (14, 33)
DCR, % (n/N evaluable)	65.4 (51/78)	66.2 (55/83)	55.7 (39/70)

Conclusions

- **The study conducted in the KRAS exon 2 WT mCRC population (not the current SoC target) did not meet its primary endpoint**
- **Safety was manageable although TRAEs were more common in patients treated with Sym004, particularly dermatologic toxicity and infusion reactions***
- **Improvement in OS was observed in the double and triple negative population subgroups†**

*Data not shown; †No RAS MUT allele frequency >20%, no BRAF V600E, no EGFR ECD [triple only] in ctDNA

Taberno J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 478O

479O: Consensus Molecular Subtypes (CMS) as predictors of benefit from bevacizumab in first line treatment of metastatic colorectal cancer: retrospective analysis of the MAX clinical trial – Mooi J, et al

Study objective

- To correlate CMS classification with survival outcomes in patients with stage IV mCRC treated with CT ± bevacizumab

Data source

- A subanalysis of the MAX study using data from 237 patients (with primary tumour blocks available)

Methods

- RNA extracted from FFPE tumour sections
- Gene expression profiling using Almac Xcel microarrays (>97,000 transcripts)
- CMS distribution
  - CMS1 (18%)
  - CMS2 (47%)
  - CMS3 (12%)
  - CMS4 (23%)

Mooi J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 479O

479O: Consensus Molecular Subtypes (CMS) as predictors of benefit from bevacizumab in first line treatment of metastatic colorectal cancer: retrospective analysis of the MAX clinical trial – Mooi J, et al

Key results

Variable		OS Analysis HR (95%CI)	p-value
CMS1 CMS2 CMS3 CMS4		1.00 0.44 (0.27, 0.72) 0.55 (0.30, 1.01) 0.57 (0.33, 0.96)	0.01
Primary tumour side	Left vs. right	0.95 (0.64, 1.39)	0.78
Treatment	CBM vs. C	0.87 (0.62, 1.22)	0.42
ECOG	1 vs. 0	1.88 (1.36, 2.59)	<0.001
Neutrophils ≥8	Yes vs. no	2.17 (1.38, 3.43)	0.001
ALP (U/L) ≥140	Yes vs. no	1.70 (1.21, 2.40)	0.002
Prior radiotherapy	Yes vs. no	1.71 (1.04, 2.80)	0.03
Primary tumour resected	Yes vs. no	0.48 (0.22, 1.07)	0.07

Mooi J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 479O

479O: Consensus Molecular Subtypes (CMS) as predictors of benefit from bevacizumab in first line treatment of metastatic colorectal cancer: retrospective analysis of the MAX clinical trial – Mooi J, et al

Conclusions

- **This study provides confirmation of the prognostic value of CMS in mCRC**
- **The prognostic differences in left- vs. right-sided primary are biologically driven**
- **Compared with CMS1 and 4, CMS2 and 3 preferentially benefit from the addition of bevacizumab to capecitabine CT as in 1L mCRC**
- **However, validation in independent cohorts for the predictive associations of CMS are required**

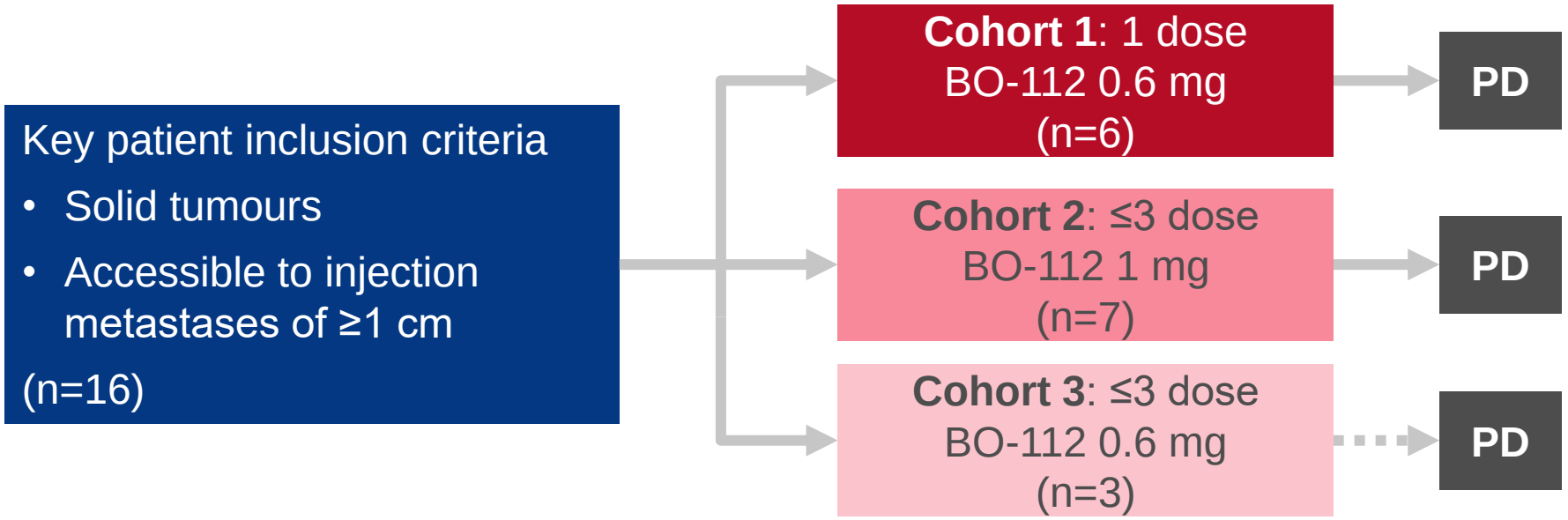
Mooi J, et al. Ann Oncol 2017;28(Suppl 5):Abstr 479O

SOLID TUMOURS

LBA20: Safety and immunobiological activity of intratumoral (IT) double-stranded RNA (dsRNA) BO-112 in solid malignancies: first in human clinical trial – Márquez Rodas I, et al

Study objective

- To explore the safety and immunobiological effects of intratumoural BO-112* in malignant tumours



PRIMARY ENDPOINT(S)

- Safety

SECONDARY ENDPOINTS

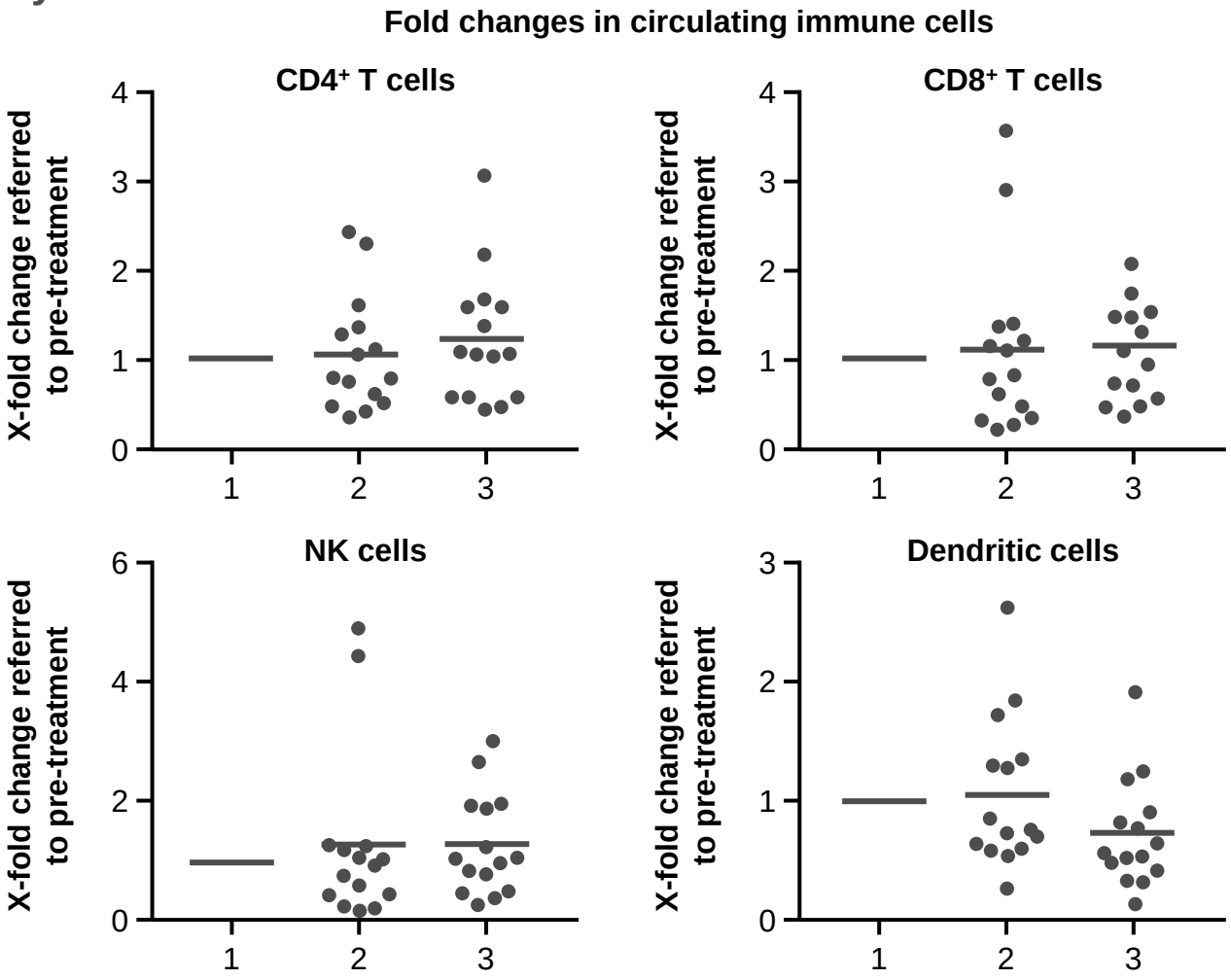
- PK, serum cytokines and circulating immune cells (immune response)

*A synthetic dsRNA with potential local and systemic anti-tumour activity

Márquez Rodas I, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA20

LBA20: Safety and immunobiological activity of intratumoral (IT) double-stranded RNA (dsRNA) BO-112 in solid malignancies: first in human clinical trial – Márquez Rodas I, et al

Key results



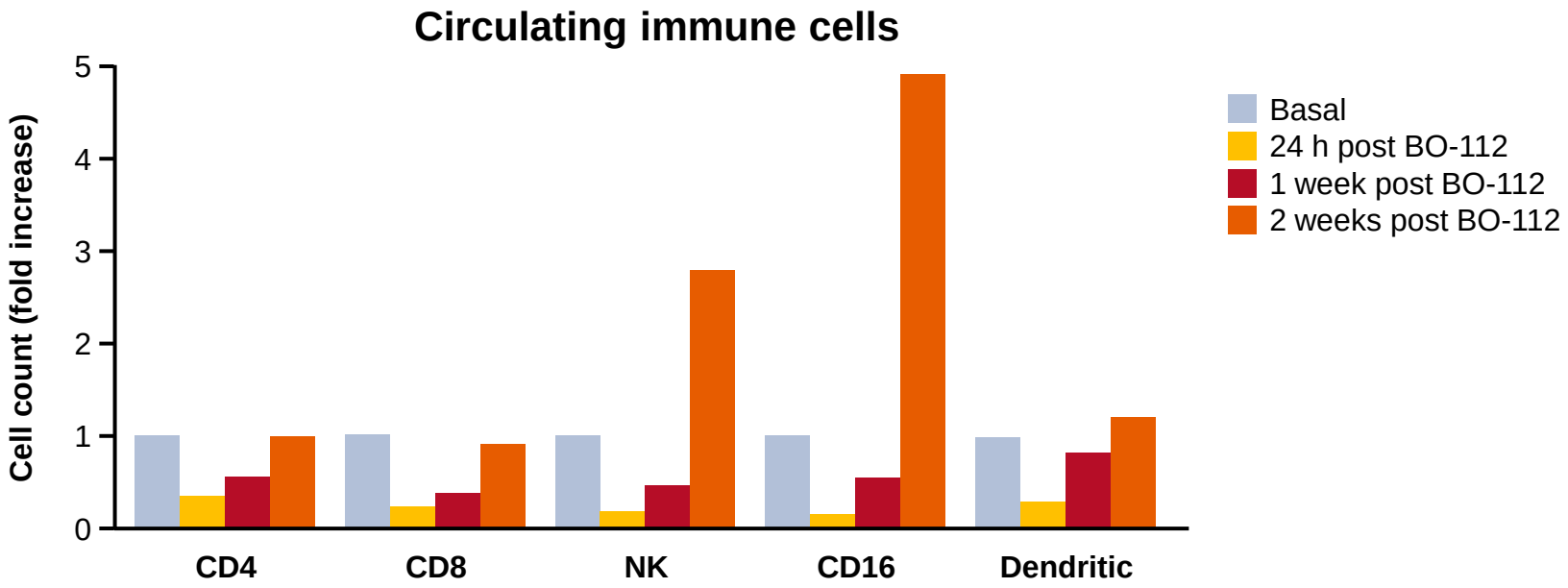
1. Basal
2. 24 h post-BO-112
3. 1 week post-BO-112

Márquez Rodas I, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA20

LBA20: Safety and immunobiological activity of intratumoral (IT) double-stranded RNA (dsRNA) BO-112 in solid malignancies: first in human clinical trial – Márquez Rodas I, et al

Key results (cont.)

Evaluable, n/N (%)		Cohort 1 (n=6)	Cohort 2 (n=7)	Cohort 3 (n=3)
Tumour	Necrosis-apoptosis	4/5 (80)	4/5 (80)	3/3 (100)
	ΔCD8+	2/5 (40)	2/5 (40)	0/3 (0)
	ΔCD4+	4/5 (80)	4/5 (80)	0/3 (0)
	ΔIFN-γ	3/5 (60)	1/1 (100)	N/A
Blood	ΔCirculating immune cells	6/6 (100)	6/6 (100)	2/3 (67)



Márquez Rodas I, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA20

LBA20: Safety and immunobiological activity of intratumoral (IT) double-stranded RNA (dsRNA) BO-112 in solid malignancies: first in human clinical trial – Márquez Rodas I, et al

Key results (cont.)

Cohort	Patient ID	Tumour	TRAE grade 1–2	TRAE grade 3–4
1	101	Endometrial neuroendocrine carcinoma	-	-
	102	Melanoma	-	-
	202	Melanoma	-	Thrombocytopenia (G4)
	203	Breast carcinoma	Myalgia	-
	204	Melanoma	Chills; erythema in injection site	-
	206	Melanoma	Pain in puncture area	-
2	103	Colorectal	-	-
	104	Ovarian carcinoma	-	-
	105	Mesothelioma	-	-
	207	Breast carcinoma	Neutropenia; pain in puncture area; inflammation in biopsy zone	Thrombocytopenia (G3)
	208	Leiomyosarcoma	-	-
	209	Melanoma	-	-
	210	Leiomyosarcoma	General malaise; fever; injection site discomfort	-
3	106	Head and Neck cancer	-	-
	211	Leiomyosarcoma	Fever, fatigue	-
	212	Adenoid cystic carcinoma	Chills; cephalea; vomiting; thrombocytopenia (G1); lymphopenia (G1)	-

Márquez Rodas I, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA20

LBA20: Safety and immunobiological activity of intratumoral (IT) double-stranded RNA (dsRNA) BO-112 in solid malignancies: first in human clinical trial – Márquez Rodas I, et al

Conclusions

- **BO-112 demonstrated activity that was consistent both with a direct anti-tumour effect and intratumoural and systemic immunity activation, driven by IFNγ pathway**
- **The safety profile of BO-112 was manageable, only 2 grade 3–4 toxicities were detected**
- **In patients who are refractory to anti-PD-1 therapy a dose of BO-112 1 mg qw x2–3 in combination with anti-PD-1 will be examined in an expansion cohort**

Márquez Rodas I, et al. Ann Oncol 2017;28(Suppl 5):Abstr LBA20