GI SLIDE DECK 2017

Selected abstracts from:

2017 Gastrointestinal Cancers Symposium

19–21 January 2017 | San Francisco, USA

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 **2017 Gastrointestinal Cancers Symposium** 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 which helps to educate and inspire further advancements in our roles as scientists, clinicians and educators. I hope you find this review of the latest developments in digestive cancers of benefit to you in your practice. If you would like to share your thoughts with us we would welcome your comments. Please send any correspondence to info@esdo.eu.

And finally, we are also very grateful to Lilly Oncology for their financial, administerial 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

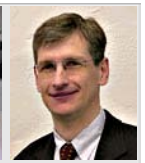
ESDO Medical Oncology Slide Deck
Editors 2017

COLORECTAL CANCERS



Prof Eric Van Cutsem	Digestive Oncology, University Hospitals, Leuven, Belgium
Prof Wolff Schmiegel	Department of Medicine, Ruhr University, Bochum, Germany
Prof Thomas Gruenberger	Department of Surgery I, Rudolf Foundation Clinic, Vienna, Austria

PANCREATIC CANCER AND HEPATOBILIARY TUMOURS

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

GASTRO-OESOPHAGEAL AND NEUROENDOCRINE TUMOURS


Emeritus Prof Philippe Rougier	University Hospital of Nantes, Nantes, France
Prof Côme Lepage	University Hospital & INSERM, Dijon, France

BIOMARKERS


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

esdo

Glossary

1L	first-line
2L	second-line
AE	adverse event
AJCC	American Joint Committee on Cancer
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BICR	blinded-independent central review
bid	twice daily
BMI	body mass index
BOR	best overall response
BSC	best supportive care
CA19-9	carbohydrate antigen 19-9
CI	confidence interval
CISH	chromogenic in situ hybridisation
CR	complete response
CRC	colorectal cancer
CT	chemotherapy
DCR	disease control rate
DFS	disease-free survival
dMMR	deficient mismatch repair
DoR	duration of response
ECC	extrahepatic cholangiocarcinoma
ECOG	Eastern Cooperative Oncology Group
ENETS	European Neuroendocrine Tumor Society
EQ-5D	EuroQol five dimensions questionnaire
ERUS	endorectal ultrasound
ESMO	European Society of Medical Oncology
(m)FOLFOX	(modified) leucovorin + 5-fluorouracil + oxaliplatin
GBC	gallbladder cancer
GEJ	gastro-oesophageal junction
GEP	gastroenteropancreatic
GEMOX	gemcitabine + oxaliplatin
GGT	gamma-glutamyl transpeptidase
GI	gastrointestinal
Gy	Gray
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HER2	human epidermal growth factor receptor 2
HR	hazard ratio
ICC	intrahepatic cholangiocarcinoma
IHC	immunohistochemistry
IR	interventional radiology
ITT	intent-to-treat
iv	intravenous
mCRC	metastatic colorectal cancer
MMR-P	mismatch repair proficient
MRI	magnetic image resonance
MSI-H	high microsatellite instability
NA	not available
NCI	National Cancer Institute
NCCN	National Comprehensive Cancer Network
NE	not evaluable
NET	neuroendocrine tumour
NR	not reached
NS	non-significant
od	once daily
ORR	overall/objective response rate
(m)OS	(median) overall survival
pCR	pathological complete response
PD	progressive disease
PD-L1	programmed death-ligand 1
PET	positron emission tomography
(m)PFS	(median) progression-free survival
po	orally
PR	partial response
PRO	patient-reported outcome
PS	performance status
q(2/3/4)w	every (2/3/4) week(s)
QLQ-C30	quality of life questionnaire C30
QoL	quality of life
R	randomised
R0/1	resection 0/1
(m)RECIST	(modified) Response Evaluation Criteria In Solid Tumors
RT	radiotherapy
SAE	serious adverse event
SBRT	stereotactic body radiation therapy
SD	stable disease
SF-36	Short Form 36
SUV	standardised uptake value
TACE	transarterial chemoembolisation
TML	tumour mutation load
TRAE	treatment-related adverse event
TTR	time to response
VAS	visual analogue scale
VEGF	vascular endothelial growth factor

Contents

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

CANCERS OF THE OESOPHAGUS AND STOMACH

1: Initial results of CALGB 80803 (Alliance): A randomized phase II trial of PET scan-directed combined modality therapy for esophageal cancer – Goodman KA, et al

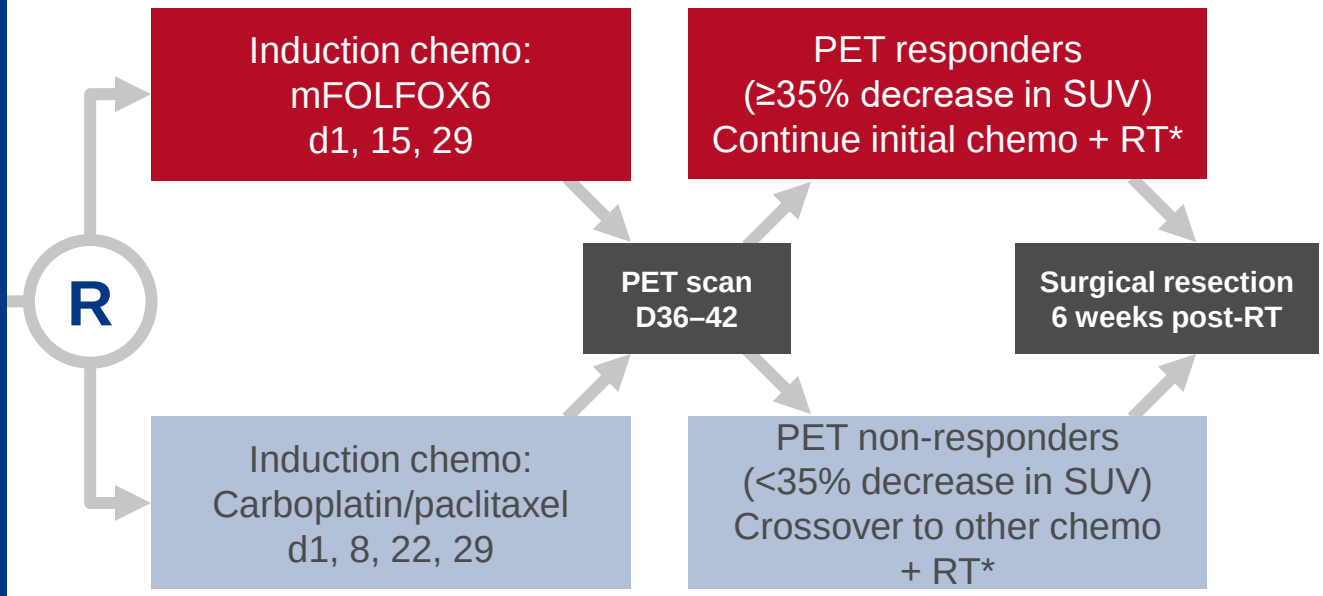
Study objective

- To evaluate the use of determining early chemotherapy responsiveness by PET imaging to direct further therapy in patients with oesophageal and GEJ cancers

Key patient inclusion criteria

- Histologically confirmed oesophageal cancer
- AJCC v.7 staging: T1N1–3 or T2–4Nany
- Tumour SUV max ≥5 on baseline PET/CT
- Tumour resectable and able to be encompassed in an RT field
- ECOG PS 0–1

(n=257)



PRIMARY ENDPOINT

- Rate of pCR of PET non-responders

SECONDARY ENDPOINTS

- 8-month PFS among PET non-responders
- Comparison of PET response between induction arms
- Comparison of pCR, PFS and OS between induction arms and PET responders and non-responders

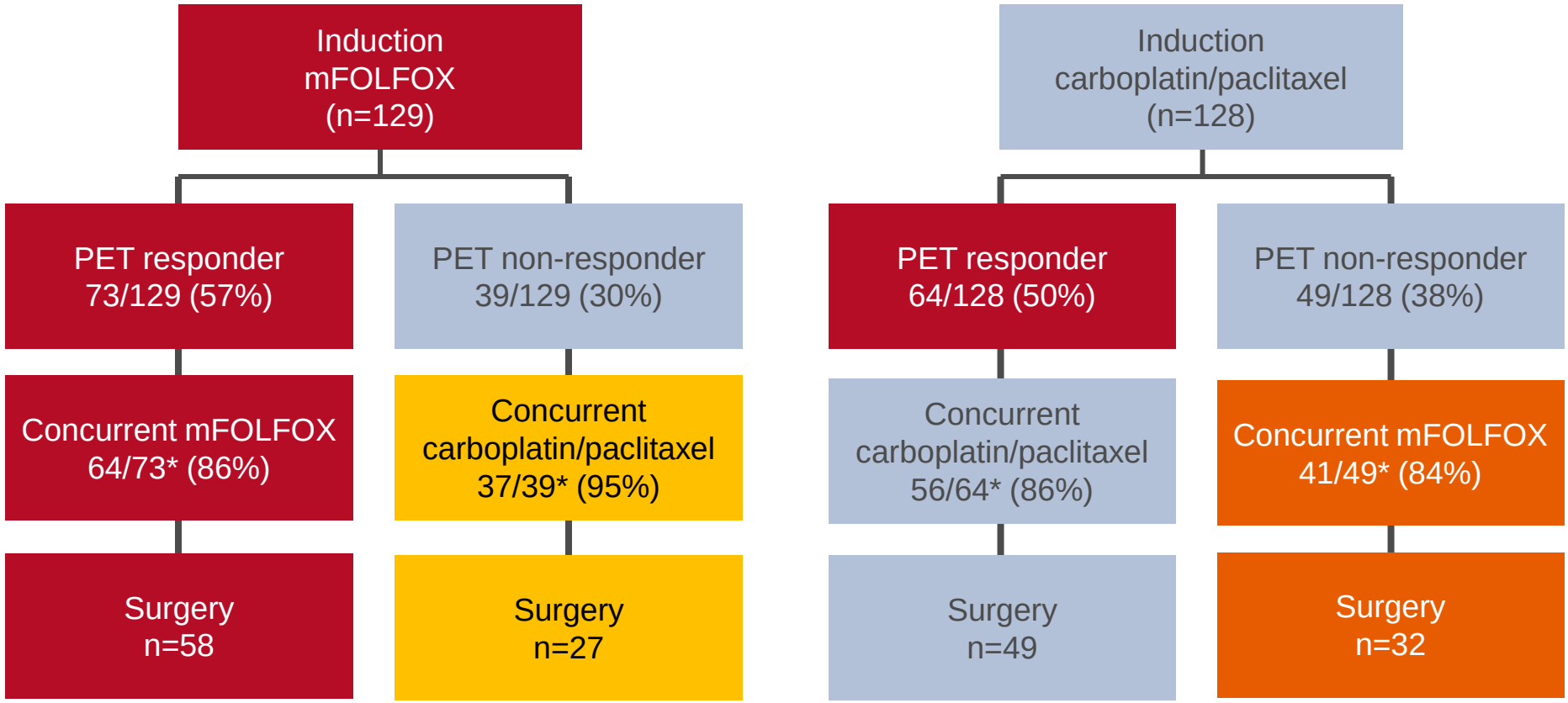
*Concurrent RT, 50.4 Gy in 28 fx

Goodman KA, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 1

1: Initial results of CALGB 80803 (Alliance): A randomized phase II trial of PET scan-directed combined modality therapy for esophageal cancer – Goodman KA, et al

Key results

Treatment course by induction therapy

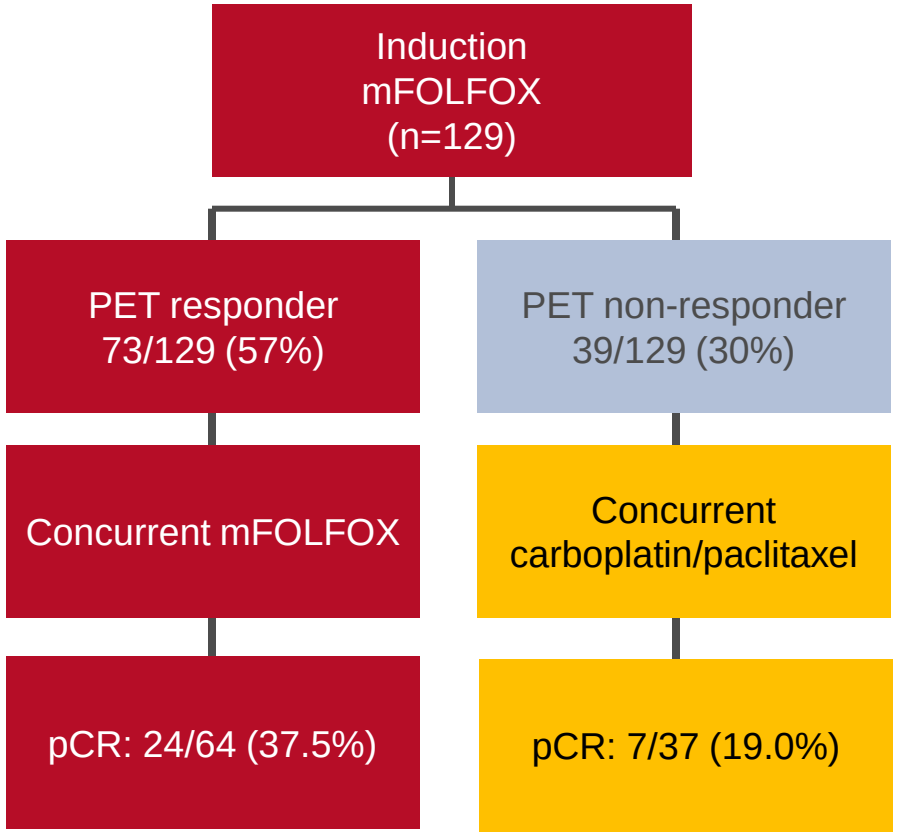


*Evaluable patients

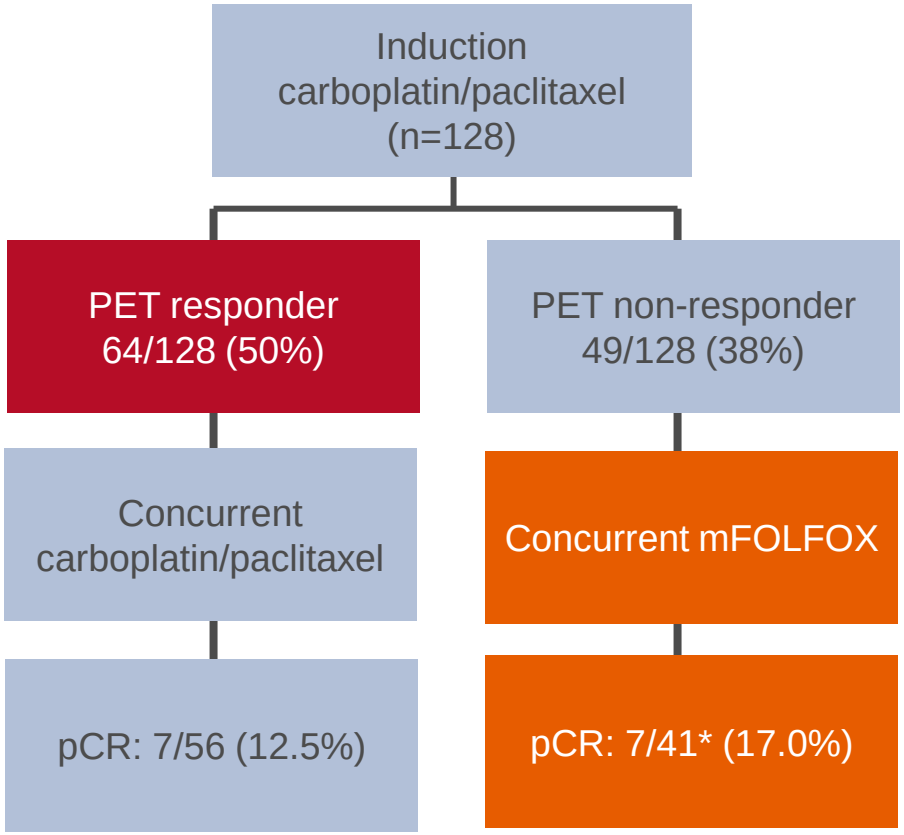
Goodman KA, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 1

1: Initial results of CALGB 80803 (Alliance): A randomized phase II trial of PET scan-directed combined modality therapy for esophageal cancer – Goodman KA, et al

Key results (cont.)



pCR rates



*One ypTON1 excluded

Goodman KA, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 1

1: Initial results of CALGB 80803 (Alliance): A randomized phase II trial of PET scan-directed combined modality therapy for esophageal cancer – Goodman KA, et al

Key results (cont.)

Subgroup	n/N	pCR rate, % (95%CI)
PET non-responders	14/78	18.0 (10, 28)
PET responders	31/120	26.0 (18, 35)
mFOLFOX6 induction	31/101	31.0 (22, 41)
Carboplatin/paclitaxel induction	14/97	14.4 (8, 23)
All patients	45/198	22.7 (17, 29)

Goodman KA, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 1

1: Initial results of CALGB 80803 (Alliance): A randomized phase II trial of PET scan-directed combined modality therapy for esophageal cancer – Goodman KA, et al

Key results (cont.)

Grade ≥3 AEs at least possibly related to treatment

AE >5% prevalence in either arm, %	Induction mFOLFOX (n=118)	Induction carboplatin/paclitaxel (n=119)	Overall (n=237)
Anaemia	5	7	6
Neutropenia	11	14	13
Thrombocytopenia	5	8	7
Dysphagia	5	6	6
Nausea	8	9	8
Fatigue	9	3	6
Anorexia	6	3	4
Dehydration	4	5	5

Goodman KA, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 1

1: Initial results of CALGB 80803 (Alliance): A randomized phase II trial of PET scan-directed combined modality therapy for esophageal cancer – Goodman KA, et al

Conclusions

- **The use of PET imaging after a short course of induction chemotherapy in order to identify and switch poor responders to an alternate chemotherapy during pre-operative chemoradiation, is feasible in patients with oesophageal and GEJ cancers**
- **This protocol resulted in a pCR of 18% in those identified as PET non-responders and 38% in those who received induction mFOLFOX and concurrent RT**
- **The use of PET imaging allows the individualisation of multimodality therapy and may improve prognosis**

Goodman KA, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 1

2: Nivolumab (ONO-4538/BMS-936558) as salvage treatment after second or later-line chemotherapy for advanced gastric or gastro-esophageal junction cancer (AGC): A double-blinded, randomized phase III trial – Kang Y-K, et al

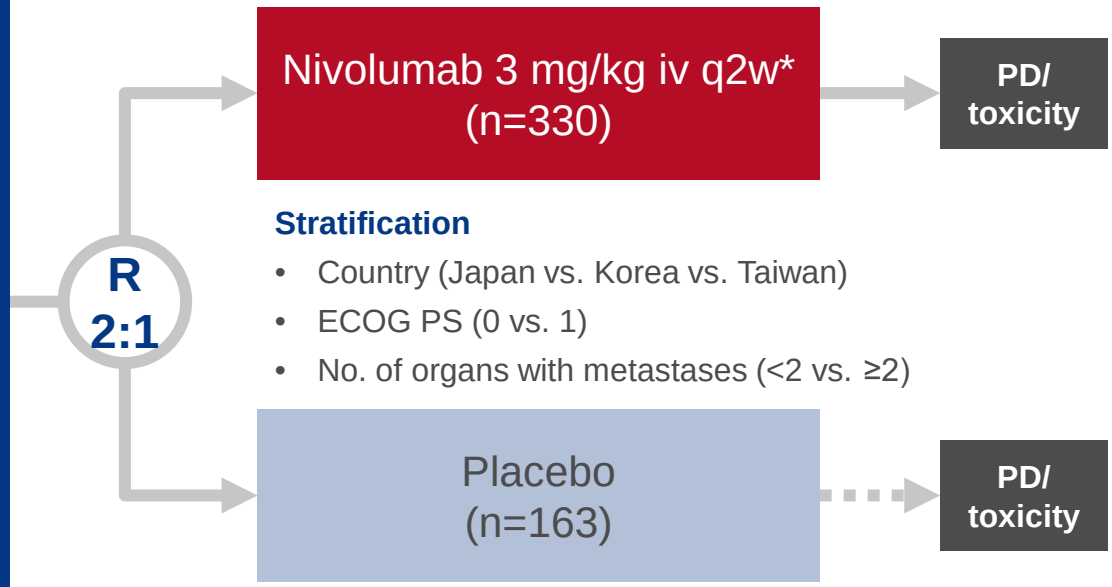
Study objective

- To evaluate the efficacy and safety of nivolumab as salvage treatment after failure of the standard chemotherapy for advanced gastric cancer in the phase 3 ONO 12 study

Key patient inclusion criteria

- Unresectable advanced or recurrent gastric or GEJ cancer
- Histologically confirmed
- ≥2 prior regimens and refractory to or intolerant of standard therapy
- Age ≥20 years
- ECOG PS 0–1

(n=493)



PRIMARY ENDPOINT

- OS (ITT population)

SECONDARY ENDPOINTS

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

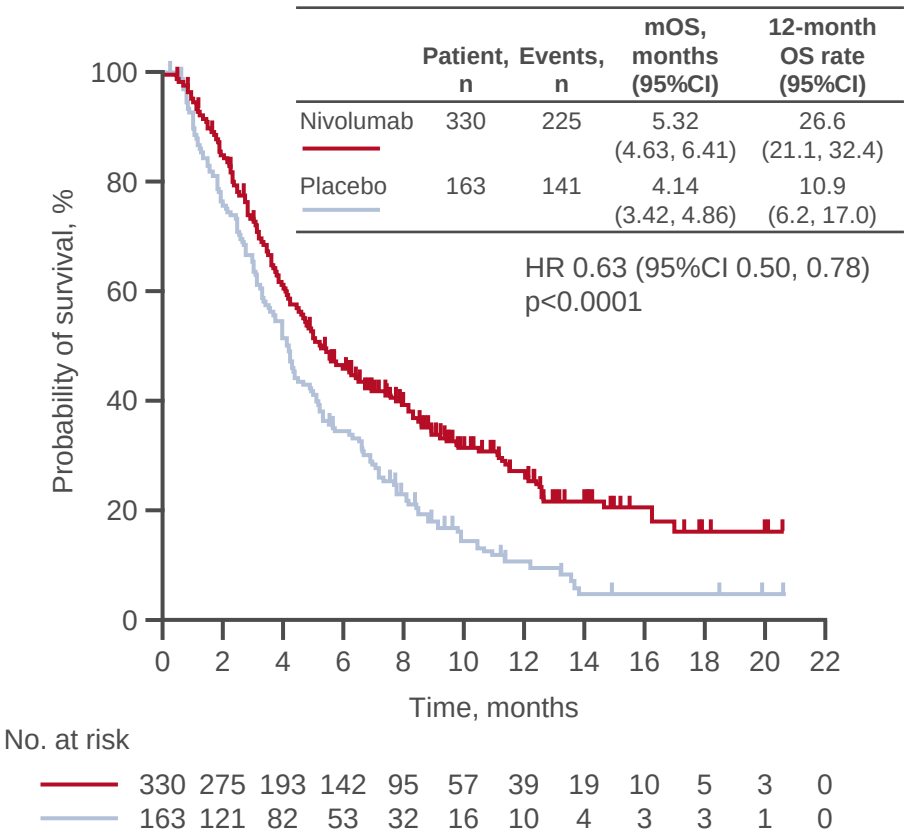
*Treatment beyond initial RECIST v1.1-defined PD permitted if patient receiving clinical benefit and tolerating study drug

Kang Y-K, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 2

2: Nivolumab (ONO-4538/BMS-936558) as salvage treatment after second or later-line chemotherapy for advanced gastric or gastro-esophageal junction cancer (AGC): A double-blinded, randomized phase III trial – Kang Y-K, et al

Key results

OS

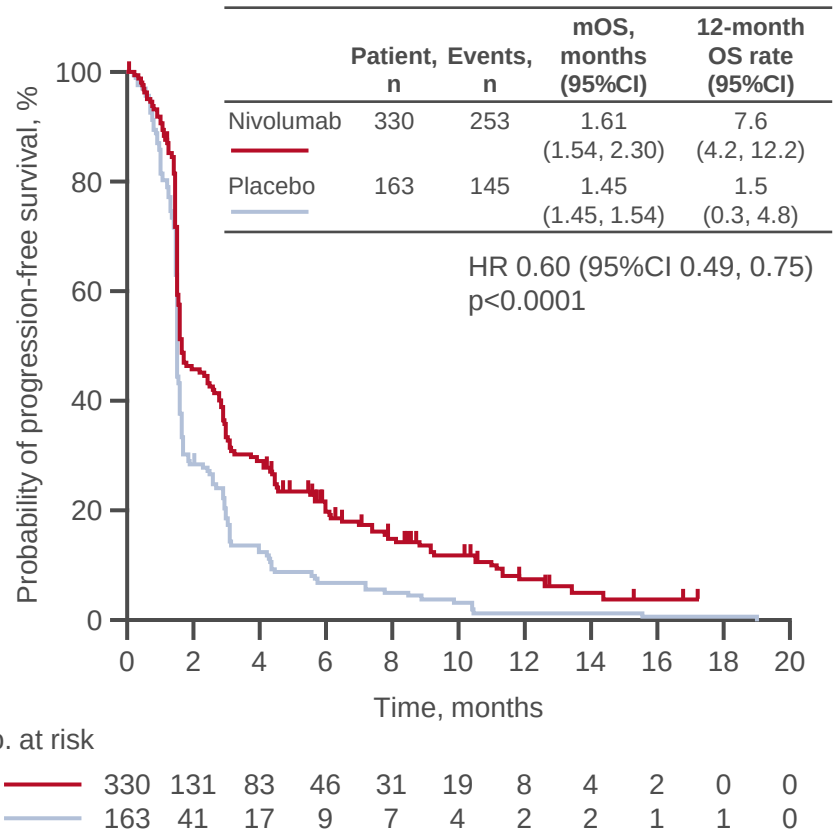


	Patient, n	Events, n	mOS, months (95%CI)	12-month OS rate (95%CI)
Nivolumab	330	225	5.32 (4.63, 6.41)	26.6 (21.1, 32.4)
Placebo	163	141	4.14 (3.42, 4.86)	10.9 (6.2, 17.0)

No. at risk

Nivolumab	330	275	193	142	95	57	39	19	10	5	3	0
Placebo	163	121	82	53	32	16	10	4	3	3	1	0

PFS



	Patient, n	Events, n	mOS, months (95%CI)	12-month OS rate (95%CI)
Nivolumab	330	253	1.61 (1.54, 2.30)	7.6 (4.2, 12.2)
Placebo	163	145	1.45 (1.45, 1.54)	1.5 (0.3, 4.8)

No. at risk

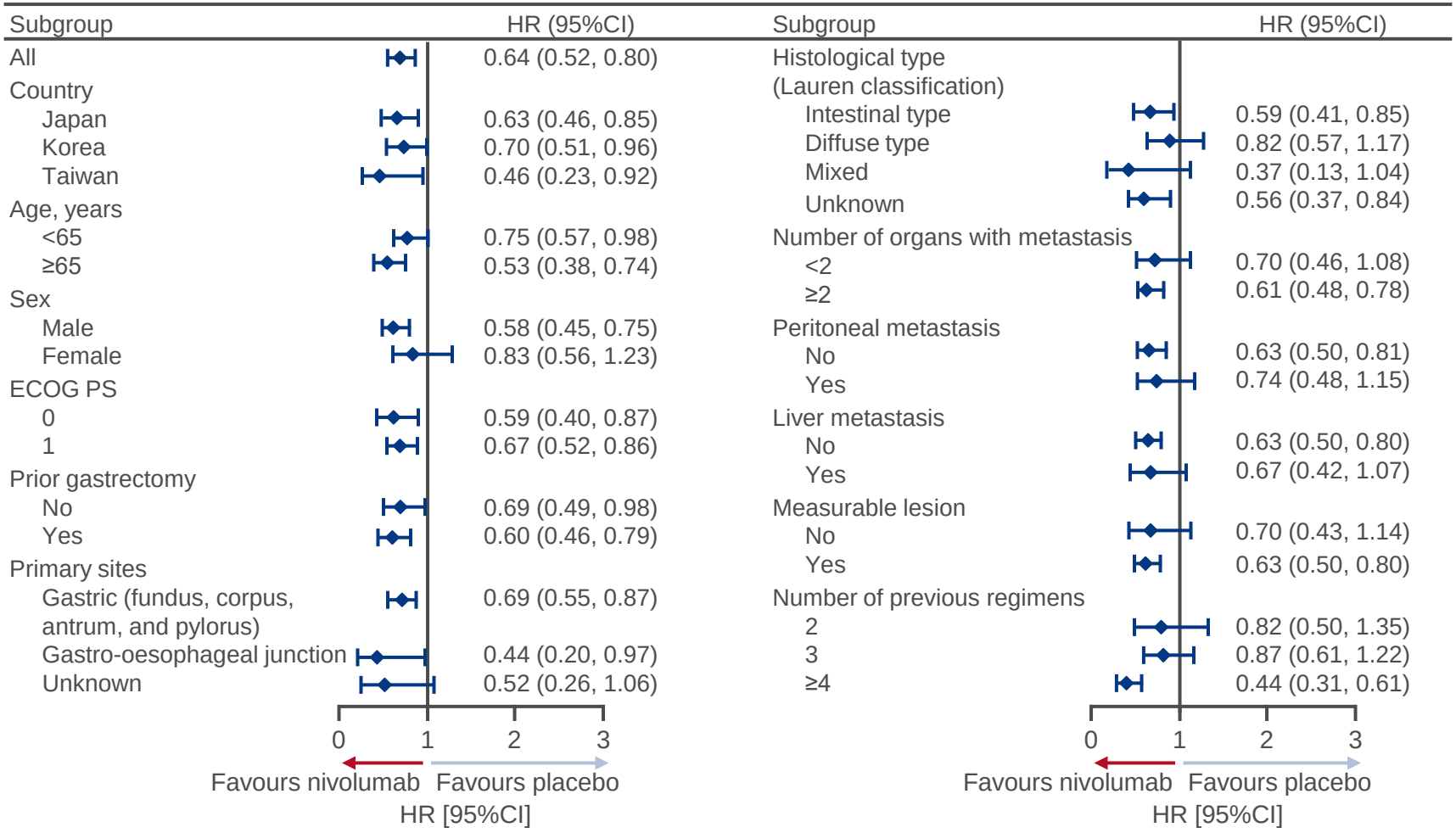
Nivolumab	330	131	83	46	31	19	8	4	2	0	0
Placebo	163	41	17	9	7	4	2	2	1	1	0

Kang Y-K, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 2

2: Nivolumab (ONO-4538/BMS-936558) as salvage treatment after second or later-line chemotherapy for advanced gastric or gastro-esophageal junction cancer (AGC): A double-blinded, randomized phase III trial – Kang Y-K, et al

Key results (cont.)

OS by subgroup



Kang Y-K, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 2

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Key results (cont.)

Characteristics	Nivolumab 3 mg/kg (n=268)	Placebo (n=131)
ORR, n (%) 95%CI p-value	30 (11.2) 7.7, 15.6 <0.0001	0 0, 2.8 —
BOR, n (%) CR PR SD PD	 0 30 (11.2) 78 (29.1) 124 (46.3)	 0 0 33 (25.2) 79 (60.3)
DCR, n (%) 95%CI p-value	108 (40.3) 34.4, 46.4 0.0036	33 (25.2) 18.0, 33.5 —
Median TTR, months (range)	1.61 (1.4–7.0)	—
Median DoR, months (95%CI)	9.53 (6.14, 9.82)	—
Tumour reduction, %	37.3	12.4

Kang Y-K, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 2

2: Nivolumab (ONO-4538/BMS-936558) as salvage treatment after second or later-line chemotherapy for advanced gastric or gastro-esophageal junction cancer (AGC): A double-blinded, randomized phase III trial – Kang Y-K, et al

Key results (cont.)

Patients, n (%)	Nivolumab 3 mg/kg (n=330)		Placebo (n=161)	
	Any	Grade 3/4	Any	Grade 3/4
Any AEs	300 (90.9)	137 (41.5)	135 (83.9)	63 (39.1)
SAEs	131 (39.7)	91 (27.6)	75 (46.6)	47 (29.2)
AEs leading to discontinuation	23 (7.0)	13 (3.9)	12 (7.5)	9 (5.6)
AEs leading to dose delay	63 (19.1)	40 (12.1)	27 (16.8)	17 (10.6)
AEs leading to death	35 (10.6)		25 (15.5)	
Any TRAEs	141 (42.7)	34 (10.3)	43 (26.7)	7 (4.3)
Serious TRAEs	33 (10.0)	21 (6.4)	8 (5.0)	4 (2.5)
TRAEs leading to discontinuation	9 (2.7)	4 (1.2)	4 (2.5)	3 (1.9)
TRAEs leading to dose delay	25 (7.6)	14 (4.2)	2 (1.2)	1 (0.6)
TRAEs leading to death	5 (1.5)		2 (1.2)	

Kang Y-K, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 2

2: Nivolumab (ONO-4538/BMS-936558) as salvage treatment after second or later-line chemotherapy for advanced gastric or gastro-esophageal junction cancer (AGC): A double-blinded, randomized phase III trial – Kang Y-K, et al

Key results (cont.)

TRAEs in >2% of patients receiving nivolumab, n (%)	Nivolumab 3 mg/kg (n=330)		Placebo (n=161)	
	Any	Grade 3/4	Any	Grade 3/4
Pruritus	30 (9.1)	0	9 (5.6)	0
Diarrhoea	23 (7.0)	2 (0.6)	3 (1.9)	0
Rash	19 (5.8)	0	5 (3.1)	0
Fatigue	18 (5.5)	2 (0.6)	9 (5.6)	2 (1.2)
Decreased appetite	16 (4.8)	4 (1.2)	7 (4.3)	1 (0.6)
Nausea	14 (4.2)	0	4 (2.5)	0
Malaise	13 (3.9)	0	6 (3.7)	0
AST increased	11 (3.3)	2 (0.6)	3 (1.9)	0
Hypothyroidism	10 (3.0)	0	1 (0.6)	0
Pyrexia	8 (2.4)	1 (0.3)	3 (1.9)	0
ALT increased	7 (2.1)	1 (0.3)	1 (0.6)	0

Kang Y-K, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 2

2: Nivolumab (ONO-4538/BMS-936558) as salvage treatment after second or later-line chemotherapy for advanced gastric or gastro-esophageal junction cancer (AGC): A double-blinded, randomized phase III trial – Kang Y-K, et al

Conclusions

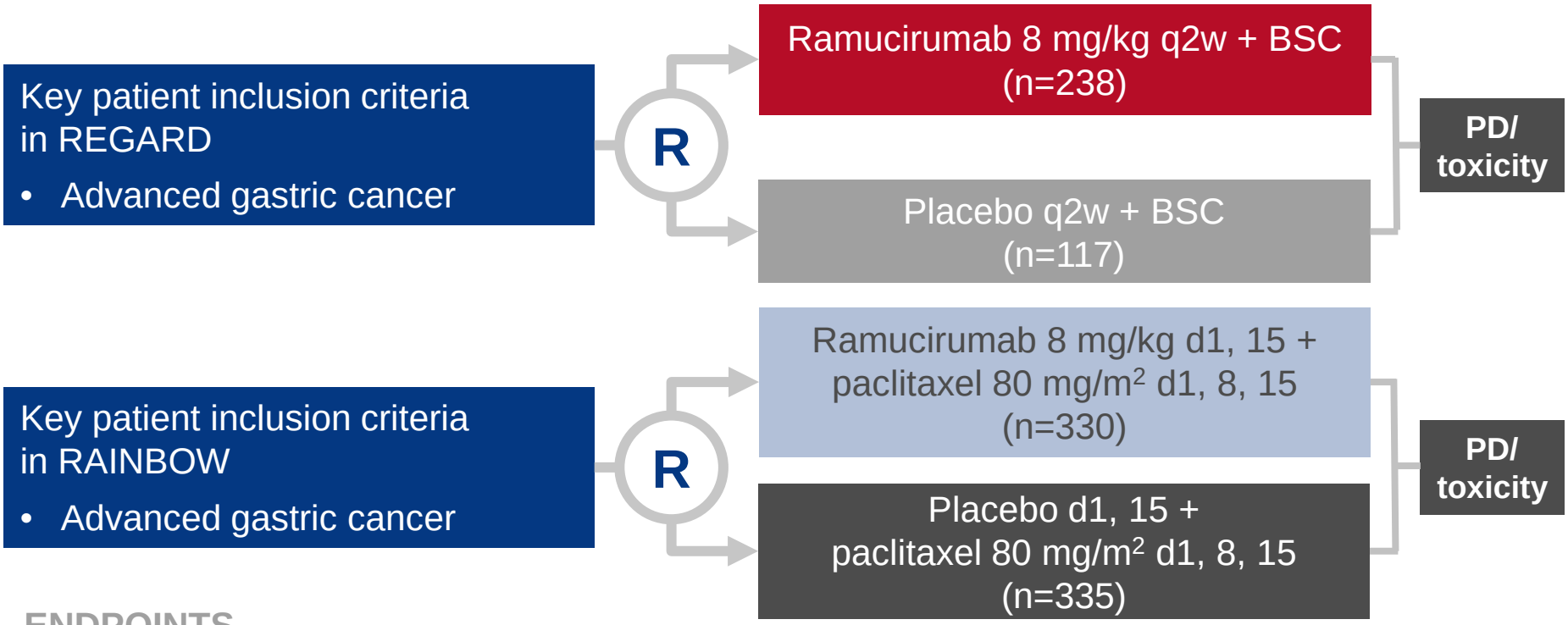
- **Nivolumab demonstrated efficacy and safety as a third or later line of treatment in patients with advanced gastric cancer**
- **Compared with placebo, nivolumab had superior OS and response rates and was well-tolerated**

Kang Y-K, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 2

3: Efficacy and safety of ramucirumab (RAM) for metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma across age subgroups in two global phase 3 trials – Muro K, et al

Study objective

- To assess the efficacy and safety of ramucirumab across a range of age groups from the REGARD and RAINBOW studies



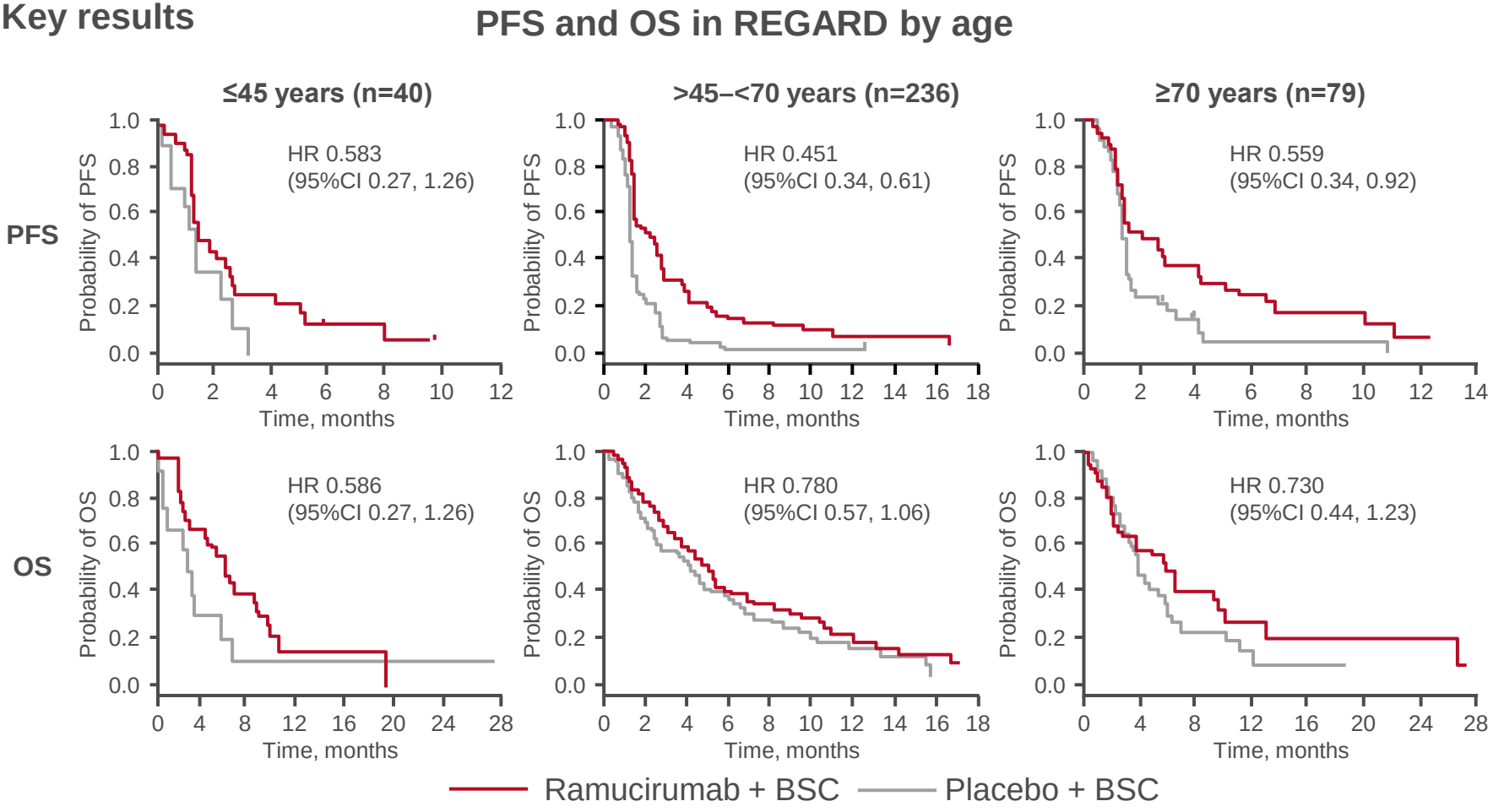
ENDPOINTS

- OS, PFS, safety by age subgroups (≤45 years, >45–<70 years, ≥70 years and ≥75 years [subgroup of ≥70 years])

Muro K, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 3

3: Efficacy and safety of ramucirumab (RAM) for metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma across age subgroups in two global phase 3 trials – Muro K, et al

Key results

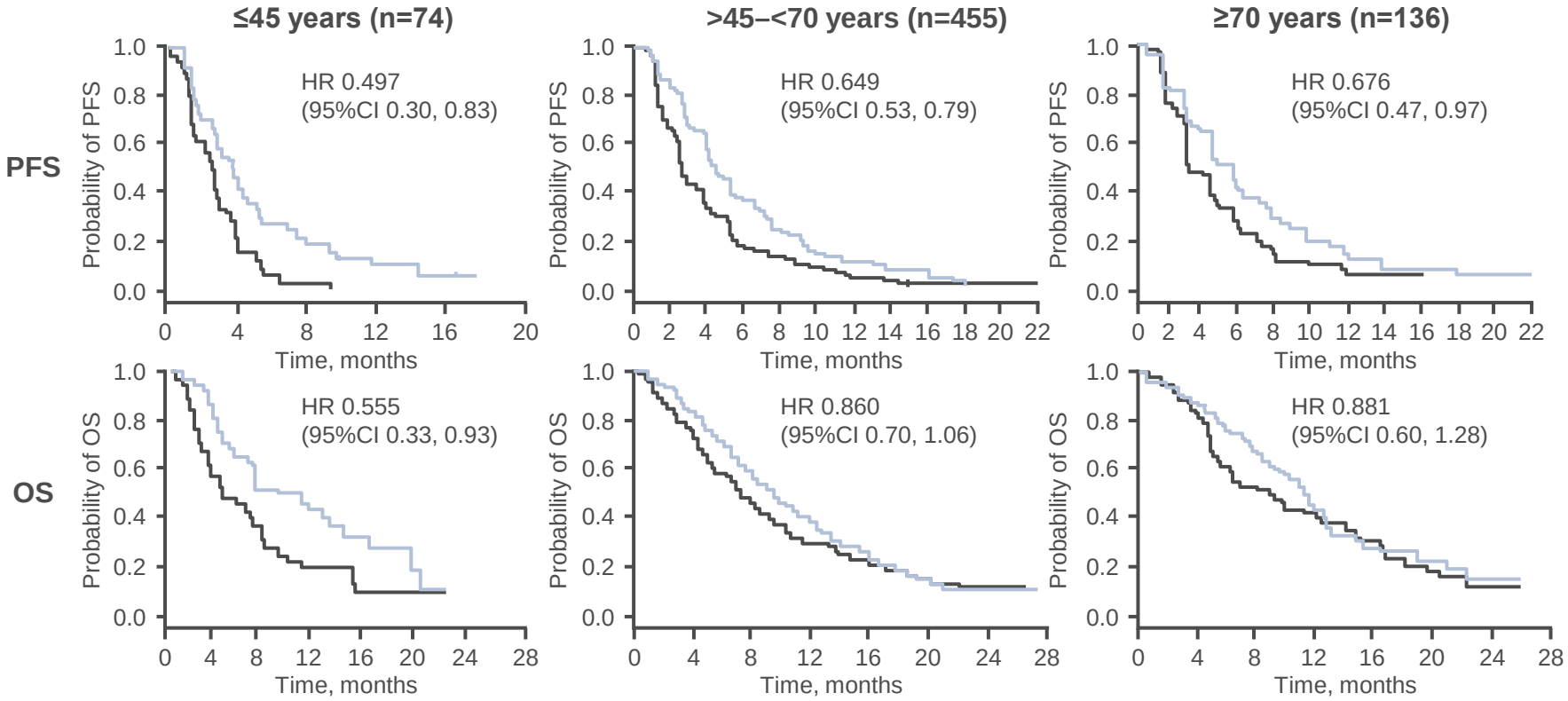


Muro K, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 3

3: Efficacy and safety of ramucirumab (RAM) for metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma across age subgroups in two global phase 3 trials – Muro K, et al

Key results (cont.)

PFS and OS in RAINBOW by age



Conclusion

- **The benefits of ramucirumab treatment were evident in young and elderly populations in the REGARD and RAINBOW studies, with comparable toxicity profiles across age groups**

Muro K, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 3

4: A randomized, double-blind, multicenter phase III study evaluating paclitaxel with and without RAD001 in patients with gastric cancer who have progressed after therapy with a fluoropyrimidine/platinum-containing regimen (RADPAC) – Al-Batran S-E, et al

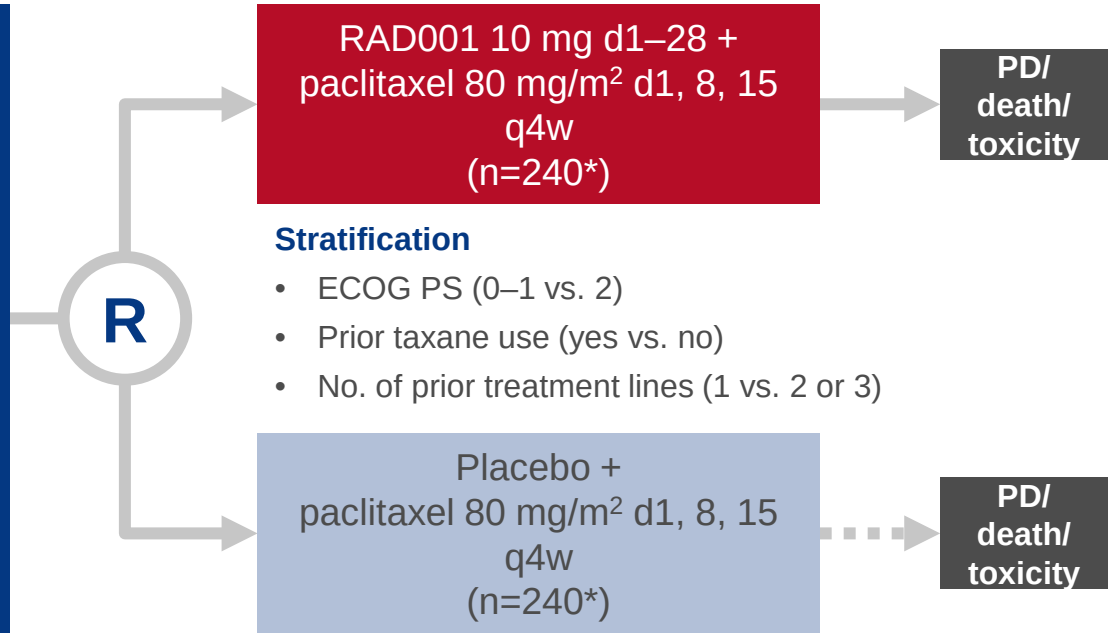
Study objective

- To evaluate RAD001 + paclitaxel in patients with gastric carcinoma who have progressed after therapy with a fluoropyrimidine/platinum-containing regimen in the RADPAC study

Key patient inclusion criteria

- Inoperable recurrent or metastatic gastric or GEJ adenocarcinoma
- Failed fluoropyrimidine/ platinum regimen
- Received 1–3 prior lines of therapy
- ECOG PS 0–2

(n=480*)



PRIMARY ENDPOINT(S)

- OS

SECONDARY ENDPOINTS

- PFS, ORR, safety

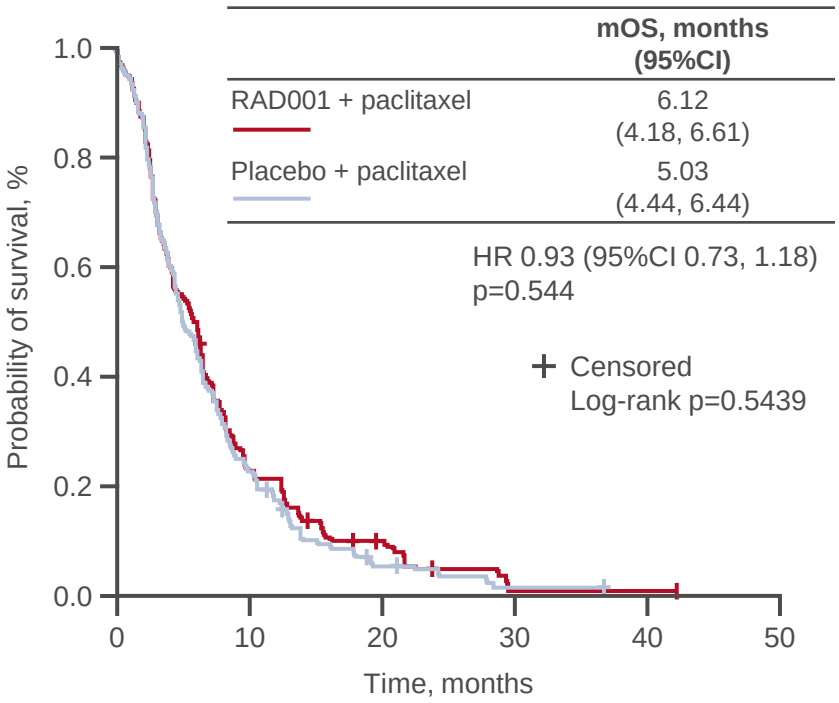
*Recruitment stopped early for low accrual

Al-Batran S-E, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 4

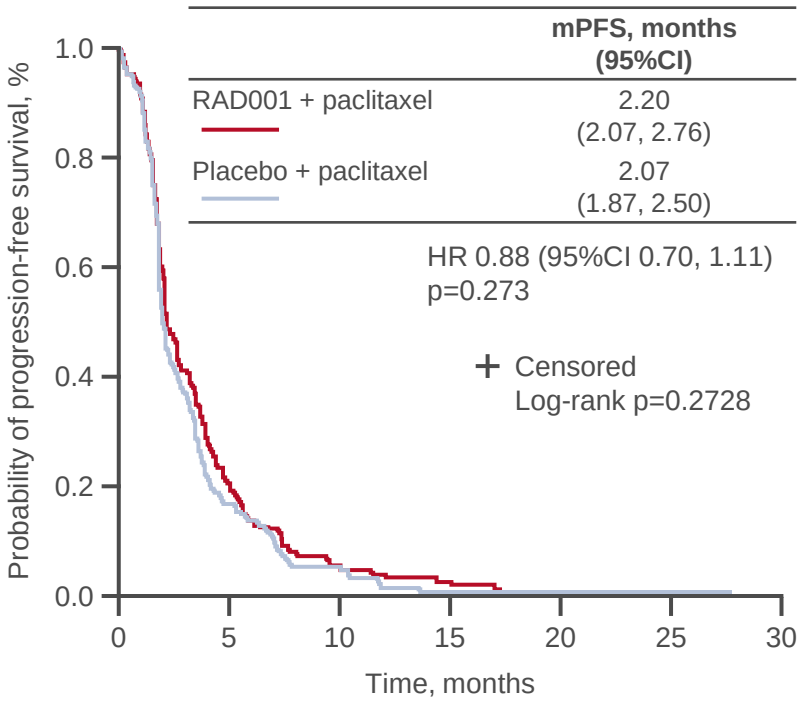
4: A randomized, double-blind, multicenter phase III study evaluating paclitaxel with and without RAD001 in patients with gastric cancer who have progressed after therapy with a fluoropyrimidine/platinum-containing regimen (RADPAC) – Al-Batran S-E, et al

Key results

OS



PFS



Al-Batran S-E, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 4

4: A randomized, double-blind, multicenter phase III study evaluating paclitaxel with and without RAD001 in patients with gastric cancer who have progressed after therapy with a fluoropyrimidine/platinum-containing regimen (RADPAC) – Al-Batran S-E, et al

Key results (cont.)

Grade 3–5 AEs occurring in ≥5% of patients, n (%)	RAD001 + paclitaxel (n=143)	Placebo + paclitaxel (n=147)
Anaemia	18 (13)	18 (12)
Neutropenia	10 (7)	10 (7)
Oral mucositis	19 (13)	1 (1)
Diarrhoea	9 (6)	5 (4)
Dyspnoea	9 (6)	5 (4)
Fatigue	10 (7)	14 (10)
Worsening of general health conditions	15 (11)	12 (8)
Infections	10 (7)	11 (8)
Nausea	7 (5)	10 (7)
Pain	10 (7)	13 (9)

Conclusions

- **Compared with paclitaxel alone, RAD001 in combination with paclitaxel did not improve outcomes**
- **Some activity with the addition of RAD001 was seen in the taxane-pretreated subgroup**

Al-Batran S-E, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 4

CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

Cancers of the pancreas, small bowel and hepatobiliary tract

PANCREATIC CANCER

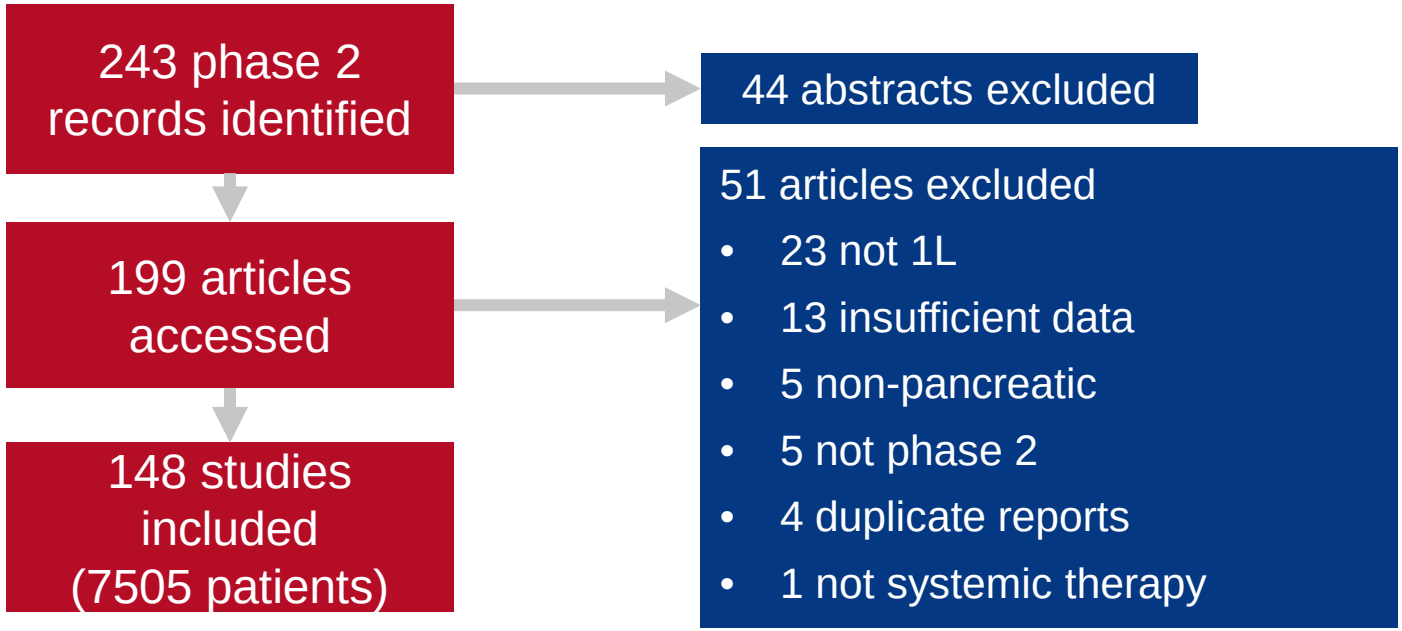
227: Correlation of phase 2 trials (Ph2t) results with outcomes of Phase 3 trials (Ph3t) of investigational agents (IA) in locally advanced and metastatic pancreas cancer (LAMPC) – Tang M, et al

Study objective

- To review phase 2 trials in advanced metastatic pancreatic cancer to identify characteristics associated with progression of phase 2 agents to phase 3 testing and to determine the correlation between outcomes of phase 2 and phase 3 trials

Methods

- Medline and clinicaltrials.gov were searched for phase 2 trials of 1L systemic treatment in advanced metastatic pancreatic cancer



Tang M, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 227

227: Correlation of phase 2 trials (Ph2t) results with outcomes of Phase 3 trials (Ph3t) of investigational agents (IA) in locally advanced and metastatic pancreas cancer (LAMPC) – Tang M, et al

Key results

- 148 phase 2 studies between 1978 and 2015 were identified
  - 7505 patients in 180 arms
  - 25 (16.9%) multi-arm trials
  - 18 (12.2%) randomised controlled trials
  - 37 (25%) trials tested biological agents
  - Limited reporting of prognostic factors
- Primary endpoint defined in 68.9% of trials
  - 41.2% ORR
  - 15.5% PFS
  - 10.1% OS
  - 2.0% Clinical benefit
- Phase 2 trial outcomes
  - 55.4% reported as successful by investigators
  - 26.4% specified and achieved target effect size
  - 14.9% proceeded to phase 3 testing

Tang M, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 227

227: Correlation of phase 2 trials (Ph2t) results with outcomes of Phase 3 trials (Ph3t) of investigational agents (IA) in locally advanced and metastatic pancreas cancer (LAMPC) – Tang M, et al

Key results (cont.)

Achievement of target effect size and relationship to phase 2 trial outcome and phase 3 testing

Pre-specified target effect size in phase 2 trial, n (%)	Investigator-determined phase 2 trial outcome		Actual phase 3 testing	
	Negative (n=66)	Positive (n=82)	No (n=126)	Yes (n=22)
Target effect size achieved	6 (9.1)	33 (40.2)	30 (23.8)	9 (40.9)
Target effect size not achieved	36 (54.6)	19 (23.2)	51 (40.5)	4 (18.2)
Target effect size not specified	21 (31.8)	27 (32.9)	40 (31.8)	8 (36.4)
Ambiguous target effect size	3 (4.6)	3 (3.7)	5 (4.0)	1 (4.6)

Tang M, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 227

227: Correlation of phase 2 trials (Ph2t) results with outcomes of Phase 3 trials (Ph3t) of investigational agents (IA) in locally advanced and metastatic pancreas cancer (LAMPC) – Tang M, et al

Key results (cont.)

Characteristics associated with progression to phase 3 testing

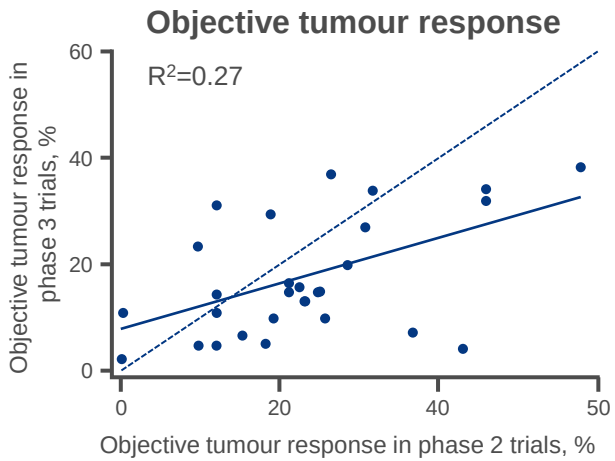
Characteristic, n (%)	No phase 3 testing	Phase 3 testing	p-value
Patients with ECOG PS 0–1	114 (78.9)	19 (84.7)	0.26
Patients with locally advanced cancer only	119 (16.2)	20 (22.0)	0.14
Mean sample size of phase 2 trial	126 (49.0)	22 (60.5)	0.19
Mean objective tumour response	126 (17.6)	22 (23.7)	0.05
Mean patient recruitment duration, months	101 (25.3)	19 (17.3)	0.03
Non-randomised design	111 (88.1)	19 (86.4)	0.82
Randomised design	15 (11.9)	3 (13.6)	
Target effect size not achieved or unspecified	96 (76.2)	13 (59.1)	0.10
Target effect size achieved	30 (23.8)	9 (40.9)	

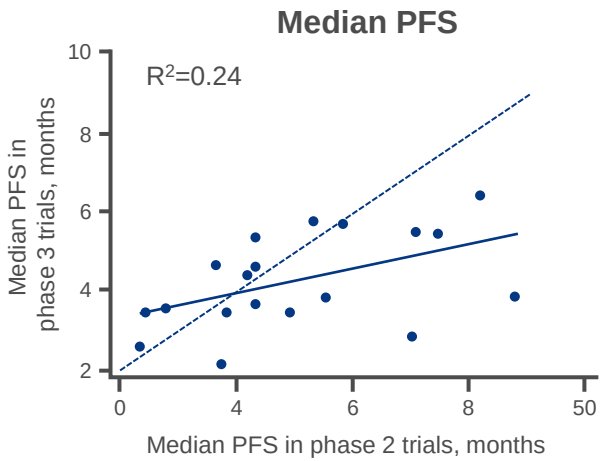
Tang M, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 227

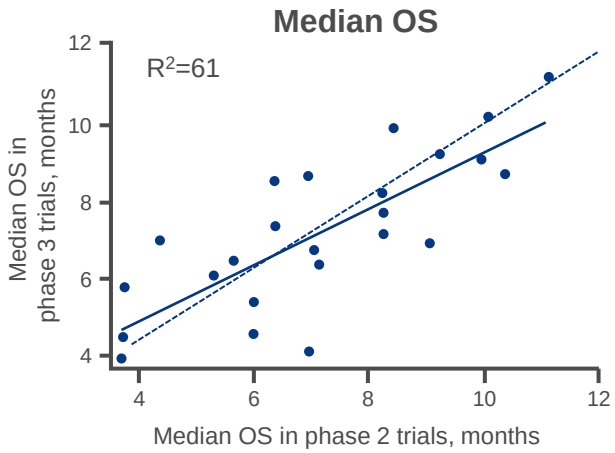
227: Correlation of phase 2 trials (Ph2t) results with outcomes of Phase 3 trials (Ph3t) of investigational agents (IA) in locally advanced and metastatic pancreas cancer (LAMPC) – Tang M, et al

Key results (cont.)

- 27 investigational agents tested in phase 2 and phase 3 trials







Tang M, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 227

227: Correlation of phase 2 trials (Ph2t) results with outcomes of Phase 3 trials (Ph3t) of investigational agents (IA) in locally advanced and metastatic pancreas cancer (LAMPC) – Tang M, et al

Conclusions

- **Advanced metastatic pancreatic phase 2 trials do not conform with NCI recommendations**
  - **Inconsistent prognostic factor reporting**
  - **Heterogeneity in baseline prognostic factors**
  - **Few trials enrich for biomarker targets**
  - **Poor statistical reporting in early trials**
  - **Investigator-reported success or progression to phase 3 does not correlate with achievement of statistical target effect size**
- **The limited success of trials in advanced metastatic pancreatic cancer may be explained by these findings**

Tang M, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 227

Cancers of the pancreas, small bowel and hepatobiliary tract

HEPATOCELLULAR CARCINOMA

223: A randomized phase II study of individualized stereotactic body radiation therapy (SBRT) versus transarterial chemoembolization (TACE) with DEBDOX beads as a bridge to transplant in hepatocellular carcinoma (HCC) – Nugent FW, et al

Study objective

- To compare stereotactic body radiation therapy (SBRT) to transarterial chemoembolisation (TACE) as a bridge to transplant in hepatocellular carcinoma

Key patient inclusion criteria

- Eligible for liver transplant
- Within Milan criteria
- ≤2 tumours
- Child-Pugh Class A/B (<9)
- Bilirubin <3.0 mg/dL
- Adequate haematological parameters

(n=30)

R

SBRT

Fiducial marker placement by IR, outpatient treatment every other day for 5 treatments, radiation dose determined to limit volume of treated liver and risk of complications, total dose 40–50 Gy in 5 fractions

(n=13)

TACE

2 treatments 1 month apart

DEBDOX® beads: 2 vial each treatment, max 100 mg doxorubicin/treatment

(n=17)

PRIMARY ENDPOINT

- Time to residual or recurrent disease

SECONDARY ENDPOINTS

- Toxicity, QoL, radiologic and pathologic response

Nugent FW, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 223

223: A randomized phase II study of individualized stereotactic body radiation therapy (SBRT) versus transarterial chemoembolization (TACE) with DEBDOX beads as a bridge to transplant in hepatocellular carcinoma (HCC) – Nugent FW, et al

Key results

Toxicity grade ≥2, n	SBRT Follow-up 2 weeks post-SBRT (n=13)	TACE Follow-up after TACE x2 (n=17)
Anorexia	0	5
Fatigue	0	6
Nausea	3	5
Pain	0	5
Main portal vein thrombus	0	1*
Liver infarction	0	1*

*After first TACE

Nugent FW, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 223

223: A randomized phase II study of individualized stereotactic body radiation therapy (SBRT) versus transarterial chemoembolization (TACE) with DEBDOX beads as a bridge to transplant in hepatocellular carcinoma (HCC) – Nugent FW, et al

Key results (cont.)

Quality of life

SF-36 questionnaire, change from baseline	SBRT (n=12)	TACE (n=17)
Physical	–0.7±7.4 (n=12) (95%CI –5.4, 4.1)	–2.7±4.3 (n=15) (95%CI –5.1, –0.3)
Mental	–0.6±9.0 (n=12) (95%CI –6.3, 5.1)	–2.6±4.6 (n=15) (95%CI –5.1, –0.0)

Nugent FW, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 223

223: A randomized phase II study of individualized stereotactic body radiation therapy (SBRT) versus transarterial chemoembolization (TACE) with DEBDOX beads as a bridge to transplant in hepatocellular carcinoma (HCC) – Nugent FW, et al

Key results (cont.)

Time to residual/recurrent disease

	SBRT (n=13)	TACE (n=17)
Patients with residual disease, n (%)	0	2 (24)
Time to residual disease from last treatment date, days	N/A	Median: 83 Range: 50–141

- Explant data
  - TACE: 6 transplanted, 3 with residual disease
  - SBRT: 5 transplanted, 2 with residual disease

Nugent FW, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 223

223: A randomized phase II study of individualized stereotactic body radiation therapy (SBRT) versus transarterial chemoembolization (TACE) with DEBDOX beads as a bridge to transplant in hepatocellular carcinoma (HCC) – Nugent FW, et al

Conclusions

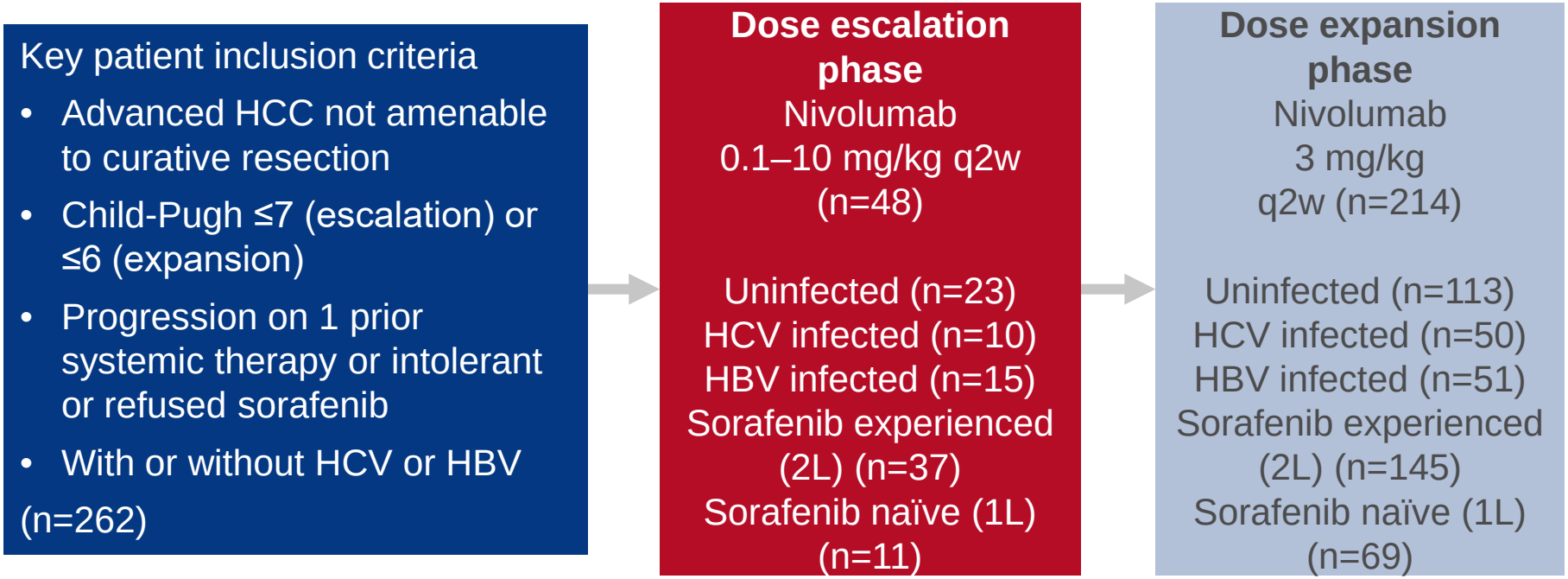
- When used as a bridge to transplant in Child-Pugh A/B patients, SBRT and TACE are equivalent in controlling the treated lesion
- SBRT may result in less acute toxicity and better QoL

Nugent FW, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 223

226: Nivolumab dose escalation and expansion in patients with advanced hepatocellular carcinoma (HCC): The CheckMate 040 study – Melero I, et al

Study objective

- To evaluate the safety, efficacy and exploratory biomarkers in patients with advanced HCC treated with nivolumab – updated interim results of the CheckMate 040 study



PRIMARY ENDPOINTS

- Safety and tolerability (dose escalation)
- ORR by RECIST v1.1 (dose expansion)

SECONDARY ENDPOINTS

- ORR, DCR, TTR, DoR, OS, biomarker, PROs

Melero I, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 226

226: Nivolumab dose escalation and expansion in patients with advanced hepatocellular carcinoma (HCC): The CheckMate 040 study – Melero I, et al

Key results

BOR in sorafenib experienced (2L), n (%)	Investigator assessment		BICR	
	Escalation (n=37)	Expansion (n=145)	Escalation (n=37)	Expansion (n=145)
Objective response by RECIST v1.1	6 (16.2)	27 (18.6)	7 (18.9)	21 (14.5)
CR	3 (8.1)	3 (2.1)	1 (2.7)	1 (0.7)
PR	3 (8.1)	24 (16.6)	6 (16.2)	20 (13.8)
SD	16 (43.2)	66 (45.5)	12 (32.4)	59 (40.7)
PD	12 (32.4)	46 (31.7)	13 (35.1)	56 (38.6)
Not evaluable	3 (8.1)	6 (4.1)	4 (10.8)	9 (6.2)
Objective response by mRECIST	–	–	8 (21.6)	27 (18.6)

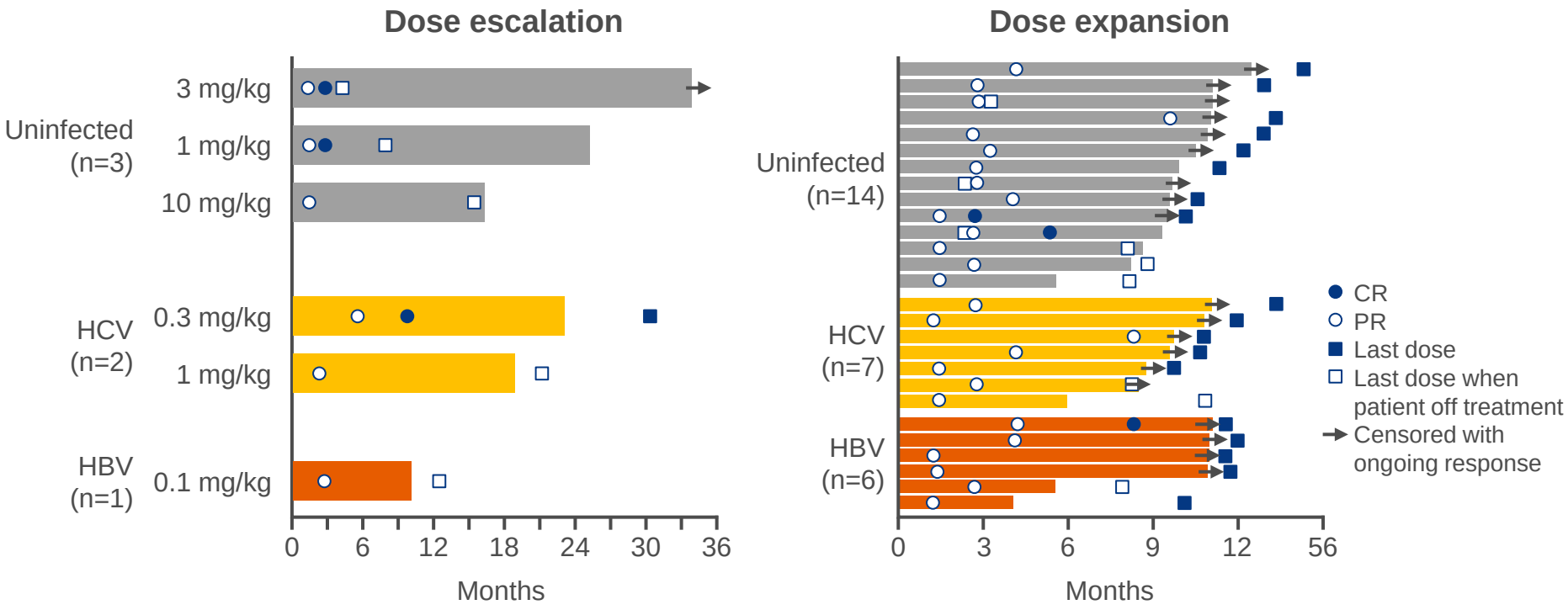
BOR in sorafenib naïve (1L), n (%)	Expansion (n=69)
Objective response	15 (21.7)
CR	0
PR	15 (21.7)
SD	30 (43.5)
PD	22 (31.9)
Not evaluable	2 (2.9)

Melero I, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 226

226: Nivolumab dose escalation and expansion in patients with advanced hepatocellular carcinoma (HCC): The CheckMate 040 study – Melero I, et al

Key results (cont.)

Time to response and duration of response in sorafenib-experienced patients (2L) by investigator assessment



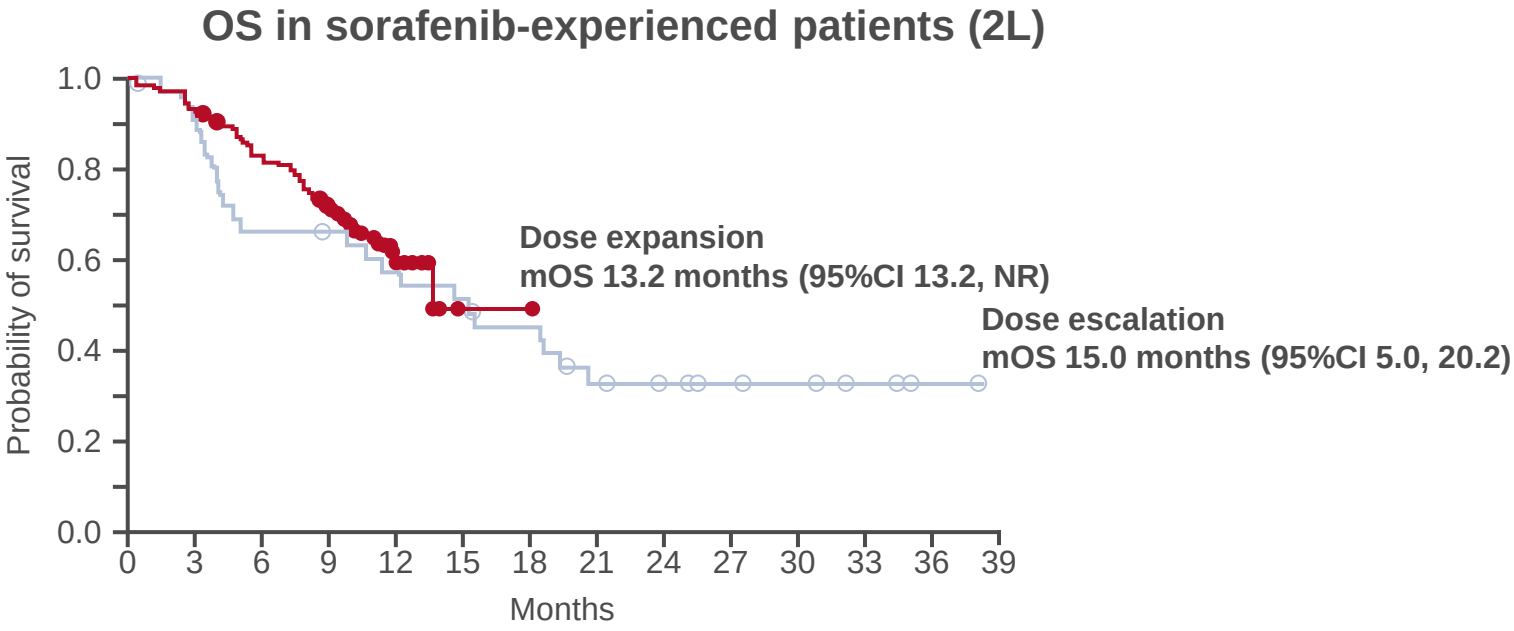
Median TTR, months (range)	1.9 (1.4–5.6)
Median DoR, months (range)	17.1 (7.2–32.5+)

Median TTR, months (range)	2.7 (1.2–9.6)
Median DoR, months (range)	NR (1.4–9.8+)

Melero I, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 226

226: Nivolumab dose escalation and expansion in patients with advanced hepatocellular carcinoma (HCC): The CheckMate 040 study – Melero I, et al

Key results (cont.)



OS rate, % (95%CI)	Dose escalation (n=37)	Dose expansion (n=145)
6 months	67 (49, 80)	82 (74, 87)
9 months	67 (49, 80)	71 (63, 78)[a]
12 months	58 (40, 72)	NC
18 months	46 (29, 62)	NC

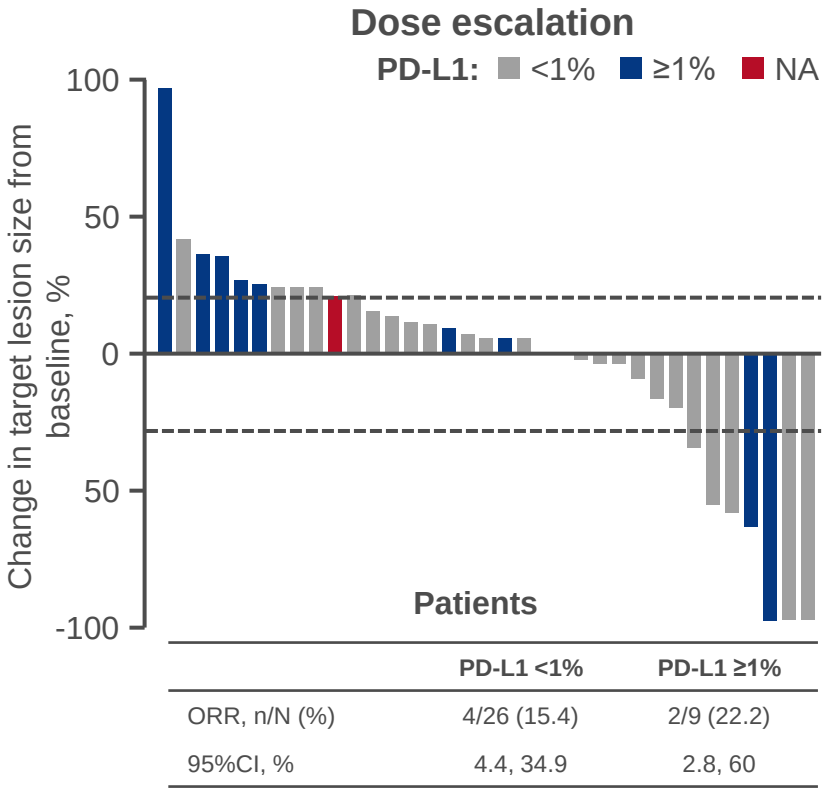
[a]Data cut-off August 8, 2016. NC, not available/not calculated

Melero I, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 226

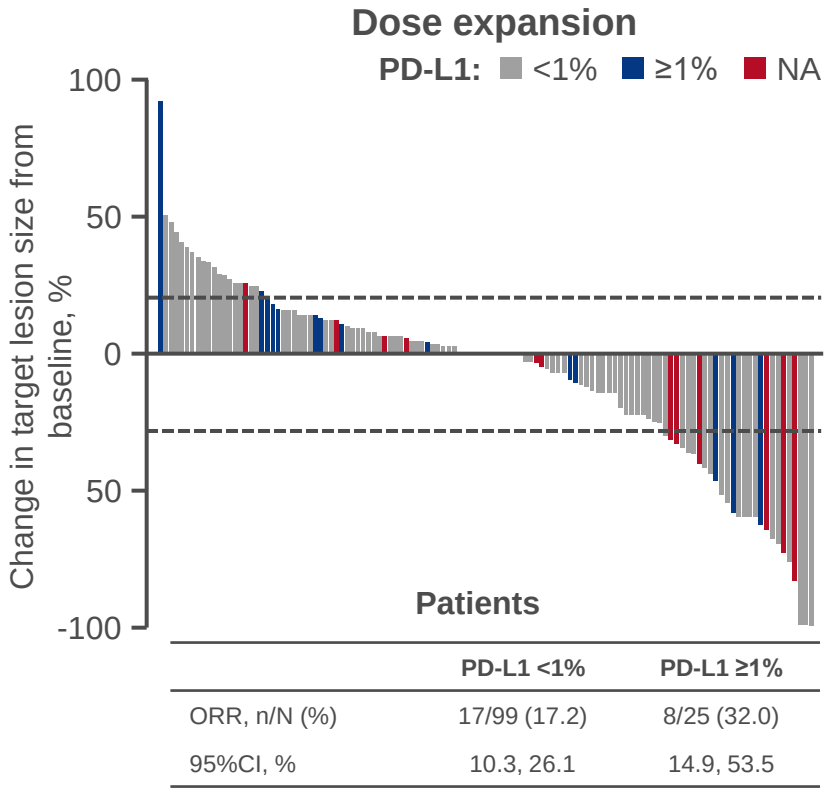
226: Nivolumab dose escalation and expansion in patients with advanced hepatocellular carcinoma (HCC): The CheckMate 040 study – Melero I, et al

Key results (cont.)

PD-L1 expression on tumour cells and response in sorafenib-experienced patients (2L)



	PD-L1 <1%	PD-L1 ≥1%
ORR, n/N (%)	4/26 (15.4)	2/9 (22.2)
95%CI, %	4.4, 34.9	2.8, 60



	PD-L1 <1%	PD-L1 ≥1%
ORR, n/N (%)	17/99 (17.2)	8/25 (32.0)
95%CI, %	10.3, 26.1	14.9, 53.5

- Responses were observed irrespective of PD-L1 expression on tumour cells

Melero I, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 226

226: Nivolumab dose escalation and expansion in patients with advanced hepatocellular carcinoma (HCC): The CheckMate 040 study – Melero I, et al

Key results (cont.)

Patients, n (%)	Uninfected (n=113)		HCV (n=50)		HBV (n=51)		All (n=214)	
	Any	Grade 3/4	Any	Grade 3/4	Any	Grade 3/4	Any	Grade 3/4
Any TRAE	84 (74)	22 (19)	40 (80)	15 (30)	35 (69)	3 (6)	159 (74)	40 (19)
TRAEs in ≥5%								
Fatigue	34 (30)	2 (2)	8 (16)	1 (2)	7 (14)	0	49 (23)	3 (1)
Pruritus	18 (16)	0	14 (28)	1 (2)	13 (25)	0	45 (21)	1 (<1)
Rash	16 (14)	2 (2)	9 (18)	0	8 (16)	0	33 (15)	2 (1)
Diarrhoea	19 (17)	2 (2)	5 (10)	0	3 (6)	1 (2)	27 (13)	3 (1)
Nausea	10 (9)	0	6 (12)	0	1 (2)	0	17 (8)	0
Dry mouth	9 (8)	0	2 (4)	0	2 (4)	0	13 (6)	0
Decreased appetite	6 (5)	0	2 (4)	1 (2)	3 (6)	0	11 (5)	1 (<1)
Laboratory TRAEs in ≥5%								
AST increased	9 (8)	4 (4)	6 (12)	5 (10)	1 (2)	0	16 (7)	9 (4)
ALT increased	7 (6)	2 (2)	7 (14)	3 (6)	3 (6)	0	17 (8)	5 (2)

Conclusion

- **Nivolumab monotherapy in sorafenib-experienced and -naïve patients advanced HCC demonstrated objective responses with no new safety signals**

Melero I, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 226

Cancers of the pancreas, small bowel and hepatobiliary tract

BILIARY TRACT CANCER

225: Gemox versus surveillance following surgery of localized biliary tract cancer: Results of the PRODIGE 12-ACCORD 18 (UNICANCER GI) phase III trial – Edeline J, et al

Study objective

- To assess the efficacy and safety of adjuvant GEMOX vs. surveillance 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
- Randomisation within 3 months of surgery

R 1:1

GEMOX
Gemcitabine 1000 mg/m^2 d1 +
oxaliplatin 85 mg/m^2 d2 (12 cycles)
(n=94)

Stratification

- Tumour site (ICC vs. ECC/Hilar vs. GBC)
- R0 vs. R1
- N0 vs. N+ vs. Nx
- Centres

Surveillance only
ACE, CA19-9 and computed tomography scans every 3 months for 2 years, then every 6 months for 3 years
(n=99)

PRIMARY ENDPOINTS

- Relapse-free survival, QoL

SECONDARY ENDPOINTS

- OS, DFS, toxicity

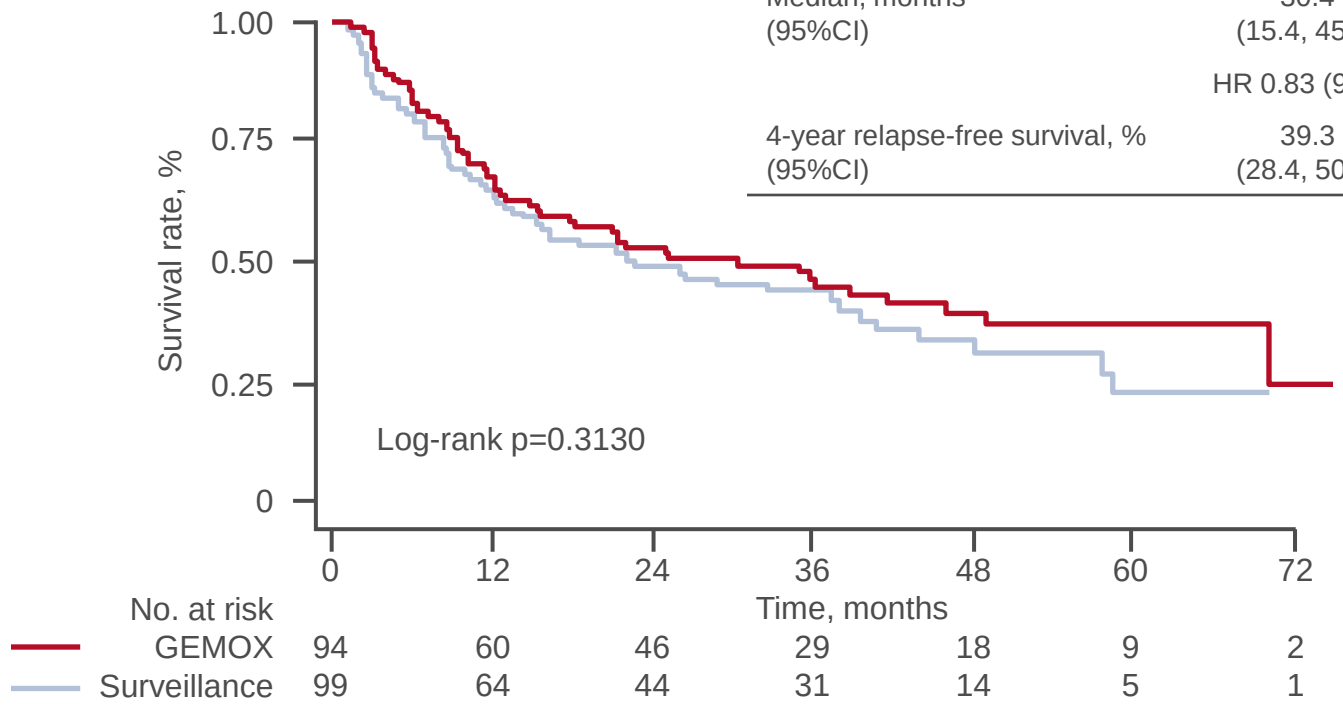
Edeline J, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 225

225: Gemox versus surveillance following surgery of localized biliary tract cancer: Results of the PRODIGE 12-ACCORD 18 (UNICANCER GI) phase III trial – Edeline J, et al

Key results

Relapse-free survival

Relapse-free survival	GEMOX	Surveillance
Median, months (95%CI)	30.4 (15.4, 45.8)	22.0 (13.6, 38.3)
	HR 0.83 (95%CI 0.58, 1.19); p=0.31	
4-year relapse-free survival, % (95%CI)	39.3 (28.4, 50.0)	33.2 (23.1, 43.7)

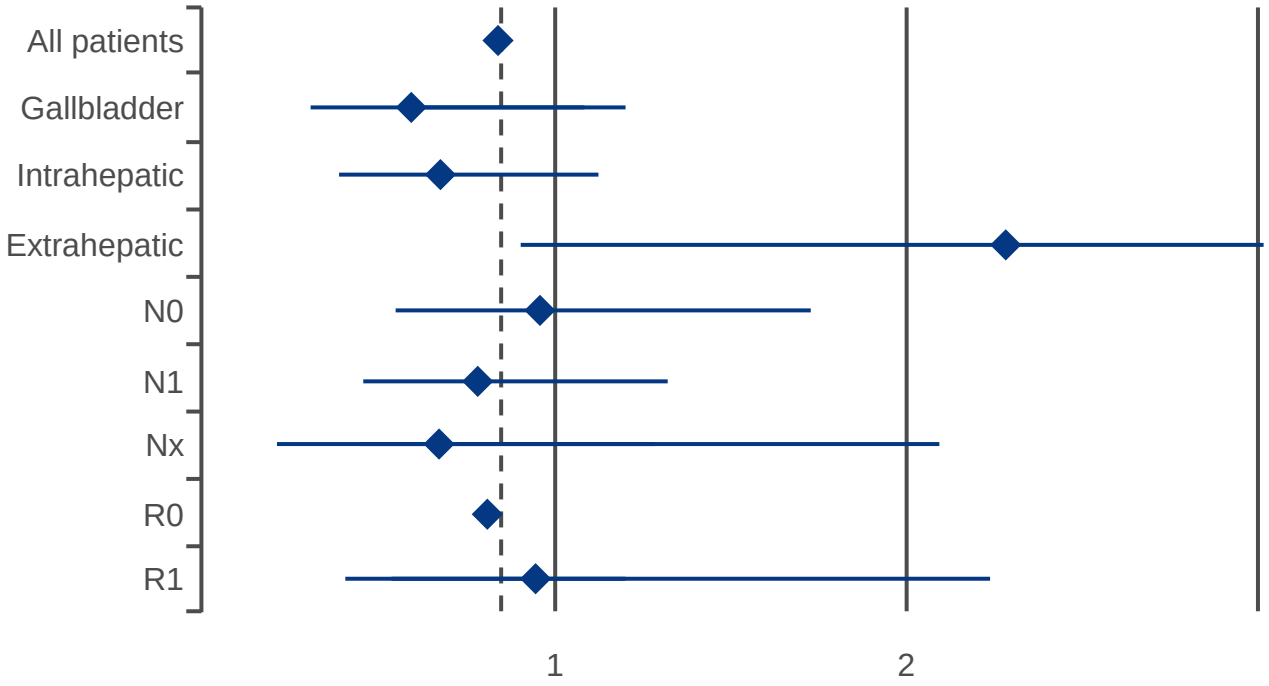


Edeline J, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 225

225: Gemox versus surveillance following surgery of localized biliary tract cancer: Results of the PRODIGE 12-ACCORD 18 (UNICANCER GI) phase III trial – Edeline J, et al

Key results (cont.)

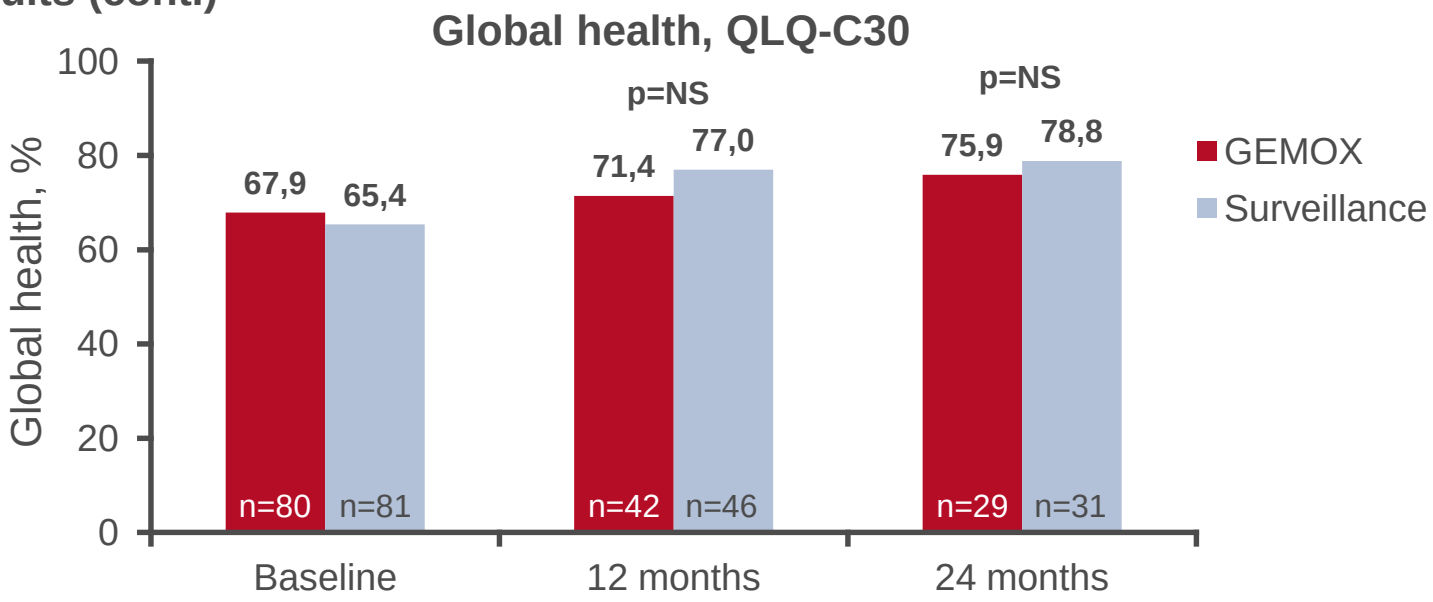
Relapse-free survival in predefined subgroups



Edeline J, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 225

225: Gemox versus surveillance following surgery of localized biliary tract cancer: Results of the PRODIGE 12-ACCORD 18 (UNICANCER GI) phase III trial – Edeline J, et al

Key results (cont.)



- The main grade 3/4 toxicities were GGT increase, alkaline phosphatase increase, peripheral sensitive neuropathy and neutrophils

Conclusions

- **Relapse-free survival did not differ between GEMOX and surveillance**
- **Adjuvant GEMOX had no detrimental effect on QoL; toxicity was as expected and manageable**

Edeline J, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 225

Cancers of the pancreas, small bowel and hepatobiliary tract

NEUROENDOCRINE TUMOUR

228: Phase II trial of cabozantinib in patients with carcinoid and pancreatic neuroendocrine tumors (pNET) – Chan JA, et al

Study objective

- To evaluate the efficacy and safety of cabozantinib in patients with advanced carcinoid or pancreatic NETs

Key patient inclusion criteria

- Well-differentiated, unresectable or metastatic grade 1–2 NETs
- Radiographic progression within 12 months of entry
- Cabozantinib or other anti-VEGF treatment naive
- Concurrent somatostatin allowed if stable dose for 2 months
- ECOG PS 0–1

(n=61)

PRIMARY ENDPOINT

- RECIST response rate

SECONDARY ENDPOINTS

- PFS, OS, safety and tolerability

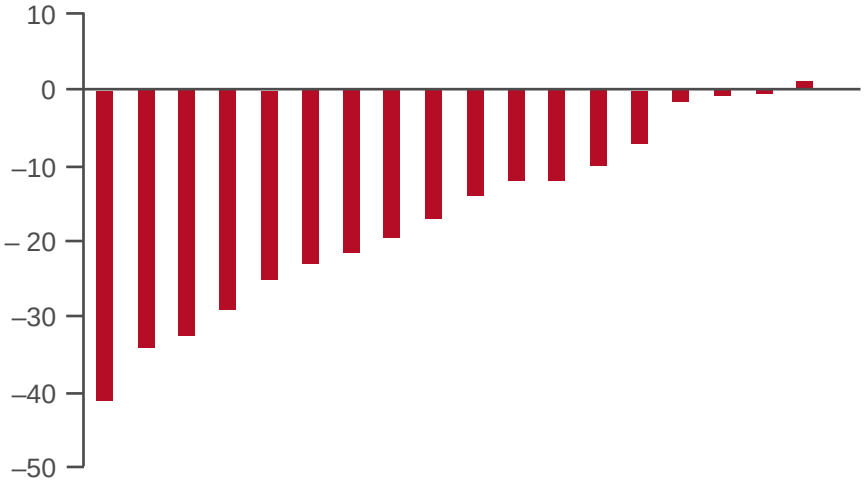
*28 day cycle, restaging every 2 cycles for the first 6 cycles, then every 3 cycles

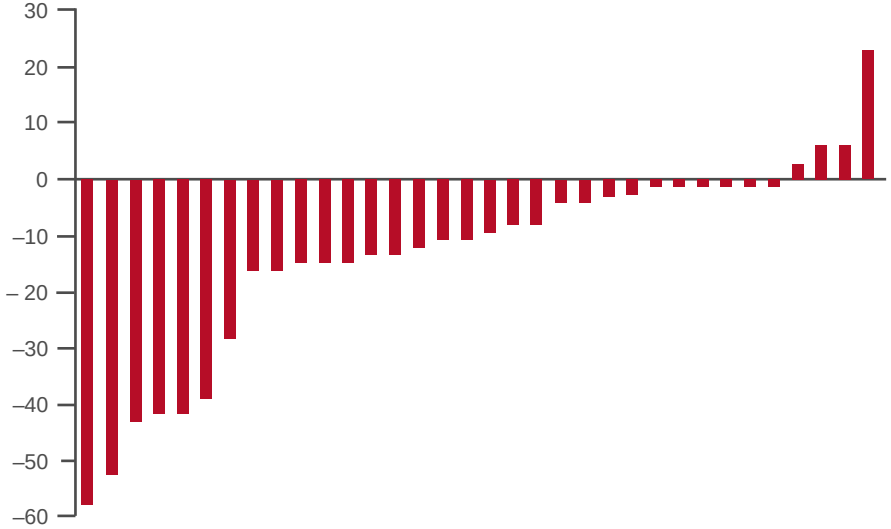
Chan JA, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 228

228: Phase II trial of cabozantinib in patients with carcinoid and pancreatic neuroendocrine tumors (pNET) – Chan JA, et al

Key results

RECIST response rate





Response, n (% [95%CI])	Pancreatic NET (n=20)	Carcinoid (n=41)
PR	3 (15 [5, 36])	6 (15 [7, 28])
SD	15 (75 [53, 89])	26 (63 [48, 76])
PD		2 (5 [1, 16])
Unknown	2 (10 [3, 30])	7* (17 [9, 31])

*Treatment stopped prior to restaging

Chan JA, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 228

228: Phase II trial of cabozantinib in patients with carcinoid and pancreatic neuroendocrine tumors (pNET) – Chan JA, et al

Key results (cont.)

Grade 3/4 TRAEs

Events occurring ≥5%, n (%)	Grade 3/4
Hypertension	8 (13)
Hypophosphatemia	7 (11)
Diarrhoea	6 (10)
Lipase or amylase increase	4 (7)
Lymphocyte decrease	4 (7)
Fatigue	3 (5)
Thrombocytopenia	3 (5)

Conclusions

- **Cabozantinib treatment of carcinoid and pancreatic NETs resulted in PRs of 15% in both groups, with mPFS of 31 months (carcinoid) and 22 months (pancreatic NETs)**
- **Toxicity was consistent with other studies**

Chan JA, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 228

224: Development of follow up recommendations for completely resected gastroenteropancreatic neuroendocrine tumours (GEP-NETS): Practice Survey of Commonwealth Neuroendocrine Tumour Collaboration (CommNETS) in conjunction with North American Neuroendocrine Tumour Society (NANETS) – Singh S, et al

Study objective

- To examine real-world practice patterns compared with published guidelines for follow-up in patients with gastroenteropancreatic neuroendocrine tumours (GEP-NETs)

Methods

- An electronic cross-sectional survey was developed and distributed to members of the Commonwealth Neuroendocrine Tumour Collaboration (CommNETS) and the North American Neuroendocrine Tumour Society (NANETS)
- Questions were regarding:
  - Demographics
  - Knowledge and use of guidelines
  - Follow-up practices according to various prognostic factors
- Descriptive statistics were reported, and results were stratified by country, patient volume and specialty

Key results

- There were 163 respondents:
  - 59 from Australia, 25 from New Zealand, 46 from Canada and 33 from US
  - 50% were medical oncologists, 23% were surgeons, 13% from nuclear medicine and 14% others

Note: Based on data from abstract only

Singh S, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 224

224: Development of follow up recommendations for completely resected gastroenteropancreatic neuroendocrine tumours (GEP-NETS): Practice Survey of Commonwealth Neuroendocrine Tumour Collaboration (CommNETS) in conjunction with North American Neuroendocrine Tumour Society (NANETS) – Singh S, et al

Key results (cont.)

- 38% responded that they were 'very familiar' with NET guidelines from NCCN; 33% for ENETS guidelines and 17% for ESMO guidelines
  - The NCCN, ENETS and ESMO guidelines were described as 'very useful' by 15%, 27% and 10% respondents, respectively
- 63% reported not using guidelines at their institution
- Grade and Ki67/mitotic count were considered the most important prognostic factors
- During the first 2 years of follow-up, every 6 months was the most common frequency (62%), for years 3–5 it was every 12 months (59%), and every 12 months was also the most common for >5 years (41%)
- The most common investigations were computed tomography scans (66%) and CgA (86%)
- When considering poor prognostic factors, an increase to the visits and tests were recommended

Conclusion

- **The results from this survey highlight the variation in follow-up practices in the real-world**

Note: Based on data from abstract only

Singh S, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 224

CANCERS OF THE COLON, RECTUM AND ANUS

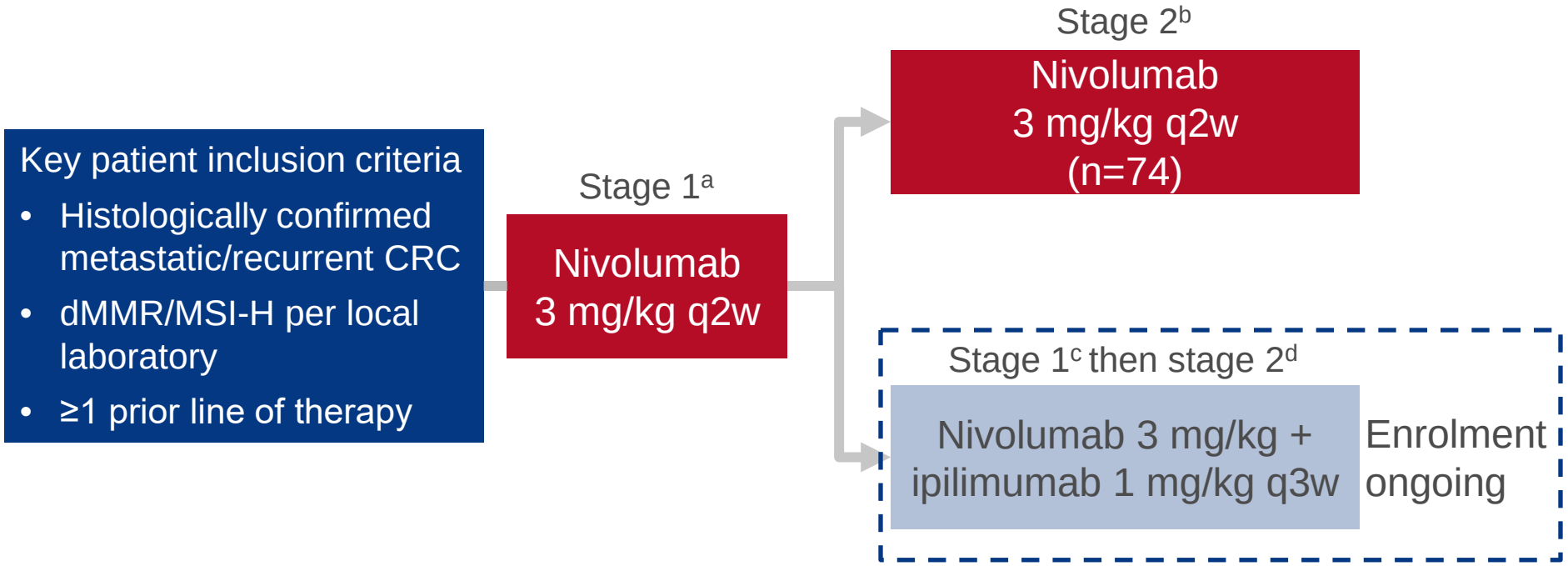
Cancers of the colon, rectum and anus

COLORECTAL CANCER

519: Nivolumab in patients with DNA mismatch repair deficient/microsatellite instability high metastatic colorectal cancer: Update from CheckMate 142 – Overman MJ, et al

Study objective

- To evaluate the efficacy and safety of nivolumab monotherapy in patients with metastatic/recurrent CRC in the CheckMate 142 study



PRIMARY ENDPOINT

- ORR per investigator assessment

[a]enrollment complete; [b]opened based on adequate ORR (CR + PR) treated in stage 1; [c]opened despite adequate ORR in stage 1; [d]opened based on adequate ORR in stage 1c

SECONDARY ENDPOINTS

- ORR per BICR
- PFS, OS, biomarkers, safety, PROs

Overman MJ, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 519

519: Nivolumab in patients with DNA mismatch repair deficient/microsatellite instability high metastatic colorectal cancer: Update from CheckMate 142 – Overman MJ, et al

Key results

Patients, n (%)	dMMR/MSI-H per local laboratory (n=74)		dMMR/MSI-H per central laboratory (n=53)	
	Investigator	BICR	Investigator	BICR
ORR	23 (31.1)	20 (27.0)	19 (35.8)	17 (32.1)
95%CI	20.8, 42.9	17.4, 38.6	23.1, 50.2	19.9, 46.3
Best overall response				
CR	0	2 (2.7)	0	1 (1.9)
PR	23 (31.1)	18 (24.3)	19 (35.8)	16 (30.2)
SD	29 (39.2)	28 (37.8)	21 (39.6)	21 (39.6)
PD	18 (24.3)	20 (27.0)	10 (18.9)	12 (22.6)
Unable to determine	4 (5.4)	6 (11.1)	3 (5.7)	3 (5.7)
Disease control for ≥12 weeks	51 (68.9)	46 (62.2)	39 (73.6)	37 (69.8)

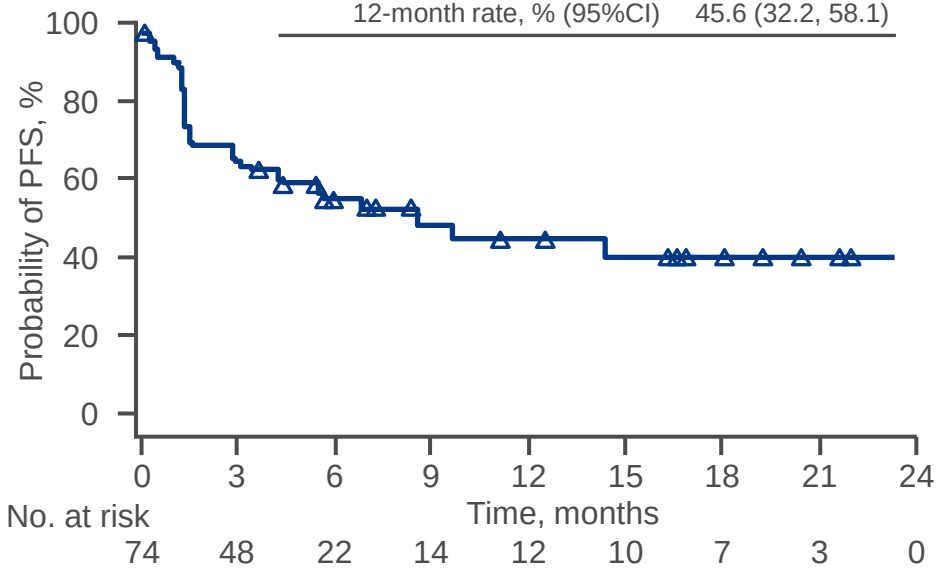
Overman MJ, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 519

519: Nivolumab in patients with DNA mismatch repair deficient/microsatellite instability high metastatic colorectal cancer: Update from CheckMate 142 – Overman MJ, et al

Key results (cont.)

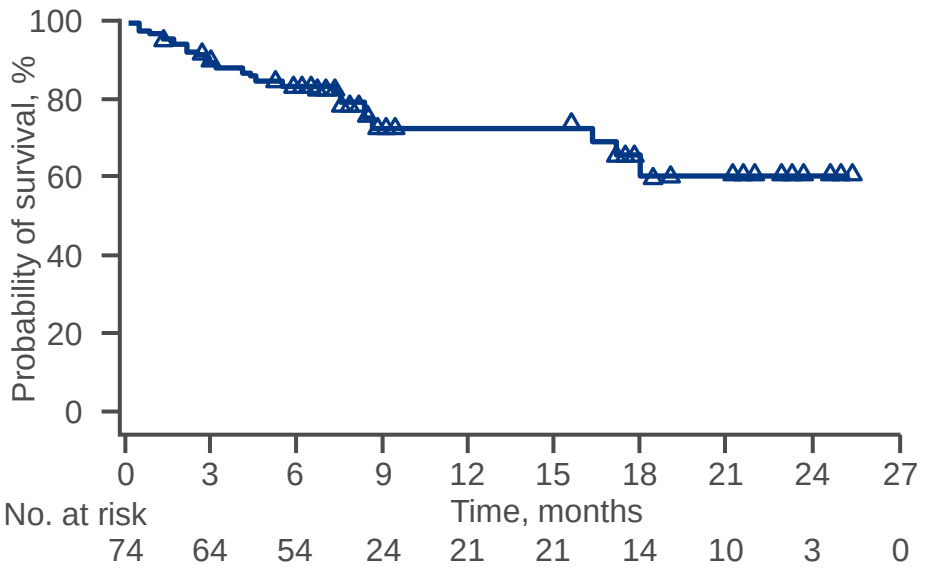
PFS

PFS per investigator	
mPFS, months (95%CI)	9.6 (4.3, NE)
12-month rate, % (95%CI)	48.4 (33.6, 61.7)
PFS per BICR	
12-month rate, % (95%CI)	45.6 (32.2, 58.1)



OS

mOS, months (95%CI)	NR (17.1, NE)
12-month OS rate, % (95%CI)	73.8 (59.8, 83.5)

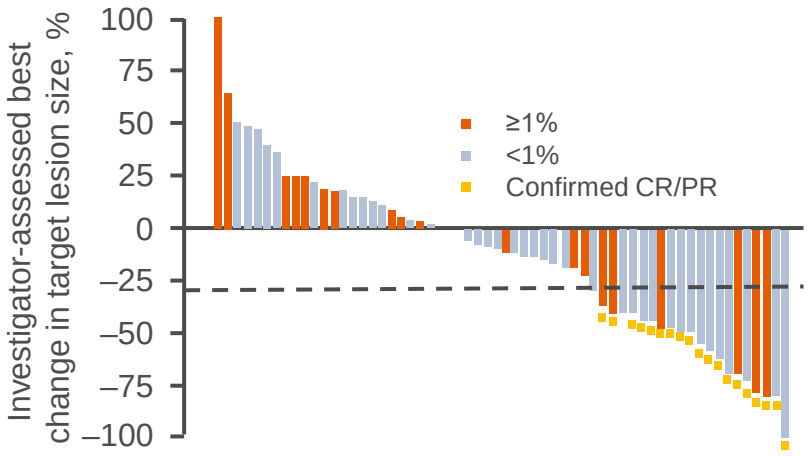


Overman MJ, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 519

519: Nivolumab in patients with DNA mismatch repair deficient/microsatellite instability high metastatic colorectal cancer: Update from CheckMate 142 – Overman MJ, et al

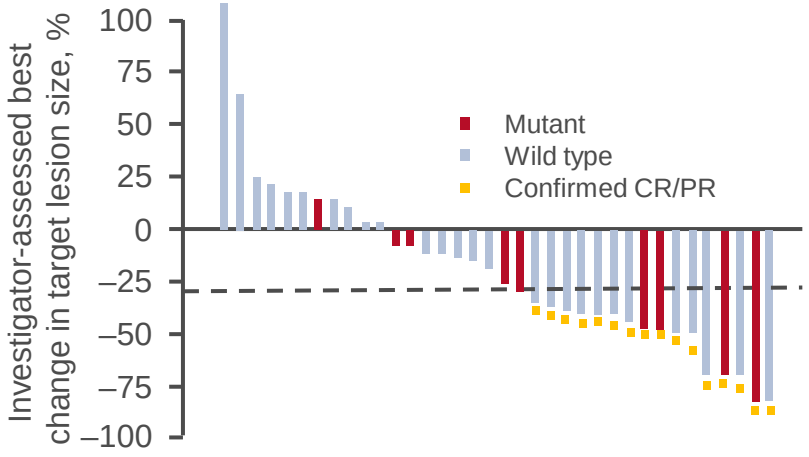
Key results (cont.)

Tumour PD-L1 expression



ORR, n/N (%)	Investigator	BICR
Tumour PD-L1 expression		
≥1%	6/21 (28.6)	7/20 (35.0)
<1%	13/45 (28.9)	11/45 (24.4)

BRAF mutation status



ORR, n/N (%)	Investigator	BICR
BRAF mutation status		
Mutant	3/12 (25.0)	2/12 (16.7)
Wild type	12/28 (42.9)	9/27 (33.3)
KRAS mutation status		
Mutant	7/26 (26.9)	6/26 (23.1)
Wild type	12/28 (42.9)	9/27 (33.3)

Overman MJ, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 519

519: Nivolumab in patients with DNA mismatch repair deficient/microsatellite instability high metastatic colorectal cancer: Update from CheckMate 142 – Overman MJ, et al

Key results (cont.)

Patients, n (%)	All patients (n=74)	
	Any grade	Grade 3–4
Any TRAE	51* (68.9)	15 (20.3)
TRAE reported in ≥10% of patients		
Fatigue	17 (23.0)	1 (1.4)
Diarrhoea	16 (21.6)	1 (1.4)
Pruritus	10 (13.5)	0
Lipase increased	9 (12.2)	6 (8.1)
Rash	8 (10.8)	0

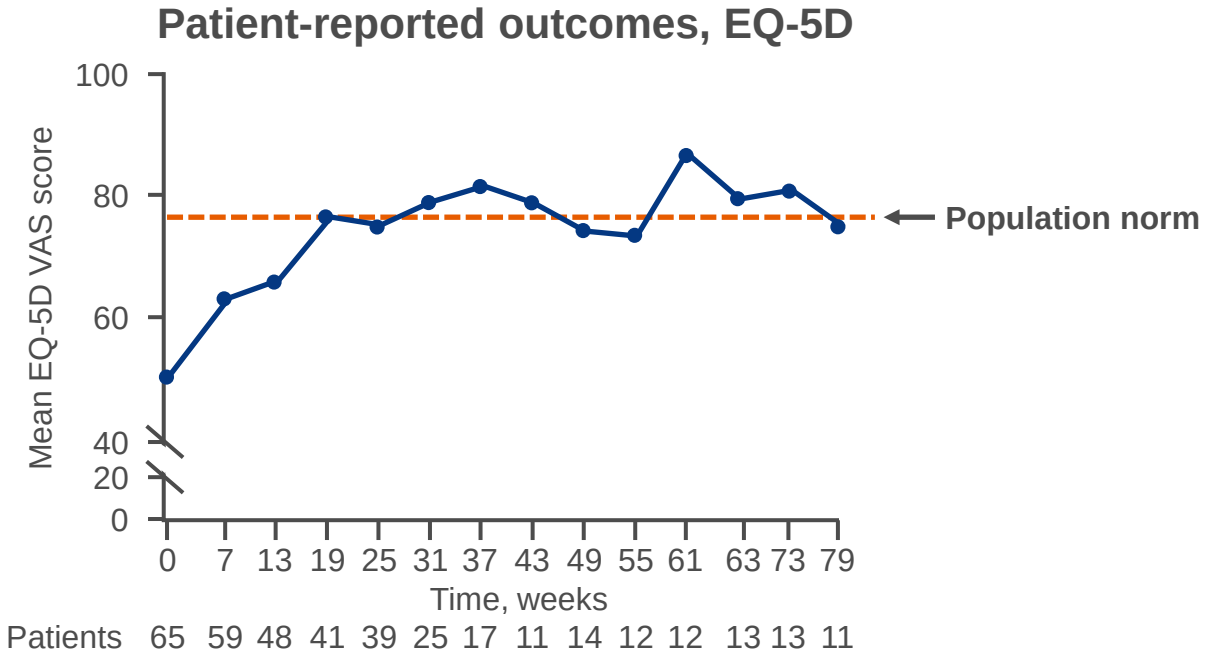
- Five (6.8%) patients discontinued therapy due to adverse events
- No deaths were reported due to study drug toxicity

*One grade 5 event of sudden death, not attributed to study drug toxicity

Overman MJ, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 519

519: Nivolumab in patients with DNA mismatch repair deficient/microsatellite instability high metastatic colorectal cancer: Update from CheckMate 142 – Overman MJ, et al

Key results (cont.)



Conclusion

- **Monotherapy with nivolumab in patients with dMMR/MSI-H mCRC provided durable responses and long-term survival, with clinically meaningful improvements in QoL and a safety profile consistent with that previously reported**

Overman MJ, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 519

520: Randomized trial of irinotecan and cetuximab with or without vemurafenib in *BRAF*-mutant metastatic colorectal cancer (SWOG 1406) – Kopetz S, et al

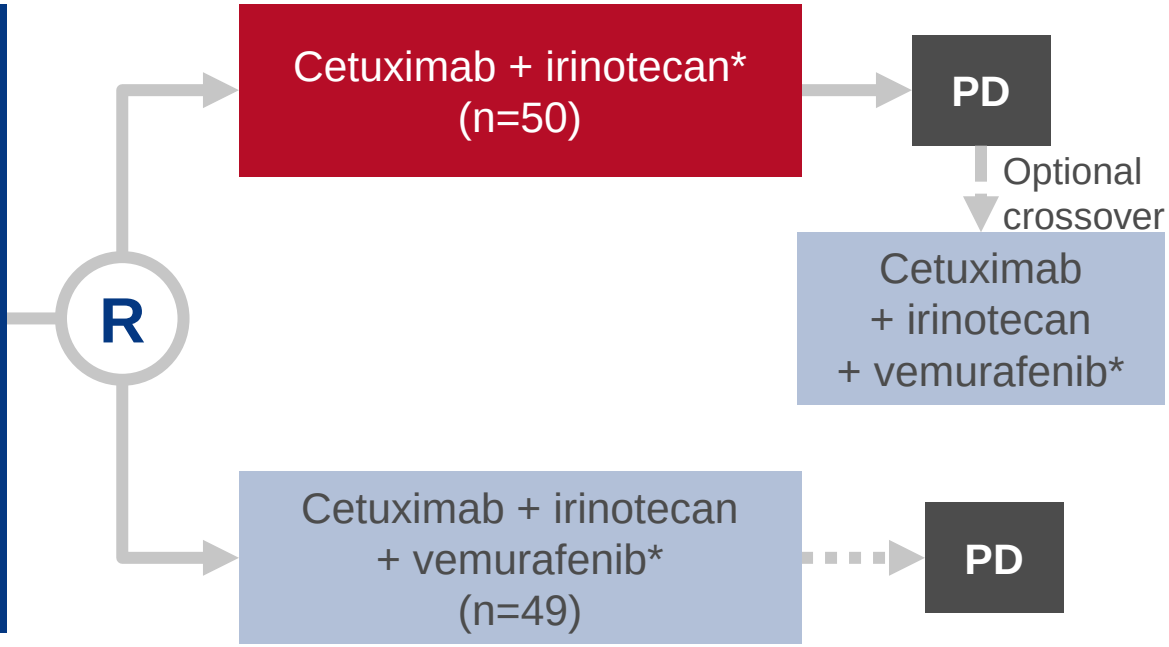
Study objective

- To assess the efficacy and safety of cetuximab + irinotecan + vemurafenib in patients with BRAF-mutant mCRC

Key patient inclusion criteria

- Metastatic adenocarcinoma of the colon or rectum
- BRAF V600E mutation
- Extended RAS wild type
- PS 0–1
- 1–2 prior systemic chemotherapy for metastatic or locally advanced disease

(n=106)



PRIMARY ENDPOINT(S)

- PFS

SECONDARY ENDPOINTS

- OS, ORR, toxicity

*Cetuximab 500 mg/m^2 iv q2w, irinotecan 180 mg/m^2 iv q2w, vemurafenib 960 mg po bid

Kopetz S, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 520

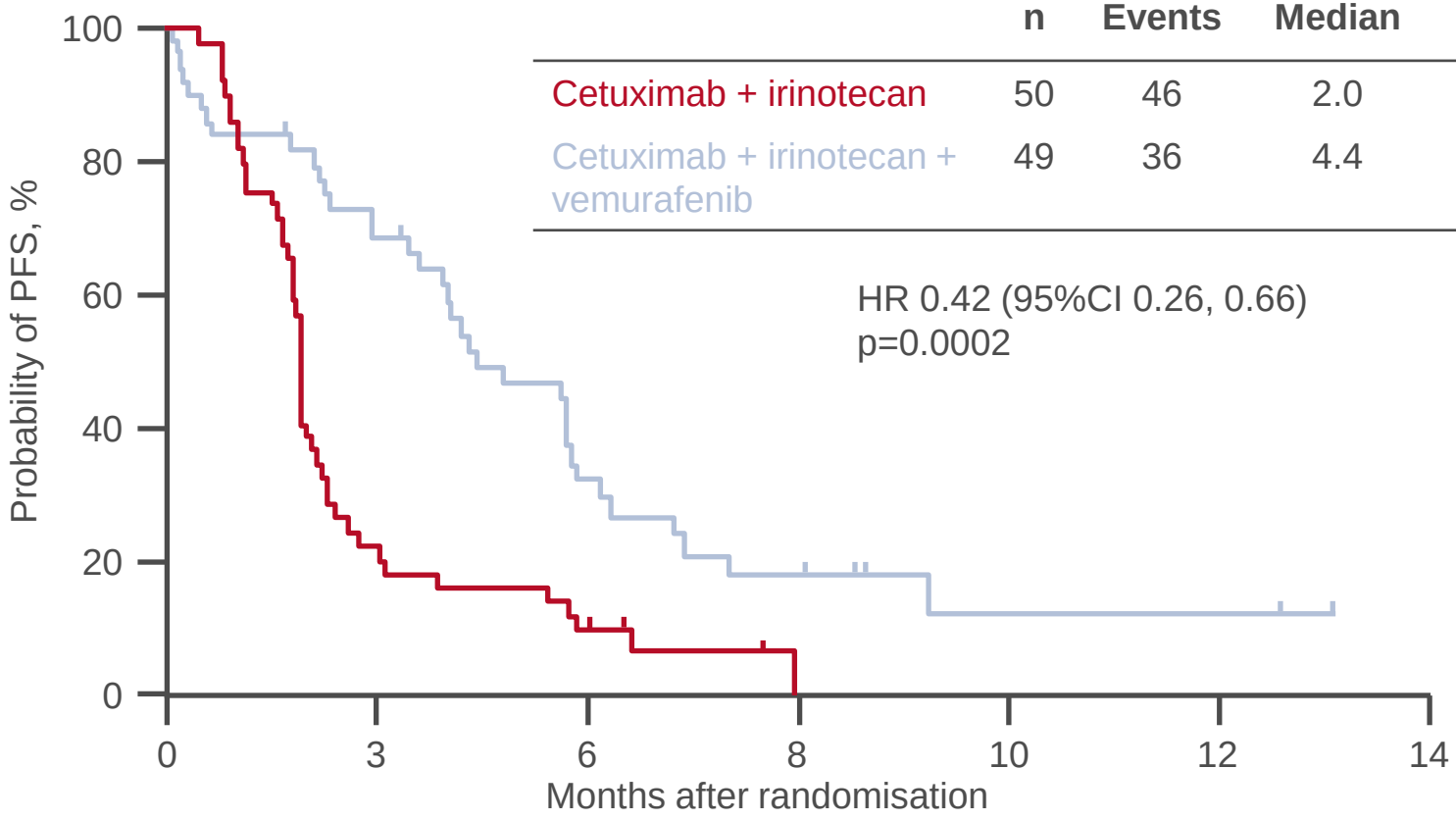
520: Randomized trial of irinotecan and cetuximab with or without vemurafenib in *BRAF*-mutant metastatic colorectal cancer (SWOG 1406) – Kopetz S, et al

Key results

PFS

	n	Events	Median	95%CI
Cetuximab + irinotecan	50	46	2.0	1.8, 2.1
Cetuximab + irinotecan + vemurafenib	49	36	4.4	3.6, 5.7

HR 0.42 (95%CI 0.26, 0.66)
p=0.0002



Kopetz S, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 520

520: Randomized trial of irinotecan and cetuximab with or without vemurafenib in *BRAF*-mutant metastatic colorectal cancer (SWOG 1406) – Kopetz S, et al

Key results (cont.)

Grade 3/4 AEs

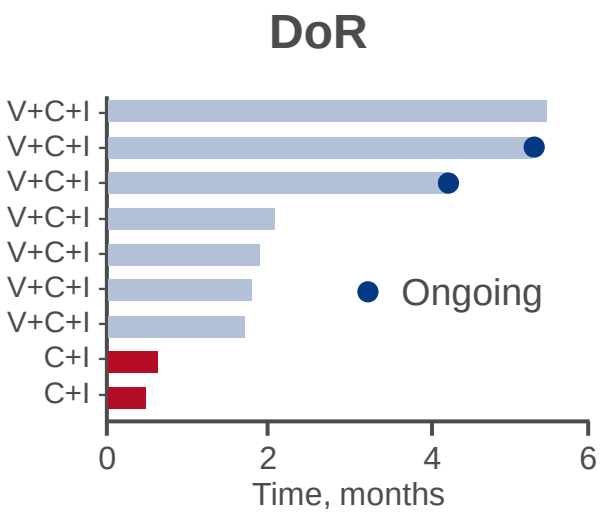
Patients, n (%)	Cetuximab + irinotecan (n=46)	Cetuximab + irinotecan + vemurafenib (n=46)
Anaemia	0 (0)	6 (13)
Dehydration	2 (4)	5 (11)
Diarrhoea	5 (11)	10 (22)
Febrile neutropenia	2 (4)	5 (11)
Fatigue	7 (15)	7 (15)
Neutropenia	3 (7)	13 (28)
Rash	3 (7)	2 (4)
Hypomagnesemia	2 (4)	0 (0)
Nausea	0 (0)	7 (15)
Arthralgia	0 (0)	3 (7)
Discontinued due to AE	4/50 (8)	9/49 (18)

Kopetz S, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 520

520: Randomized trial of irinotecan and cetuximab with or without vemurafenib in *BRAF*-mutant metastatic colorectal cancer (SWOG 1406) – Kopetz S, et al

Key results (cont.)

Patients, %	Cetuximab + irinotecan (n=46)	Cetuximab + irinotecan + vemurafenib (n=46)	p-value
PR	4	16	0.001
SD	17	48	
PD	56	12	
DCR	22	67	



Conclusions

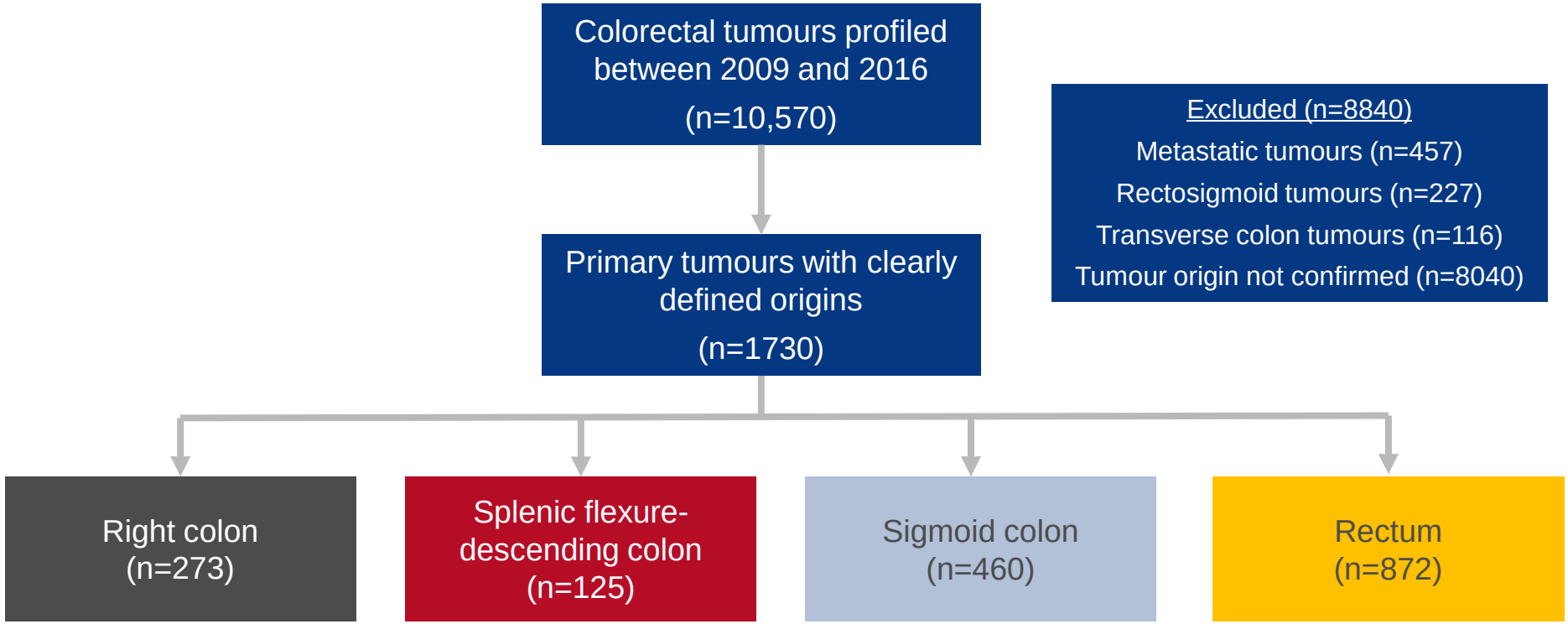
- **In patients with BRAF mutant CRC, cetuximab + irinotecan + vemurafenib improved PFS**
- **Neutropenia, anaemia and nausea were the notable toxicities and are similar to a previous study**

Kopetz S, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 520

522: Molecular variances between rectal and left-sided colon cancers – Marshall J, et al

Study objective

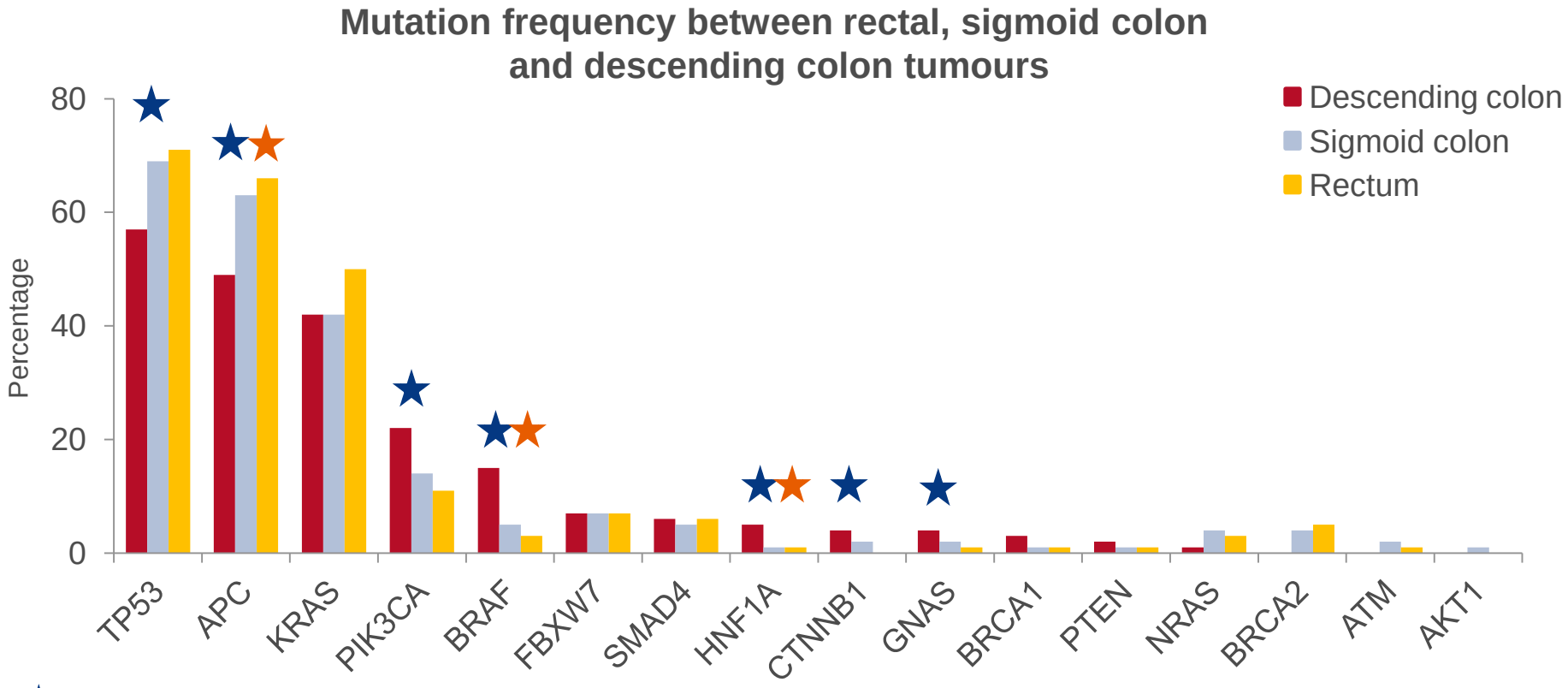
- Retrospective analysis to identify the molecular variations among left-sided CRC tumours (rectal, sigmoid colon and descending colon including splenic flexure)



Marshall J, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 522

522: Molecular variances between rectal and left-sided colon cancers – Marshall J, et al

Key results



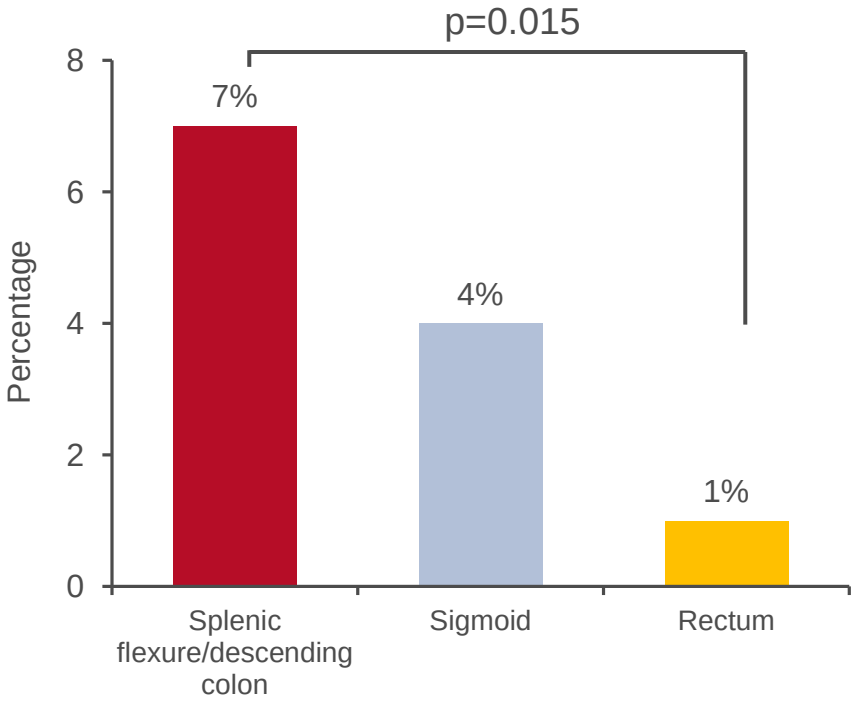
★ Significant difference between rectal and descending colon tumours ($p<0.05$)
★ Significant difference between sigmoid colon and descending colon tumours ($p<0.05$)
No significant differences between rectal and sigmoid colon tumours

Marshall J, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 522

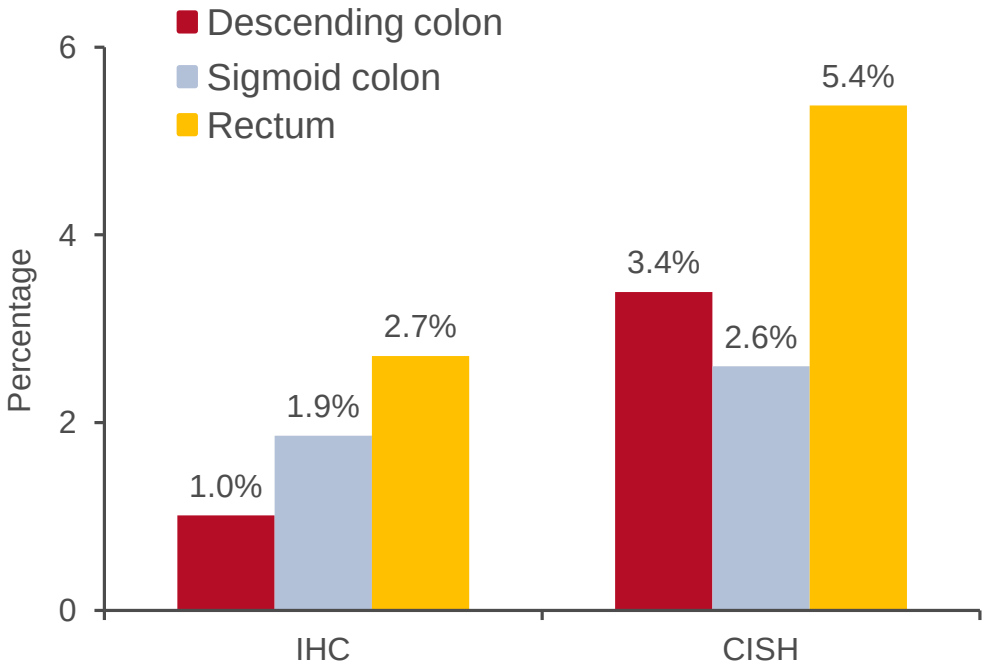
522: Molecular variances between rectal and left-sided colon cancers – Marshall J, et al

Key results (cont.)

Frequency of microsatellite instability



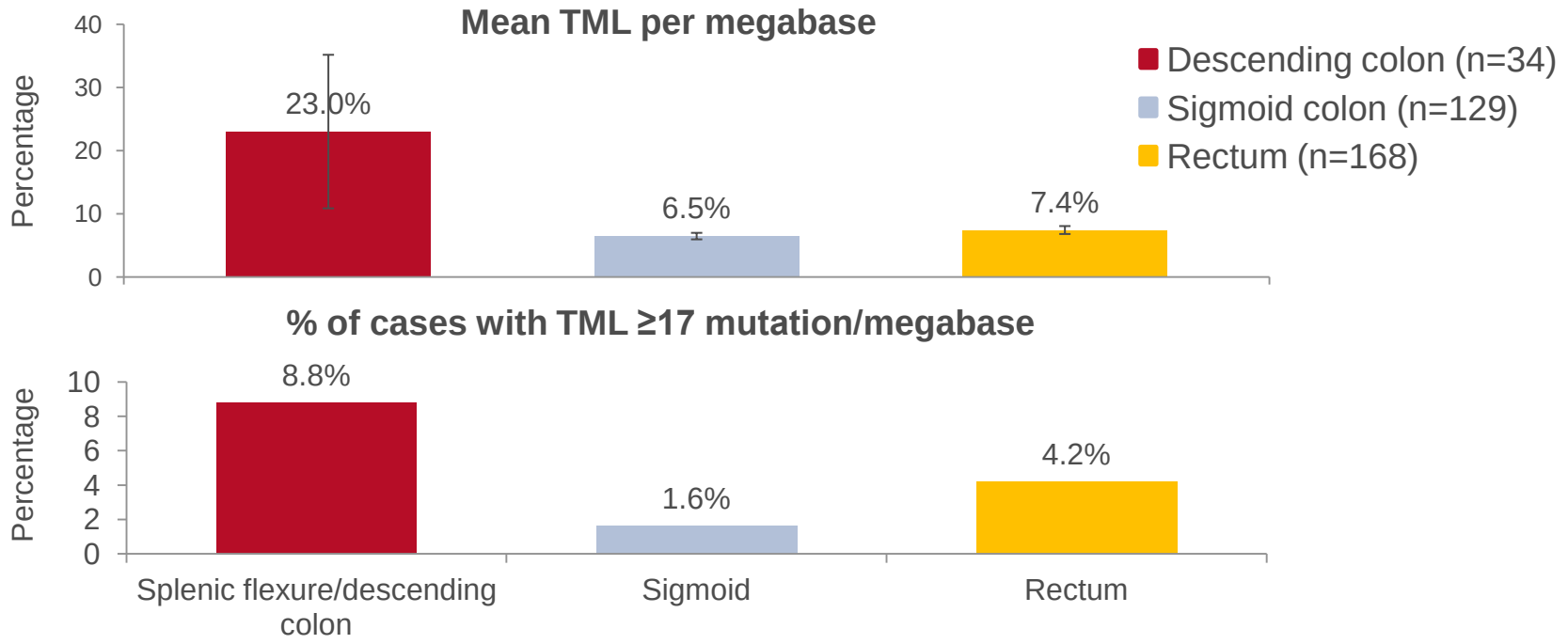
HER2/Neu: overexpression and amplification



Marshall J, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 522

522: Molecular variances between rectal and left-sided colon cancers – Marshall J, et al

Key results (cont.)



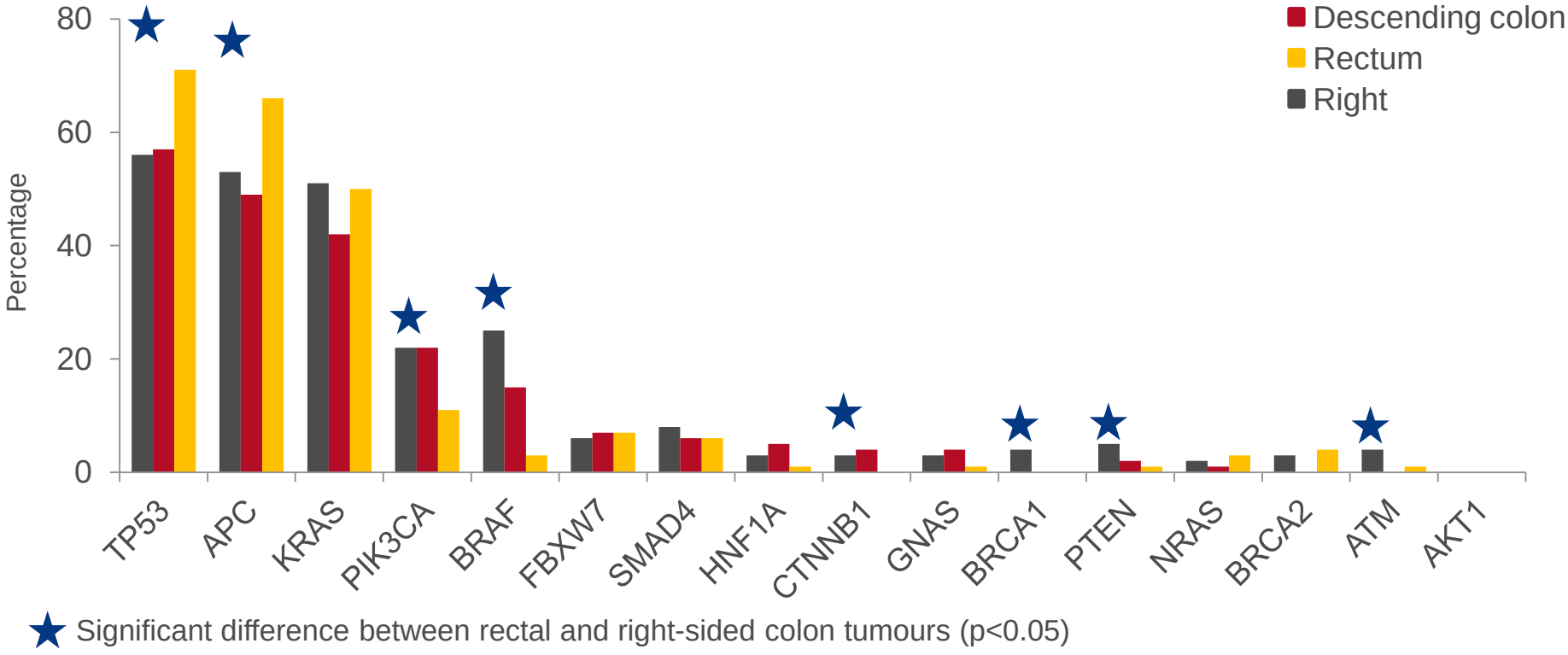
- TML was calculated using only somatic non-synonymous missense mutations sequenced with a 592-gene panel
- No significant difference was seen between the three cohorts

Marshall J, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 522

522: Molecular variances between rectal and left-sided colon cancers – Marshall J, et al

Key results (cont.)

Mutation frequency comparison between rectal and right-sided colon cancers



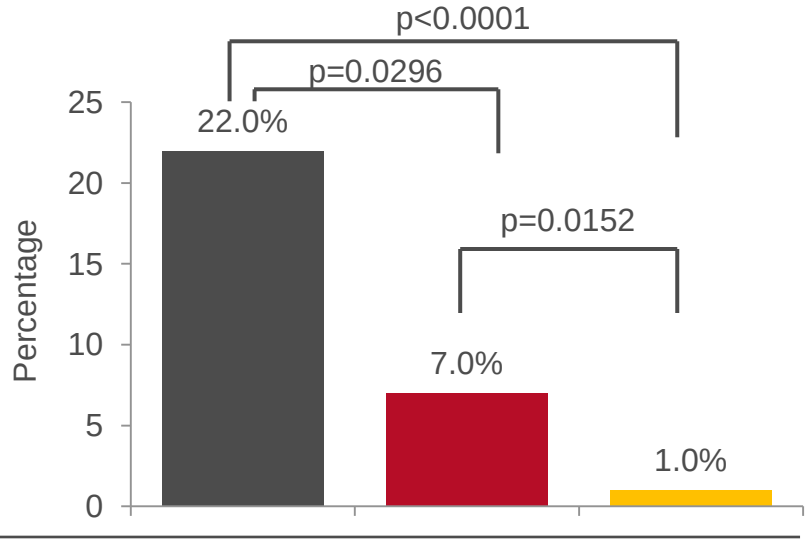
★ Significant difference between rectal and right-sided colon tumours ($p<0.05$)

Marshall J, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 522

522: Molecular variances between rectal and left-sided colon cancers – Marshall J, et al

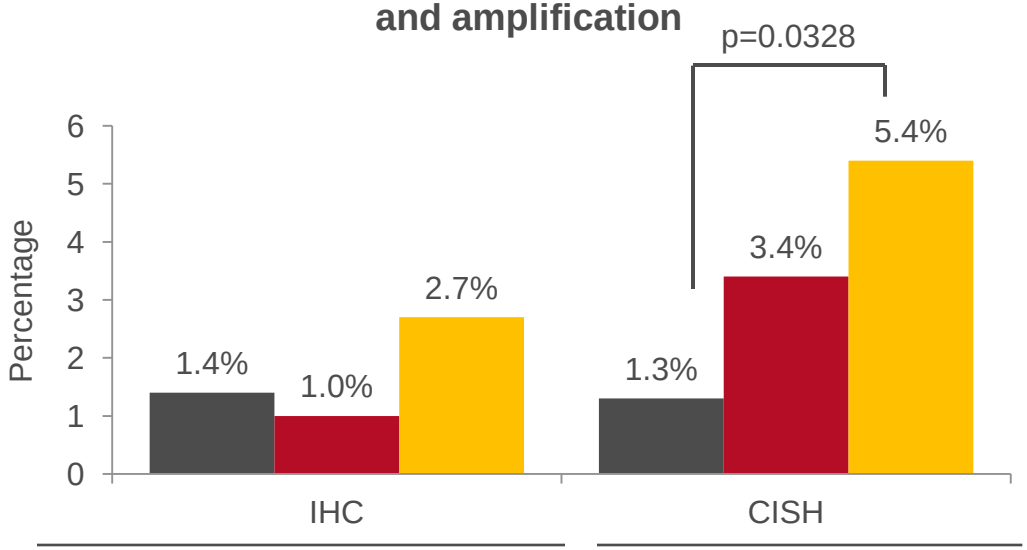
Key results (cont.)

Frequency of microsatellite instability



	Right colon (n=112)	Descending (n=42)	Rectum (n=134)
Deficient	25	3	1
Proficient	87	39	133

HER2/Neu: overexpression and amplification



HER2/ Neu	Right colon (n=221)	Descending (n=99)	Rectum (n=590)	Right colon (n=158)	Descending (n=59)	Rectum (n=279)
Positive	3	1	16	2	2	15
Negative	218	98	574	156	57	264

Conclusions

- There is a continuum of molecular alterations from left to right in CRC
- Molecular features in rectal cancers are different from those in left-sided colon tumours

Marshall J, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 522

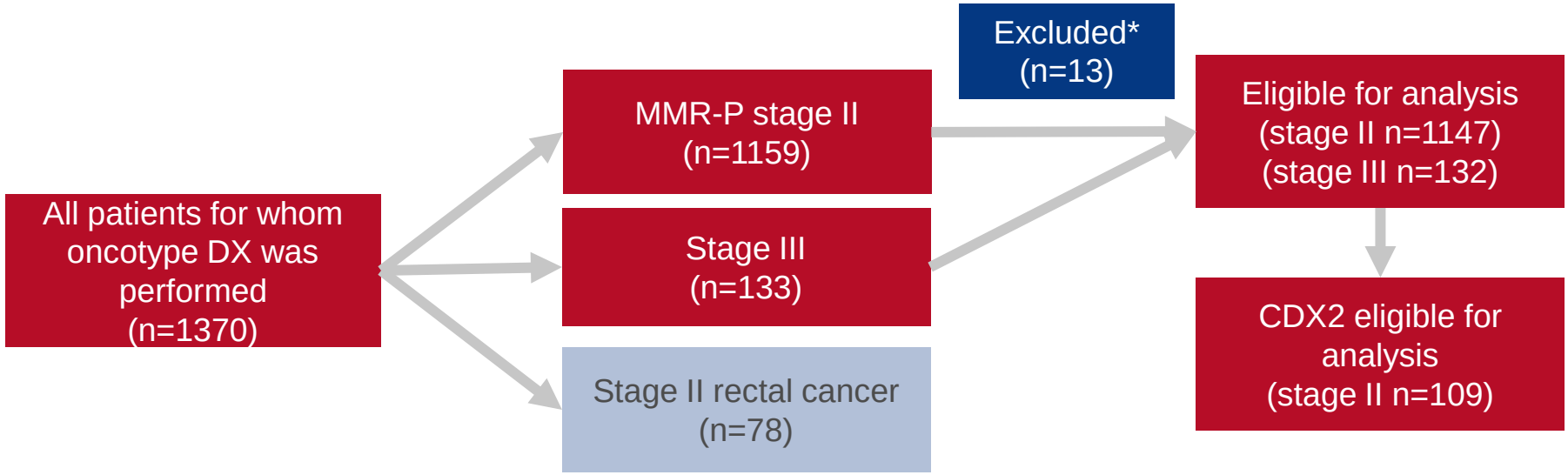
523: Sidedness matters: Surrogate biomarkers prognosticate colorectal cancer upon anatomic location – Ben-Aharon I, et al

Study objective

- To evaluate whether the 12-gene oncotype DX score and/or CDX2 status correlate with primary tumour location, and whether location reflects differential prognosis in stage II and stage III CRC

Methods

- Retrospective analysis of patients with T3 MMR-P stage II CRC for whom the 12-gene assay was performed, and a subgroup of patients with stage III CRC
- CDX2 expression reviewed in those diagnosed in 2016



*Pathological report not available

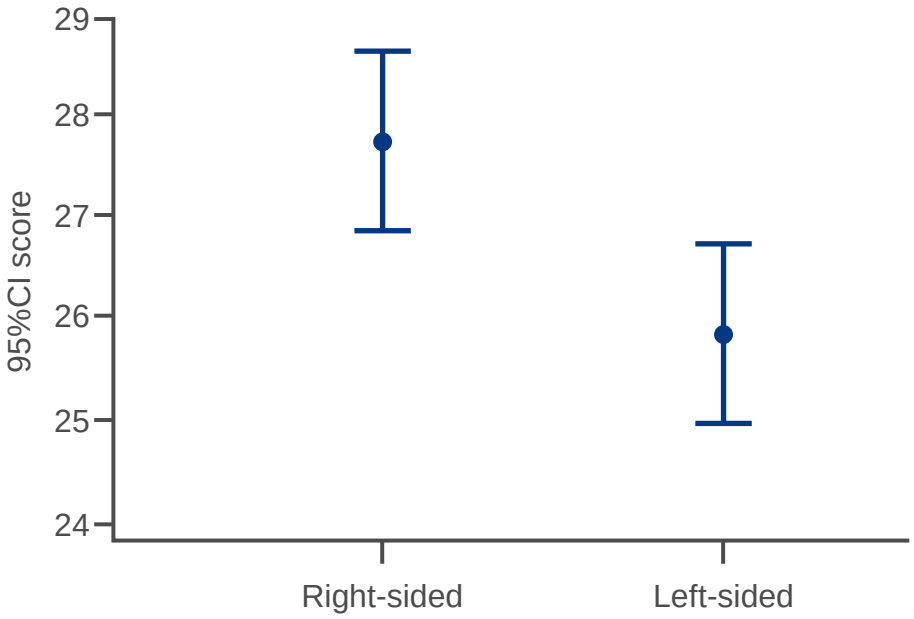
Ben-Aharon I, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 523

523: Sidedness matters: Surrogate biomarkers prognosticate colorectal cancer upon anatomic location – Ben-Aharon I, et al

Key results

- In stage II tumours, recurrence score was higher in right-sided tumours

	n (%)	Mean score (range)
Right-sided	551 (48.03)	27.72 (6–71)
Left-sided	596 (51.97)	25.79 (6–54)
Total	1147 (100)	p=0.002



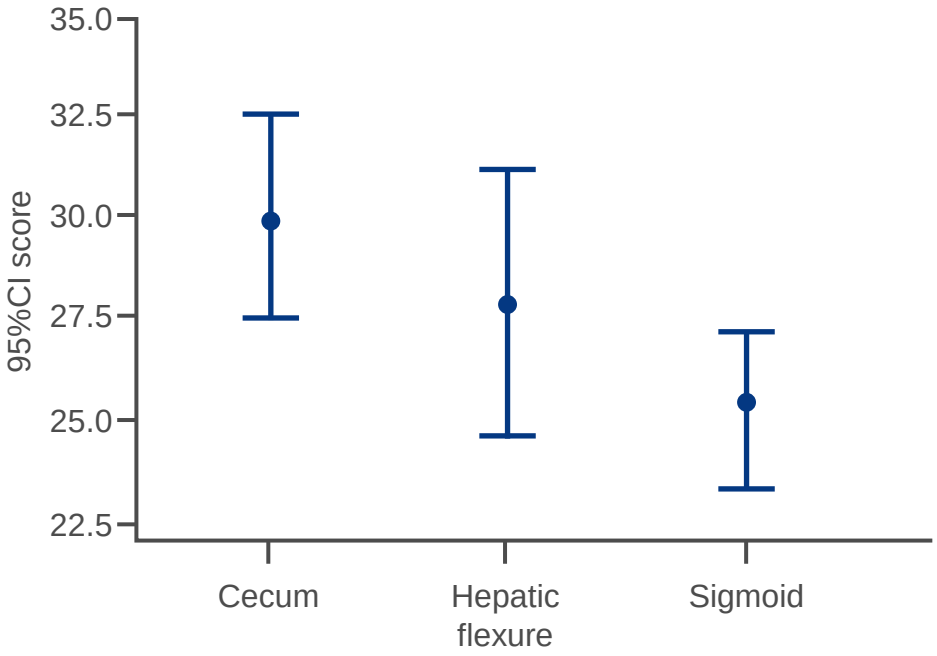
Ben-Aharon I, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 523

523: Sidedness matters: Surrogate biomarkers prognosticate colorectal cancer upon anatomic location – Ben-Aharon I, et al

Key results (cont.)

- Recurrence score gradually decreased across the colon

	n	Mean score (range)
Cecum	95	29.75 (8–71)
Hepatic flexure	38	27.76 (7–57)
Sigmoid	306	24.49 (0–52)
		p=0.014



Ben-Aharon I, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 523

523: Sidedness matters: Surrogate biomarkers prognosticate colorectal cancer upon anatomic location – Ben-Aharon I, et al

Key results (cont.)

- Right-sided tumours exhibited more CDX2-negative tumours then left-sided tumours
- CDX2-negative tumours had a higher oncotype DX score

	Right-side, n (%)	Left-side, n (%)
CDX2-positive	34 (64.2)	47 (83.9)
CDX2-negative	19 (35.8)	9 (16.1)
Total (n=109)	53	56
		p=0.029

	Mean oncotype score	Standard deviation
CDX2-positive	24.42	10.30
CDX2-negative	32.00	12.686
		p=0.020

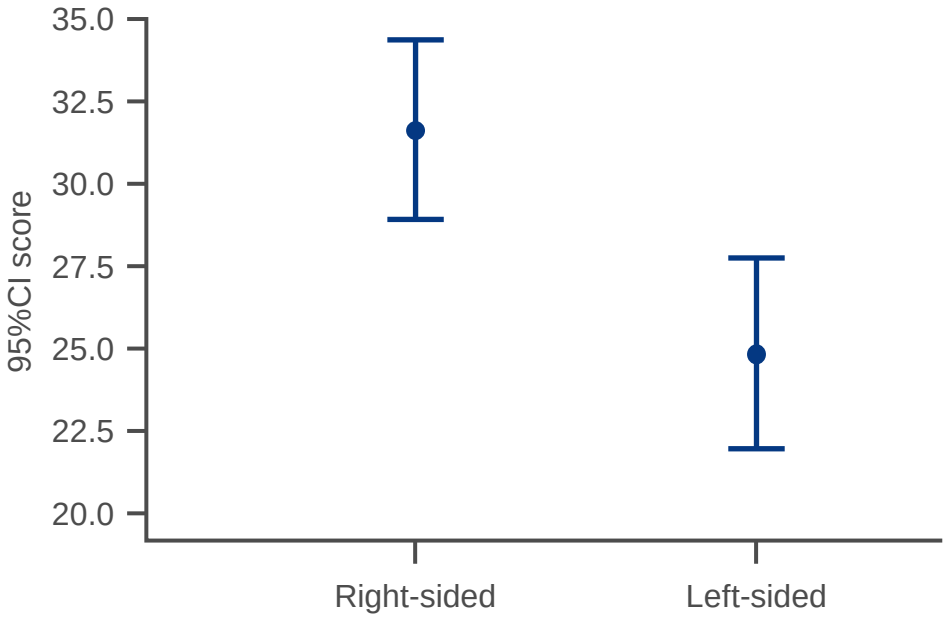
Ben-Aharon I, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 523

523: Sidedness matters: Surrogate biomarkers prognosticate colorectal cancer upon anatomic location – Ben-Aharon I, et al

Key results (cont.)

- In stage III tumours, recurrence score was higher in right-sided tumours than left-sided tumours, and higher than stage II tumours

	n (%)	Mean score (range)
Right-sided	60 (45.4)	31.15 (3–63)
Left-sided	72 (54.6)	24.6 (7–52)
Total	132 (100)	p=0.001



Ben-Aharon I, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 523

523: Sidedness matters: Surrogate biomarkers prognosticate colorectal cancer upon anatomic location – Ben-Aharon I, et al

Key results (cont.)

- Recurrence scores for stage II and III rectal cancer were higher than left-sided tumours

	n	Mean score
Stage II left colon	596	25.79
Stage II rectal	78	27.06*
Stage III left colon	72	24.6
Stage III rectal	14	27.15**

*p=0.04; **p=0.05

Conclusion

- **These results indicate that in MMR-P stage II CRC, right-sided tumours may display worse prognosis compared with left-sided tumours using these prognostic tools**

Ben-Aharon I, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 523

Cancers of the colon, rectum and anus

RECTAL CANCER

521: The International Watch & Wait database (IWWD) for rectal cancer: An update – van der Valk M, et al

Study objective

- To assess the characteristics of patients with rectal cancer included in the International Watch and Wait database (IWWD)

Methods

- An international, multicentre, observational study
- As of August 2016, 775 patients from 11 countries were included in the database
  - 679 (90%) patients were included due to a clinical complete response, all other patients were excluded from this analysis

Note: Based on data from abstract only

van der Valk M, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 521

521: The International Watch & Wait database (IWWD) for rectal cancer: An update – van der Valk M, et al

Key results

Characteristic, n (%)		Patients (n=679)
Sex, male		449 (66)
Mean age, years		63.6
Mean BMI, kg/m^2		26.7
Imaging	Endo/rectoscopy	598 (87)
	MRI	434 (64)
	ERUS	42 (6)
	Computed tomography-pelvis	172 (25)
T stage	cT1	13 (2)
	cT2	146 (28)
	cT3	335 (64)
	cT4	27 (5)
N stage	cN0	208 (40)
	cN1	185 (35)
	cN2	132 (25)
M stage	M0	635 (99)
	M+	8 (1)

Note: Based on data from abstract only

van der Valk M, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 521

521: The International Watch & Wait database (IWWD) for rectal cancer: An update – van der Valk M, et al

Key results (cont.)

- In 90% of cases induction treatment consisted of chemo-radiotherapy
- Median follow-up time was 2.6 years (range 0–24)
- Local regrowth occurred in 167 (25%) patients
  - 84% of which occurred in the first 2 years of follow-up
  - Local regrowth was endoluminal in 161 (96%) and in the loco-regional lymph nodes in 7 (4%)
- Distant metastasis occurred in 49 (7%)
- The 3-year OS rate was 91%
  - 87% for patients with local regrowth

Conclusion

- **This is the largest database of patients with rectal cancer where surgery was omitted after induction therapy, and illustrates differences in imaging and induction therapy**

Note: Based on data from abstract only

van der Valk M, et al. J Clin Oncol 2017; 35 (suppl 4): abstr 521