GI SLIDE DECK 2016

Selected abstracts on **Non-Colorectal Cancer** from:

18th World Congress on Gastrointestinal Cancer

29 June–2 July 2016 | Barcelona, Spain

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 2016. This slide set specifically focuses on the **18th World Congress on Gastrointestinal Cancer 2016** and is available in English 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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ESDO Medical Oncology Slide Deck
Editors 2016

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

1L	first line
5FU	5-fluorouracil
AE	adverse event
BCLC	Barcelona Clinic Liver Cancer
BID	twice daily
BSC	best supportive care
CA-19.9	carbohydrate antigen-19.9
Cap-RT	capecitabine + radiotherapy
CgA	Chromogranin A
CI	confidence interval
CR	complete response
CRT	chemoradiotherapy
CT	chemotherapy
D	day
DCR	disease control rate
ECC	epirubicin, cisplatin, capecitabine
ECOG	Eastern Cooperative Oncology Group
EGFR	endothelial growth factor receptor
EOC	epirubicin, oxaliplatin, capecitabine
EORTC-QLQC30	European Organization for Research and Treatment of Cancer core quality of life questionnaire
EOX	epirubicin, oxaliplatin, capecitabine
FOLFOX	leucovorin, fluorouracil, oxaliplatin
GC	gastric cancer
GEJ	gastroesophageal junction
GemCap	gemcitabine, capecitabine
Gem-RT	gemcitabine + radiotherapy
GI	gastrointestinal
HCC	hepatocellular carcinoma
HER2	human epidermal growth factor receptor 2
HR	hazard ratio
IHC	immunohistochemistry
ISH	in situ hybridisation
KPS	Karnofsky performance status
LAR	long-acting release
LLOQ	lower limit of quantitation
Lu	lutetium
LV	leucovorin
LV5FU2-CDDP	leucovorin, 5-fluorouracil, cisplatin
MDT	multidisciplinary team
MSEC	metastatic squamous-cell oesophageal cancer
nal-IRI	nanoliposomal irinotecan
(P)NET	(pancreatic) neuroendocrine tumour
NGS	next generation sequencing
NR	not reached
OR	odds ratio
ORR	overall response rate
(m)OS	(median) overall survival
PD	progressive disease
PDAC	pancreatic ductal adenocarcinoma
PD-L1	programmed death-ligand 1
(m)PFS	(median) progression-free survival
PR	partial response
PS	performance status
q(2/3/4/6/8)w	every (2/3/4/6/8) weeks
QD	once daily
QoL	quality of life
R	randomised
RECIST	Response Evaluation Criteria In Solid Tumors
RR	response rate
RT	radiotherapy
SAE	serious adverse event
SRC	signet ring cell
SSA	somatostatin analogue
TTP	time to progression
VEGF	vascular endothelial growth factor
W	week
WHO	World Health Organization

Contents

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CANCERS OF THE OESOPHAGUS AND STOMACH

LBA-002: A multicenter randomized phase III trial of neo-adjuvant chemotherapy followed by surgery and chemotherapy or by surgery and chemoradiotherapy in resectable gastric cancer: First results from the CRITICS study – Verheij M, et al

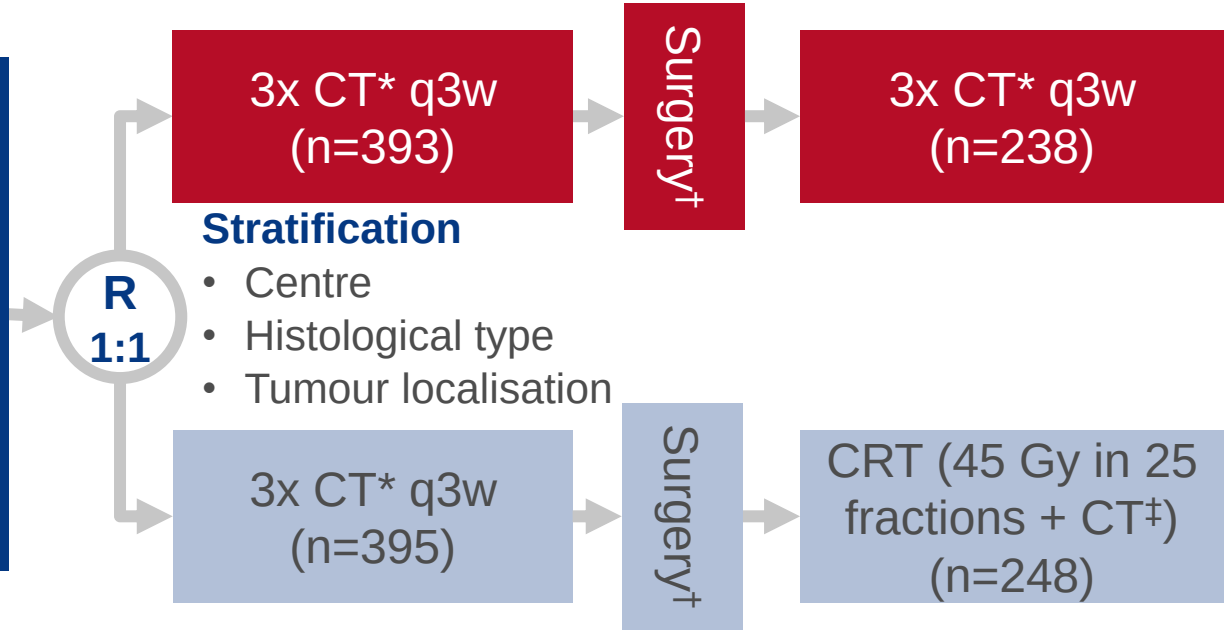
Study objective

- To examine the effect of optimal local and systemic therapy on survival in patients with resectable GC

Key patient inclusion criteria

- Stage Ib–IVa resectable GC or GEJ
- No distant metastases
- WHO PS ≤1
- Age ≥18 years

(n=788)



PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

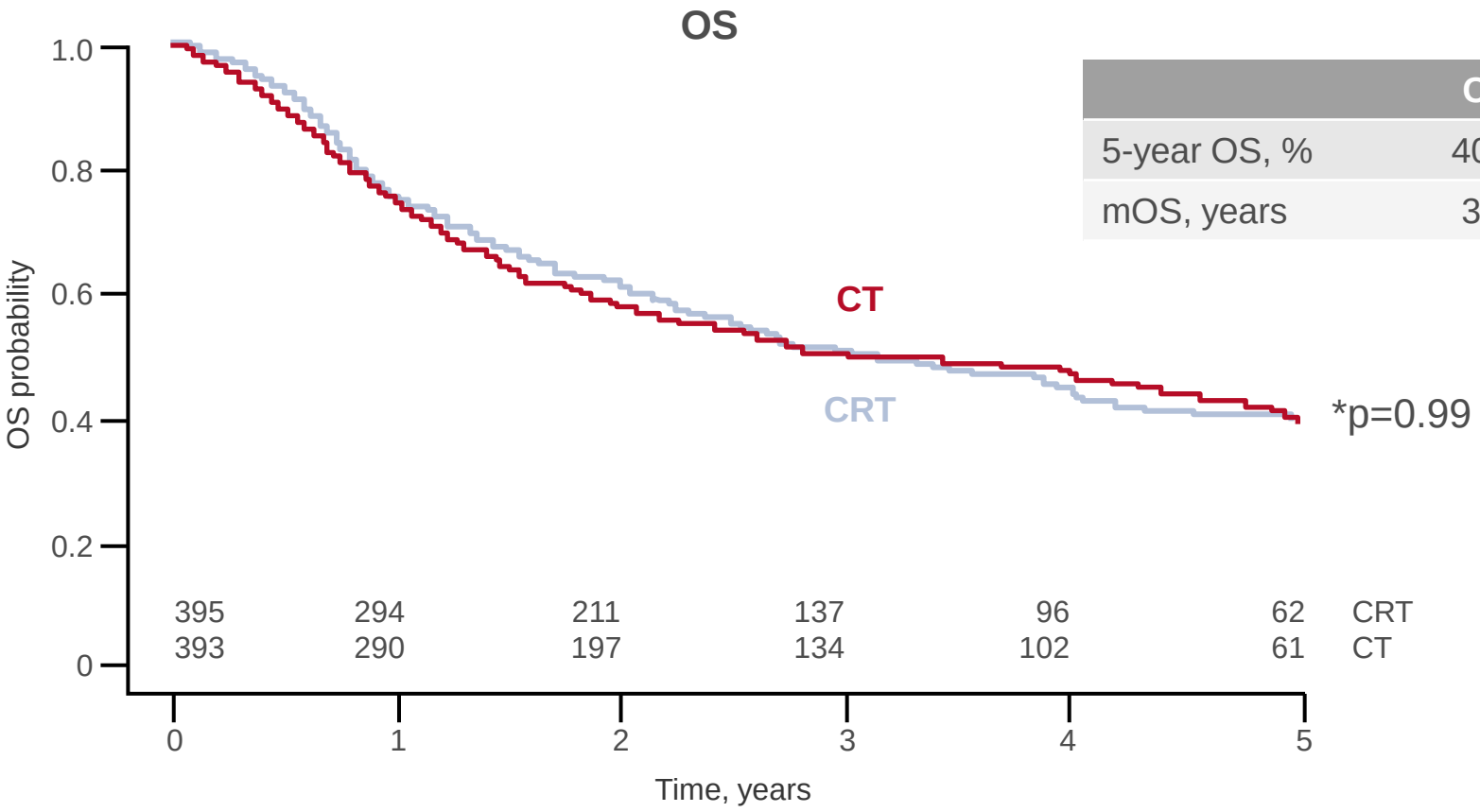
- PFS
- Safety, QoL

*ECC (epirubicin 50 mg/m^2 D1; cisplatin 60 mg/m^2 D1; capecitabine 1000 mg/m^2 BID D1–14) or EOC (epirubicin 50 mg/m^2 D1, oxaliplatin 130 mg/m^2 D1, capecitabine 625 mg/m^2 BID D1–21);
†Total/partial gastrectomy and *en bloc* N1 + N2 lymph nodes;
‡cisplatin 20 mg/m^2 qw, capecitabine 575 mg/m^2 BID.

Verheij et al. Ann Oncol 2016; 27 (suppl 2): abstr LBA-02

LBA-002: A multicenter randomized phase III trial of neo-adjuvant chemotherapy followed by surgery and chemotherapy or by surgery and chemoradiotherapy in resectable gastric cancer: First results from the CRITICS study – Verheij M, et al

Key results



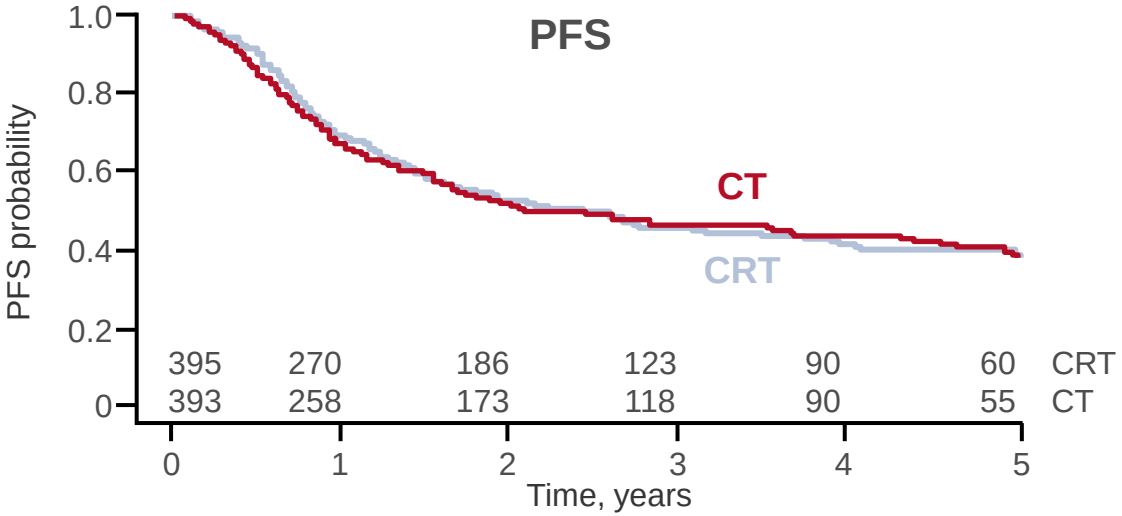
	CT	CRT
5-year OS, %	40.8	40.9
mOS, years	3.5	3.3

*Log-rank test.

Verheij et al. Ann Oncol 2016; 27 (suppl 2): abstr LBA-02

LBA-002: A multicenter randomized phase III trial of neo-adjuvant chemotherapy followed by surgery and chemotherapy or by surgery and chemoradiotherapy in resectable gastric cancer: First results from the CRITICS study – Verheij M, et al

Key results (cont.)



	CT	CRT
5-year PFS, %	38.5	39.5
mPFS, years	2.3	2.5

*p=0.99

Pre-operative AEs in ≥8% of patients	Grade 3	Grade 4	Sum (%)
Neutropenia	171	76	247 (31)
Febrile neutropenia	53	10	63 (8)
Diarrhoea	94	5	99 (13)
Nausea	83	1	84 (11)
Anorexia	71	2	73 (9)
Vomiting	58	3	61 (8)
Fatigue	57	8	65 (8)

Grade 5 AEs, all	Sum (%)
Cardiovascular	7
GI	3
Infectious	2
Total	12 (2)

*Log-rank test.

Verheij et al. Ann Oncol 2016; 27 (suppl 2): abstr LBA-02

LBA-002: A multicenter randomized phase III trial of neo-adjuvant chemotherapy followed by surgery and chemotherapy or by surgery and chemoradiotherapy in resectable gastric cancer: First results from the CRITICS study – Verheij M, et al

Key results (cont.)

Post-operative AEs in ≥10% of patients	CT (n=238)			CRT (n=248)		
	Grade 3	Grade 4	Sum (%)	Grade 3	Grade 4	Sum (%)
Neutropenia	63	18	81 (34)*	7	3	10 (4)*
Febrile neutropenia	4	1	5 (2)	6	0	6 (2)
Anorexia	20	0	20 (8)	30	0	30 (12)
Nausea	27	0	27 (11)	22	0	22 (9)
Fatigue	20	0	20 (8)	25	0	25 (10)

- Any surgery-related complications: 145 (22%) patients; in-hospital deaths: 15 (2%)

Conclusions

- **No difference in OS was observed with CT vs CRT in patients with resectable GC**
- **The 5-year OS and mOS were comparable with other studies in Western countries**
- **Ongoing analyses may detect subgroups that specifically benefit from treatment, but the current data do not clearly identify any preferred adjuvant strategy**
- **As <50% of patients could complete full treatment, more emphasis on pre-operative strategies should be considered**

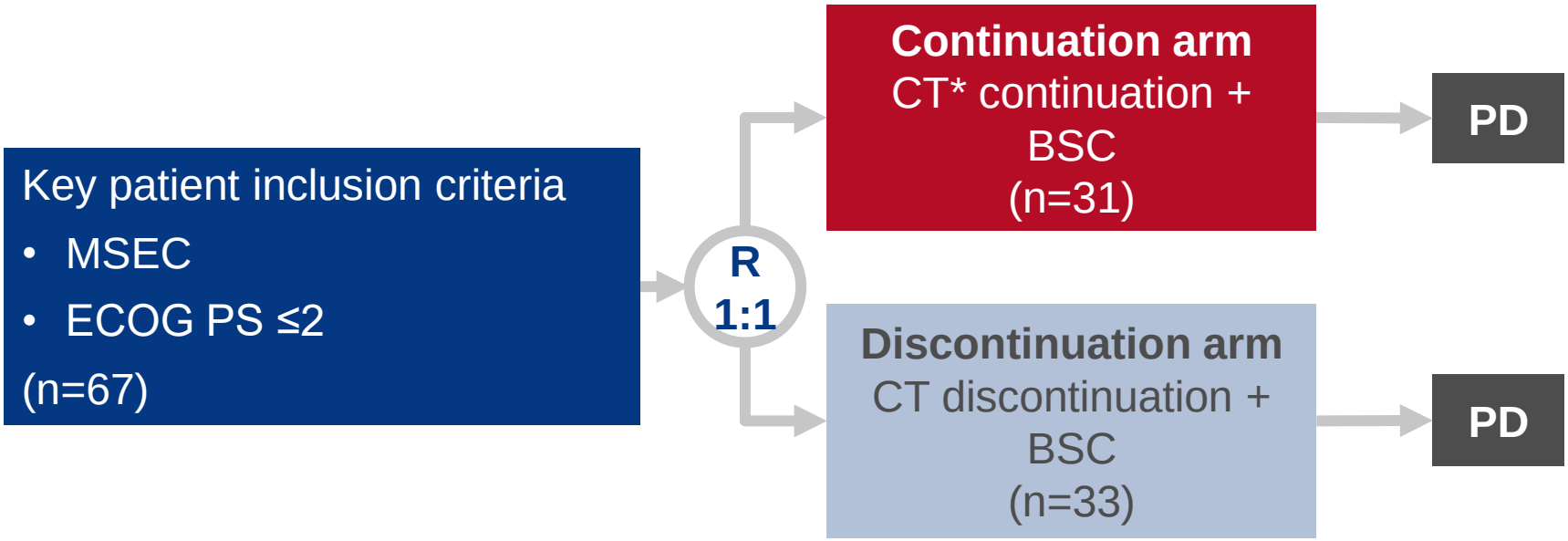
*p<0.001.

Verheij et al. Ann Oncol 2016; 27 (suppl 2): abstr LBA-02

LBA-04: The E-DIS study, a randomized discontinuation trial of first-line chemotherapy (CT) in patients with metastatic squamous-cell esophageal cancer (MSEC): efficacy and quality of life results – Adenis A, et al

Study objective

- To assess the benefit of 1L chemotherapy in MSEC patients free from progression after 6 weeks of chemotherapy



PRIMARY ENDPOINT

- 9-month survival rate

SECONDARY ENDPOINTS

- OS, PFS, QoL

Note: Based on data from abstract only

*LV5FU2-CDDP q2w (n=7), FOLFOX (n=24).

Adenis et al. Ann Oncol 2016; 27 (suppl 2): abstr LBA-04

LBA-04: The E-DIS study, a randomized discontinuation trial of first-line chemotherapy (CT) in patients with metastatic squamous-cell esophageal cancer (MSEC): efficacy and quality of life results – Adenis A, et al

Key results

	Continuation (n=31)	Discontinuation (n=33)
9-month survival rate, % (85% CI)	50 (37, 62)	48 (34, 60)
PFS, months (95% CI)	4 (2.8, 5.8)	1.4 (1.4, 2.7)
OS, months (95% CI)	8.5 (6.6, 12)	8.8 (5.9, 13.4)
Time until definite deterioration of global health status,* months (95% CI)	6.7 (3.3, 11.9)	4.4 (2.9, 6.3)

Conclusion

- **Both continuation and discontinuation of 1L chemotherapy were observed to be adequate for patients with MSEC**

Note: Based on data from abstract only

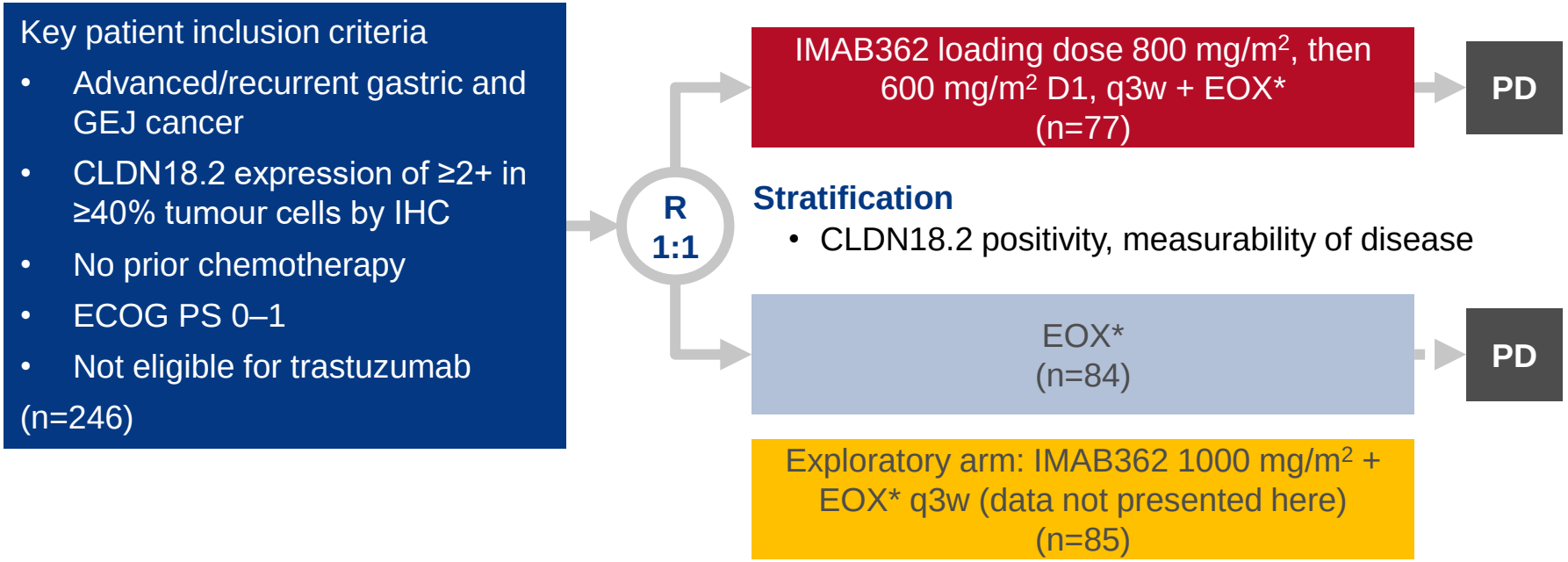
*Assessed with EORTC-QLCC30.

Adenis et al. Ann Oncol 2016; 27 (suppl 2): abstr LBA-04

LBA-06: IMAB362: A novel immunotherapeutic antibody targeting the tight-junction protein component CLAUDIN18.2 in gastric cancer – Al-Batran SE, et al

Study objective

- To evaluate the efficacy and safety of 1L IMAB362 + EOX compared with EOX alone in patients with advanced/recurrent gastric and GEJ cancer and CLDN18.2 expression



PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

- OS, safety

*Epirubicin 50 mg/m^2 + oxaliplatin 130 mg/m^2 D1 + capecitabine 625 mg/m^2 BID, D1–21; QD22).

Al-Batran et al. Ann Oncol 2016; 27(suppl 2): abstr LBA-06

LBA-06: IMAB362: A novel immunotherapeutic antibody targeting the tight-junction protein component CLAUDIN18.2 in gastric cancer – Al-Batran SE, et al

Key results

	IMAB362 + EOX	EOX	HR	p-value
mPFS (months)	7.9	4.8	0.47	<0.001
mOS (months)	13.2	8.4	0.51	<0.001
High CLDN18.2 expression subgroup*				
mOS (months)	16.7	9.0	0.45	<0.0005

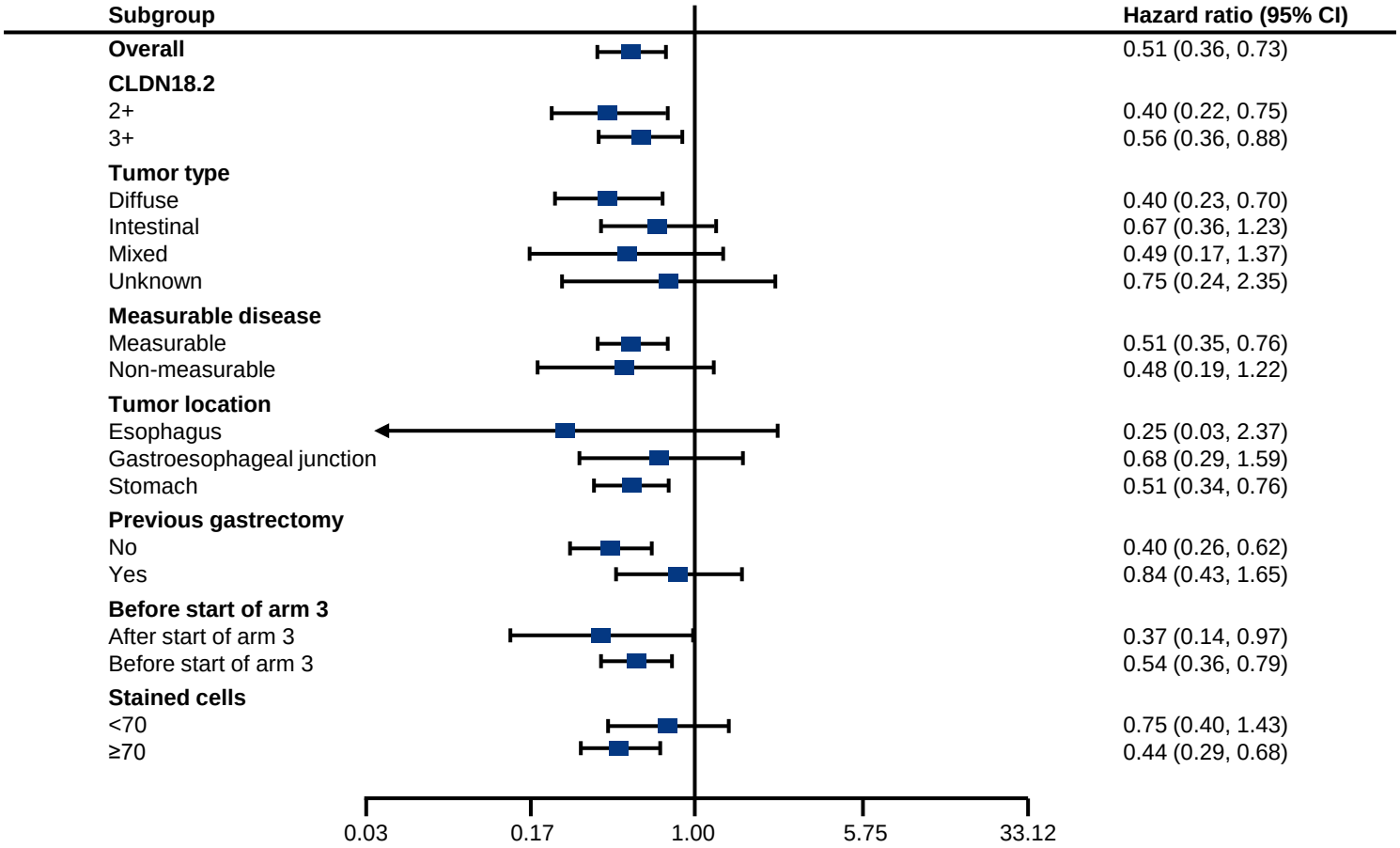
*≥2+ intensity in ≥70% tumour cells.

Al-Batran et al. Ann Oncol 2016; 27(suppl 2): abstr LBA-06

LBA-06: IMAB362: A novel immunotherapeutic antibody targeting the tight-junction protein component CLAUDIN18.2 in gastric cancer – Al-Batran SE, et al

Key results (cont.)

- OS subgroup analysis

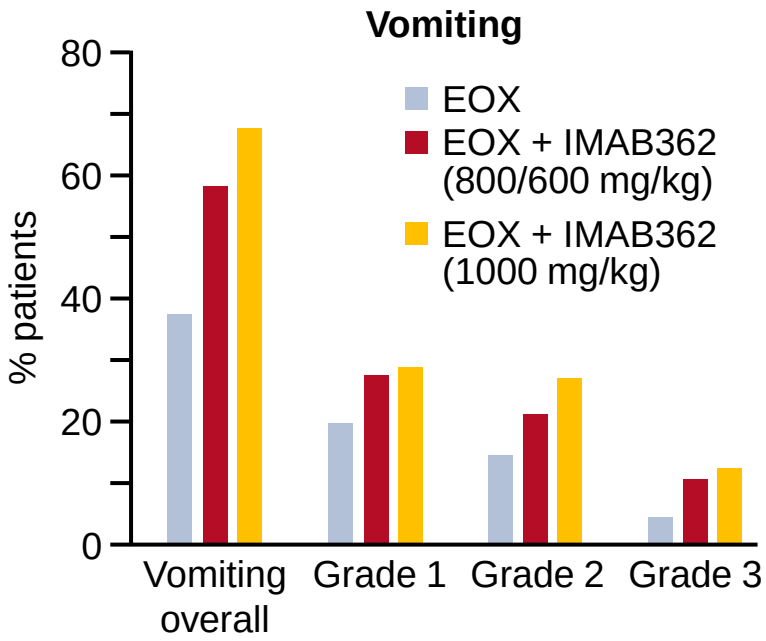


Al-Batran et al. Ann Oncol 2016; 27(suppl 2): abstr LBA-06

LBA-06: IMAB362: A novel immunotherapeutic antibody targeting the tight-junction protein component CLAUDIN18.2 in gastric cancer – Al-Batran SE, et al

Key results (cont.)

- Grade 3/4 events were not significantly increased by IMAB362



Conclusion

- **IMAB362 + EOX significantly improved mPFS and mOS compared with EOX alone, and was well tolerated**

Al-Batran et al. Ann Oncol 2016; 27(suppl 2): abstr LBA-06

O-005: Comparative molecular analyses of esophageal adenocarcinoma, esophageal squamous cell carcinoma, and gastric adenocarcinoma, and impact of molecular profile on outcome – Salem M, et al

Study objective

- To compare the molecular characteristics of oesophageal adenocarcinoma, oesophageal squamous cell carcinoma and gastric adenocarcinoma

Study design

- Between 2009 and 2015, 1892 gastroesophageal tumours were examined by Caris Life Sciences including IHC (protein expression), ISH (gene amplification) and NGS sequencing
- Only tumours with clear oesophageal or gastric origins were included
- Chi-square test was used to determine the differences between histological subtypes, and the Kaplan-Meier methodology was used to estimate survival

Salem et al. Ann Oncol 2016; 27 (suppl 2): abstr O-005

O-005: Comparative molecular analyses of esophageal adenocarcinoma, esophageal squamous cell carcinoma, and gastric adenocarcinoma, and impact of molecular profile on outcome – Salem M, et al

Key results

Site, %	Oesophageal squamous cell adenocarcinoma (n=113)	Oesophageal adenocarcinoma (n=882)	Gastric adenocarcinoma (n=897)
Primary	70	65	67
Metastatic	30	34	30
Unclear		1	3

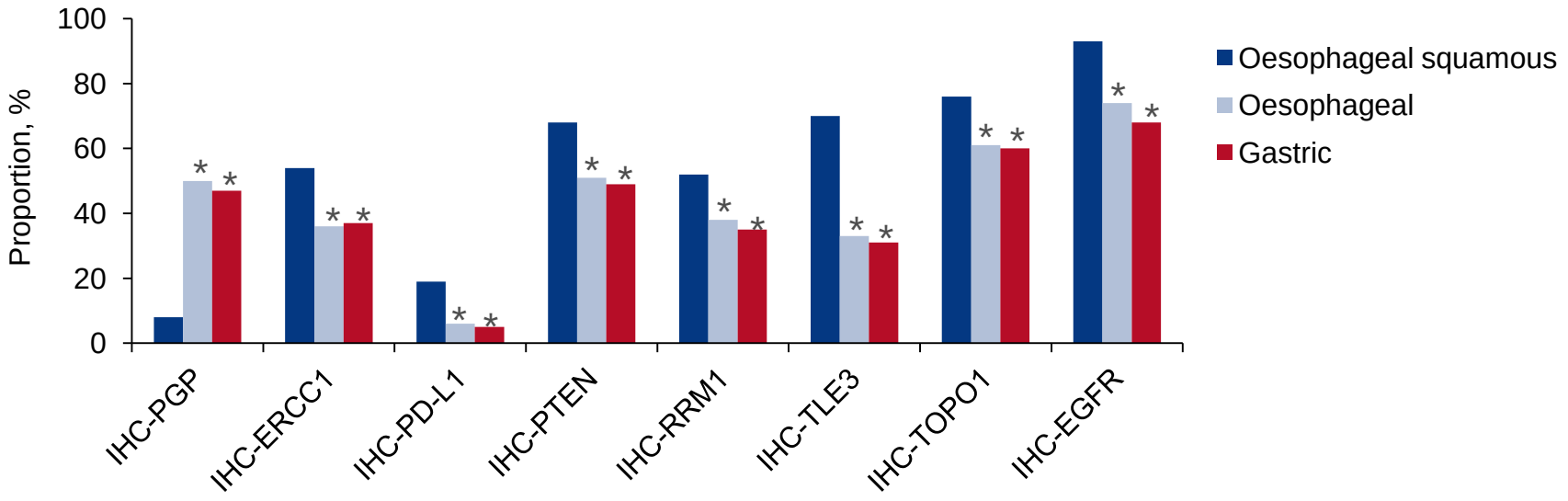
- Both oesophageal squamous cell adenocarcinomas (71% vs. 29%) and oesophageal adenocarcinomas (86% vs. 14%) were more prevalent in males then females ($p<0.0001$), respectively

Salem et al. Ann Oncol 2016; 27 (suppl 2): abstr O-005

O-005: Comparative molecular analyses of esophageal adenocarcinoma, esophageal squamous cell carcinoma, and gastric adenocarcinoma, and impact of molecular profile on outcome – Salem M, et al

Key results (cont.)

	Oesophageal squamous cell adenocarcinoma (n=113)	Oesophageal adenocarcinoma (n=882)	Gastric adenocarcinoma (n=897)
ISH-HER2, %	0	21*	10*
IHC-HER2/Neu, %	0	12*	6*



*p<0.05.

Salem et al. Ann Oncol 2016; 27 (suppl 2): abstr O-005

O-005: Comparative molecular analyses of esophageal adenocarcinoma, esophageal squamous cell carcinoma, and gastric adenocarcinoma, and impact of molecular profile on outcome – Salem M, et al

Key results (cont.)

- TP53 is the most mutated gene in all three cancer types (70% in both oesophageal squamous and oesophageal adenocarcinomas and 46% in gastric adenocarcinoma)
- KRAS mutation occurred more frequently in oesophageal (p=0.01) and gastric adenocarcinomas (p=0.03) than oesophageal squamous cell adenocarcinoma, where it was completely absent
- APC occurred more frequently in oesophageal adenocarcinoma (p=0.04) and was completely absent in oesophageal squamous cell adenocarcinoma

Conclusions

- **This molecular comparison of gastroesophageal tumours demonstrated that the tumour profile of oesophageal adenocarcinomas is similar to that of gastric adenocarcinomas, but differs from that of oesophageal squamous cell carcinoma, which suggests that treatment of gastroesophageal tumours should be based on its histological subtype rather than anatomical site**
- **Low frequency mutations in several druggable genes may have potential therapeutic value including HER2, PD-L1, BRCA1/2, PIK3CA, PTEN, FGFR2**

Salem et al. Ann Oncol 2016; 27 (suppl 2): abstr O-005

O-006: Survival impact of histology for resectable gastric cancer: A multicenter U.S. observation study – Greenleaf E, et al

Study objective

- To assess compare the impact of gastric cancer histologies on survival in a large sample of patients with resectable gastric cancer in the US

Study design

- Patients with stages 0–III gastric cancer who underwent definitive surgical resection between 2003 and 2012 were identified from the ACS National Cancer Database
- Treatment groups were stratified based on commonly presented histology, including intestinal type, diffuse type, signet ring cell (SRC), mucinous and mixed cell type
- Based on tumour aggressiveness, histology cohorts were combined to form two distinct cohorts – intestinal/mucinous and diffuse/SRC
- Propensity score matching was performed to determine mortality rates after matching for demographic, surgery-related and tumour-related variables

Note: Based on data from abstract only

Greenleaf et al. Ann Oncol 2016; 27 (suppl 2): abstr O-006

O-006: Survival impact of histology for resectable gastric cancer: A multicenter U.S. observation study – Greenleaf E, et al

Key results

- Of 8367 patients with resectable cancer, 2328 (27.8%) had intestinal type, 916 (10.9%) had diffuse type, 654 (7.8%) had mucinous, 4008 (47.9%) had SRC and 461 (5.6%) had mixed cell type

Intestinal/mucinous	Diffuse/SRC
Older	Younger
More comorbidities	Less comorbidity
	More frequently underwent total gastrectomy
Negative surgical margins	Positive surgical margins
No lymph node involvement	Diffuse type more frequently lymph node positive
Stage I no difference in mortality	
Stage II mortality 40.06%	Stage II mortality 50.50% ($p<0.0001$)
Stage III mortality 52.43%	Stage III mortality 65.70% ($p<0.0001$)

Note: Based on data from abstract only

Greenleaf et al. Ann Oncol 2016; 27 (suppl 2): abstr O-006

O-006: Survival impact of histology for resectable gastric cancer: A multicenter U.S. observation study – Greenleaf E, et al

Conclusions

- **Patients with gastric tumours with diffuse type and SRC histologies have worse survival than those with intestinal type and mucinous tumours, regardless of other prognostic factors and therapeutic intervention**
- **Further research is required to determine whether a different or more aggressive treatment strategy should be employed for these patients**

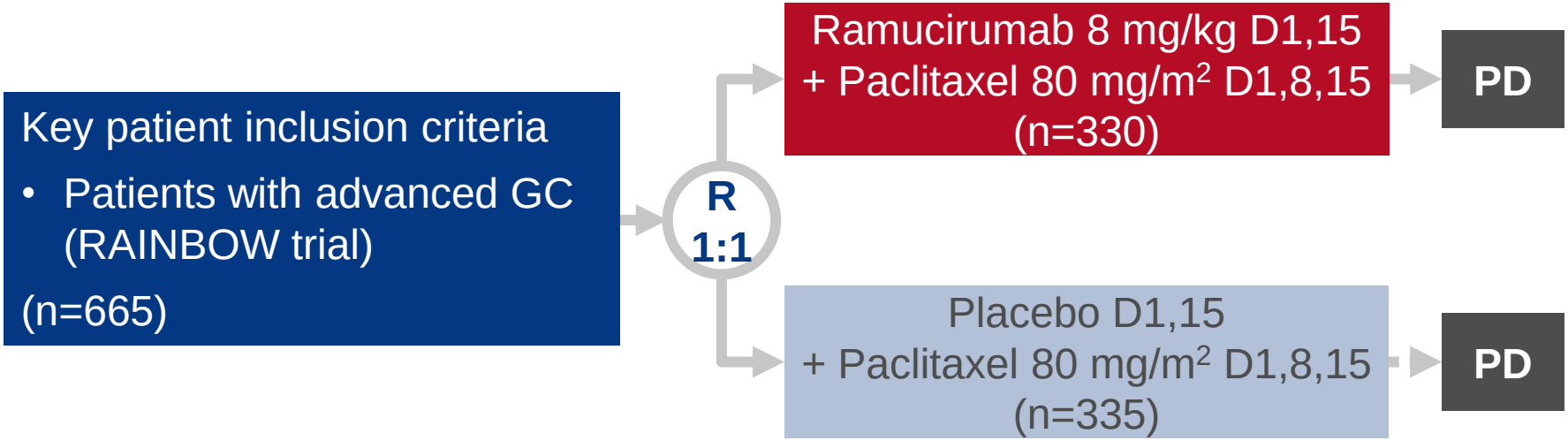
Note: Based on data from abstract only

Greenleaf et al. Ann Oncol 2016; 27 (suppl 2): abstr O-006

O-007: Biomarker analyses of second-line Ramucirumab in patients with advanced gastric cancer from RAINBOW, a global, randomized, double-blind, phase 3 study – Van Cutsem E, et al

Study objective

- To evaluate the predictive and prognostic value of plasma markers in patients with advanced GC



Subanalysis of the RAINBOW trial:

- VEGF markers and cytokines were assessed
- Patient data were divided into low- and high-marker subgroups, using:
  - The lower limit of quantitation as the cut-off point for those markers with >20% of samples below the limit of quantitation
  - The median marker level as the cut-off point

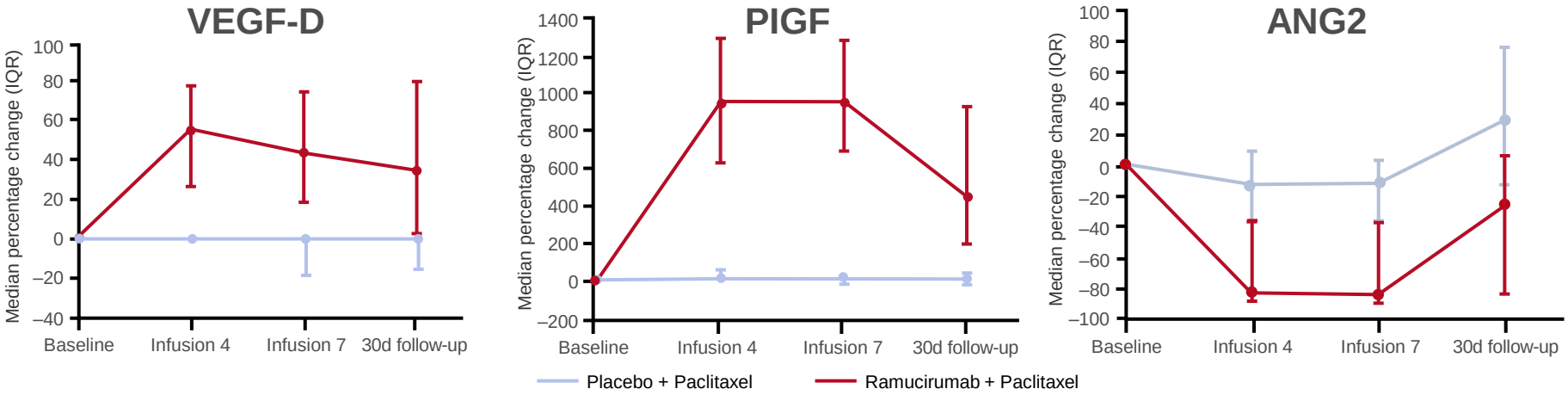
Van Cutsem et al. Ann Oncol 2016; 27 (suppl 2): abstr O-007

O-007: Biomarker analyses of second-line Ramucirumab in patients with advanced gastric cancer from RAINBOW, a global, randomized, double-blind, phase 3 study – Van Cutsem E, et al

Key results

Analysis of predictive markers	Cut-off point (value, pg/mL)	OS, interaction p-value	PFS, interaction p-value
VEGF-C	LLOQ (261.8)	0.2723	0.9946
VEGF-D	LLOQ (656.1)	0.9165	0.9530
sVEGFR-1	Median (119.0)	0.6590	0.9864
sVEGFR-2	Median (11625.0)	0.5295	0.7852
Placental growth factor	Median (21.2)	0.6693	0.3303

Percentage change from baseline in selected biomarkers



LLOQ, lower limit of quantitation.

Van Cutsem et al. Ann Oncol 2016; 27 (suppl 2): abstr O-007

O-007: Biomarker analyses of second-line Ramucirumab in patients with advanced gastric cancer from RAINBOW, a global, randomized, double-blind, phase 3 study – Van Cutsem E, et al

Key results (cont.)

	OS		PFS	
	HR* (95% CI)	p-value	HR* (95% CI)	p-value
C-reactive protein	2.1 (1.6, 2.7)	<0.0001	1.5 (1.2, 2.0)	0.0007
Hepatocyte growth factor	1.9 (1.3, 2.7)	0.0007	1.8 (1.3, 2.6)	0.0009
Intercellular adhesion molecule-3	1.4 (1.0, 1.8)	0.0377	1.4 (1.0, 1.8)	0.0382
Interleukin-8	1.5 (1.1, 1.9)	0.0039	1.3 (1.0, 1.7)	0.0401
Serum amyloid A	1.8 (1.4, 2.4)	<0.0001	1.3 (1.0, 1.7)	0.0420
Vascular cell adhesion molecule-1	1.6 (1.3, 2.0)	0.0001	1.4 (1.1, 1.7)	0.0074

*High vs low expression level.

Van Cutsem et al. Ann Oncol 2016; 27 (suppl 2): abstr O-007

O-007: Biomarker analyses of second-line Ramucirumab in patients with advanced gastric cancer from RAINBOW, a global, randomized, double-blind, phase 3 study – Van Cutsem E, et al

Conclusions

- **There are no known consistently predictive biomarkers to guide patient selection, despite multiple approved anticancer therapies that target angiogenesis**
- **The exploratory plasma analyses available from the RAINBOW study do not identify a predictive biomarker for ramucirumab**
- **However, this analysis revealed pharmacodynamic trends with VEGF-D, PlGF + ANG2**
- **Several prognostic markers were identified**

Van Cutsem et al. Ann Oncol 2016; 27 (suppl 2): abstr O-007

CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

Cancers of the pancreas, small bowel and hepatobiliary tract

PANCREATIC CANCER

O-002: Utilization and trends in palliative therapy for stage IV pancreatic adenocarcinoma patients: A U.S. population based study – Kulaylat A, et al

Study objective

- To characterise the trends, factors and outcomes associated with utilisation of palliative therapies among patients with metastatic pancreatic adenocarcinoma in the US

Study design

- Patients with clinical stage 4 pancreatic adenocarcinoma were identified from the US National Cancer Database between 2003 and 2011
- Patients were stratified by receipt of palliative therapy (surgery, radiation, systemic therapy, pain management or a combination thereof) and compared with those without these designations
- Linear regression, multivariable logistic regression, and survival analyses using multivariate proportional hazards models were performed

Note: Based on data from abstract only

Kulaylat et al. Ann Oncol 2016; 27 (suppl 2): abstr O-002

O-002: Utilization and trends in palliative therapy for stage IV pancreatic adenocarcinoma patients: A U.S. population based study – Kulaylat A, et al

Key results

- A total of 68,075 patients with stage IV disease were identified, 10,105 (14.8%) of whom received specified palliative therapy
- Among the palliative cohort, the majority received systemic therapy (42.2%), followed by a surgical intervention (21.6%), pain management alone (17.3%), radiation (9.1%) and a combination of modalities (9.8%)
- Utilisation of palliative therapies increased from 12.2% in 2003 to 15.9% in 2011 ($p<0.001$)
  - This trend was not observed among patients with inoperable stage 1 (7.2–8.5%, $p=0.646$), stage 2 (10.1–10.2%, $p=0.204$) or stage 3 disease (13.5–12.5%, $p=0.651$)
- Patients were less likely to undergo palliation with age >60 years (OR 0.88, $p<0.001$), and particularly for those >80 years (OR 0.66, $p<0.001$)
- Utilisation did not differ between males and females ($p=0.58$). Lower utilisation of palliative measures was observed for black (OR 0.83, $p<0.001$) and Hispanic (OR 0.79, $p<0.001$) ethnicities vs Caucasians

Note: Based on data from abstract only

Kulaylat et al. Ann Oncol 2016; 27 (suppl 2): abstr O-002

O-002: Utilization and trends in palliative therapy for stage IV pancreatic adenocarcinoma patients: A U.S. population based study – Kulaylat A, et al

Key results (cont.)

- Palliative therapy was used more in the presence of associated comorbidities, with 10% higher odds in those with one comorbidity (95% CI 1.05, 1.16), and 14% higher odds in those with two or more (95% CI 1.06, 1.23)
- Utilisation was lower for privately insured patients compared with patients with government or no insurance (OR 0.92, p=0.004)
- Community cancer centres were less likely to offer palliative therapies than comprehensive community and academic centres and there were significant regional variations
- Overall, survival was slightly worse in patients receiving palliative therapies (HR 1.02; 95% CI 1.01, 1.05), with median survival of 3.6 months
- When stratifying by type of palliative therapy, those receiving surgery or combination therapy had similar survival to non-palliative patients
  - Those undergoing systemic palliative therapy, however, demonstrated prolonged survival (median 4.7 months, HR 0.88; 95% CI 0.85, 0.91), while those undergoing palliative radiation (median 3.2 months, HR 1.12; 95% CI 1.05, 1.20) or pain management alone (median 1.6 months, HR 1.79; 95% CI 1.71, 1.89) experienced worse survival

Note: Based on data from abstract only

Kulaylat et al. Ann Oncol 2016; 27 (suppl 2): abstr O-002

O-002: Utilization and trends in palliative therapy for stage IV pancreatic adenocarcinoma patients: A U.S. population based study – Kulaylat A, et al

Conclusions

- **Palliation of symptoms remains underutilised in the US, particularly in non-Caucasian, older patients with more comorbidities, and across all stages of inoperable disease, despite the continued dismal prognosis of pancreatic cancer**
- **Although palliation does not improve survival, increased awareness of palliative options may help increase its utilisation for end-of-life symptom control**

Note: Based on data from abstract only

Kulaylat et al. Ann Oncol 2016; 27 (suppl 2): abstr O-002

O-003: Long-term outcome from the SCALOP trial: A multi-centre randomized phase II trial of Gemcitabine or Capecitabine-based chemoradiation (CRT) for locally advanced pancreatic cancer (LAPC) – Mukherjee S, et al

Study objective

- To evaluate the efficacy and safety of CRT with gemcitabine vs capecitabine following induction CT in patients with locally advanced pancreatic cancer

Key patient inclusion criteria

- Locally advanced pancreatic adenocarcinoma
- Responding/stable disease after 3 cycles GemCap*
- WHO PS 0–2
- Maximum tumour diameter 7 cm

(n=74)

R 1:1

Cap-RT
GemCap* (1 cycle) followed by Capecitabine (830 mg/m^2 BID on RT days) + RT† (n=38)

→ PD

Stratification
- Centre
- WHO performance status [0 vs 1]
- Disease location [head vs body or tail]

Gem-RT
GemCap* (1 cycle) followed by Gemcitabine (300 mg/m^2 qw) + RT† (n=36)

→ PD

PRIMARY ENDPOINT

- 9-month PFS (reported previously)

SECONDARY ENDPOINTS

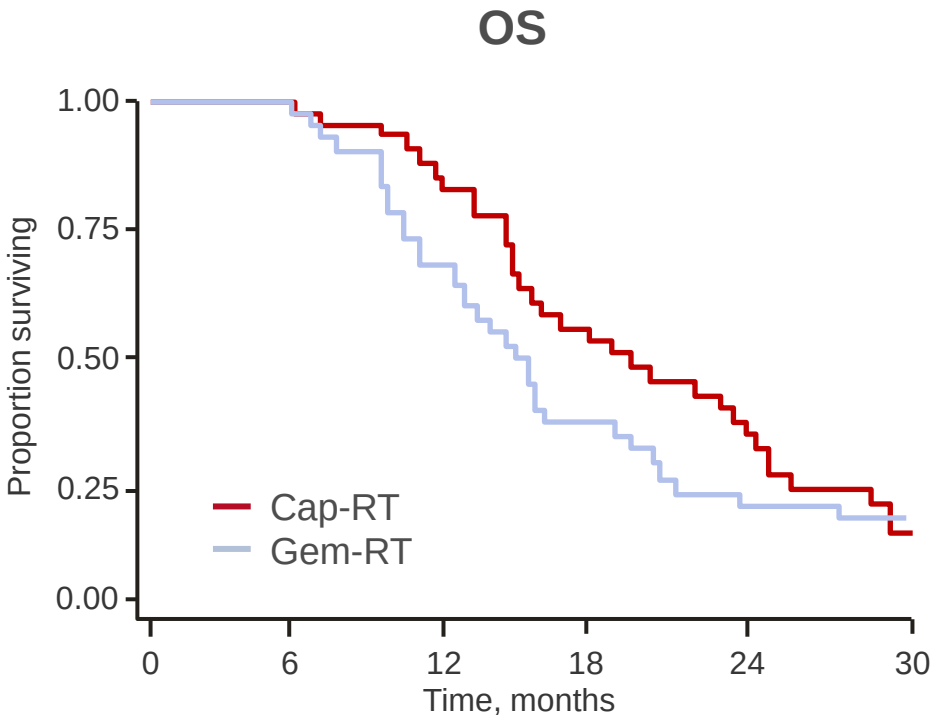
- OS, PFS (time to event), ORR (RECIST)
- Safety, treatment compliance

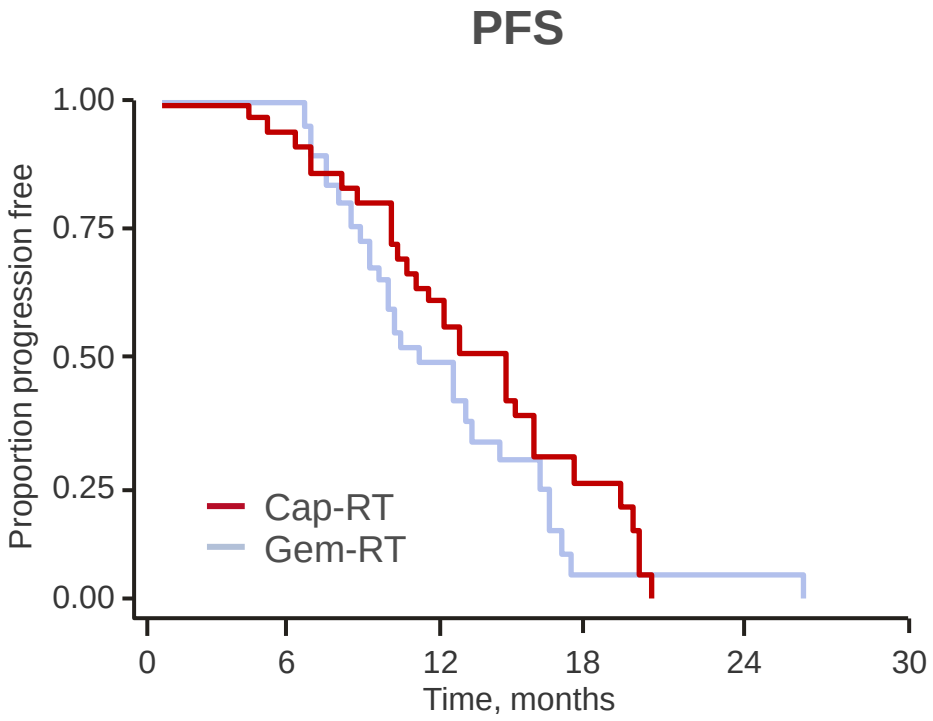
*Gemcitabine 1000 mg/m^2 D1,8,15 + capecitabine 830 mg/m^2 BID D1–21 of 28-day cycle; †50.4 Gy in 28 fractions.

Mukherjee et al. Ann Oncol 2016; 27 (suppl 2): abstr O-003

O-003: Long-term outcome from the SCALOP trial: A multi-centre randomized phase II trial of Gemcitabine or Capecitabine-based chemoradiation (CRT) for locally advanced pancreatic cancer (LAPC) – Mukherjee S, et al

Key results





	Cap-RT	Gem-RT
mPFS, months	17.6	14.6
HR (95% CI); p-value	0.73 (0.46, 1.18); 0.203	

	Cap-RT	Gem-RT
mPFS, months	12.0	10.4
HR (95% CI); p-value	0.73 (0.44, 1.23); 0.244	

Cap, capecitabine; Gem, gemcitabine.

Mukherjee et al. Ann Oncol 2016; 27 (suppl 2): abstr O-003

O-003: Long-term outcome from the SCALOP trial: A multi-centre randomized phase II trial of Gemcitabine or Capecitabine-based chemoradiation (CRT) for locally advanced pancreatic cancer (LAPC) – Mukherjee S, et al

Key results (cont.)

OS by variables at baseline		HR (95% CI)	p-value
Age	<65 years	1.00	
	≥65 years	0.54 (0.33, 0.88)	0.013
Sex	Male	1.00	
	Female	1.12 (0.69, 1.80)	0.654
WHO PS	0	1.00	
	1–2	2.09 (1.24, 3.52)	0.006
CA19.9	<613	1.00	
	≥613	4.11 (2.38, 7.12)	<0.001
GHS*	-	0.95 (0.85, 1.06)	0.395
Tumour diameter†	-	1.28 (1.08, 1.51)	0.005

*HRs were calculated for every 10-point difference in scores;
†HRs were calculated for every 1 cm increase.

Mukherjee et al. Ann Oncol 2016; 27 (suppl 2): abstr O-003

O-003: Long-term outcome from the SCALOP trial: A multi-centre randomized phase II trial of Gemcitabine or Capecitabine-based chemoradiation (CRT) for locally advanced pancreatic cancer (LAPC) – Mukherjee S, et al

Key results (cont.)

OS treatment arm at start of CRT	Patients, n	mOS, months	HR (95% CI)	p-value
Capecitabine-RT	25	13.9	0.40 (0.17, 0.91)	0.029
Gemcitabine-RT	29	9.5	1.00	-

Conclusions

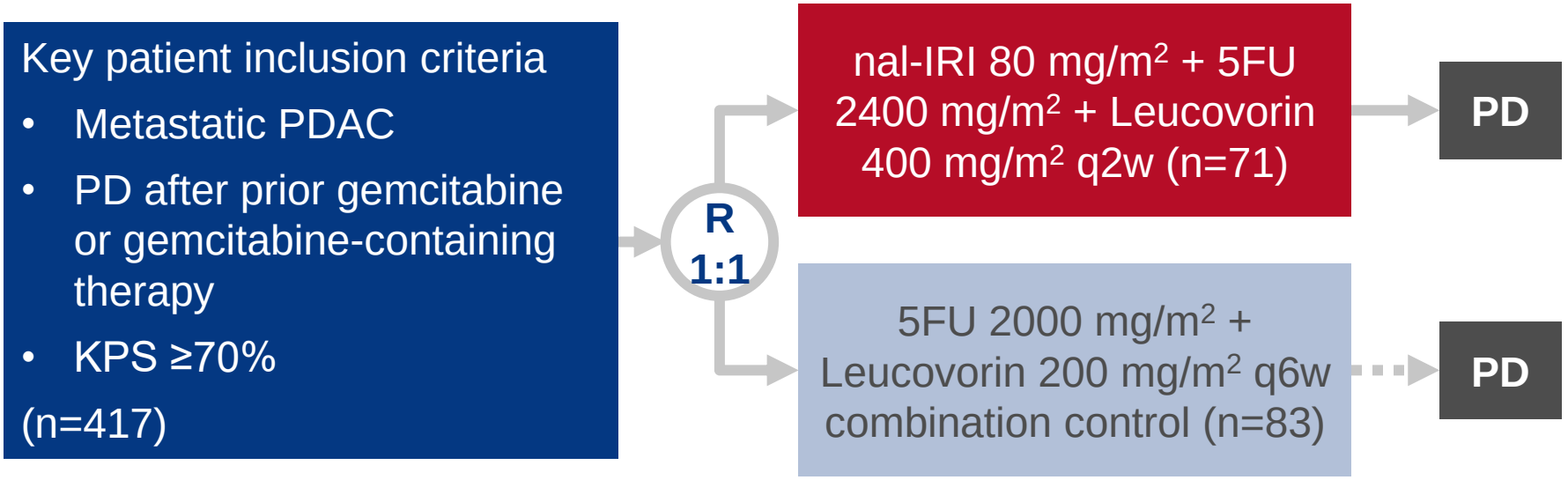
- **In the overall population, survival with capecitabine-RT was no longer superior to gemcitabine-RT in patients with locally advanced pancreatic cancer compared with the initial survival analysis**
- **However, in patients receiving CRT, survival was significantly superior with capecitabine-RT vs gemcitabine-RT**
- **Age, WHO PS, tumour diameter and CA-19.9 levels all significantly influenced OS**

Mukherjee et al. Ann Oncol 2016; 27 (suppl 2): abstr O-003

O-004: Effects of nal-IRI (MM-398) ± 5-fluorouracil on quality of life (QoL) in NAPOLI-1: A phase 3 study in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) previously treated with gemcitabine – Hubner R, et al

Study objective

- To evaluate the impact on QoL of nal-IRI (MM-398) with 5FU + leucovorin compared with 5FU + leucovorin alone in patients with metastatic pancreatic ductal adenocarcinoma (PDAC)



PRIMARY ENDPOINT

- OS (previously reported)

SECONDARY ENDPOINTS

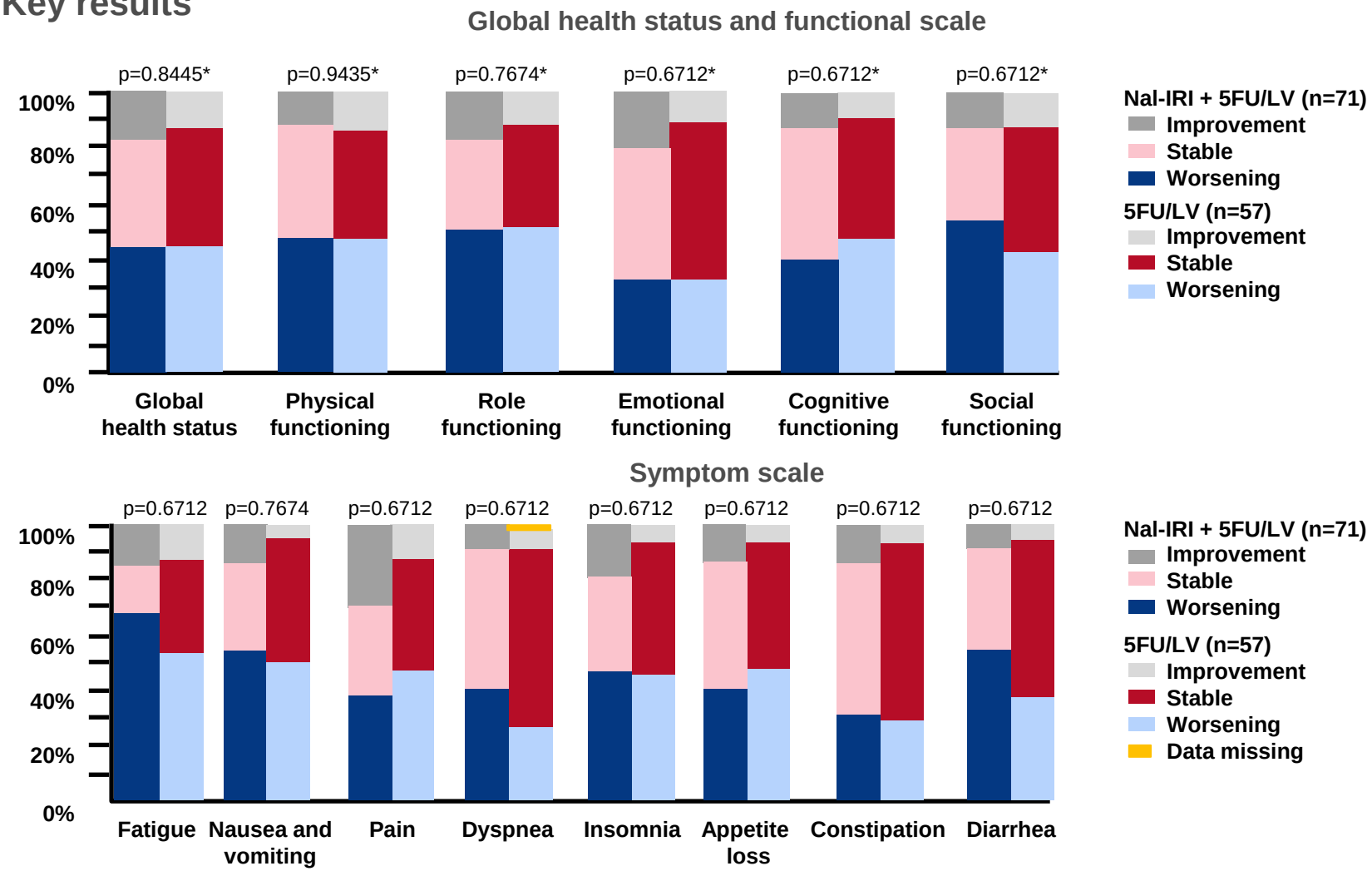
- QoL and global health (EORTC-QLQC30)

nal-IRI, nanoliposomal irinotecan.

Hubner et al. Ann Oncol 2016; 27 (suppl 2): abstr O-004

O-004: Effects of nal-IRI (MM-398) ± 5-fluorouracil on quality of life (QoL) in NAPOLI-1: A phase 3 study in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) previously treated with gemcitabine – Hubner R, et al

Key results



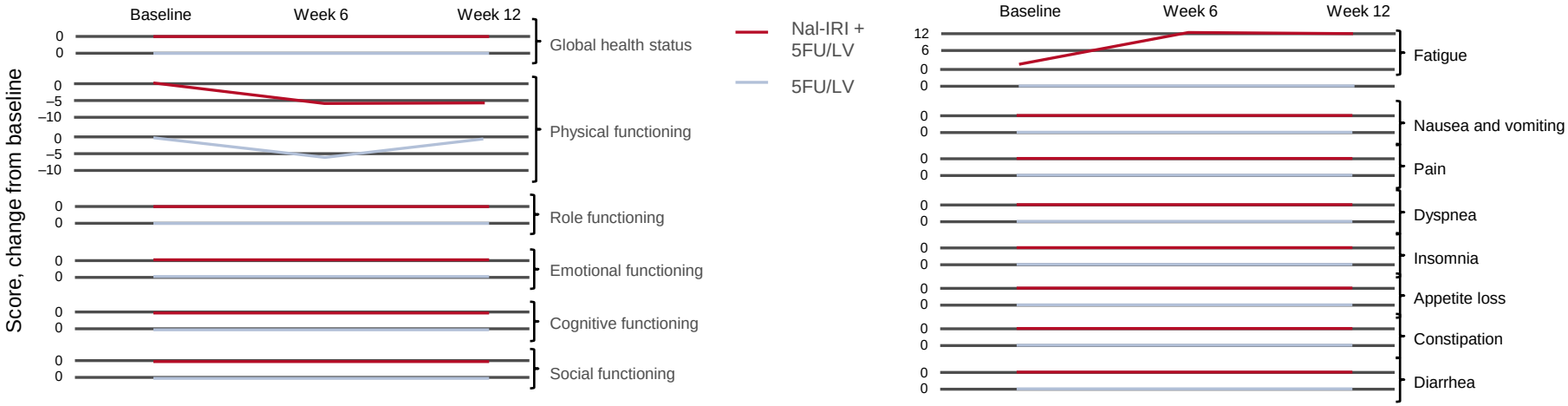
* 'Benjamini-Hochberg-adjusted p-value.

Hubner et al. Ann Oncol 2016; 27 (suppl 2): abstr O-004

O-004: Effects of nal-IRI (MM-398) ± 5-fluorouracil on quality of life (QoL) in NAPOLI-1: A phase 3 study in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) previously treated with gemcitabine – Hubner R, et al

Key results (cont.)

Global health status, functional and symptom scales



- No appreciable change from baseline in either arm
  - Observed median change from baseline to week 6 in physical functioning score was 6.7 points in both arms
  - Observed median change from baseline to week 6 in fatigue score was ~11 points in the nal-irinotecan + 5-FU + leucovorin arm

Hubner et al. Ann Oncol 2016; 27 (suppl 2): abstr O-004

O-004: Effects of nal-IRI (MM-398) ± 5-fluorouracil on quality of life (QoL) in NAPOLI-1: A phase 3 study in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) previously treated with gemcitabine – Hubner R, et al

Conclusions

- **Overall, over 12 weeks, patients treated with nal-IRI + 5FU + leucovorin had no deterioration in QoL**
- **No significant difference in global health status and functional scale scores were observed between treatment arms at baseline, or over the 12 weeks of the study**
- **As nal-IRI has been previously shown to improve OS, these data support it as a new treatment option for patients with metastatic PDAC previously treated with gemcitabine-based therapy**

Hubner et al. Ann Oncol 2016; 27 (suppl 2): abstr O-004

Cancers of the pancreas, small bowel and hepatobiliary tract

HEPATOCELLULAR CARCINOMA

LBA-03: Efficacy and safety of regorafenib versus placebo in patients with hepatocellular carcinoma (HCC) progressing on sorafenib: Results of the international, randomized phase 3 RESORCE trial – Bruix J, et al

Study objective

- To evaluate the efficacy and safety of regorafenib in patients with intermediate or advanced HCC who had disease progression on sorafenib

Key patient inclusion criteria

- HCC BCLC stage B or C
- Received and tolerated sorafenib for ≥20 days at ≥400 mg/day
- Documented radiological progression on sorafenib
- Child-Pugh A liver function
- ECOG PS 0–1

(n=573)

R 2:1

Regorafenib 160 mg/day
W1–3 of each 4-week cycle
+ BSC (n=379)

→ **PD/ death/ toxicity**

Stratification

- Geographic region (Asia vs ROW)
- ECOG PS, α-fetoprotein, extra-hepatic spread, macroscopic vascular invasion

Placebo QD
W1–3 of each 4-week cycle
+ BSC (n=194)

→ **PD/ death/ toxicity**

PRIMARY ENDPOINT

- OS

SECONDARY ENDPOINTS

- PFS, TTP, RR and DCR

Note: Based on data from abstract only

BCLC, Barcelona Clinic Liver Cancer.

Bruix et al. Ann Oncol 2016; 27 (suppl 2): abstr LBA-03

LBA-03: Efficacy and safety of regorafenib versus placebo in patients with hepatocellular carcinoma (HCC) progressing on sorafenib: Results of the international, randomized phase 3 RESORCE trial – Bruix J, et al

Key results

	Regorafenib (n=379)	Placebo (n=194)	HR	95% CI	p-value
Median OS, months	10.6	7.8	–	–	–
Median PFS, months	3.1	1.5	–	–	–
Median TTP, months	3.2	1.5	0.44	0.36, 0.55	<0.001
ORR, %	10.6	4.1	–	–	0.005
DCR*, %	65.2	36.1	–	–	<0.001

- There was a 38% reduction in the risk of death in the regorafenib group compared with the placebo group (HR 0.62; 95% CI 0.50, 0.78; p<0.001)
- Compared with placebo, the risk of progression or death with regorafenib reduced by 54% (HR 0.46; 95% CI 0.37, 0.56; p<0.001)

Note: Based on data from abstract only

*Complete and partial responses + stable disease by mRECIST.

Bruix et al. Ann Oncol 2016; 27 (suppl 2): abstr LBA-03

LBA-03: Efficacy and safety of regorafenib versus placebo in patients with hepatocellular carcinoma (HCC) progressing on sorafenib: Results of the international, randomized phase 3 RESORCE trial – Bruix J, et al

Key results (cont.)

	Regorafenib (n=379)	Placebo (n=194)
Grade ≥3 AEs, %	79.7	58.5
Most common grade ≥3 AE, %		
Hypertension	15.2	4.7
Hand-foot skin reaction	12.6	0.5
Fatigue	9.1	4.7
Diarrhoea	3.2	0
Dose modifications due to AEs, %	68.2	31.1
Death up to 30 days after last dose, %	13.4	19.7

Note: Based on data from abstract only

Bruix et al. Ann Oncol 2016; 27 (suppl 2): abstr LBA-03

LBA-03: Efficacy and safety of regorafenib versus placebo in patients with hepatocellular carcinoma (HCC) progressing on sorafenib: Results of the international, randomized phase 3 RESORCE trial – Bruix J, et al

Conclusions

- **In patients with HCC who had progressed under sorafenib, treatment with regorafenib significantly improved OS**
- **Regorafenib therapy was well tolerated and observed AEs were in line with its known safety profile**

Note: Based on data from abstract only

Bruix et al. Ann Oncol 2016; 27 (suppl 2): abstr LBA-03

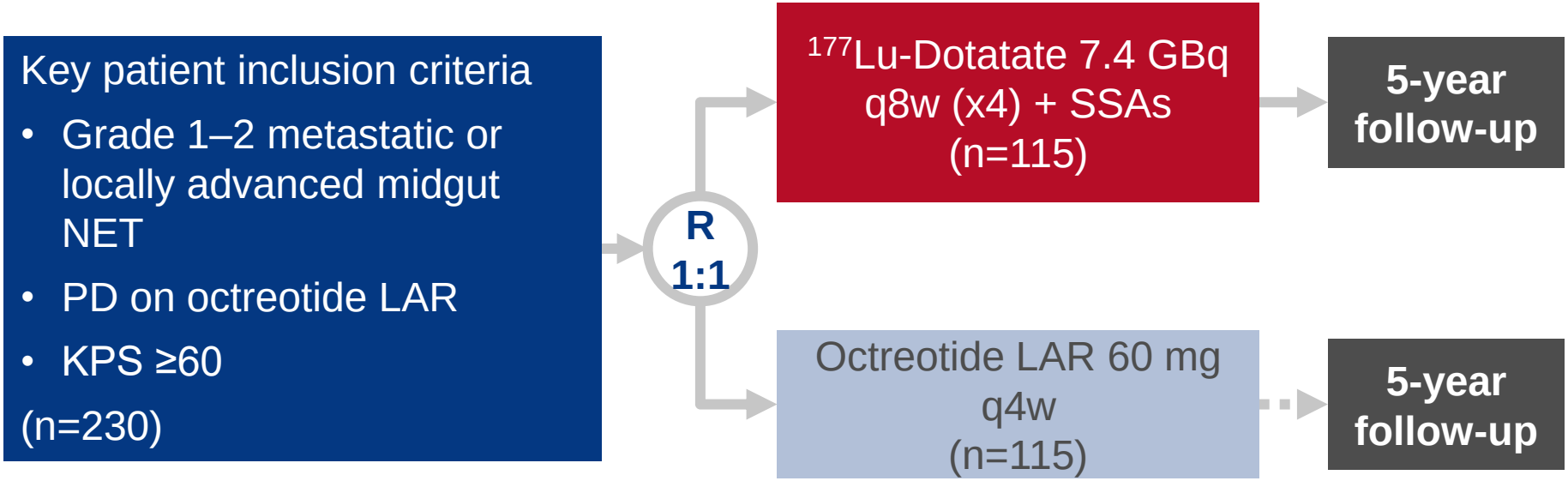
Cancers of the pancreas, small bowel and hepatobiliary tract

NEUROENDOCRINE TUMOUR

O-009: NETTER-1 phase III: Efficacy and safety results in patients with midgut neuroendocrine tumors treated with 177Lu-dotatate – Ruszniewski P, et al

Study objective

- To evaluate the efficacy and safety of ^{177}Lu-dotatate compared with octreotide LAR in patients with advanced, progressive somatostatin receptor positive midgut NETs



PRIMARY ENDPOINT

- PFS (RECIST 1.1)

SECONDARY ENDPOINTS

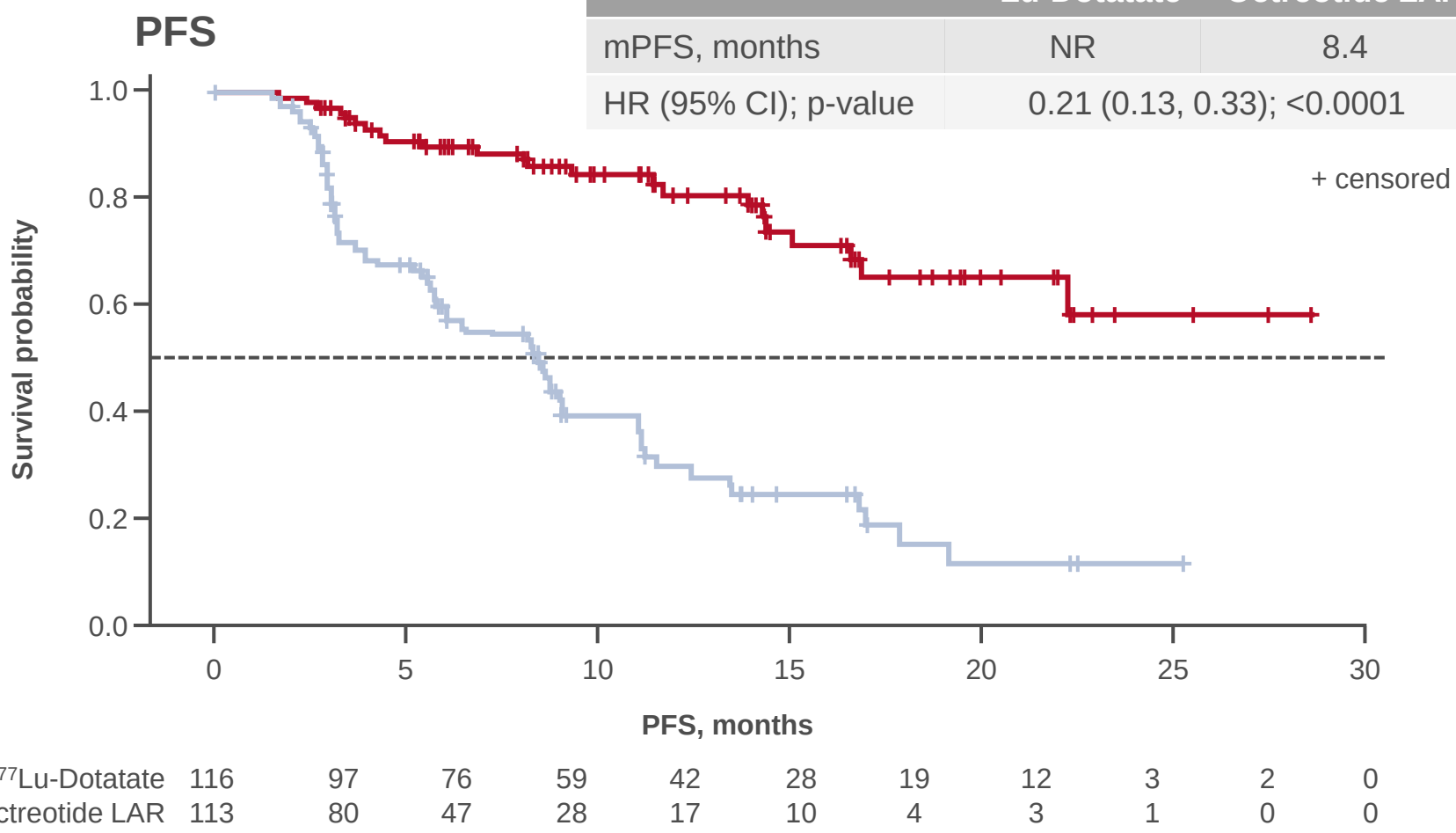
- ORR, OS, TTP, safety and QoL

Ruszniewski et al. Ann Oncol 2016; 27 (suppl 2): abstr O-009

O-009: NETTER-1 phase III: Efficacy and safety results in patients with midgut neuroendocrine tumors treated with 177Lu-dotatate – Ruszniewski P, et al

Key results

	^{177}Lu-Dotatate	Octreotide LAR
mPFS, months	NR	8.4
HR (95% CI); p-value	0.21 (0.13, 0.33); <0.0001	



Ruszniewski et al. Ann Oncol 2016; 27 (suppl 2): abstr O-009

O-009: NETTER-1 phase III: Efficacy and safety results in patients with midgut neuroendocrine tumors treated with 177Lu-dotatate – Ruszniewski P, et al

Key results (cont.)

	^{177}Lu-Dotatate (n=101)	Octreotide LAR (n=100)	p-value
CR, n	1	0	
PR, n	17	3	
ORR, % (95% CI)	18 (10, 25)	3 (0, 6)	0.0008
OS (interim), HR (95% CI)	0.398 (0.21, 0.77)		0.0043

Treatment-related AEs, n (%)	^{177}Lu-Dotatate (n=111)	Octreotide LAR (n=110)
Any AE	95 (86)	34 (31)
SAE	10 (9)	1 (1)
Withdrawal	5 (5)	0 (0)

Ruszniewski et al. Ann Oncol 2016; 27 (suppl 2): abstr O-009

O-009: NETTER-1 phase III: Efficacy and safety results in patients with midgut neuroendocrine tumors treated with 177Lu-dotatate – Ruszniewski P, et al

Key results (cont.)

Grade 3/4 AEs occurring in ≥1%, %	^{177}Lu-Dotatate (n=111)	Octreotide LAR (n=110)
Nausea	4	2
Vomiting	7	0
Diarrhoea	3	2
Abdominal pain	3	5
Fatigue/asthenia	2	2
Thrombocytopenia	2	0
Lymphopenia	9	0
Leukopenia	1	0
Neutropenia	1	0

Conclusions

- **^{177}Lu-Dotatate was superior to octreotide LAR for PFS and OS in patients with progressive metastatic midgut NETs**
- **^{177}Lu-Dotatate showed a favourable tolerability profile with no clinically relevant findings**
- **^{177}Lu-Dotatate may be a major therapeutic benefit for these patients who have limited treatment options after progressing under SSAs**

Ruszniewski et al. Ann Oncol 2016; 27 (suppl 2): abstr O-009

O-008: Impact of chromogranin A, grade, and mitotic rate in small, non-functional pancreatic neuroendocrine tumors: A U.S population based study – Mirkin K, et al

Study objective

- To evaluate in the US population, the survival impact of selected factors Chromogranin A levels (CgA), mitotic rate and histologic grade of the tumour in patients with non-functional pancreatic neuroendocrine tumours (PNETs)

Study design

- The US National Cancer Data Base was reviewed between 1998 and 2012 to identify patients with stages 1–3 non-functional PNETs of ≤2 cm
- Clinicopathologic characteristics were collected for the identified patient population
- Statistical analysis comprised univariate and multivariate survival analyses

Note: Based on data from abstract only

Mirkin et al. Ann Oncol 2016; 27 (suppl 2): abstr O-008

O-008: Impact of chromogranin A, grade, and mitotic rate in small, non-functional pancreatic neuroendocrine tumors: A U.S population based study – Mirkin K, et al

Key results

	Well differentiated (n=824)	Moderately differentiated (n=94)	Poorly differentiated (n=54)	p-value*
Earlier clinical stage disease (Stage I), %	93.2	86.2	85.2	0.015
Lower mitotic rate, %	31.7	12.8	1.9	<0.0001
Undergoing surgery, %	88.0	68.1	31.5	<0.0001
Positive lymph nodes, n	0.35	0.56	0.94	<0.0001
Earlier pathological stage disease (Stage I), %	61.0	38.3	9.3	<0.0001

- Patients with high mitotic rates had poorer differentiated disease (p<0.001) and were less likely to undergo surgery (p<0.0001) than those with medium or low mitotic rates
- After controlling for disease characteristics only mitotic rate >20 mitoses/10 HPF significantly impacted survival (HR 10.6; p=0.002)
- Patients with low CgA values (≤100 ng/mL) had fewer comorbidities, well differentiated disease, lower mitotic rate and tended to undergo surgical resection (all p<0.0001) than those with high CgA levels (>100 ng/mL)

Note: Based on data from abstract only

*Well differentiated vs moderately and poorly differentiated.

Mirkin et al. Ann Oncol 2016; 27 (suppl 2): abstr O-008

O-008: Impact of chromogranin A, grade, and mitotic rate in small, non-functional pancreatic neuroendocrine tumors: A U.S population based study – Mirkin K, et al

Conclusions

- **Both grade and very high CgA levels were significantly associated with survival in patients with non-functional, small PNETs**
- **Survival appeared to be negatively impacted by mitotic rate >20 mitoses/10 HPF only, although this was a rare occurrence**
- **In this select population, both poor grade and elevated CgA levels should be considered as poor prognostic indicators, but surgical resection appears to improve survival in these patients**

Note: Based on data from abstract only

Mirkin et al. Ann Oncol 2016; 27 (suppl 2): abstr O-008

Cancers of the pancreas, small bowel and hepatobiliary tract

GENERAL

O-001: The influence of multidisciplinary teams on diagnosis and treatment – Basta Y, et al

Study objective

- To assess the influence of MDTs on the diagnosis and management of patients with potential GI cancers

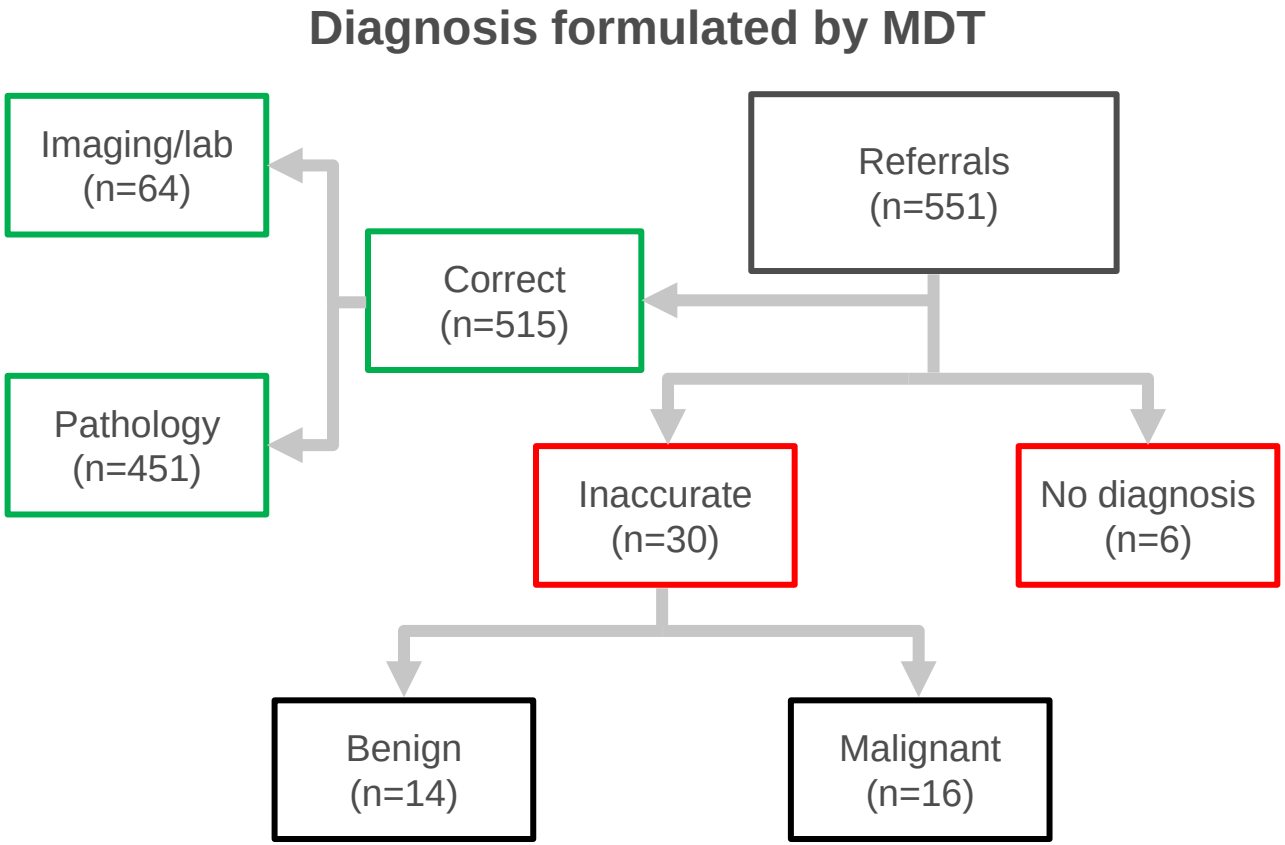
Study design

- A total of 551 patients were prospectively discussed 691 times at 74 GI oncology MDT meetings over a 6-month period
- Diagnoses by MDTs were validated using pathology or follow-up
- Factors influencing correct diagnosis were identified with a Poisson regression model
- Implementation of MDT-decisions was assessed using electronic patient records and reasons to deviate from these decisions were searched manually in the records

Basta et al. Ann Oncol 2016; 27 (suppl 2): abstr O-001

O-001: The influence of multidisciplinary teams on diagnosis and treatment – Basta Y, et al

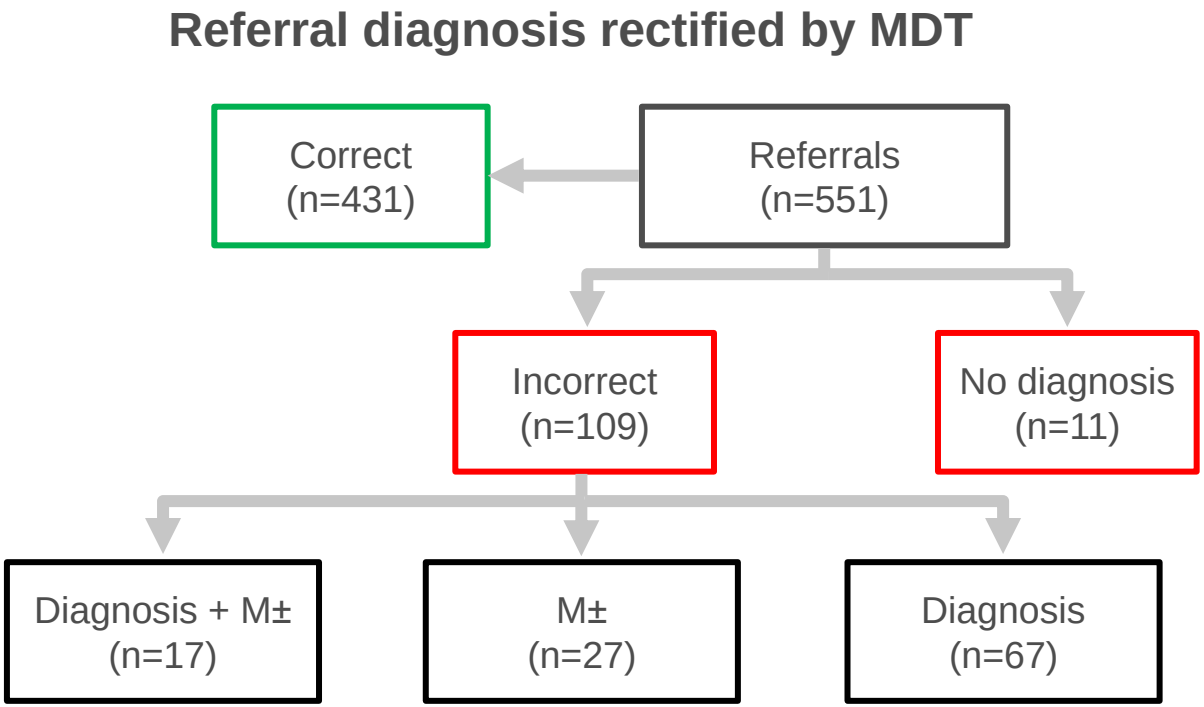
Key results



Basta et al. Ann Oncol 2016; 27 (suppl 2): abstr O-001

O-001: The influence of multidisciplinary teams on diagnosis and treatment – Basta Y, et al

Key results (cont.)



M±, alteration of stage.

Basta et al. Ann Oncol 2016; 27 (suppl 2): abstr O-001

O-001: The influence of multidisciplinary teams on diagnosis and treatment – Basta Y, et al

Key results (cont.)

Factors influencing correct decision	RR (95% CI)	p-value
Treating physician	1.2 (1.02, 1.47)	0.045
Additional tests needed	0.8 (0.75, 0.93)	<0.001
Number of patients discussed	1.0 (0.98, 1.01)	-
Duration of meeting	1.0 (0.99, 1.00)	-

Reason for deviation from advised treatment plan, n	N=32
Patient wishes	15
Patient physical condition	14
Second opinion	1
Incorrect diagnosis	2

Conclusions

- **In patients with potential GI cancers, MDTs rectified 21.8% of referral diagnoses**
- **The presence of the treating physician was the most important factor to ensure a correct diagnosis**
- **The number of correct diagnoses were not influenced by the number of patients discussed or the duration of the meeting**

Basta et al. Ann Oncol 2016; 27 (suppl 2): abstr O-001