GI SLIDE DECK 2015

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

EUROPEAN CANCER CONGRESS (ECC)

25–29 September 2015

Vienna, Austria

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 2015. This slide set specifically focuses on the European Cancer Congress 2015 Meeting 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 2015

COLORECTAL CANCERS



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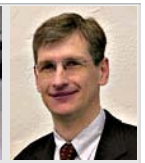
PANCREATIC CANCER AND HEPATOBILIARY TUMOURS

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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Glossary

5-FU	5-fluorouracil
5-HIAA	5-hydroxyindoleacetic acid
ADC	adenocarcinoma
AE	adverse event
AJCC/UICC	American Joint Committee on Cancer/ Union for International Cancer Control
CA-125	cancer antigen 125
CI	confidence interval
CEA	carcinoembryonic antigen
CR	complete response
CRT	chemoradiotherapy
CT	chemotherapy
CTL	cytotoxic T lymphocytes
DCR	disease control rate
DFS	disease-free survival
EBV	Epstein–Barr virus
ECF	epirubicin/cisplatin/5-fluorouracil
ECOG	Eastern Cooperative Oncology Group
ECX	epirubicin/cisplatin/capecitabine
FLOT	docetaxel/5-fluorouracil/leucovorin/oxaliplatin
GC	gastric cancer
GEC	gastroesophageal adenocarcinoma
GEJ	gastroesophageal junction
GI	gastrointestinal
Gy	Gray
HCC	hepatocellular carcinoma
H. pylori	*Helicobacter pylori*
HR	hazard ratio
HR-QoL	health-related quality of life
ITT	intent-to-treat
IV	intravenous
LAR	long-acting release
mAb	monoclonal antibody
NCI−CTC	National Cancer Institute common toxicity criteria
(m)NET	(metastatic) neuroendocrine tumour
NS	non-significant
OP	operation
OSCC	oesophageal squamous cell carcinoma
ORR	overall/objective response rate
(m)OS	(median) overall survival
pCR	pathological complete response
PD	progressive disease
PD-L1	programmed death-ligand 1
(m)PFS	(median) progression-free survival
PO	by mouth (orally)
PR	partial response
PS	performance status
pSR	pathological sub-total response
Q2W	every 2 weeks
QoL	quality of life
RECIST	Response Evaluation Criteria In Solid Tumors
RT	radiotherapy
SAE	serious adverse event
SCC	squamous cell carcinoma
SD	stable disease
SSA	somatostatin analogue
TEAE	treatment-emergent adverse event
TID	three times daily
TNM	Tumour, Node, Metastasis
TTP	time to progression
TTR	time to response
TRG	tumour regression grading
TSH	thyroid-stimulating hormone
ULN	upper limit of normal
WHO	World Health Organisation

Contents

- Hepatocellular carcinoma 6
- Oesophageal and gastric cancer 10
- Anal cancer 34
- Neuroendocrine tumours 38
- Peritoneal carcinomatosis 45

HEPATOCELLULAR CARCINOMA

2205: Treatment strategy for recurrent hepatocellular carcinoma after curative hepatectomy: Repeat hepatectomy vs. salvage living donor liver transplantation – Yamashita YI et al

Study objective

- To investigate the efficacy of repeat hepatectomy vs. salvage living donor liver transplantation (LDLT) in patients with recurrent HCC following curative hepatectomy

Study design

- A total of 159 patients within Milan criteria who had undergone curative hepatectomy for recurrent HCC were included in the analysis:
  - Group 1: Repeat hepatectomy (n=146)
  - Group 2: Salvage LDLT (n=13)
- Operative results and patient prognoses were compared between the groups using:
  - Univariate analyses (χ^2 test, Student's t-test)
  - Survival analysis (Kaplan-Meier method, log-rank test)

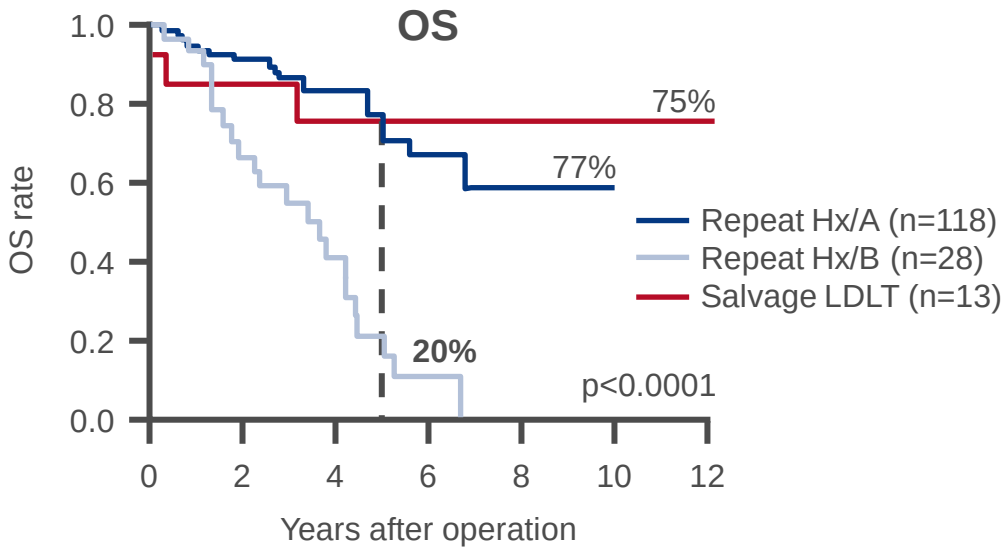
Yamashita et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2205

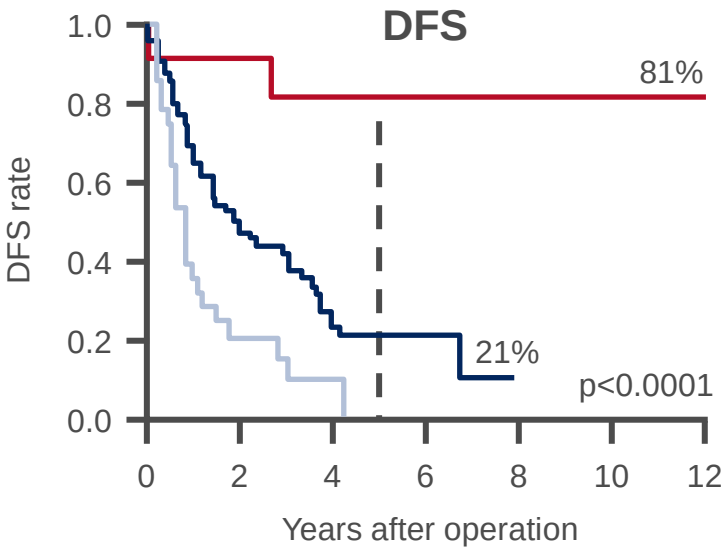
2205: Treatment strategy for recurrent hepatocellular carcinoma after curative hepatectomy: Repeat hepatectomy vs. salvage living donor liver transplantation – Yamashita YI et al

Key results

	Repeat hepatectomy (n=146)	Salvage LDLT (n=13)	p-value
OS, %	61	75	0.1714
DFS, %	16	81	0.0002

Survival according to liver damage (grade A/B)





Hx, hepatectomy

Yamashita et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2205

2205: Treatment strategy for recurrent hepatocellular carcinoma after curative hepatectomy: Repeat hepatectomy vs. salvage living donor liver transplantation – Yamashita YI et al

Key results (cont.)

Short-term surgical outcomes	Repeat hepatectomy (n=146)	Salvage LDLT (n=13)	p-value
Surgical outcome			
Operation time, min	229.1	862.9	<0.0001
Blood loss, g	596.3	24,690.0	<0.0001
Intraoperative transfusion, %	18	100	<0.0001
Post-operative course			
Mortality, %	0	7.7	0.0818
Morbidity (≥Clavien II), %	26	62	0.0111
Hospital stay, days	20	35	0.0180

Conclusions

- **Repeat hepatectomy should be indicated for patients with recurrent HCC and grade A liver damage after curative resection**
- **The prognosis of patients with grade B liver damage after repeat hepatectomy is poor; therefore, salvage LDLT would be a potent option in such patients**

Yamashita et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2205

OESOPHAGEAL AND GASTRIC CANCER

36LBA: Pathological response to neoadjuvant 5-FU, oxaliplatin and docetaxel (FLOT) versus epirubicin, cisplatin and 5-FU (ECF) in patients with locally advanced, resectable gastric/esophagogastric junction (EGJ) cancer: Data from the phase II part of the FLOT4 phase III study of the AIO – Pauligk C* et al

Study objective

- To report pathological remission rates of a phase 2/3 study comparing perioperative FLOT with ECF(X) in resectable stages upon request of the German Cancer Aid in order to further sponsor the trial

Key patient inclusion criteria

- Gastric cancer or adenocarcinoma of the gastro-oesophageal junction (GEJ) type I–III
- Medically and technically operable stages
- T2-4, every N, M0 or every T, N+, M0

(n=265)

R

4xFLOT - OP - 4xFLOT
(n=128)

FLOT: docetaxel 50 mg/m², d1;
5-FU 2600 mg/m², d1;
leucovorin 200 mg/m², d1;
oxaliplatin 85 mg/m², d1, q2w

3xECF(X) - OP - 3xECF(X)
(n=137)

ECF(X): epirubicin 50 mg/m², d1;
cisplatin 60 mg/m², d1;
5-FU 200 mg/m² (or capecitabine 1250 mg/m² po divided into two doses d1–d21), q3w

PRIMARY ENDPOINT(S)

- Pathological CR (pCR)

*Presented by S-E Al-Batran

Pauligk et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 36LBA

36LBA: Pathological response to neoadjuvant 5-FU, oxaliplatin and docetaxel (FLOT) versus epirubicin, cisplatin and 5-FU (ECF) in patients with locally advanced, resectable gastric/esophagogastric junction (EGJ) cancer: Data from the phase II part of the FLOT4 phase III study of the AIO – Pauligk C* et al

Key results

- 265 patients from the phase 2 part of the trial were evaluable on ITT basis; median age was 62 years; 76.2% of patients were male
- The primaries were stomach in 47.9% and GEJ in 52.1% of patients
- 80.8% of patients had tumours of clinical stage T3/T4 at baseline and 78.1% were N+, with no difference between arms
- FLOT was associated with significantly higher rates of pCR and pCR + pSR vs. ECF

Pathological regression, n (%)	ECF/ECX (n=137)	FLOT (n=128)	p-value (2-sided)
Complete (pCR)	8 (5.8)	20 (15.6)	0.015
Subtotal (pSR)	23 (16.8)	27 (21.1)	
pCR + pSR	31 (22.6)	47 (36.7)	0.015
Partial (pPR)	28 (20.4)	23 (18.0)	
Minor (pMR)	44 (32.1)	45 (35.2)	
No response (pNR)	8 (5.8)	4 (3.1)	

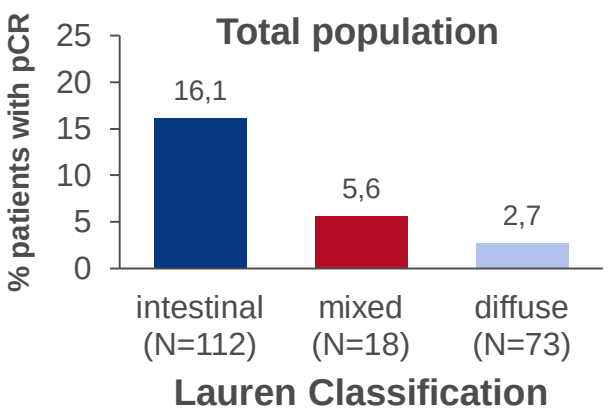
pSR, pathological sub-total response

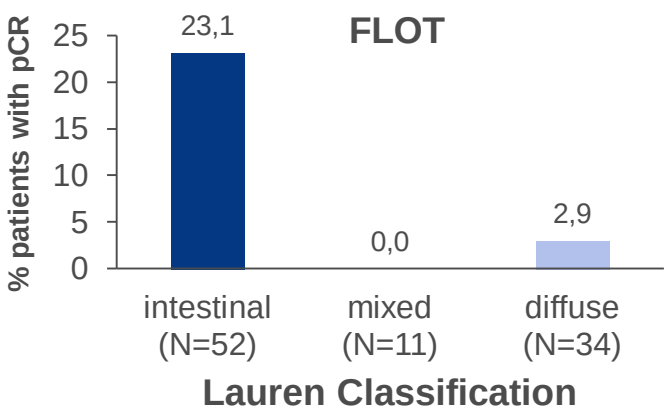
*Presented by S-E Al-Batran

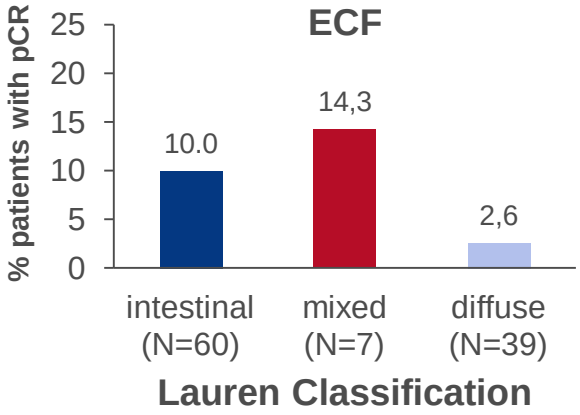
Pauligk et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 36LBA

36LBA: Pathological response to neoadjuvant 5-FU, oxaliplatin and docetaxel (FLOT) versus epirubicin, cisplatin and 5-FU (ECF) in patients with locally advanced, resectable gastric/esophagogastric junction (EGJ) cancer: Data from the phase II part of the FLOT4 phase III study of the AIO – Pauligk C* et al

Key results







Conclusion

- **FLOT shows significantly more pathological response than ECF/ECX in patients with resectable gastric and GEJ cancer**

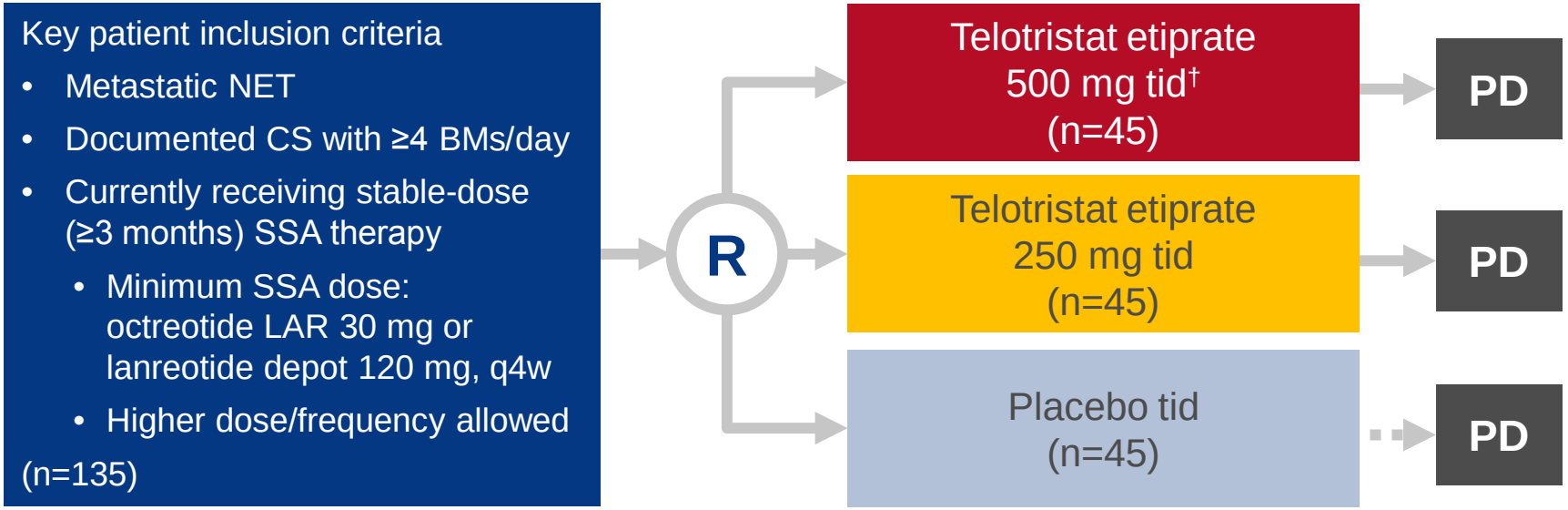
*Presented by S-E Al-Batran

Pauligk et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 36LBA

37LBA: Telotristat etiprate is effective in treating patients with carcinoid syndrome that is inadequately controlled by somatostatin analog therapy (the phase 3 TELESTAR clinical trial) – Kulke MH et al

Study objective

- To assess the effectiveness of telotristat* etiprate in reducing mean number of daily BMs averaged over the 12-week double-blind period of a phase 3 global trial, TELESTAR



†Including a blinded titration step of one week of 250 mg tid

PRIMARY ENDPOINT(S)

- Change from baseline in daily BM frequency

SECONDARY ENDPOINTS

- Changes in urinary 5-hydroxyindoleacetic acid, cutaneous flushing episodes and abdominal pain

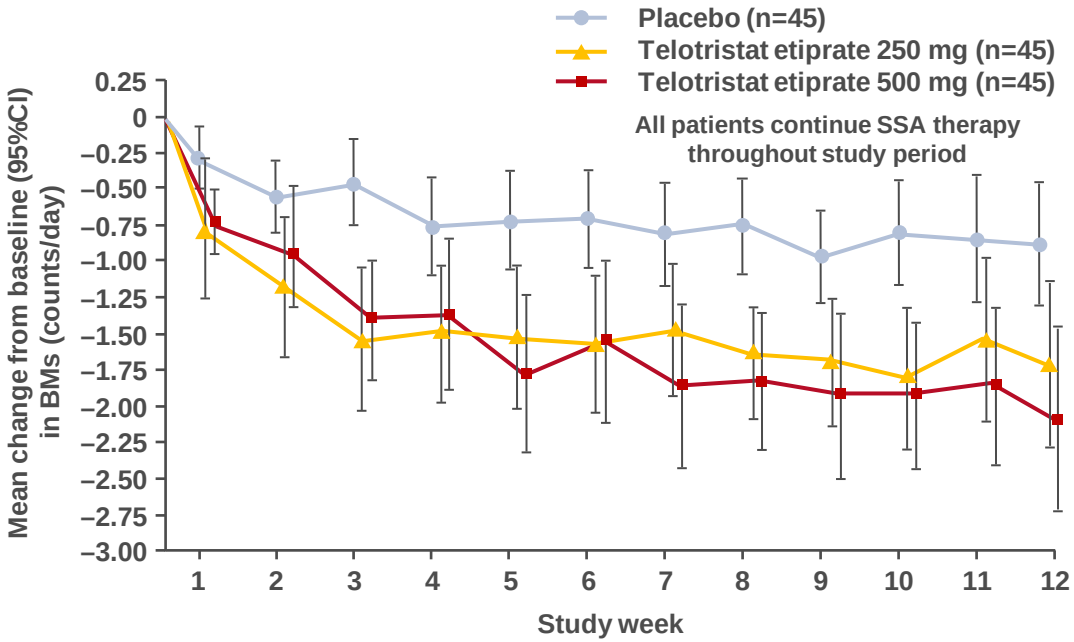
*Investigational drug targeting tryptophan hydroxylase (TPH) that triggers excess serotonin production within mNET cells.
BM, bowel movement; CS, carcinoid syndrome.

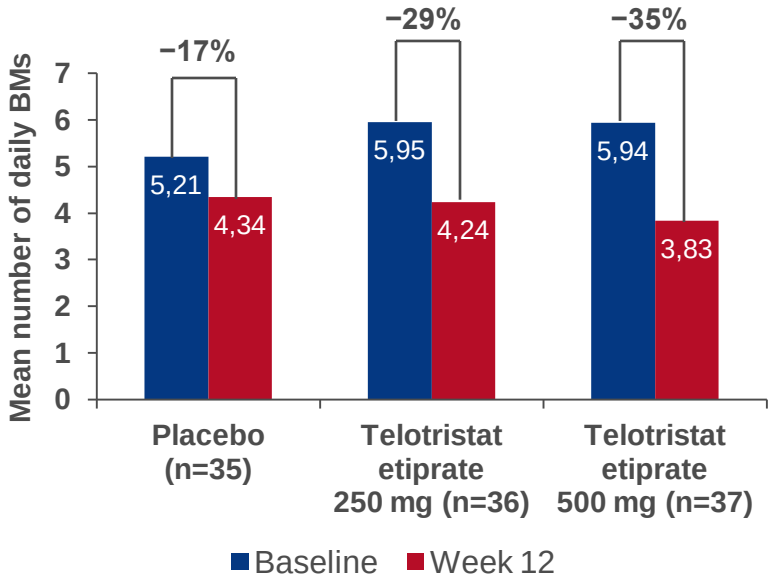
Kulke et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 37LBA

37LBA: Telotristat etiprate is effective in treating patients with carcinoid syndrome that is inadequately controlled by somatostatin analog therapy (the phase 3 TELESTAR clinical trial) – Kulke MH et al

Key results

- Demographics were similar across the three treatment groups; mean age was 64 years and baseline mean number of BMs/day was 5.7
- Both telotristat etiprate groups reduced mean BM frequency greater than placebo ($p<0.001$) (figure)

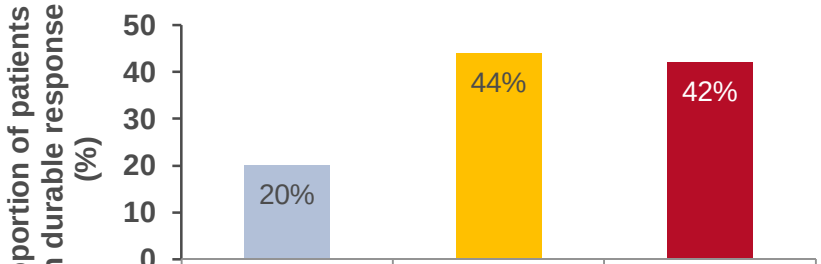




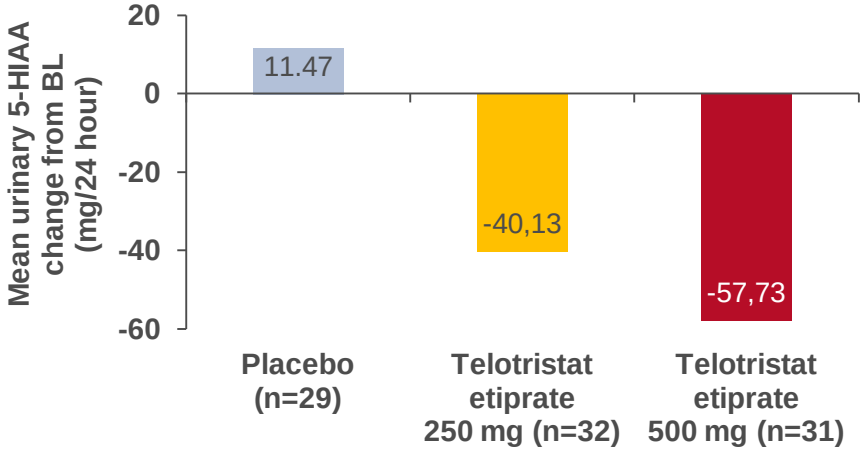
Kulke et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 37LBA

37LBA: Telotristat etiprate is effective in treating patients with carcinoid syndrome that is inadequately controlled by somatostatin analog therapy (the phase 3 TELESTAR clinical trial) – Kulke MH et al

Key results (cont.)



Odds ratio (95%CI)	-	3.49 (1.33, 9.16)	3.11 (1.20, 8.10)
p-value		0.011	0.020



- Reductions in flushing and abdominal pain were greater with telotristat etiprate vs. placebo; however, differences were not statistically significant
- SAEs and discontinuations were uncommon and were similar between groups
- Events of depression and nausea were mild or moderate and did not lead to treatment discontinuation

Conclusion

- **Telotristat etiprate provided statistically significant and clinically meaningful reductions in BM frequency and represents a promising new class of treatment for patients with severe carcinoid syndrome**

Kulke et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 37LBA

104: CDH2 negative esophageal squamous cell carcinoma with cytotoxic T-lymphocyte signatures is a good responder subtype to definitive chemoradiotherapy – Tanaka Y et al

Study objective

- To investigate whether immunoactivation is induced by CRT, and to assess the prognosis in OSCCs with immunoreactive subtype

Study design

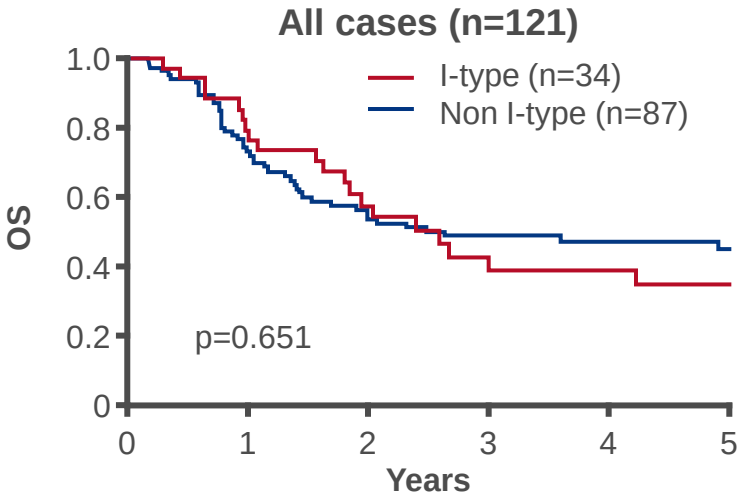
- Sixty biopsy samples from 30 locally advanced OSCC patients (stage II/III: n=14/16) before and 3–4 weeks after CRT
- Affymetrix arrays (HG-U133Plus2.0)
- USV clustering of all 60 samples
- Selection of up-regulated genes after CRT from cases with CR and identification of immunoreactive subtype by clustering
- Additionally, gene expression profiles were obtained from another 125 samples
  - Survival analysis was performed in 121 of 125 cases whose clinical data was available

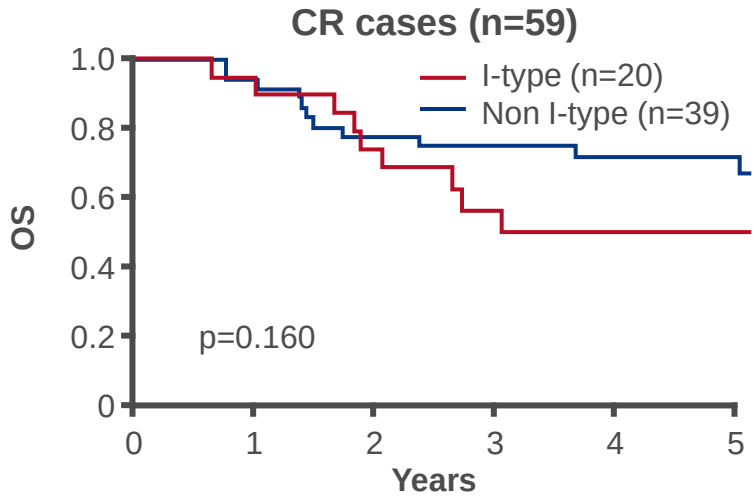
Tanaka et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 104

104: CDH2 negative esophageal squamous cell carcinoma with cytotoxic T-lymphocyte signatures is a good responder subtype to definitive chemoradiotherapy – Tanaka Y et al

Key results

- 1,014 up-regulated genes were identified in 19 CR cases, including at least 235 immune activation-related genes, in particular CTL-related genes such as IFNγ, PRF1 and GZMB
- Clustering analysis with expression profiles of these 235 genes allowed the immune-activated cases, designated as I-type, to be distinguished from other cases





- A series of mesenchymal transition-related genes were over-expressed in I-type OSCC with early relapse vs. epithelial type markers that were over-expressed in I-type OSCC without early relapse

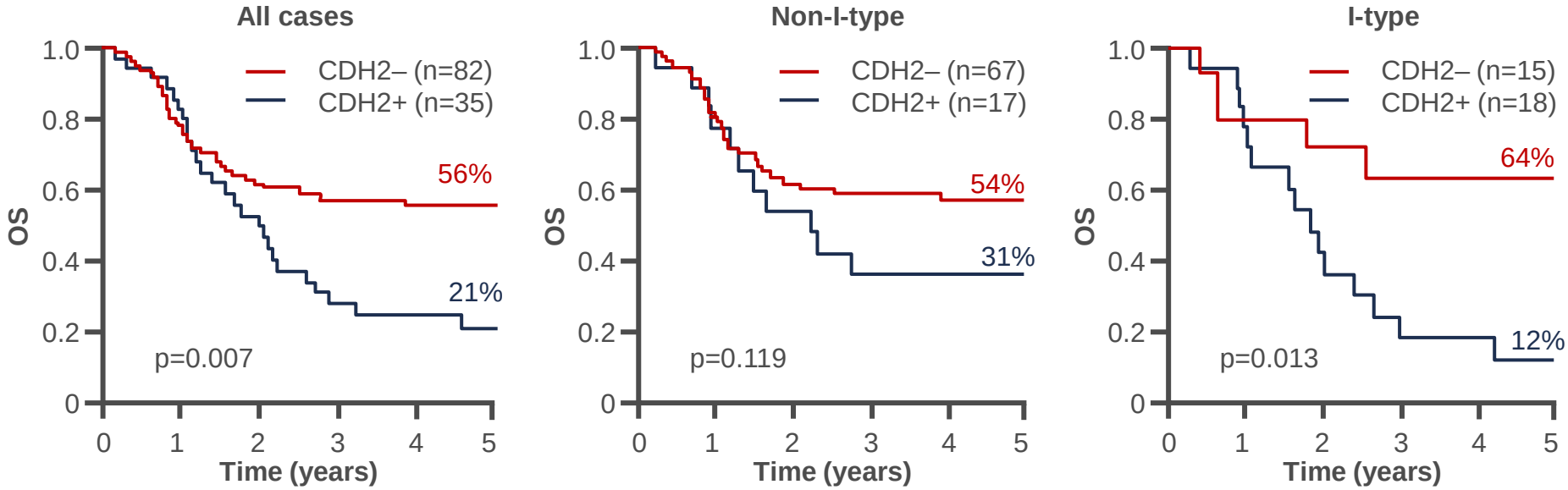
IFNγ, interferon gamma; GZMB, granzyme B; PRF1, perforin 1

Tanaka et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 104

104: CDH2 negative esophageal squamous cell carcinoma with cytotoxic T-lymphocyte signatures is a good responder subtype to definitive chemoradiotherapy – Tanaka Y et al

Key results

- OS in CDH2 negative cases was significantly better than CDH2 positive cases in the oesophageal cancer analysis (figure)
- OS and recurrence rate of CDH2-negative cases in the I-type was significantly better than that of CDH2-positive cases in the I-type (figure)



Conclusion

- **CRT may activate CTL in a certain subtype and immunoreactive OSCCs with epithelial phenotype may receive the benefit of the immune activation therapy**

CDH, cadherin; CTL, cytotoxic T-lymphocyte

Tanaka et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 104

901: Reporting adverse events (AEs) in cancer surgery randomized trial: A systemic analysis of published trials in oesogastric (OG) and gynecological (GY) cancer patients – Meghelli L et al

Study objective

- To analyse the quality of the description of surgical AEs in published cancer surgery clinical trials

Study design

- Systematic review of all consecutive fully published trials issued between 01/1990 and 11/2014 in English, including >50 patients and investigating surgery in oesogastric (OG) or gynaecological (GY) patients using an 18-item questionnaire based on CONSORT recommendations
- The questionnaire was weighted using a 4-point Likert-scale by 15 experts (9 surgeons and 6 methodologists)

Leila et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 901

901: Reporting adverse events (AEs) in cancer surgery randomized trial: A systemic analysis of published trials in oesogastric (OG) and gynecological (GY) cancer patients – Meghelli L et al

Key results

- 179 published studies (133 OG and 46 GY) were analysed
  - Postoperative AEs were described in 89.9% of these studies
  - 43.6% assessed multimodal treatments
  - Morbidity was the primary objective in 31.3% of the studies
- The items of greatest importance to the expert panel are shown below

Item	Score	n (%) of publications reporting these items	95%CI
Use of a validated severity grading scale (NCI-CT, Dindo-Clavien…)	3.9	30 (16.8)	11.3, 22.2
Precise definition of AEs (NCI-CT, Dindo-Clavien…)	3.8	48 (26.8)	20.3, 33.3
Discussion of harms/benefit balance	3.7	128 (71.5)	64.9, 78.1
AEs reported by arm	3.6	154 (86.0)	81, 91.1
AEs reported by grade	3.6	15 (8.4)	4.3, 12.4
Exhaustive list of AEs	3.6	64 (35.8)	28.7, 42.8

Leila et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 901

901: Reporting adverse events (AEs) in cancer surgery randomized trial: A systemic analysis of published trials in oesogastric (OG) and gynecological (GY) cancer patients – Meghelli L et al

Key results (cont.)

- Pure surgical trials had a higher mean AE grading score than trials that involved multimodal treatments (20.2 [SD 7.7] vs. 13.6 [SD 10.2]; p=0.01)
- Trials with morbidity as their primary objective were also better in terms of AE reporting compared with trials with other primary objectives (mean AE grading score 23.9 [SD 7.18] vs. 14.3 [SD 8.8]; p<0.001)
- The period of publication, continent of the sponsor, impact factor of the journal publishing the study or the number of enrolled patients did not impact the score

Conclusions

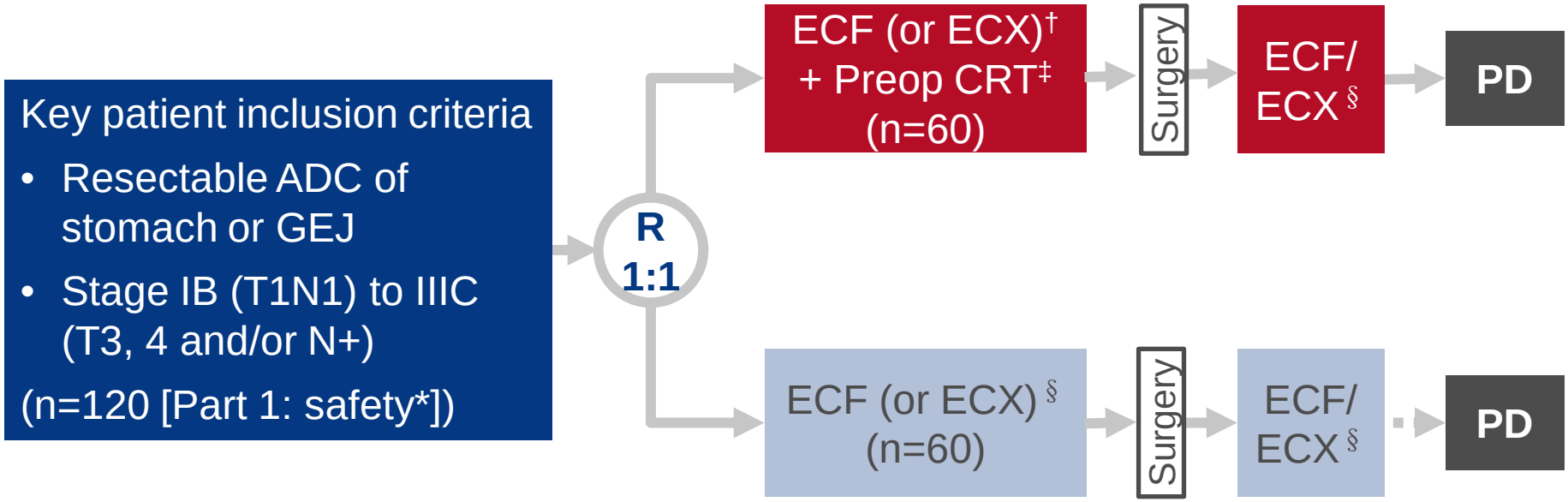
- **This is the largest systematic review of AE reporting in surgical trials. Overall the review showed that surgical AEs were poorly reported**
- **The reporting of AEs was inaccurate irrespective of the journal's impact factor**
- **Consensus on how to report surgical AEs is needed**

Leila et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 901

2200: TOPGEAR: A randomized phase II/III trial of perioperative ECF chemotherapy versus preoperative chemoradiation plus perioperative ECF chemotherapy for resectable gastric cancer. Interim results from an international, intergroup trial of the AGITG/TROG/NCIC CTG/EORTC – Leong T et al

Study objective

- To investigate the efficacy* and safety of preoperative CRT + perioperative ECF CT vs. perioperative ECF CT alone in patients with resectable GC



PART 1 (phase 2, reported here)

- Toxicity
- Feasibility, accrual, pathological response

PART 2 (phase 3, reported later)

- OS

*Efficacy data will be reported later; †2 cycles q21d; ‡45 Gy; § 3 cycles q21d

Leong et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2200

2200: TOPGEAR: A randomized phase II/III trial of perioperative ECF chemotherapy versus preoperative chemoradiation plus perioperative ECF chemotherapy for resectable gastric cancer. Interim results from an international, intergroup trial of the AGITG/TROG/NCIC CTG/EORTC – Leong T et al

Key results

	CT (n=60)	CRT (n=60)
Preoperative CT compliance, n (%)		
Commenced all cycles	56 (93.3)	59 (98.3)
Completed all cycles	32 (53.3)	39 (65)
Dose reductions	29 (48.3)	24 (40)
Surgery compliance		
Received surgery, n (%)	54 (90)	51 (85)
Non-curative surgery, n (%)	3 (5)	3 (5)
Median interval to surgery, weeks	4.9	5.7
	CT (n=48)	**CRT (n=53)**
Postoperative CT compliance		
Commenced all cycles	34 (64)	24 (50)
Completed all cycles	21 (40)	14 (29)
Dose reductions	22 (42)	22 (46)

Leong et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2200

2200: TOPGEAR: A randomized phase II/III trial of perioperative ECF chemotherapy versus preoperative chemoradiation plus perioperative ECF chemotherapy for resectable gastric cancer. Interim results from an international, intergroup trial of the AGITG/TROG/NCIC CTG/EORTC – Leong T et al

Key results (cont.)

- Surgical complications: 21.6 vs. 22.2% in the CRT vs. CT group, respectively

Grade ≥3 AEs in ≥10% of patients, n (%)	CT (n=60)	CRT (n=60)
GI toxicity	19 (31.7)	18 (30.0)
Nausea	4 (6.7)	8 (13.3)
Dysphagia	5 (8.3)	6 (10)
Anorexia	7 (11.7)	6 (10)
Diarrhoea	7 (11.7)	10 (16.7)
Haematological toxicity	30 (50.0)	31 (51.7)
Neutropenia	24 (40.0)	27 (45.0)
Febrile neutropenia	5 (8.3)	6 (10.0)
Leukocytes	5 (8.3)	6 (10.0)

Conclusions

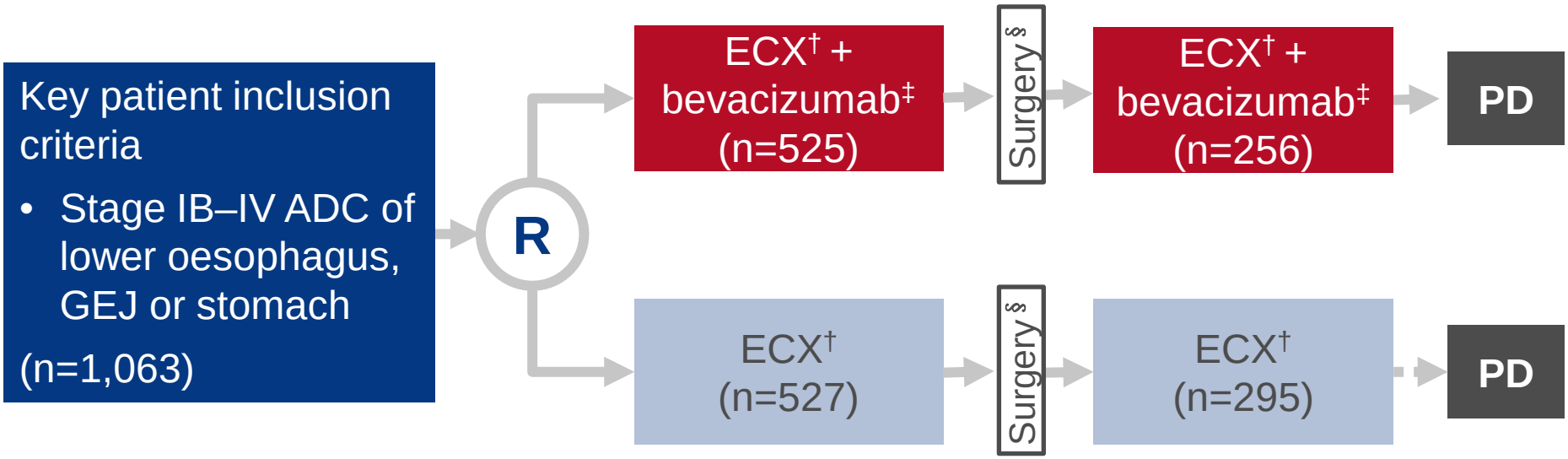
- **Preoperative CRT is feasible in patients with resectable GC and has an acceptable safety profile**
- **Preoperative CRT does not affect surgical compliance or surgical morbidity**

Leong et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2200

2201: Peri-operative chemotherapy ± bevacizumab for resectable gastro-oesophageal adenocarcinoma: Results from the UK Medical Research Council randomised ST03 trial (ISRCTN 46020948) – Cunningham D et al

Study objective

- To evaluate the efficacy* and safety of perioperative bevacizumab + ECX vs. perioperative ECX alone in patients with resectable GEC



PRIMARY ENDPOINT(S)

- OS (all patients)

SECONDARY ENDPOINTS

- Response, curative resection rate, DFS, PFS
- Safety

*Efficacy data reported later; †Epirubicin 50 mg/m^2 IV d1, cisplatin 60 mg/m^2 IV d1, capecitabine 1,250 mg/m^2 po daily, 3 cycles q3w; †7.5 mg/kg IV d1, 3 cycles q3w then 6 maintenance doses; ‡7.5mg/kg on d1; §5–6 week break pre-surgery, and 6–10 week break post-surgery

Cunningham et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2201

2201: Peri-operative chemotherapy ± bevacizumab for resectable gastro-oesophageal adenocarcinoma: Results from the UK Medical Research Council randomised ST03 trial (ISRCTN 46020948) – Cunningham D et al

Key results

	ECX + Bev	ECX	HR (95%CI)	p-value
mOS, months	34.46	33.97	1.067 (0.891, 1.279)	0.4784
3-year OS, % (95%CI)	47.6 (42.3, 52.7)	48.9 (43.6, 53.8)	-	-

- PFS: HR 1.026, p=0.7683; DFS: HR 1.006, p=0.9425

n (%)	ECX + Bev	ECX	p-value
ORR	170 (40)	180 (42)	0.488
CR	11 (3)	21 (5)	-
PR	159 (37)	159 (37)	-
SD	228 (53)	219 (51)	-
PD	21 (5)	21 (5)	-
*Mandard TRG Grade 1–3	133 (38)	145 (39)	0.813†

- Postoperative wound healing complications:
  - 12% with ECX + bevacizumab vs. 7% with ECX alone
- Anastomotic leaks in patients undergoing oesophago-gastrectomy:
  - 23% ECX + bevacizumab vs. 9% with ECX alone

*For patients undergoing surgical resection; †vs. grade 4–5
Bev, bevacizumab

Cunningham et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2201

2201: Peri-operative chemotherapy ± bevacizumab for resectable gastro-oesophageal adenocarcinoma: Results from the UK Medical Research Council randomised ST03 trial (ISRCTN 46020948) – Cunningham D et al

Key results (cont.)

Grade ≥3 AEs in ≥7% of patients, %	ECX + Bevacizumb (n=525)	ECX (n=527)
Preoperative AEs		
Neutropenia	26	27
Lethargy	8	8
Nausea	4	7
Postoperative AEs		
Neutropenia	32	32
Lethargy	10	7
Nausea	6	8

Conclusions

- **Perioperative bevacizumab + ECX did not improve survival, tumour response or the likelihood of curative resection vs. ECX alone in patients with resectable GEC**
- **Preoperative bevacizumab may be associated with an increased postoperative anastomotic leak in patients undergoing oesophago-gastrectomy**

Cunningham et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2201

2202: Incorporation of N0 stage with insufficient numbers of lymph nodes into N1 stage in the seventh edition of the TNM classification improves prediction of prognosis in gastric cancer: Results of a single-institution study of 1258 Chinese patients – Li B

Study objective

- To examine the prognosis of patients designated “node-negative with examined lymph nodes (eLNs) ≤15”
- To assess the added value of incorporating this into the pN1 category of the seventh edition of the AJCC/UICC TNM classification system

Study design

- Non-randomised, single-centre study

Key patient inclusion criteria

- Patients with GC
- Patients with eLNs >15 or node-negative with eLNs ≤15
- Undergoing radical gastric resection

(n=1258)

- Node-negative patients with eLNs ≤15 were incorporated into pN1, and this designation was compared with the current 7th Ed UICC definition
- Endpoints:
  - OS
  - Homogeneity, discriminatory ability, and monotonicity of gradients of the two systems

Note: Based on data from abstract only.

Li et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2202

2202: Incorporation of N0 stage with insufficient numbers of lymph nodes into N1 stage in the seventh edition of the TNM classification improves prediction of prognosis in gastric cancer: Results of a single-institution study of 1258 Chinese patients – Li B

Key results

- Node-negative patients with eLNs ≤15 had worse survival than those with eLNs >15:

	Node –ve & eLNs ≤15	eLNs >15	p-value
3-year OS, %	84.0	94.6	<0.001
5-year OS, %	78.6	93.4	<0.001

- In univariate and multivariate analyses, the hypothetical N stage showed superiority to the 7th edition pN staging

- The TNM system was found to be the optimum prognostic stratification based on the following tests:

	Node –ve & eLNs ≤15	eLNs >15
Linear trend χ^2 score	314.418	295.911
Likelihood ratio χ^2 score	304.860	299.295
AIC* values	4243.832	4260.239

Conclusion

- **The incorporation of "node-negative patients with eLNs ≤15" into the pN1 stage in the 7th edition of the TNM classification may be considered of added value**

Note: Based on data from abstract only.

*Akaike information criterion

Li et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2202

2203: Association with programmed death ligand-1 (PDL-1) expression and *Helicobacter pylori* infection in patients with "non diffusive type" gastric carcinoma radically resected – Di Bartolomeo M et al

Study objective

- To evaluate the association between the presence of *H. pylori*, PD-L1 expression and lymphocyte infiltrate in resected GC samples

Study design

- Tissue specimens were collected from 346 patients from the phase 3 randomised trial ITACA-S who had radically resected GC
- 55 cases with non-diffuse type carcinoma and with paired normal mucosae adequate for *H. pylori* analysis were selected for evaluation
- Endpoints measured
  - Malignant sections:
    - PD-L1 expression by immunohistochemistry using anti-PD-L1 (Anti-B7-H1, Anti-CD274) mAb
    - Intratumoural and peritumoural lymphocytes infiltrate score (morphological analysis)*
  - Non-malignant sections:
    - *H. pylori* infection (haematoxylin and eosin, and Giemsa staining)

*from Klintrup K, et al. *Eur J Cancer* 2005; 41: 2645–54

Di Bartolomeo et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2203

2203: Association with programmed death ligand-1 (PDL-1) expression and *Helicobacter pylori* infection in patients with "non diffusive type" gastric carcinoma radically resected – Di Bartolomeo M et al

Key results

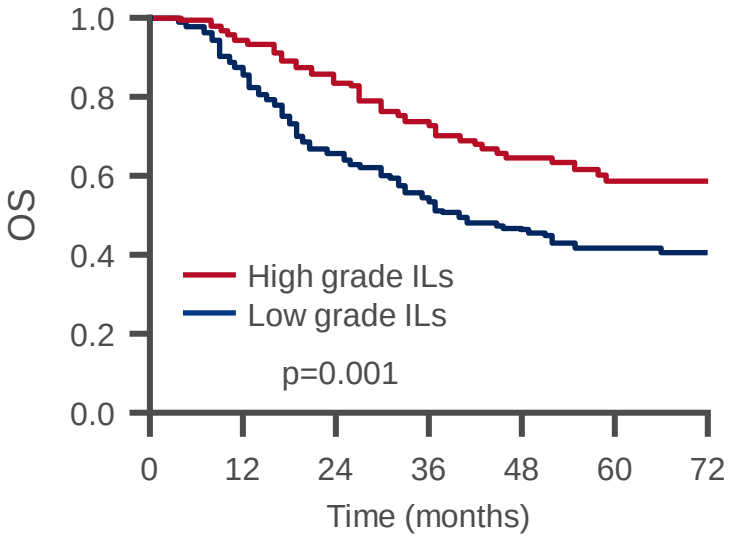
- *H. pylori* infection was significantly associated with PD-L1 expression (p=0.010):
  - 23/55 (42%) samples were positive for *H. pylori* infection
  - 87% (95%CI 66.4, 97.2%) of these vs. 53% (95%CI 34.7, 70.9%) in *H. pylori*-negative samples were positive for PD-L1 expression (p=0.010)
- PD-L1 was overexpressed in EBV-positive patients and in 4 of 5 patients with microsatellite instability
- PD-L1 overexpression was not associated with N stage (p=0.45) or T stage (p=0.23)
- Neither PD-L1 expression (p=0.377) nor *H. pylori* infection (p=78) were significantly associated with lymphocytic infiltrate

Di Bartolomeo et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2203

2203: Association with programmed death ligand-1 (PDL-1) expression and *Helicobacter pylori* infection in patients with "non diffusive type" gastric carcinoma radically resected – Di Bartolomeo M et al

Key results (cont.)

- An exploratory analysis on the entire dataset of 346 patients showed an association between infiltrating lymphocytes and OS (p=0.001; graph)
- Multivariable Cox analysis confirmed infiltrating lymphocytes and stage to be independent prognostic factors (table)



	HR	95%CI		p-value
Infiltrating lymphocytes				
Low	1.77	1.23	2.56	0.002
High				
Stage				
IIB vs. IB–IIA	3.76	1.43	9.89	<0.001
IIIA vs. IB–IIA	4.26	1.61	11.22	
IIIB vs. IB–IIA	6.95	2.74	17.63	
IIIC vs. IB–IIA	15.68	6.33	38.88	

Conclusion

- **These findings show an association between *H. pylori* infection and PD-L1 expression in GC, supporting further research on immunotherapy in patients with *H. pylori*-positive, non-diffuse type GC**

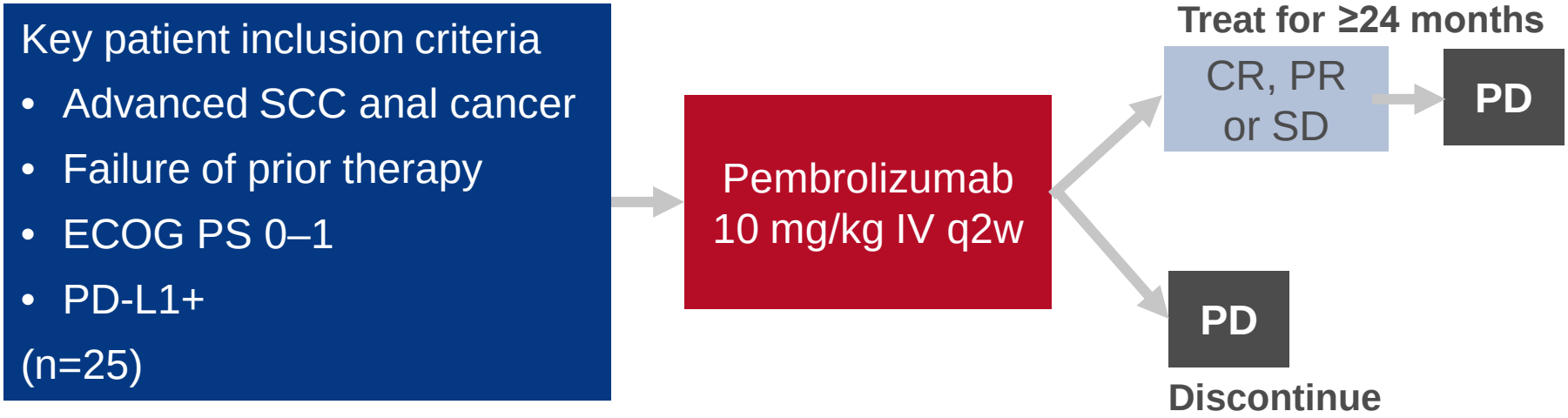
Di Bartolomeo et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2203

ANAL CANCER

500: Pembrolizumab (MK-3475) for PD-L1-positive squamous cell carcinoma (SCC) of the anal canal: Preliminary safety and efficacy results from KEYNOTE-028 – Ott PA et al

Study objective

- To assess the efficacy and safety of pembrolizumab in patients with PD-L1+ advanced SCC anal carcinoma



PRIMARY ENDPOINT(S)

- ORR (RECIST v1.1)

SECONDARY ENDPOINTS

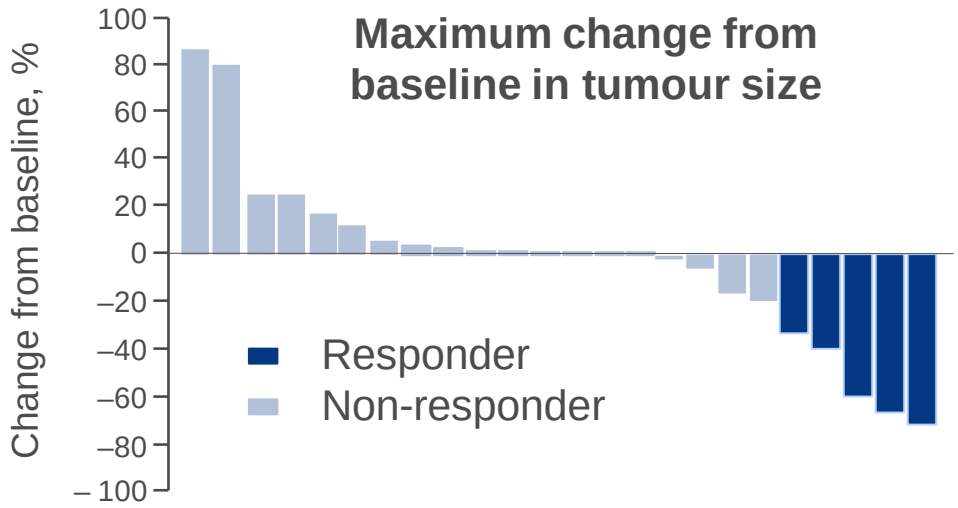
- PFS, OS, duration of response
- Safety

Ott et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 500

500: Pembrolizumab (MK-3475) for PD-L1-positive squamous cell carcinoma (SCC) of the anal canal: Preliminary safety and efficacy results from KEYNOTE-028 – Ott PA et al

Key results

Best response	n (%)	95%CI
ORR	5 (20)	6.8, 40.7
CR	0	0.0, 13.7
PR	5 (20)	6.8, 40.7
SD	11 (44)	24.4, 65.1
PD	8 (32)	14.9, 53.5
Not assessed	1 (4)	0.1, 20.4



Ott et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 500

500: Pembrolizumab (MK-3475) for PD-L1-positive squamous cell carcinoma (SCC) of the anal canal: Preliminary safety and efficacy results from KEYNOTE-028 – Ott PA et al

Key results (cont.)

- mTTR: 15.6 weeks (range 7.1, 21.0)
- Median SD duration: 3.6 months (range 1.8, 11.0)
- mPFS: 3.0 months (95%CI 1.7, 7.3); 6-month PFS: 31.6%; 12-month PFS: 19.7%

Grade 3–4 AEs occurring in ≥1 patient, n (%)	n=25
TSH increased	1 (4)
Colitis, grade 3	1 (4)
Diarrhoea, grade 3	1 (4)
General physical health deterioration	1 (4)

Conclusions

- **Pembrolizumab demonstrated promising antitumour activity in patients with heavily pre-treated PD-L1+ advanced SCC anal carcinoma**
- **The safety profile was manageable and consistence with previous studies**
- **These data support future studies of pembrolizumab in advanced anal carcinoma**

Ott et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 500

NEUROENDOCRINE TUMOURS

5LBA: Everolimus in advanced nonfunctional neuroendocrine tumors (NET) of lung or gastrointestinal (GI) origin: Efficacy and safety results from the placebo-controlled, double-blind, multicenter, Phase 3 RADIANT-4 study – Yao J et al

Study objective

- To investigate the efficacy and safety of everolimus in patients with advanced, non-functional, progressive lung or GI NETs

Key patient inclusion criteria

- Well differentiated (G1/G2), advanced, progressive, non-function NET of lung/GI origin
- Absence of active or any history of carcinoid syndrome
- ≤6 months of radiological PD

(n=302)

R 2:1

Everolimus 10 mg/day (n=205) → PD

Stratification

- Prior SSA (yes vs. no)
- Tumour origin (stratum A vs. B*)
- WHO PS (1 vs. 2)

Placebo (n=97) → PD

PRIMARY ENDPOINT(S)

- PFS

SECONDARY ENDPOINTS

- OS, ORR, DCR
- Safety, HRQoL, WHO PS

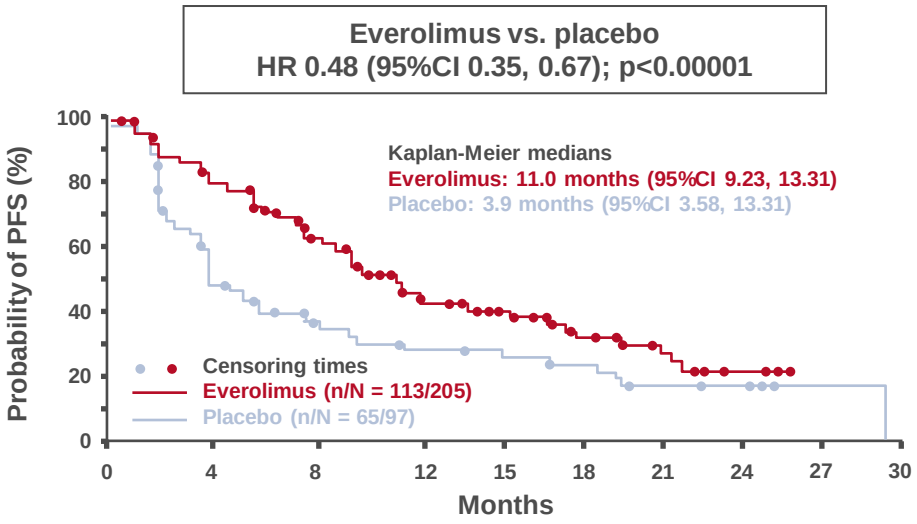
*Stratum A (better prognosis) – appendix, caecum, jejunum, ileum, and NET of unknown primary; stratum B (worse prognosis) – lung, stomach, rectum and colon (except caecum)

Yao et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 5LBA

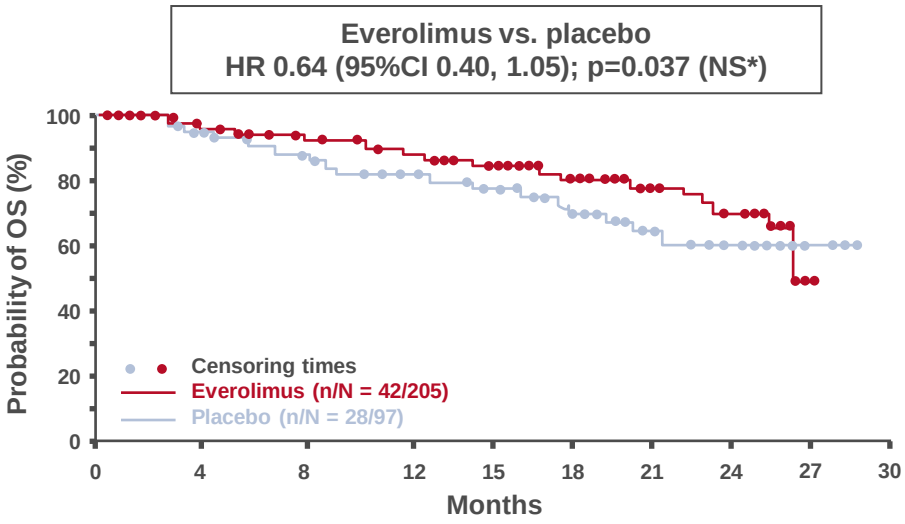
5LBA: Everolimus in advanced nonfunctional neuroendocrine tumors (NET) of lung or gastrointestinal (GI) origin: Efficacy and safety results from the placebo-controlled, double-blind, multicenter, Phase 3 RADIANT-4 study – Yao J et al

Key results

PFS



OS (interim analysis)



Best overall response, n (%)	Everolimus (n=205)	Placebo (n=97)
ORR (CR + PR)	4 (2.0)	1 (1.0)
DCR (CR + PR + SD)	169 (82.4)	63 (64.9)
PD	19 (9.3)	26 (26.8)
Unknown	17 (8.3)	8 (8.2)

*Significance defined as p ≤0.0002

Yao et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 5LBA

5LBA: Everolimus in advanced nonfunctional neuroendocrine tumors (NET) of lung or gastrointestinal (GI) origin: Efficacy and safety results from the placebo-controlled, double-blind, multicenter, Phase 3 RADIANT-4 study – Yao J et al

Key results (cont.)

TEAEs grade 3–4 in ≥3% of patients, %	Everolimus (n=205)	Placebo (n=97)
Stomatitis	9	0
Diarrhoea	7	2
Fatigue	3	1
Anaemia	4	1
Hyperglycaemia	3	0
Deaths, n (%)	**Everolimus (n=205)**	**Placebo (n=97)**
All	41 (20.3)	28 (28.6)
On-treatment	7 (3.5)	3 (3.1)
Due to study indication	4 (2.0)	1 (1.0)

Conclusions

- **Everolimus significantly improved PFS vs. placebo in patients with advanced, non-functional, progressive lung or GI NET**
- **Interim OS analysis favoured everolimus vs. placebo**
- **The safety profile for everolimus was consistent with previous studies**
- **Everolimus is the first targeted agent to show robust antitumour activity with acceptable tolerability across a broad spectrum of NETs**

Yao et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 5LBA

6LBA: ^{177}Lu-Dotatate significantly improves progression-free survival in patients with midgut neuroendocrine tumours: Results of the phase III NETTER-1 trial – Strosberg J* et al

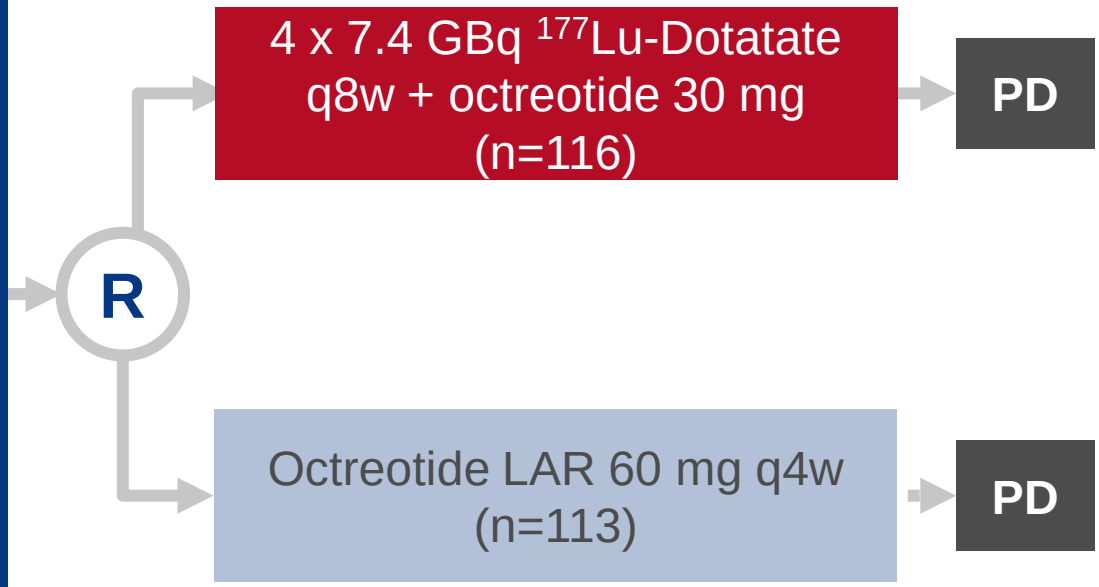
Study objective

- To assess the efficacy and safety of ^{177}Lu-Dotatate + octreotide 30 mg vs. octreotide LAR 60 mg (off-label use) in patients with inoperable, somatostatin receptor positive, mid-gut NET, with PD following octreotide LAR 30 mg (on-label use)

Key patient inclusion criteria

- Metastatic/locally advanced, inoperable, midgut NET
- Ki67 index ≤20% (grade 1–2)
- Somatostatin-receptor positive disease
- PD with octreotide LAR 30–40 mg q3–4w

(n=229)



PRIMARY ENDPOINT(S)

- PFS

SECONDARY ENDPOINTS

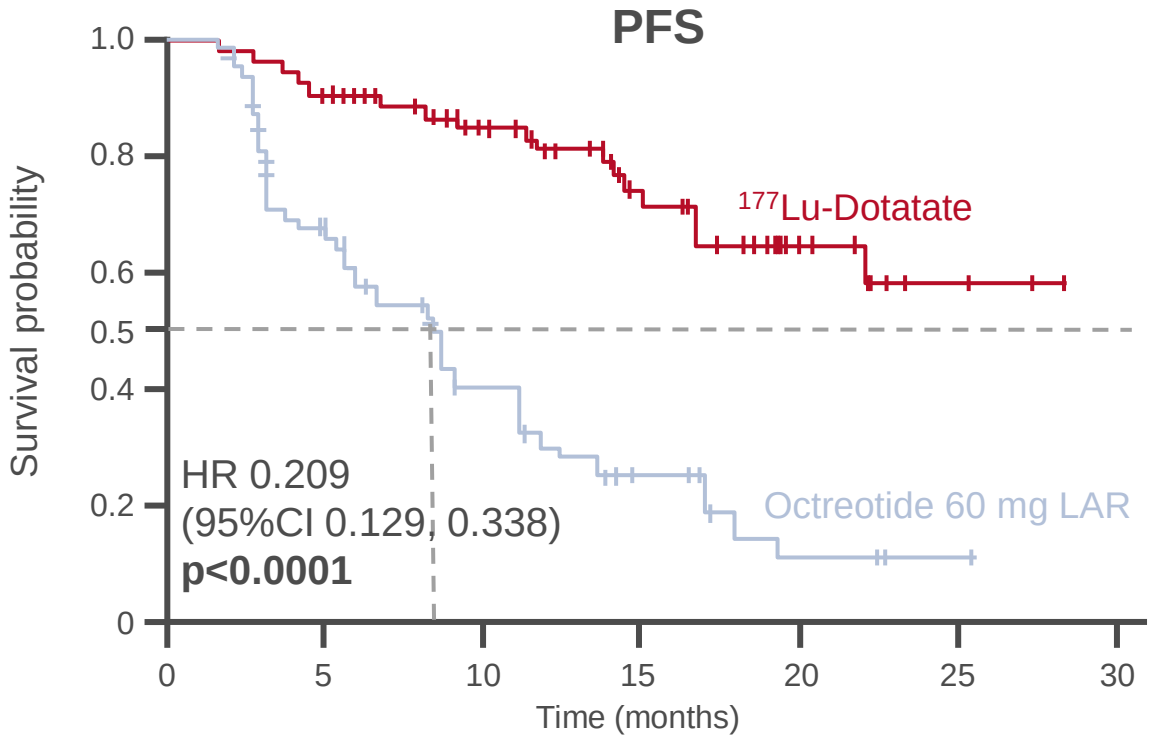
- ORR, OS, TTP, safety, tolerability, QoL

*Presented by P Ruszniewski

Strosberg et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 6LBA

6LBA: ^{177}Lu-Dotatate significantly improves progression-free survival in patients with midgut neuroendocrine tumours: Results of the phase III NETTER-1 trial – Strosberg J* et al

Key results



n=229 (ITT)
No. events: 90

- ^{177}Lu-Dotatate: 23
- Octreotide 60 mg LAR: 67

- Interim OS: 13 deaths with ^{177}Lu-Dotatate vs. 22 with octreotide LAR 60 mg

*Presented by P Ruszniewski

Strosberg et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 6LBA

6LBA: ^{177}Lu-Dotatate significantly improves progression-free survival in patients with midgut neuroendocrine tumours: Results of the phase III NETTER-1 trial – Strosberg J* et al

Key results (cont.)

	^{177}Lu-Dotatate (n=101)	Octreotide LAR 60 mg (n=100)
CR, n	1	0
PR, n	18	3
ORR, n (95%CI)	19 (11, 26)	3 (0, 6)*
PD, n (%)	5 (4)	27 (24)
SD, n (%)	77 (66)	70 (62)

- SAEs: 26 vs. 24% (treatment-related, 9 vs. 1%); discontinuations due to AEs: 6 vs. 9% (treatment-related, 5 vs. 0%) with ^{177}Lu-Dotatate vs. octreotide LAR 60 mg, respectively

Conclusions

- **^{177}Lu-Dotatate was superior to octreotide LAR 60 mg in terms of PFS and ORR in patients with progressive metastatic midgut NETs**
- **Interim analysis suggested longer OS with ^{177}Lu-Dotatate vs. octreotide LAR 60 mg**
- **Current safety data confirmed the results of a previous phase 1–2 study**
  - **^{177}Lu-Dotatate had a favourable safety profile**
- **^{177}Lu-Dotatate appears to be a major advance in this patient population**

*Presented by P Ruszniewski

*p<0.0004

Strosberg et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 6LBA

PERITONEAL CARCINOMATOSIS

2204: Predicting incomplete cytoreduction and aborted hyperthermic intraperitoneal chemotherapy procedures in patients with peritoneal carcinomatosis – Milovanov V et al

Study objective

- To develop a risk scoring system to evaluate the risk of incomplete cytoreduction (IC) and aborted hyperthermic intraperitoneal chemotherapy (HIPEC) procedures in patients with peritoneal carcinomatosis

Study design

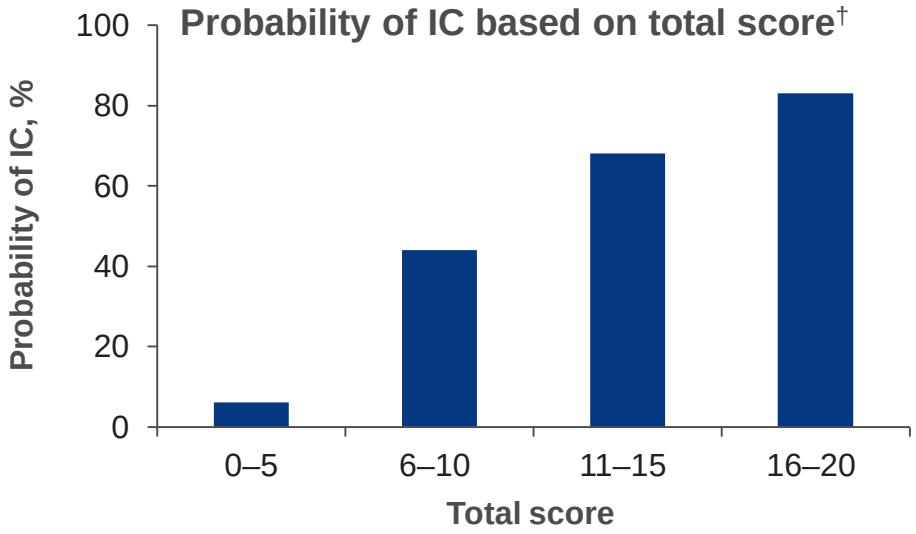
- Data were analysed from 452 attempts of cytoreductive surgery (CRS) or HIPEC procedures using univariate analysis and multivariate binary logistic regressions
  - Patient population:
    - Procedures: complete cytoreduction (n=335); IC/HIPEC (n=45); aborted HIPEC (n=72)
    - Tumour origin: appendiceal (n=305), ovarian (n=61), colon (n=56), mesothelioma (n=30)
- Preoperative risk factors for IC/HIPEC were selected to develop a risk predictive model
- Data on all CRS/HIPEC attempts were randomly divided into two subsets
  - Subset 1: development of a weighted model (n=225)
  - Subset 2: validation of the weight model (n=225)

Milovanov et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2204

2204: Predicting incomplete cytoreduction and aborted hyperthermic intraperitoneal chemotherapy procedures in patients with peritoneal carcinomatosis – Milovanov V et al

Key results

Variable	β-coefficients* (95%CI); p-value (n=305)	Score†
C-reactive protein >2.5 mg/L	6 (2.6, 13.2); <0.001	6
CA-125 >3x ULN	4 (1.3, 13.5); 0.017	4
Neutrophil-lymphocyte ratio >2.6	3 (1.4, 6.7); 0.004	3
CEA >3x ULN	3 (1.3, 7.3); 0.011	3
High grade tumour	2 (1.1, 5.2); 0.038	2
Prior surgical score ≥2	2 (1.1, 2.4); 0.021	2



*Multivariate logistic regression;
†For patients with peritoneal carcinomatosis of appendiceal origin

Milovanov et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2204

2204: Predicting incomplete cytoreduction and aborted hyperthermic intraperitoneal chemotherapy procedures in patients with peritoneal carcinomatosis – Milovanov V et al

Conclusions

- **Clinical implications of high cumulative scores may include:**
  - **Laparoscopy prior to CRS/HIPEC to determine resectability**
  - **Avoiding surgery in patients with major comorbidities**
  - **Preoperative systemic chemotherapy to decrease tumour burden**
- **External validation of the model is required**

Milovanov et al. *Ann Oncol* 2015; 26 (suppl 6): abstr 2204