# GI SLIDE DECK 2017

## Selected abstracts from:


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 American Society of Clinical Oncology Annual Meeting** and is available in English, French and Japanese.

The area of clinical research in oncology is a challenging and ever changing environment. Within this environment, we all value access to scientific data and research that helps to educate and inspire further advancements in our roles as scientists, clinicians and educators. I hope you find this review of the latest developments in digestive cancers of benefit to you in your practice. If you would like to share your thoughts with us we would welcome your comments. Please send any correspondence to info@esdo.eu.

Finally, we are also very grateful to Lilly Oncology for their financial, administrative and logistical support in the realisation of this activity.

Yours sincerely,

**Eric Van Cutsem**
**Wolff Schmiegel**
**Phillippe Rougier**
**Thomas Seufferlein**

(ESDO Governing Board)

esdo

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 | GEJ | gastro-oesophageal junction | PFS | progression-free survival |
| 2L | second-line | GI | gastrointestinal | PK | pharmacokinetics |
| AE | adverse event | HA | hyaluronan | PPE | Palmar-Plantar erythrodysesthesia |
| AFP | alpha-fetoprotein | HBV | hepatitis B virus | | |
| ALT | alanine aminotransferase | HCC | hepatocellular carcinoma | PO | orally |
| AST | aspartate aminotransferase | HCV | hepatitis C virus | PR | partial response |
| BCLC | Barcelona Clinic Liver Cancer | HER2 | human epidermal growth factor receptor 2 | PRO | patient-reported outcome |
| bid | twice daily | | | PS | performance status |
| BSC | best supportive care | HFSR | hand-foot skin reaction | q(2/3/4)w | every (2/3/4) week(s) |
| BW | body weight | HR | hazard ratio | QoL | quality of life |
| CA19-9 | carbohydrate antigen 19-9 | IQR | interquartile range | R | randomised |
| CAPOX | capecitabine-oxaliplatin | (m)ITT | (modified) intent-to-treat | RECIST | Response Evaluation Criteria In Solid Tumors |
| CI | confidence interval | IV | intravenous | | |
| CRC | colorectal cancer | KPS | Karnofsky performance status | RFS | relapse-free survival |
| DCR | disease control rate | MSI | microsatellite instability | SAE | serious adverse event |
| DFS | disease-free survival | MVI | macroscopic portal vein invasion | SD | stable disease |
| DoR | duration of response | | | SIRT | selective internal radiation therapy |
| ECOG | Eastern Cooperative Oncology Group | NA | not available | | |
| | | NR | not reached | TEAE | treatment-emergent adverse event |
| EGFR | endothelial growth factor receptor | ORR | overall/objective response rate | | |
| | | | | TRAE | treatment-related adverse event |
| EHS | extrahepatic spread | OS | overall survival | | |
| FOLFIRI | folinic acid + fluorouracil + irinotecan | PD | progressive disease | TTP | time to progression |
| | | PDA | pancreatic ductal adenocarcinoma | TTR | time to response |
| (m)FOLFOX | (modified) leucovorin + 5-fluorouracil + oxaliplatin | | | XELOX | oxaliplatin + capecitabine |
| | | PD-(L)1 | programmed death-(ligand) 1 | | |

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# CANCERS OF THE OESOPHAGUS AND STOMACH

# 4003: KEYNOTE-059 cohort 1: Efficacy and safety of pembrolizumab (pembro) monotherapy in patients with previously treated advanced gastric cancer – Fuchs CS, et al

## Study objective

- To evaluate the safety and efficacy of pembrolizumab in the global phase 2 study in patients with gastric and GEJ cancer – data for Cohort 1 of KEYNOTE-059

Key patient inclusion criteria – Cohort 1

- Measurable recurrent/metastatic disease
- ≥2 prior chemotherapy regimens
- HER2/neu (-) or HER2/neu (+) in previously treated with HER2-targeted therapy
- No systemic steroid therapy or prior PD-1/PD-L1 therapy
- ECOG PS 0–1

→ Pembrolizumab 200 mg q3w (n=259)

→ Patients treated for 24 months or until PD, toxicity, intolerability, or other reason

### CO-PRIMARY ENDPOINTS

- ORR (RECIST v1.1), safety

### SECONDARY ENDPOINTS

- DoR (central review), PFS, OS, microsatellite instability, gene expression profile

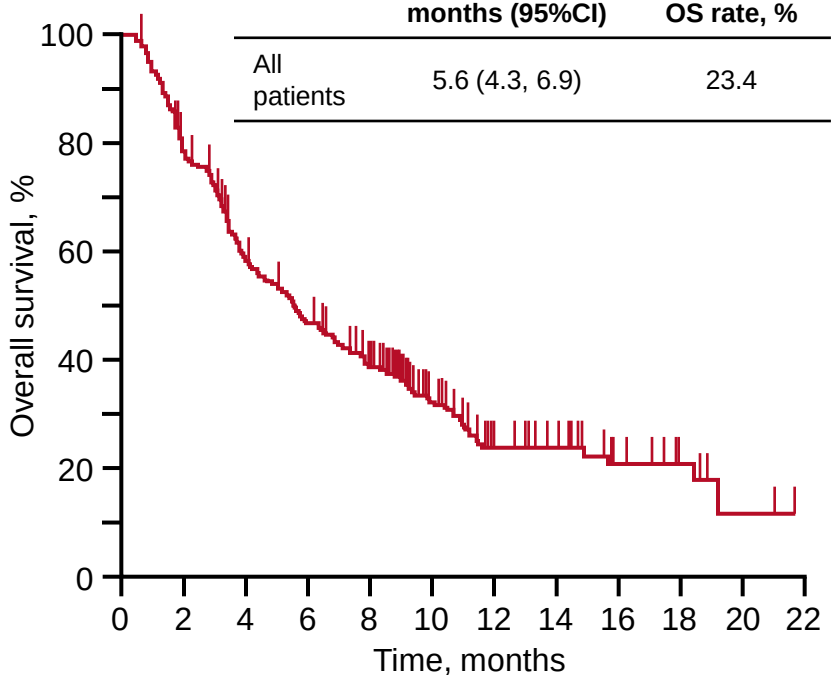
Fuchs CS, et al. J Clin Oncol 2017;35(Suppl):Abstr 4003

# 4003: KEYNOTE-059 cohort 1: Efficacy and safety of pembrolizumab (pembro) monotherapy in patients with previously treated advanced gastric cancer – Fuchs CS, et al

## Key results

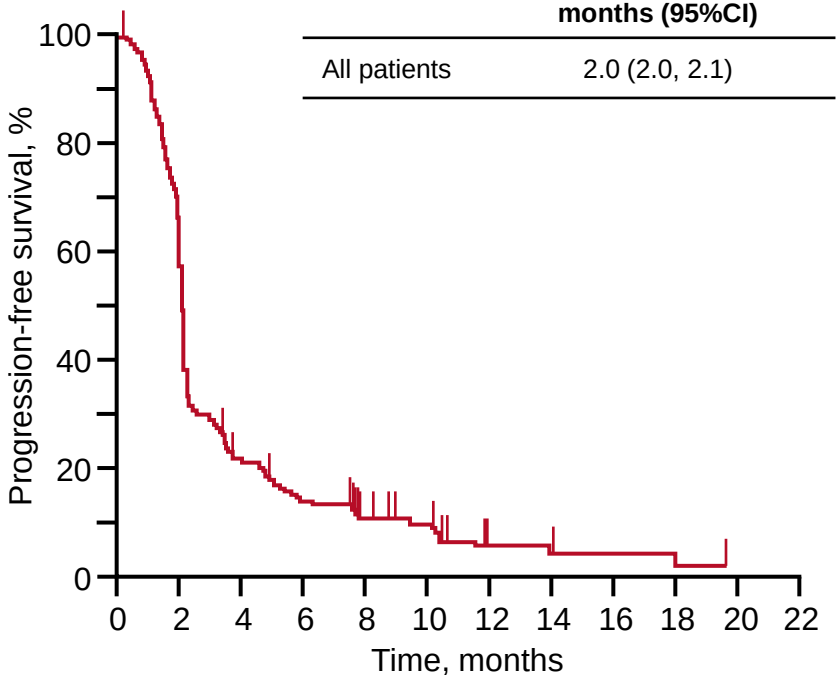
### OS

| | Median OS, months (95%CI) | 12-month OS rate, % |
|---|---|---|
| All patients | 5.6 (4.3, 6.9) | 23.4 |




### PFS

| | Median PFS, months (95%CI) |
|---|---|
| All patients | 2.0 (2.0, 2.1) |

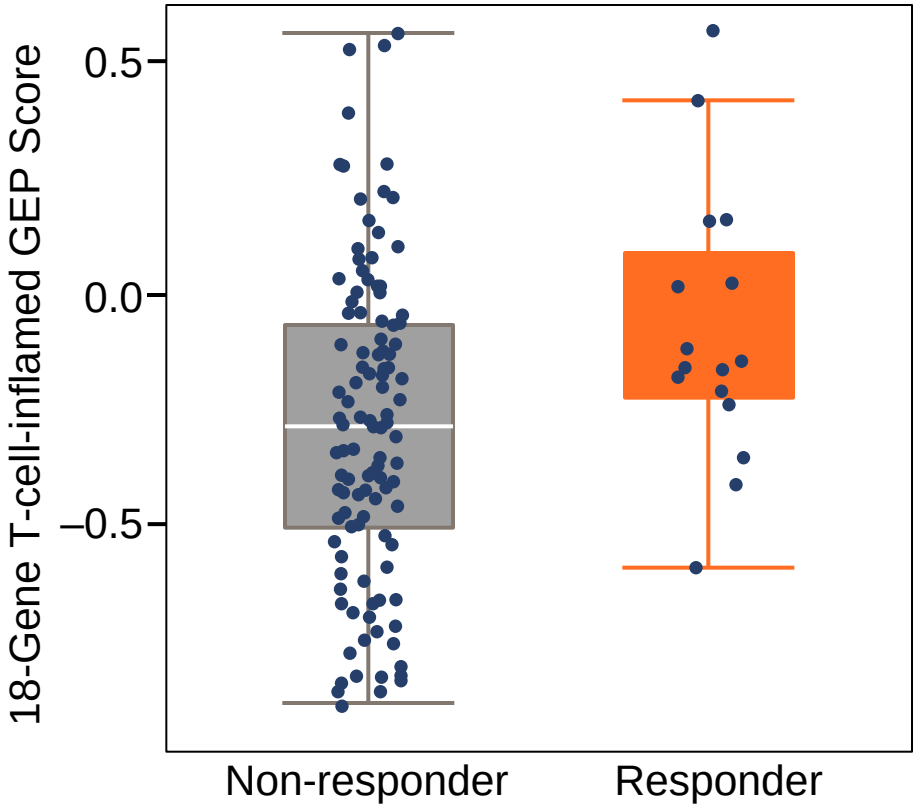



Fuchs CS, et al. J Clin Oncol 2017;35(Suppl):Abstr 4003

# 4003: KEYNOTE-059 cohort 1: Efficacy and safety of pembrolizumab (pembro) monotherapy in patients with previously treated advanced gastric cancer – Fuchs CS, et al

**Key results (cont.)**

- T-cell-inflamed GEP score was significantly associated with improved response to pembrolizumab (p=0.014)




Fuchs CS, et al. J Clin Oncol 2017;35(Suppl):Abstr 4003

# 4003: KEYNOTE-059 cohort 1: Efficacy and safety of pembrolizumab (pembro) monotherapy in patients with previously treated advanced gastric cancer – Fuchs CS, et al

## Key results (cont.)

| Patients, n (%) | All patients (n=259) | |
|---|---|---|
| | All grades (in >5%) | Grade 3/4 |
| TRAEs, % | | |
| Fatigue | 18.9 | 2.3 |
| Pruritus | 8.9 | 0 |
| Rash | 8.5 | 0.8 |
| Hypothyroidism | 7.7 | 0.4 |
| Decreased appetite | 7.3 | 0 |
| Anaemia | 6.9 | 2.7 |
| Nausea | 6.9 | 0.8 |
| Diarrhoea | 6.6 | 1.2 |
| Arthralgia | 5.8 | 0.4 |
| Immune-mediated AEs, % | | |
| Any | 17.8 | 4.6 |
| Hypothyroidism | 8.9 | 0.4 |
| Hyperthyroidism | 3.5 | 0 |
| Colitis | 2.3 | 1.2 |
| Pneumonitis | 1.9 | 0.8 |
| Thyroiditis | 1.5 | 0.4 |
| Infusion reaction | 1.5 | 0 |
| Severe skin reactions | 1.5 | 1.5 |

Fuchs CS, et al. J Clin Oncol 2017;35(Suppl):Abstr 4003

# 4003: KEYNOTE-059 cohort 1: Efficacy and safety of pembrolizumab (pembro) monotherapy in patients with previously treated advanced gastric cancer – Fuchs CS, et al

## Conclusions

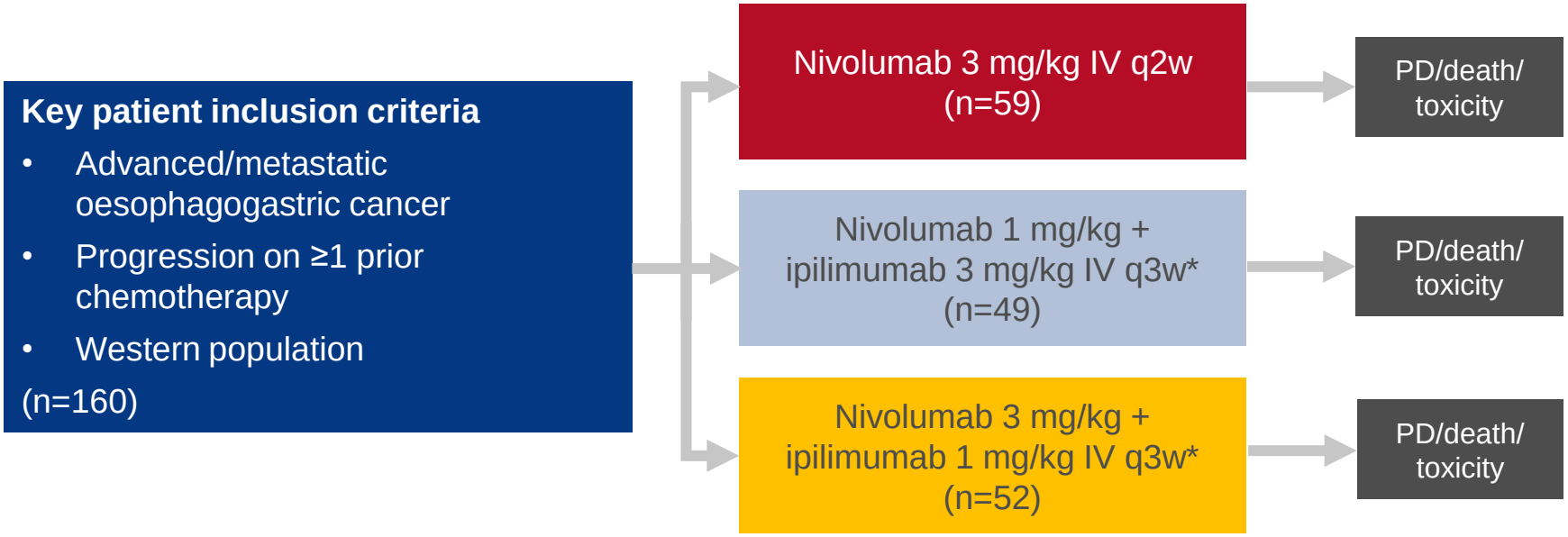
- In patients with advanced gastric or GEJ cancer progressing after ≥2 prior lines of therapy, pembrolizumab showed promising anti-tumour activity and durable responses
- In patients with PD-L1-positive tumours, ORR was higher, but there were also responses observed in patients with PD-L1-negative tumours
- Pembrolizumab was well tolerated
- In patients with gastric or GEJ cancer who have progressed after ≥2 prior lines of therapy pembrolizumab may be a potential treatment option

Fuchs CS, et al. J Clin Oncol 2017;35(Suppl):Abstr 4003

# 4014: Nivolumab ± ipilimumab in pts with advanced (adv)/metastatic chemotherapy-refractory (CTx-R) gastric (G), esophageal (E), or gastroesophageal junction (GEJ) cancer: CheckMate 032 study – Janjigian YY, et al

## Study objective

- To evaluate the long-term survival, efficacy, and safety of nivolumab alone and in combination with ipilimumab in the oesophagogastric cohort of the CheckMate 032 study




### PRIMARY ENDPOINT

- ORR (RECIST v1.1)

### SECONDARY ENDPOINTS

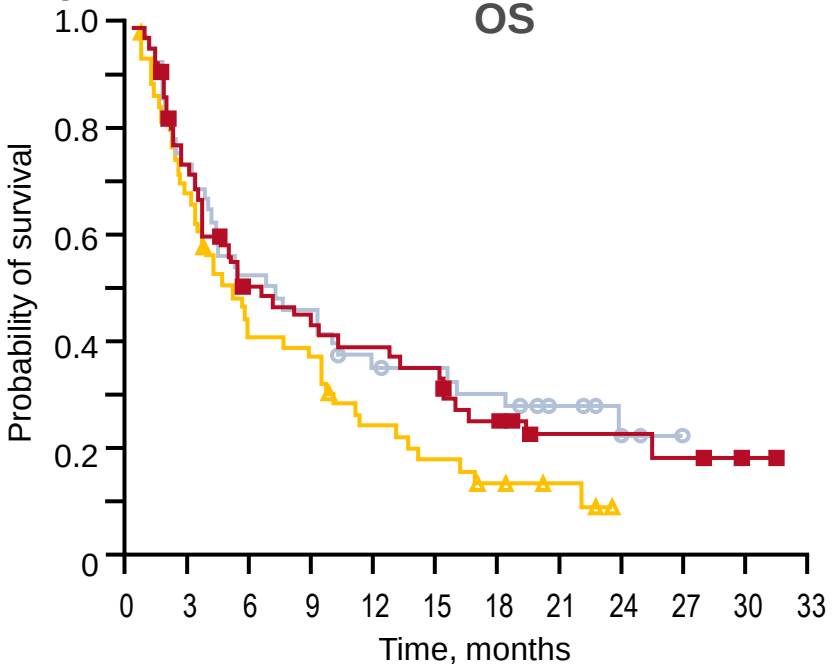
- OS, PFS, TTR, DoR, safety, PD-L1 tumour expression

*Administered for 4 cycles followed by nivolumab 3 mg/kg IV q2w

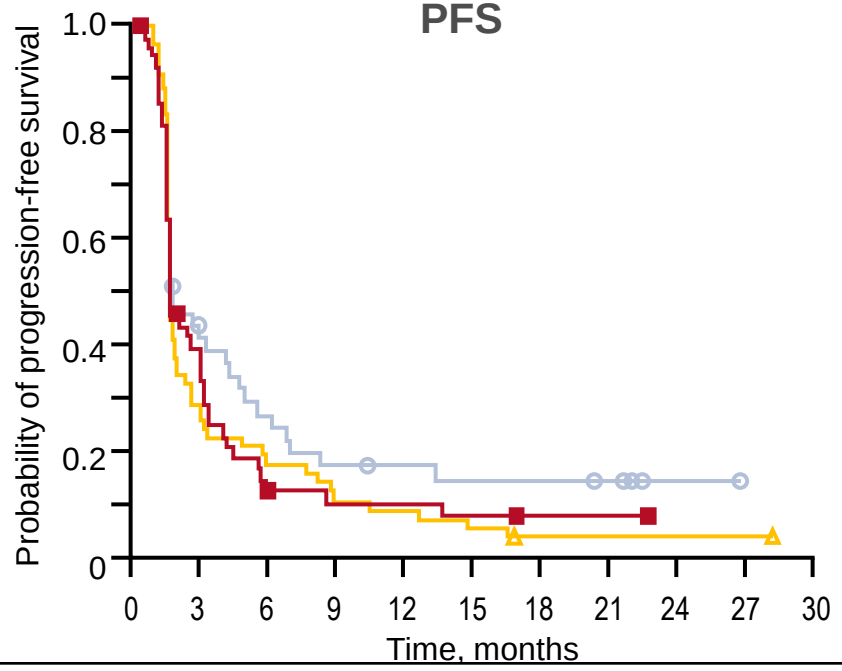
Janjigian YY, et al. J Clin Oncol 2017;35(Suppl):Abstr 4014

# 4014: Nivolumab ± ipilimumab in pts with advanced (adv)/metastatic chemotherapy-refractory (CTx-R) gastric (G), esophageal (E), or gastroesophageal junction (GEJ) cancer: CheckMate 032 study – Janjigian YY, et al

## Key results




| | mOS, months (95%CI) | OS rate, % | |
|---|---|---|---|
| | | 12-month | 18-month |
| Nivolumab 3 mg/kg | 6.2 (3.4, 12.4) | 39 | 25 |
| Nivolumab 1 mg/kg + ipilimumab 3 mg/kg | 6.9 (3.7, 11.5) | 35 | 28 |
| Nivolumab 3 mg/kg + ipilimumab 1 mg/kg | 4.8 (3.0, 8.4) | 24 | 13 |



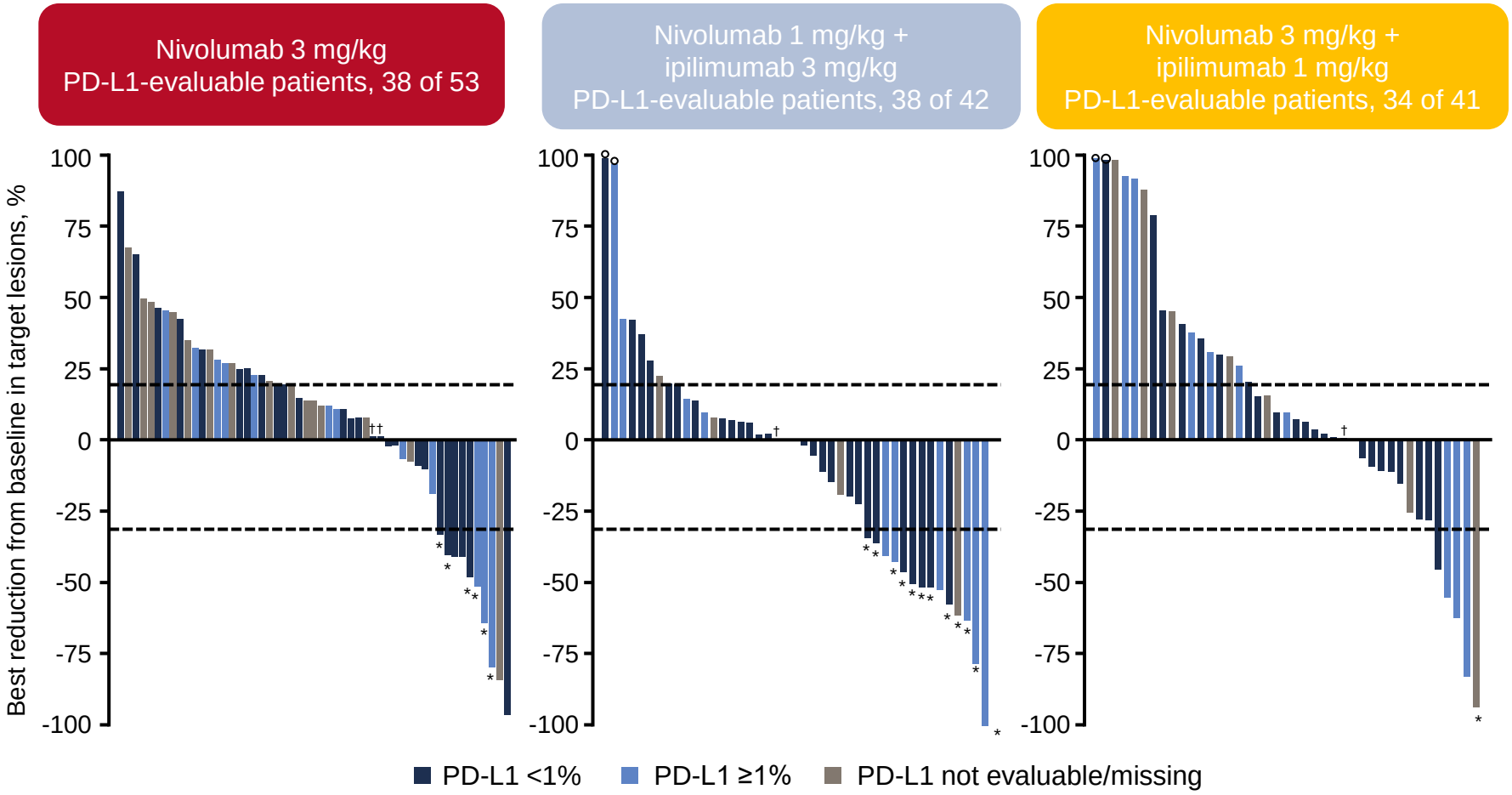

| | mPFS, months (95%CI) | PFS rate, % | |
|---|---|---|---|
| | | 6-month | 12-month |
| Nivolumab 3 mg/kg | 1.4 (1.2, 1.5) | 17 | 8 |
| Nivolumab 1 mg/kg + ipilimumab 3 mg/kg | 1.4 (1.2, 3.8) | 24 | 17 |
| Nivolumab 3 mg/kg + ipilimumab 1 mg/kg | 1.6 (1.4, 2.6) | 12 | 10 |

Janjigian YY, et al. J Clin Oncol 2017;35(Suppl):Abstr 4014

# 4014: Nivolumab ± ipilimumab in pts with advanced (adv)/metastatic chemotherapy-refractory (CTx-R) gastric (G), esophageal (E), or gastroesophageal junction (GEJ) cancer: CheckMate 032 study – Janjigian YY, et al

## Key results (cont.)

### Best reduction in target lesions




Janjigian YY, et al. J Clin Oncol 2017;35(Suppl):Abstr 4014

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## Key results (cont.)

| | Nivolumab 3 mg/kg (n=59) | | Nivolumab 1 mg/kg + ipilimumab 3 mg/kg (n=49) | | Nivolumab 3 mg/kg + ipilimumab 1 mg/kg (n=52) | |
|---|---|---|---|---|---|---|
| | Any grade | Grade 3/4 | Any grade | Grade 3/4 | Any grade | Grade 3/4 |
| Any TRAE | 41 (69) | 10 (17) | 41 (84) | 23 (47) | 39 (75) | 14 (27) |
| Serious TRAEs | 6 (10) | 3 (5) | 21 (34) | 17 (35) | 13 (25) | 9 (17) |
| TRAEs leading to treatment discontinuation | 2 (3) | 2 (3) | 10 (20) | 10 (20) | 7 (13) | 5 (10) |
| TRAEs in ≥15% of patients in any arm | | | | | | |
| ALT increased | 5 (8) | 2 (3) | 8 (16) | 7 (14) | 5 (10) | 2 (4) |
| AST increased | 7 (12) | 3 (5) | 8 (16) | 5 (10) | 2 (4) | 1 (2) |
| Decreased appetite | 9 (15) | 0 | 5 (10) | 0 | 3 (6) | 0 |
| Diarrhea | 9 (15) | 1 (2) | 15 (31) | 7 (14) | 5 (10) | 1 (2) |
| Fatigue | 20 (34) | 1 (2) | 14 (29) | 3 (6) | 10 (19) | 0 |
| Pruritus | 10 (17) | 0 | 9 (18) | 1 (2) | 12 (23) | 0 |
| Rash | 5 (8) | 0 | 10 (20) | 0 | 8 (15) | 0 |

Janjigian YY, et al. J Clin Oncol 2017;35(Suppl):Abstr 4014

# 4014: Nivolumab ± ipilimumab in pts with advanced (adv)/metastatic chemotherapy-refractory (CTx-R) gastric (G), esophageal (E), or gastroesophageal junction (GEJ) cancer: CheckMate 032 study – Janjigian YY, et al

## Conclusions

- In patients with chemotherapy-refractory oesophagogastric cancer, nivolumab alone or in combination with ipilimumab demonstrated clinical activity irrespective of PD-L1 status
- Safety profile was consistent with previous findings

Janjigian YY, et al. J Clin Oncol 2017;35(Suppl):Abstr 4014

# 4004: Perioperative chemotherapy with docetaxel, oxaliplatin, and fluorouracil/ leucovorin (FLOT) versus epirubicin, cisplatin, and fluorouracil or capecitabine (ECF/ECX) for resectable gastric or gastroesophageal junction (GEJ) adenocarcinoma (FLOT4-AIO): A multicenter, randomized phase 3 – Al-Batran S-E, et al

## Study objective

- To evaluate the efficacy of FLOT vs. ECF/ECX as a perioperative treatment for patients with resectable gastric or GEJ adenocarcinoma

**Key patient inclusion criteria**

- Gastric cancer or adenocarcinoma of the gastro-oesophageal junction type I–III
- Medically and technically operable
- cT2–4/cN-any/cMO or cT-any/ cN+/cMO

(n=716)

R

FLOT x4 – RESECTION – FLOT x4 (n=356)

**Stratification**

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

ECF/ECX x3 – RESECTION – ECF/ECX x3

### PRIMARY ENDPOINT

- OS

### SECONDARY ENDPOINTS

- PFS, complete resection rate, surgical morbidity/mortality, safety

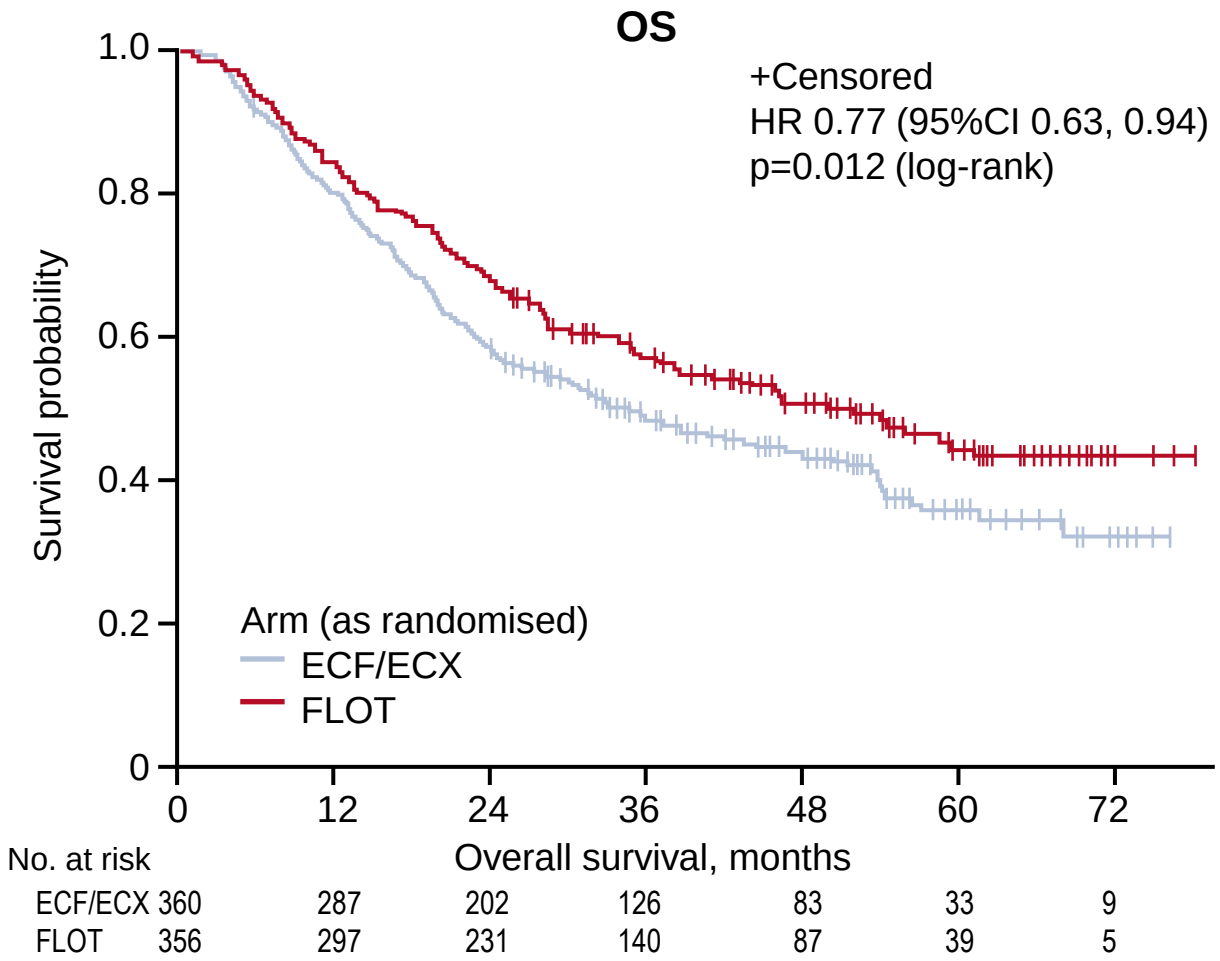
FLOT: docetaxel 50 mg/m$^2$ D1; 5FU 2600 mg/m$^2$ D1; leucovorin 200 mg/m$^2$ D1; oxaliplatin 85 mg/m$^2$ D1q2w

ECF/ECX: epirubicin 50 mg/m$^2$ D1; cisplatin 60 mg/m$^2$ D1; 5FU 200 mg/m$^2$ (or capecitabine 1250 mg/m2 PO divided into 2 doses D1–D21) q3w

Al-Batran S-E, et al. J Clin Oncol 2017;35(Suppl):Abstr 4004

# 4004: Perioperative chemotherapy with docetaxel, oxaliplatin, and fluorouracil/ leucovorin (FLOT) versus epirubicin, cisplatin, and fluorouracil or capecitabine (ECF/ECX) for resectable gastric or gastroesophageal junction (GEJ) adenocarcinoma (FLOT4-AIO): A multicenter, randomized phase 3 – Al-Batran S-E, et al

## Key results

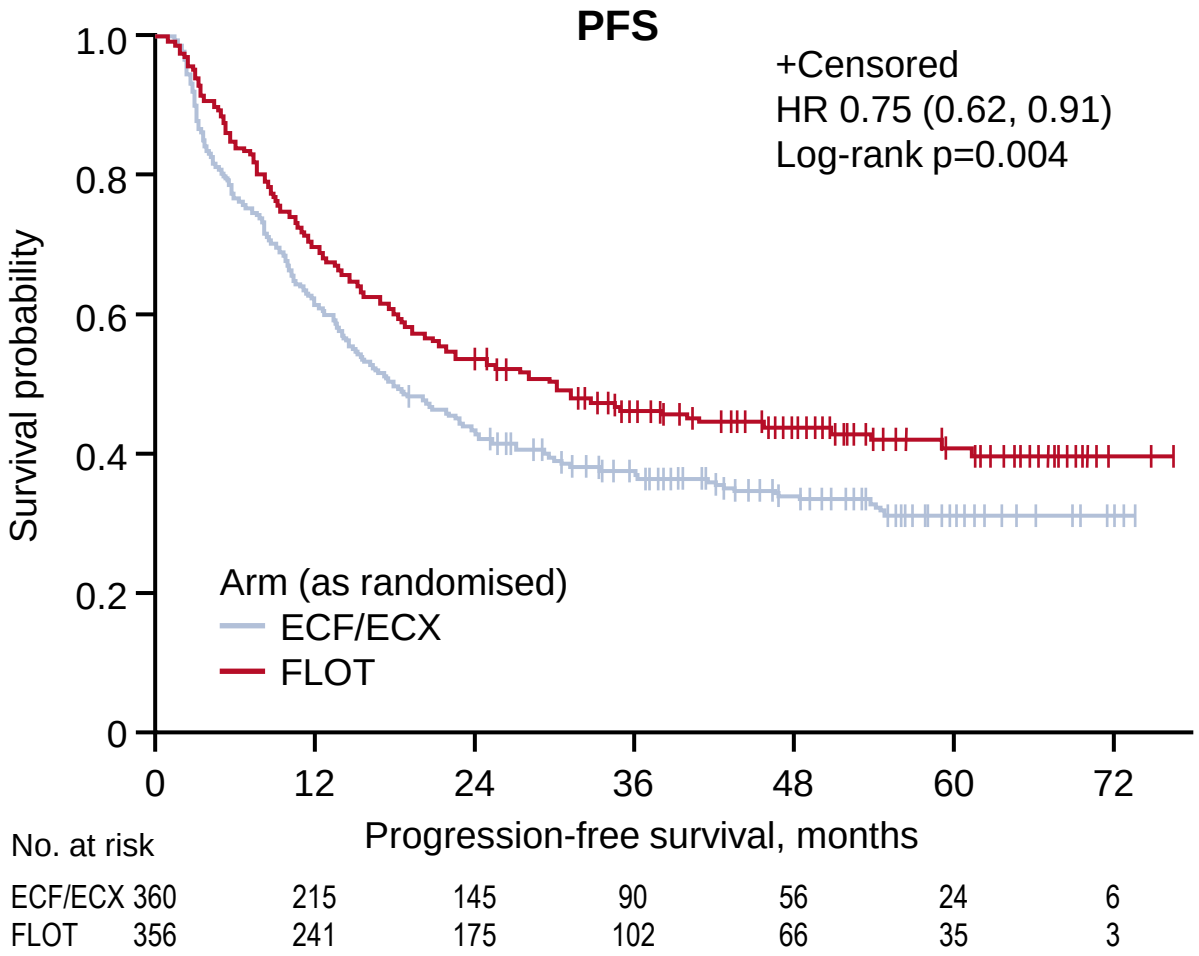



| | ECF/ECX | FLOT |
|---|---|---|
| mOS, months (95%CI) | 35 (27, 46) | 50 (38, NA) |
| Projected OS rate, % | | |
| 2-year | 59 | 68 |
| 3-year | 48 | 57 |
| 5-year | 36 | 45 |

Al-Batran S-E, et al. J Clin Oncol 2017;35(Suppl):Abstr 4004

# 4004: Perioperative chemotherapy with docetaxel, oxaliplatin, and fluorouracil/ leucovorin (FLOT) versus epirubicin, cisplatin, and fluorouracil or capecitabine (ECF/ECX) for resectable gastric or gastroesophageal junction (GEJ) adenocarcinoma (FLOT4-AIO): A multicenter, randomized phase 3 – Al-Batran S-E, et al

## Key results (cont.)




| | ECF/ECX | FLOT |
|---|---|---|
| mPFS, months (95%CI) | 18 (15, 22) | 30 (21, 44) |
| Projected PFS rate, % | | |
| 2-year | 43 | 53 |
| 3-year | 37 | 46 |
| 5-year | 31 | 41 |

Al-Batran S-E, et al. J Clin Oncol 2017;35(Suppl):Abstr 4004

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## Key results (cont.)

| | ECF/ECX (n=354) | FLOT (n=354) | p-value |
|---|---|---|---|
| Grade 3/4 AEs, n (%) | | | |
| Diarrhoea | 13 (4) | 34 (10) | 0.002 |
| Vomiting | 27 (8) | 7 (2) | <0.001 |
| Nausea | 55 (16) | 26 (7) | 0.001 |
| Fatigue | 38 (11) | 25 (7) | - |
| Infections | 30 (9) | 63 (18) | <0.001 |
| Leukopenia | 75 (21) | 94 (27) | - |
| Neutropenia | 139 (39) | 181 (51) | 0.002 |
| Sensory | 7 (2) | 24 (7) | 0.002 |
| Thromboembolic | 22 (6) | 9 (3) | 0.03 |
| Anaemia | 20 (6) | 9 (3) | 0.04 |
| Any SAE, n (%) | 220 (62) | 215 (61) | - |
| Treatment-related SAE, n (%) | 137 (34) | 139 (35) | - |
| Toxic death, n (%) | 2 (<1) | 2 (<1) | - |

Al-Batran S-E, et al. J Clin Oncol 2017;35(Suppl):Abstr 4004

# 4004: Perioperative chemotherapy with docetaxel, oxaliplatin, and fluorouracil/ leucovorin (FLOT) versus epirubicin, cisplatin, and fluorouracil or capecitabine (ECF/ECX) for resectable gastric or gastroesophageal junction (GEJ) adenocarcinoma (FLOT4-AIO): A multicenter, randomized phase 3 – Al-Batran S-E, et al

## Conclusions

- In comparison to ECF/ECX, FLOT demonstrated increased rates of curative surgery and prolonged PFS and OS
- The results with FLOT were consistent across subgroups and sensitivity analyses
- Surgical morbidity and mortality, re-surgeries or hospitalization times were not increased
- In perioperative treatment of patients with adenocarcinoma of the stomach or GEJ, FLOT offers a new standard of care

Al-Batran S-E, et al. J Clin Oncol 2017;35(Suppl):Abstr 4004

# CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

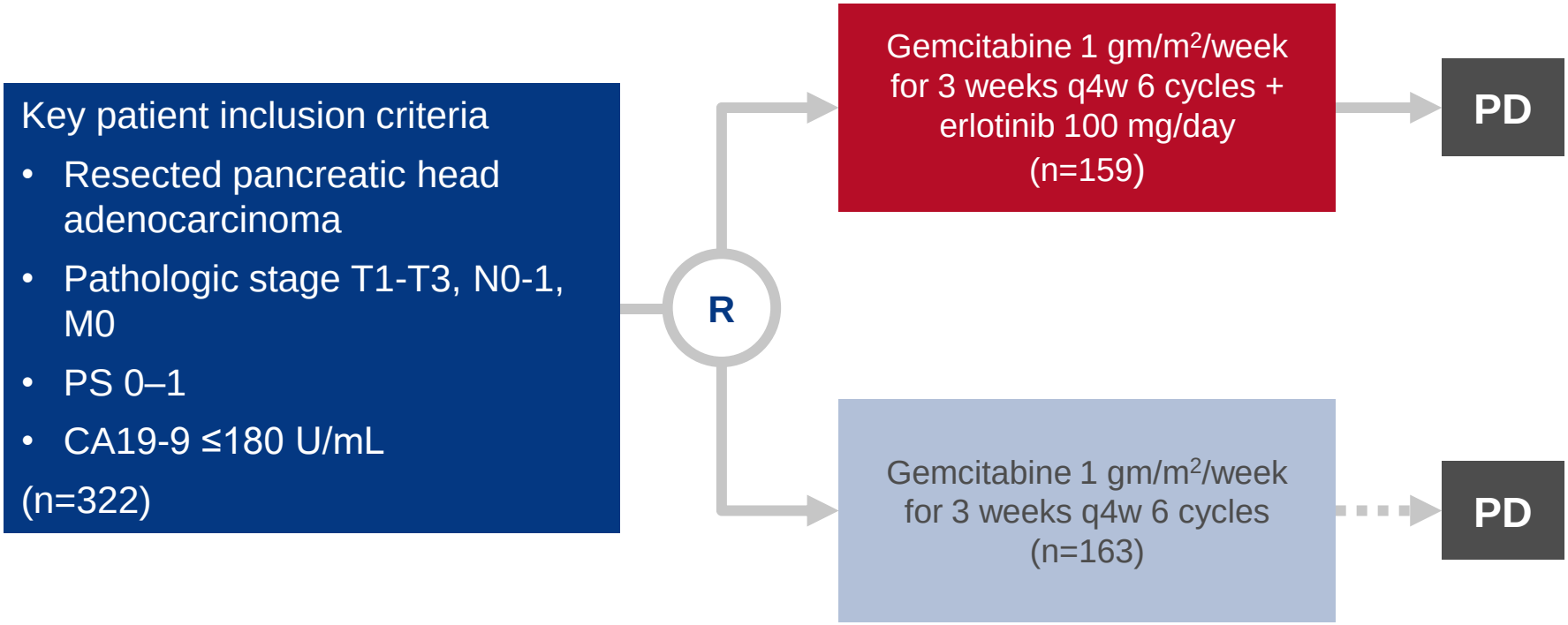
Cancers of the pancreas, small bowel and hepatobiliary tract

# PANCREATIC CANCER

# 4007: Results of the randomized phase II portion of NRG Oncology/RTOG 0848 evaluating the addition of erlotinib to adjuvant gemcitabine for patients with resected pancreatic head adenocarcinoma – Safran H, et al

## Study objective

- To evaluate the addition of erlotinib to adjuvant gemcitabine for patients with resected pancreatic head adenocarcinoma




### PRIMARY ENDPOINT

- OS

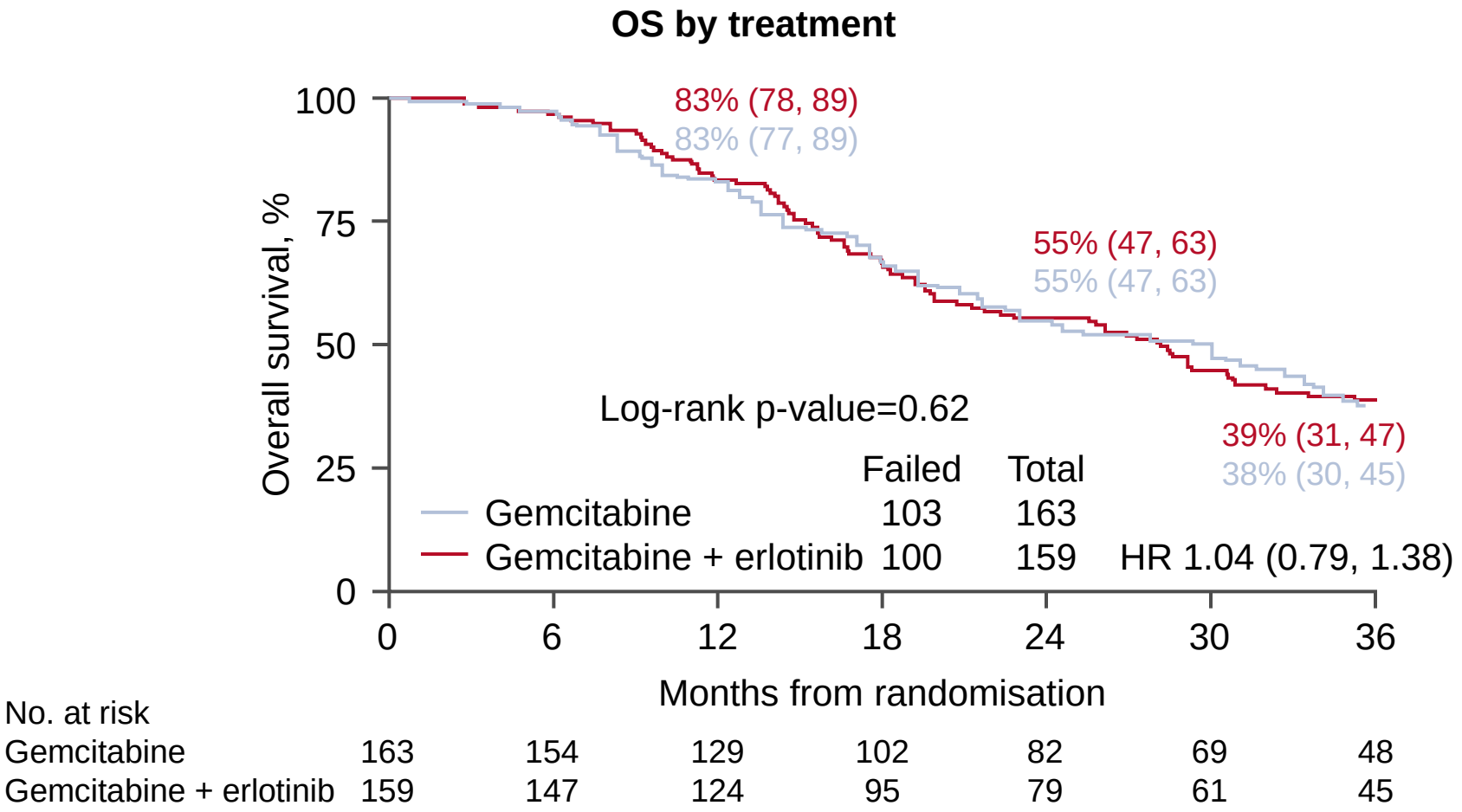
### SECONDARY ENDPOINTS

- Safety

Safran H, et al. J Clin Oncol 2017;35(Suppl):Abstr 4007

# 4007: Results of the randomized phase II portion of NRG Oncology/RTOG 0848 evaluating the addition of erlotinib to adjuvant gemcitabine for patients with resected pancreatic head adenocarcinoma – Safran H, et al

## Key results




Safran H, et al. J Clin Oncol 2017;35(Suppl):Abstr 4007

# 4007: Results of the randomized phase II portion of NRG Oncology/RTOG 0848 evaluating the addition of erlotinib to adjuvant gemcitabine for patients with resected pancreatic head adenocarcinoma – Safran H, et al

## Key results (cont.)

| AEs, n (%) | Gemcitabine + erlotinib (n=157) | | | | Gemcitabine (n=161) | | | |
|---|---|---|---|---|---|---|---|---|
| | G2 | G3 | G4 | G5 | G2 | G3 | G4 | G5 |
| Overall highest grade | 23 (15) | 101 (64) | 27 (17) | 3 (2) | 21 (13) | 99 (62) | 32 (20) | 2 (1) |
| Blood and lymphatic system disorders | 48 (31) | 32 (20) | 2 (1) | 0 (0) | 56 (35) | 30 (19) | 1 (1) | 0 (0) |
| GI disorders | 54 (34) | 42 (27) | 2 (1) | 0 (0) | 62 (39) | 35 (22) | 0 (0) | 0 (0) |
| Diarrhoea | 29 (19) | 16 (10) | 0 (0) | 0 (0) | 26 (16) | 3 (2) | 0 (0) | 0 (0) |
| Hepatobiliary disorders | 0 (0) | 1 (1) | 0 (0) | 1 (1) | 1 (1) | 3 (2) | 1 (1) | 0 (0) |
| Infections/infestations | 21 (13) | 24 (15) | 6 (4) | 1 (1) | 24 (15) | 10 (6) | 9 (6) | 0 (0) |
| Metabolism and nutrition disorders | 39 (25) | 42 (27) | 4 (3) | 0 (0) | 43 (27) | 39 (22) | 3 (2) | 0 (0) |

## Conclusions

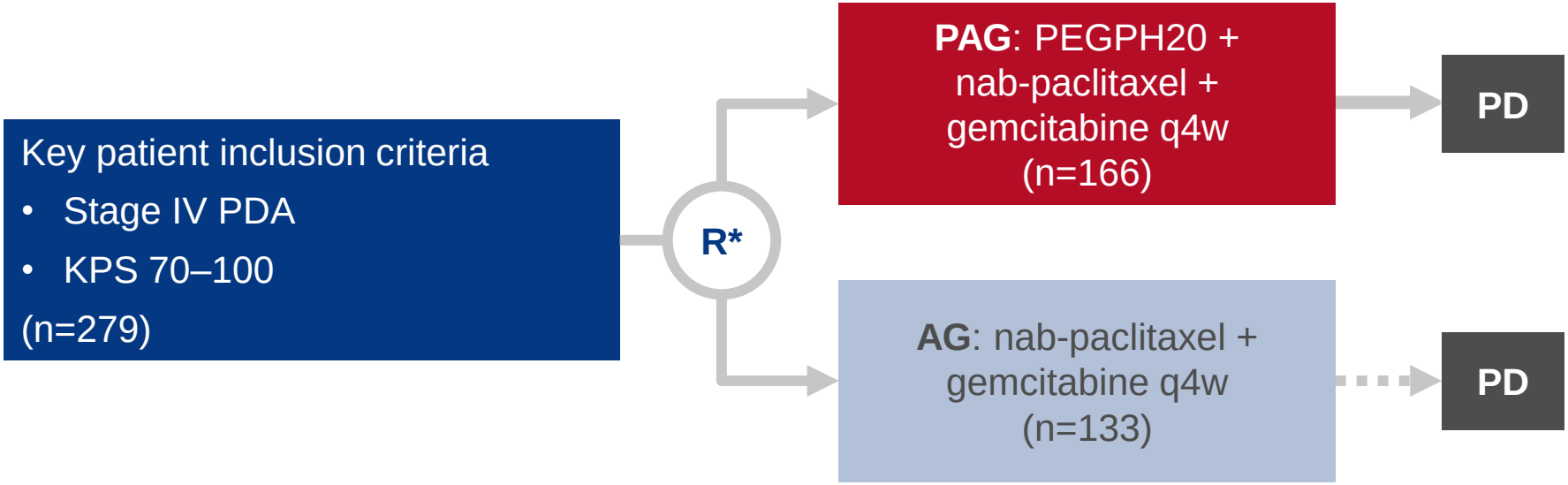
- **Addition of erlotinib to gemcitabine did not increase OS vs. gemcitabine alone**
- **A modest increase in grade ≥3 GI toxicity was seen with the addition of erlotinib**

Safran H, et al. J Clin Oncol 2017;35(Suppl):Abstr 4007

# 4008: Randomized phase II study of PEGPH20 plus nab-paclitaxel/gemcitabine (PAG) vs AG in patients (Pts) with untreated, metastatic pancreatic ductal adenocarcinoma (mPDA) – Hingorani SR, et al

**Study objective**

- To evaluate the efficacy and rate of thromboembolic events in patients with untreated metastatic PDA treated with PAG or AG




**CO-PRIMARY ENDPOINTS**

- PFS, thromboembolic event rate

**SECONDARY ENDPOINTS**

- PFS by HA level, ORR, OS

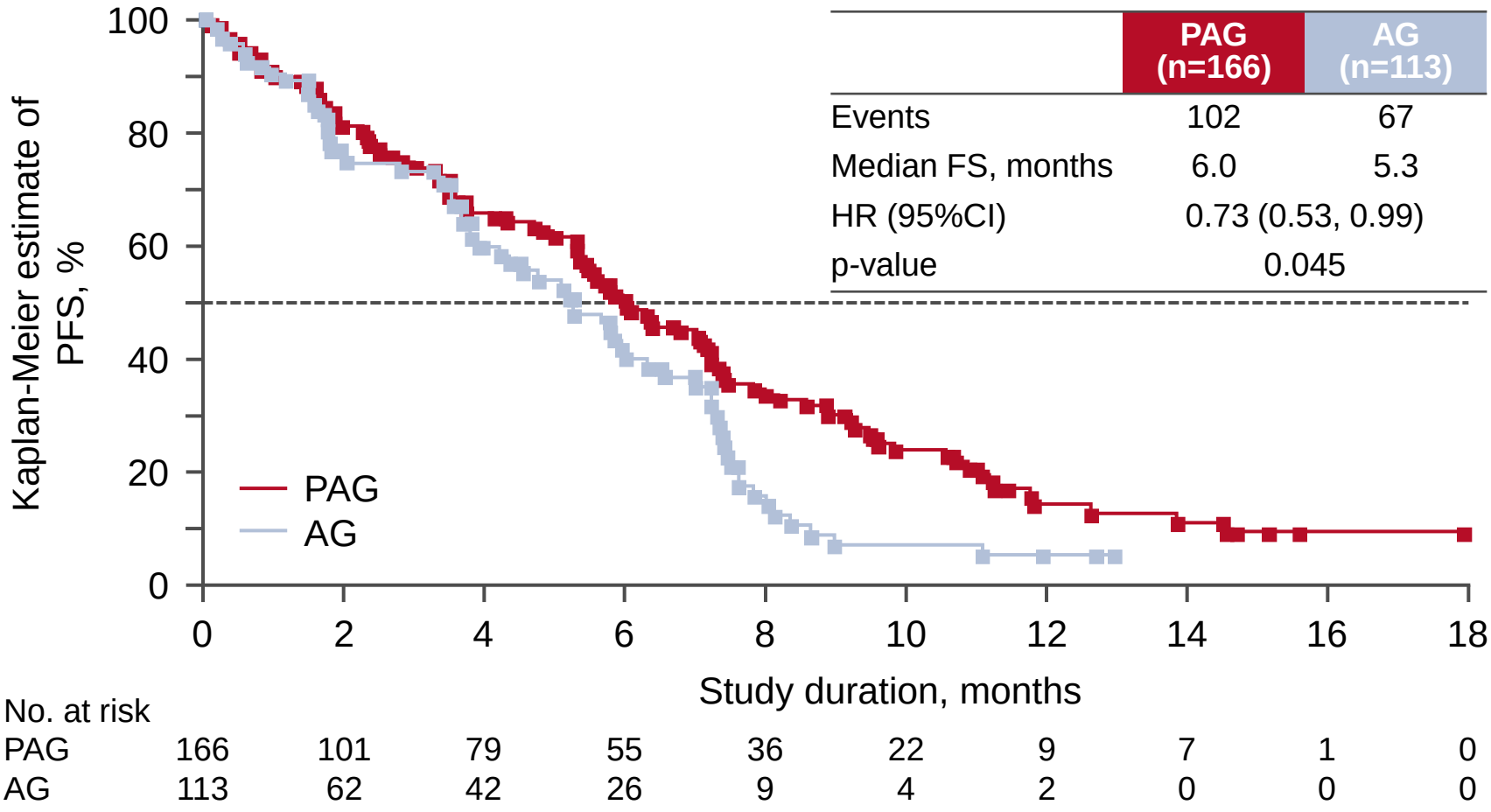
*In Stage 2, randomisation was 2:1 to PAG vs. AG

Hingorani SR, et al. J Clin Oncol 2017;35(Suppl):Abstr 4008

# 4008: Randomized phase II study of PEGPH20 plus nab-paclitaxel/gemcitabine (PAG) vs AG in patients (Pts) with untreated, metastatic pancreatic ductal adenocarcinoma (mPDA) – Hingorani SR, et al

## Key results

### PFS (combined stages 1 and 2)




| | PAG (n=166) | AG (n=113) |
|---|---|---|
| Events | 102 | 67 |
| Median FS, months | 6.0 | 5.3 |
| HR (95%CI) | 0.73 (0.53, 0.99) | |
| p-value | 0.045 | |

No. at risk

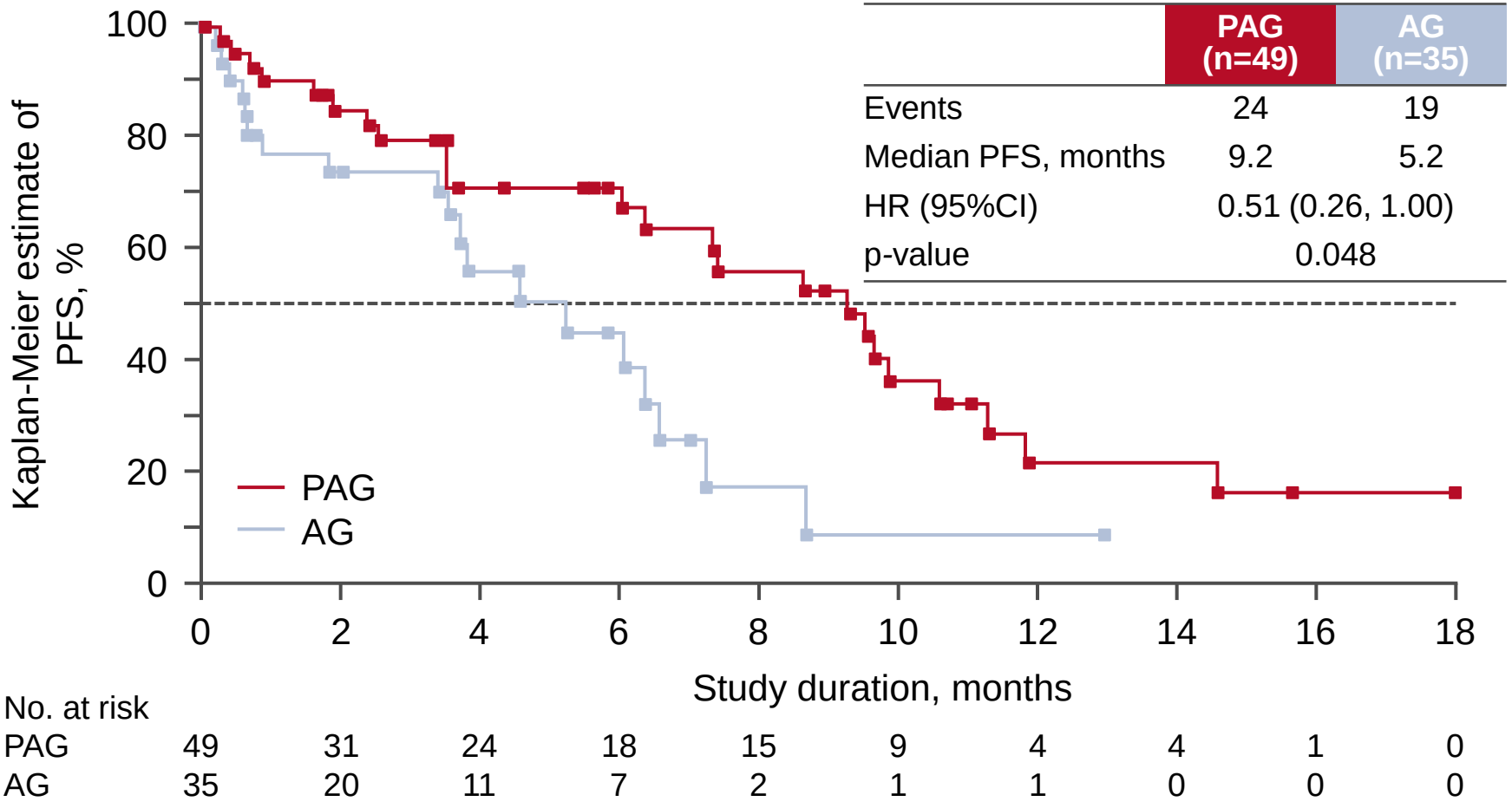
| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| PAG | 166 | 101 | 79 | 55 | 36 | 22 | 9 | 7 | 1 | 0 |
| AG | 113 | 62 | 42 | 26 | 9 | 4 | 2 | 0 | 0 | 0 |

Hingorani SR, et al. J Clin Oncol 2017;35(Suppl):Abstr 4008

# 4008: Randomized phase II study of PEGPH20 plus nab-paclitaxel/gemcitabine (PAG) vs AG in patients (Pts) with untreated, metastatic pancreatic ductal adenocarcinoma (mPDA) – Hingorani SR, et al

## Key results (cont.)

**PFS in HA-high population (combined stages 1 and 2)**




| | PAG (n=49) | AG (n=35) |
|---|---|---|
| Events | 24 | 19 |
| Median PFS, months | 9.2 | 5.2 |
| HR (95%CI) | 0.51 (0.26, 1.00) | |
| p-value | 0.048 | |

| No. at risk | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| PAG | 49 | 31 | 24 | 18 | 15 | 9 | 4 | 4 | 1 | 0 |
| AG | 35 | 20 | 11 | 7 | 2 | 1 | 1 | 0 | 0 | 0 |

Hingorani SR, et al. J Clin Oncol 2017;35(Suppl):Abstr 4008

# 4008: Randomized phase II study of PEGPH20 plus nab-paclitaxel/gemcitabine (PAG) vs AG in patients (Pts) with untreated, metastatic pancreatic ductal adenocarcinoma (mPDA) – Hingorani SR, et al

## Key results (cont.)

| | Enoxaparin prophylaxis dose | Thromboembolism rate, n/N (%) | |
|---|---|---|---|
| | | PAG | AG |
| Stage 1 | N/A | 32/74 (43) | 15/61 (25) |
| Stage 2* | 40 mg/day | 5/18 (28) | 2/7 (29) |
| | 1 mg/kg/day | 7/68 (10) | 2/32 (6) |

## Conclusions

- **Both primary endpoints (PFS and thromboembolism event rate) were met, with the largest improvement in the secondary endpoint of PFS in HA-high patients**
- **There were no differences in bleeding events between treatment arms**
- **Data support HA as a potential predictive biomarker for use of PEGPH20**

*Thromboembolism rates for all stage 2 patients were 12/86 (14%) and 4/49 (10%) in the PAG and AG arms, respectively

Hingorani SR, et al. J Clin Oncol 2017;35(Suppl):Abstr 4008

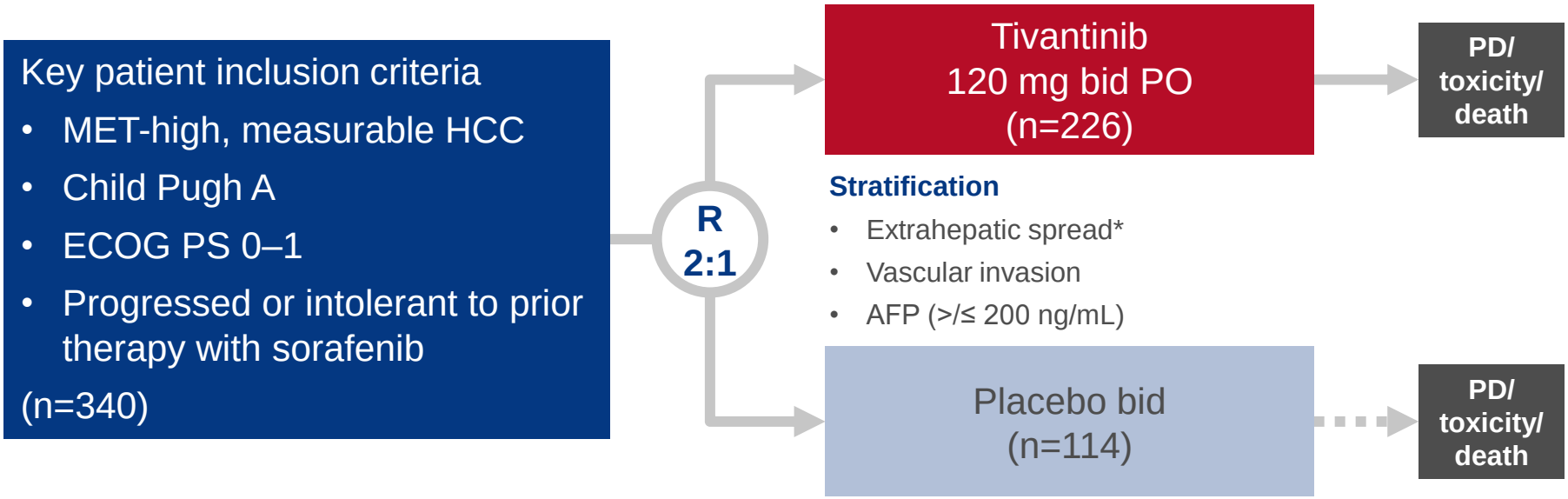
Cancers of the pancreas, small bowel and hepatobiliary tract

# HEPATOCELLULAR CARCINOMA

# 4000: Second-line tivantinib (ARQ 197) vs placebo in patients (Pts) with MET-high hepatocellular carcinoma (HCC): Results of the METIV-HCC phase III trial – Rimassa L, et al

## Study objective

- To evaluate efficacy and safety of 2L tivantinib in patients with MET-high HCC who had progressed or were intolerant to sorafenib




## PRIMARY ENDPOINT

- OS

## SECONDARY ENDPOINTS

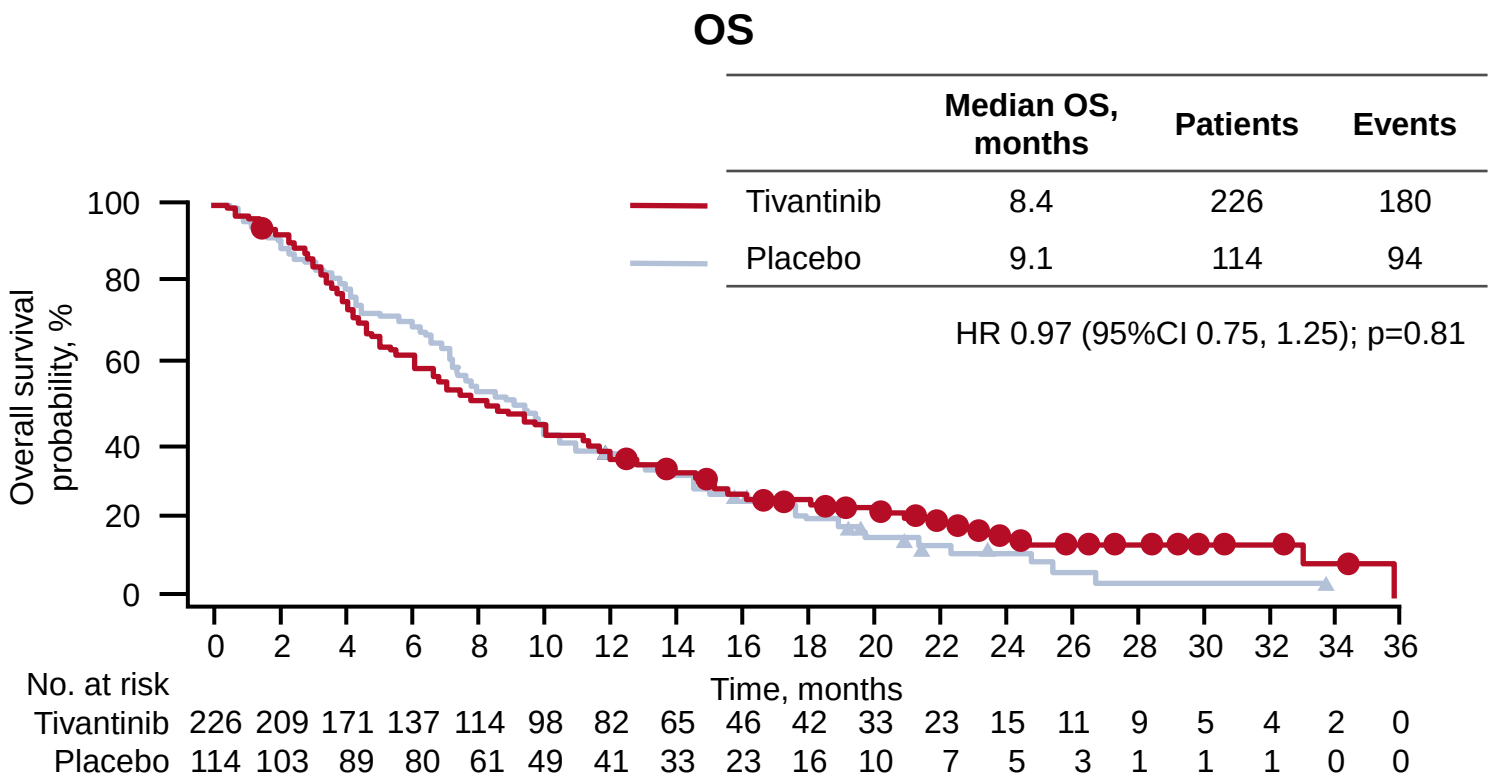
- PFS, safety, TTP, ORR, DCR, PD type, PK, biomarkers, PRO

*Includes perihepatic lymph nodes >2 cm in smallest diameter

Rimassa L, et al. J Clin Oncol 2017;35(Suppl):Abstr 4000

# 4000: Second-line tivantinib (ARQ 197) vs placebo in patients (Pts) with MET-high hepatocellular carcinoma (HCC): Results of the METIV-HCC phase III trial – Rimassa L, et al

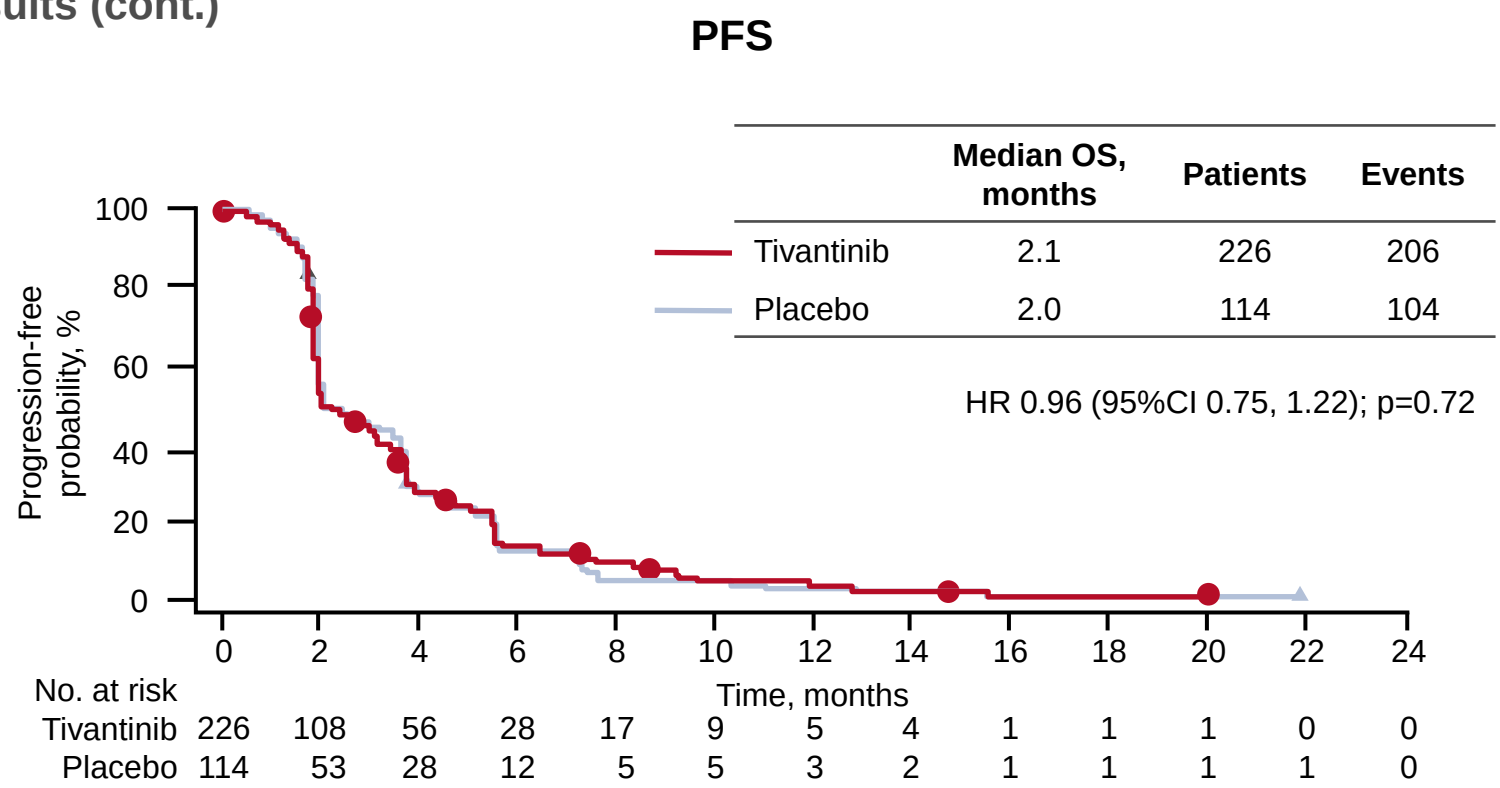
## Key results




Rimassa L, et al. J Clin Oncol 2017;35(Suppl):Abstr 4000

# 4000: Second-line tivantinib (ARQ 197) vs placebo in patients (Pts) with MET-high hepatocellular carcinoma (HCC): Results of the METIV-HCC phase III trial – Rimassa L, et al

## Key results (cont.)




- Median TTP: 2.4 vs. 3.0 months for tivantinib vs. placebo (HR 0.96 [95%CI 0.74, 1.25]; p=0.76)
- DCR: 49.5% vs. 50% for tivantinib vs. placebo, with no objective responses in either arm

Rimassa L, et al. J Clin Oncol 2017;35(Suppl):Abstr 4000

# 4000: Second-line tivantinib (ARQ 197) vs placebo in patients (Pts) with MET-high hepatocellular carcinoma (HCC): Results of the METIV-HCC phase III trial – Rimassa L, et al

## Key results (cont.)

| TEAEs (>15%), n (%) | Tivantinib | | Placebo | |
|---|---|---|---|---|
| | All grades | Grade ≥3 | All grades | Grade ≥3 |
| Abdominal pain | 69 (30.7) | 9 (4.0) | 44 (38.6) | 5 (4.4) |
| Fatigue | 58 (25.8) | 3 (1.3) | 31 (27.2) | 5 (4.4) |
| Asthenia | 48 (21.3) | 7 (3.1) | 25 (21.9) | 2 (1.8) |
| Ascites | 46 (20.4) | 16 (7.1) | 24 (21.1) | 9 (7.9) |
| Decreased appetite | 36 (16.0) | 2 (0.9) | 21 (18.4) | 3 (0.6) |
| Pruritus | 24 (10.7) | 3 (1.3) | 21 (18.4) | 0 (0) |
| Peripheral oedema | 54 (24.0) | 1 (0.4) | 19 (16.7) | 0 (0) |
| Anaemia | 42 (18.7) | 11 (4.9) | 17 (14.9) | 7 (6.1) |
| Diarrhoea | 50 (22.2) | 4 (1.8) | 17 (14.9) | 2 (1.8) |
| Nausea | 50 (22.2) | 1 (0.4) | 13 (11.4) | 1 (0.9) |
| Other TEAEs of relevance | | | | |
| Neutropenia | 28 (12.4) | 9 (4.0) | 5 (4.4) | 1 (0.9) |
| Bradycardia | 31 (13.8) | 1 (0.4) | 0 (0) | 0 (0) |

Rimassa L, et al. J Clin Oncol 2017;35(Suppl):Abstr 4000

# 4000: Second-line tivantinib (ARQ 197) vs placebo in patients (Pts) with MET-high hepatocellular carcinoma (HCC): Results of the METIV-HCC phase III trial – Rimassa L, et al

**Conclusions**

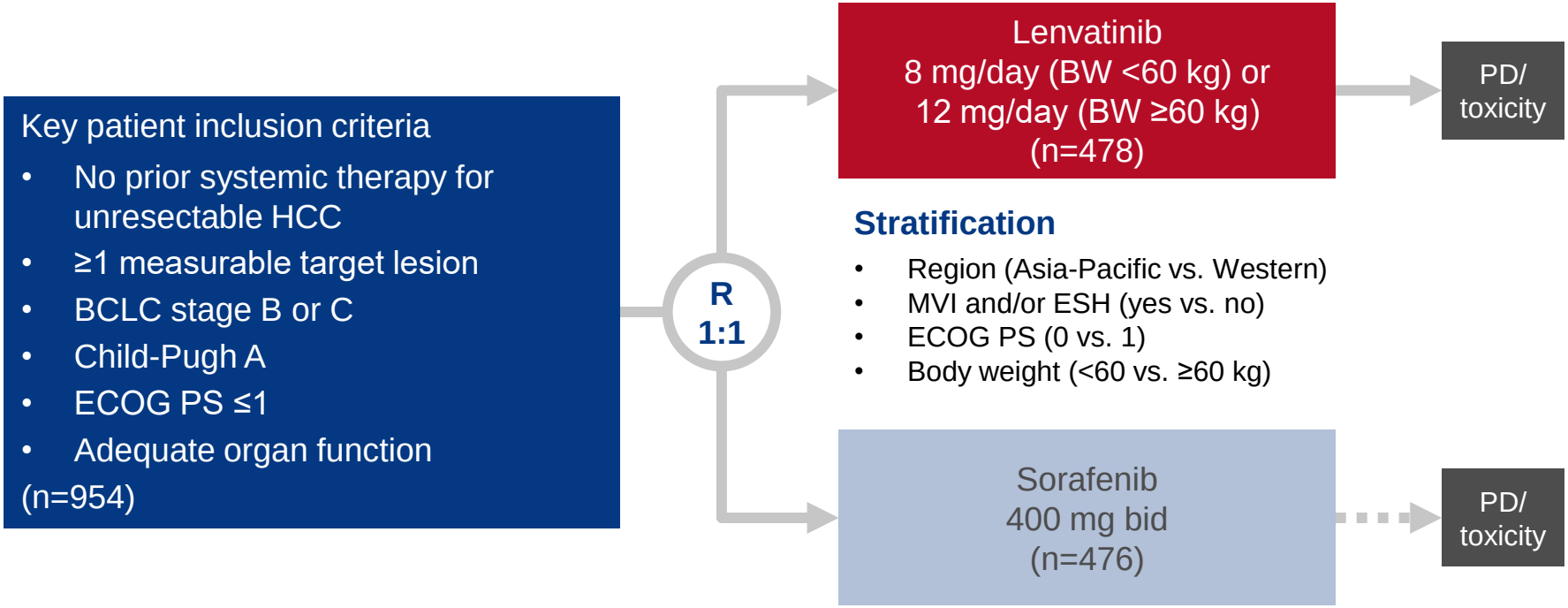
- **In MET-high patients with HCC who had progressed on or were intolerant to sunitinib, tivantinib 120 mg bid did not improve OS or PFS**
- **OS was longer than expected for MET-high patients on placebo**
- **Adverse events with tivantinib appeared to be manageable at the final established dose of 120 mg bid**

Rimassa L, et al. J Clin Oncol 2017;35(Suppl):Abstr 4000

# 4001: Phase III trial of lenvatinib (LEN) vs sorafenib (SOR) in first-line treatment of patients (pts) with unresectable hepatocellular carcinoma (uHCC) – Cheng A-L, et al

## Study objective

- To evaluate the efficacy and safety of lenvatinib as a 1L treatment for patients with HCC




## PRIMARY ENDPOINT

- OS

*Study excluded patients with ≥50% liver occupation; clear bile duct invasion; and portal vein invasion at the main portal vein

## SECONDARY ENDPOINTS

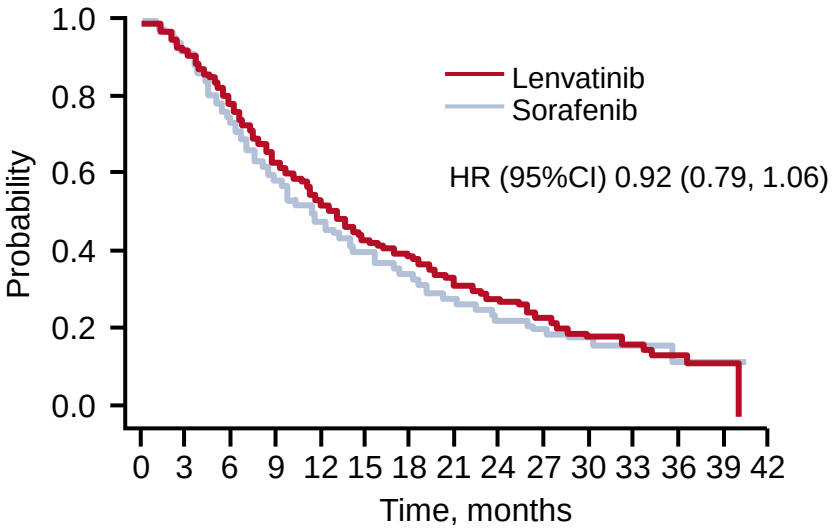
- PFS, TTP, ORR, QoL, PK lenvatinib exposure parameters, biomarkers

Cheng A-L, et al. J Clin Oncol 2017;35(Suppl):Abstr 4001

# 4001: Phase III trial of lenvatinib (LEN) vs sorafenib (SOR) in first-line treatment of patients (pts) with unresectable hepatocellular carcinoma (uHCC) – Cheng A-L, et al

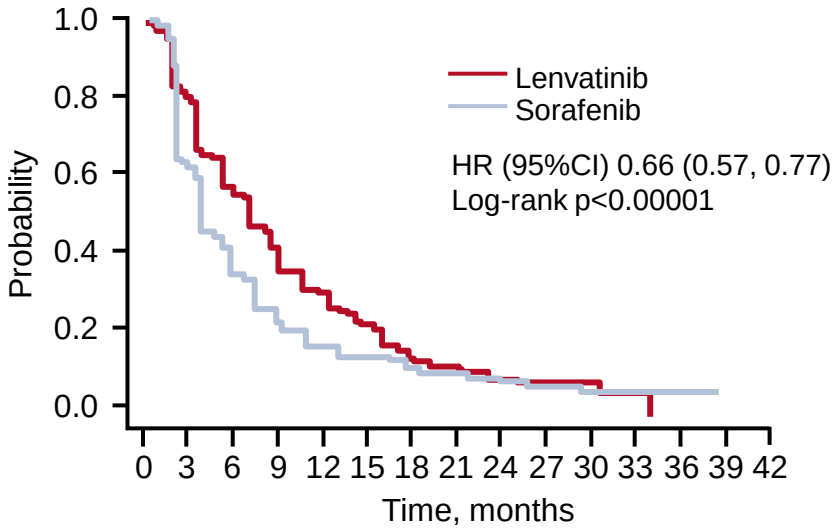
## Key results

### OS




| | Median OS, months (95%CI) |
|---|---|
| Lenvatinib | 13.6 (12.1, 14.9) |
| Sorafenib | 12.3 (10.4, 13.9) |

### PFS




| | Median OS, months (95%CI) |
|---|---|
| Lenvatinib | 7.4 (6.9, 8.8) |
| Sorafenib | 3.7 (3.6, 4.8) |

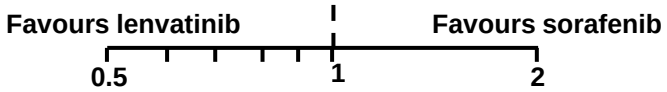
Cheng A-L, et al. J Clin Oncol 2017;35(Suppl):Abstr 4001

# 4001: Phase III trial of lenvatinib (LEN) vs sorafenib (SOR) in first-line treatment of patients (pts) with unresectable hepatocellular carcinoma (uHCC) – Cheng A-L, et al

## Key results (cont.)

### OS by subgroup

| Characteristic | Subgroup | Events / patients | | HR (95%CI) Lenvatinib vs. sorafenib | Median, months | |
|---|---|---|---|---|---|---|
| | | Lenvatinib | Sorafenib | | Lenvatinib | Sorafenib |
| Overall | | 351/478 | 350/476 | 0.92 (0.79, 1.06) | 13.6 | 12.3 |
| Age | <65 years | 203/270 | 204/283 | 0.94 (0.77, 1.15) | 12.4 | 11.4 |
| | ≥65 years | 148/208 | 146/193 | 0.84 (0.66, 1.07) | 14.6 | 13.4 |
| Sex | Male | 293/405 | 293/401 | 0.91 (0.77, 1.07) | 13.4 | 12.4 |
| | Female | 58/73 | 57/75 | 0.84 (0.56, 1.26) | 15.3 | 11.4 |
| Region | Asia-Pacific | 243/321 | 248/319 | 0.86 (0.72, 1.02) | 13.5 | 11.0 |
| | Western | 108/157 | 102/157 | 1.08 (0.82, 1.42) | 13.6 | 14.2 |
| ECOG PS | 0 | 221/304 | 223/301 | 0.88 (0.73, 1.06) | 14.6 | 12.8 |
| | 1 | 130/174 | 127/175 | 0.97 (0.76, 1.25) | 10.7 | 10.3 |
| Body weight | <60 kg | 110/153 | 113/146 | 0.85 (0.65, 1.11) | 13.4 | 10.3 |
| | ≥60 kg | 241/325 | 237/330 | 0.95 (0.79, 1.14) | 13.7 | 12.5 |
| MVI, EHS or both | Yes | 250/329 | 259/336 | 0.87 (0.73, 1.04) | 11.5 | 9.8 |
| | No | 101/149 | 91/140 | 1.05 (0.79, 1.40) | 18.0 | 18.0 |
| AFP at baseline | <200 ng/mL | 167/255 | 193/266 | 0.91 (0.74, 1.12) | 19.5 | 16.3 |
| | ≥200 ng/mL | 182/222 | 154/187 | 0.78 (0.63, 0.98) | 10.4 | 8.2 |
| Aetiology | HBV | 196/259 | 186/244 | 0.83 (0.68, 1.02) | 13.4 | 10.2 |
| | HCV | 75/103 | 97/135 | 0.91 (0.66, 1.26) | 15.3 | 14.1 |
| BCLC staging | Stage B | 71/104 | 65/92 | 0.91 (0.65, 1.28) | 18.5 | 17.3 |
| | Stage C | 280/374 | 285/384 | 0.92 (0.77, 1.08) | 11.8 | 10.3 |
| Post-treatment anticancer therapy | Yes | 143/206 | 175/243 | 0.84 (0.67, 1.06) | 19.5 | 17.0 |
| | No | 208/272 | 175/233 | 0.91 (0.74, 1.11) | 10.5 | 7.9 |




Cheng A-L, et al. J Clin Oncol 2017;35(Suppl):Abstr 4001

# 4001: Phase III trial of lenvatinib (LEN) vs sorafenib (SOR) in first-line treatment of patients (pts) with unresectable hepatocellular carcinoma (uHCC) – Cheng A-L, et al

## Key results (cont.)

| Patients, n (%) | Lenvatinib (n=476) | Sorafenib (n=475) |
|---|---|---|
| Any TEAEs | 470 (99) | 472 (99) |
| Treatment-related TEAEs | 447 (94) | 452 (95) |
| Any TEAEs grade ≥3 | 357 (75) | 316 (67) |
| Treatment-related TEAEs grade ≥3 | 270 (57) | 231 (49) |
| Any serious AEs | 205 (43) | 144 (30) |
| Treatment-related serious AEs | 84 (18) | 48 (10) |
| Dose modifications | | |
| Dose reductions due to related TEAEs | 176 (37) | 181 (38) |
| Dose reductions or interruption due to related TEAEs | 252 (53) | 236 (50) |
| Discontinuation due to related TEAEs | 42 (9) | 34 (7) |

Cheng A-L, et al. J Clin Oncol 2017;35(Suppl):Abstr 4001

# 4001: Phase III trial of lenvatinib (LEN) vs sorafenib (SOR) in first-line treatment of patients (pts) with unresectable hepatocellular carcinoma (uHCC) – Cheng A-L, et al

## Conclusions

- In patients with unresectable HCC, lenvatinib demonstrated non-inferiority compared with sorafenib in OS (13.6 vs. 12.3 months)
- In this patient population, lenvatinib compared with sorafenib provided significant and clinically meaningful improvement in PFS, TTP, and ORR
- The safety profiles of lenvatinib and sorafenib seem consistent with those previously reported in patients with HCC
- In patients with advanced HCC, lenvatinib may be a potential treatment option

Cheng A-L, et al. J Clin Oncol 2017;35(Suppl):Abstr 4001

# 4002: Phase III multi-centre open-label randomized controlled trial of selective internal radiation therapy (SIRT) versus sorafenib in locally advanced hepatoceullar carcinoma: The SIRveNIB study – Chow P, et al

## Study objective

- To assess the efficacy of SIRT with Y90 resin microspheres compared with sorafenib in patients with locally advanced HCC not amenable to curative therapies

**Key patient inclusion criteria**

- Locally advanced HCC without extrahepatic metastases
- At least one lesion ≥10 mm
- Child-Pugh A or B (≤7 points)
- ≤2 prior administrations of hepatic artery-directed therapy
- ECOG PS 0–1

(n=360)

R

SIRT with Y90 microspheres* (n=182) → PD

**Stratification**

- Site
- Portal vein thrombosis

Sorafenib 400 mg bid (n=178) → PD

## PRIMARY ENDPOINT

- OS

## SECONDARY ENDPOINTS

- Tumour response rate, DCR, PFS, TTP

*Single injection

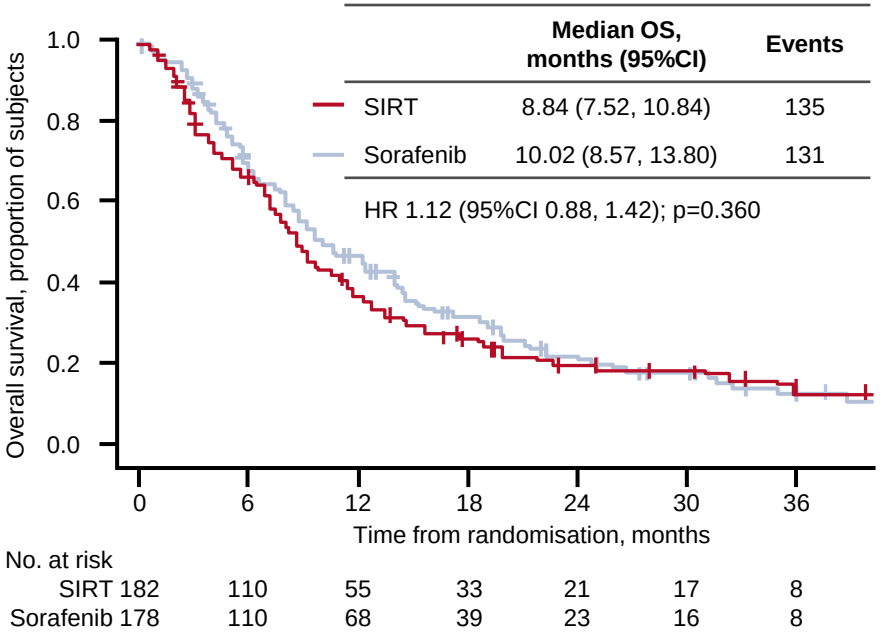
Chow P, et al. J Clin Oncol 2017;35(Suppl):Abstr 4002

# 4002: Phase III multi-centre open-label randomized controlled trial of selective internal radiation therapy (SIRT) versus sorafenib in locally advanced hepatoceullar carcinoma: The SIRveNIB study – Chow P, et al

## Key results

### OS

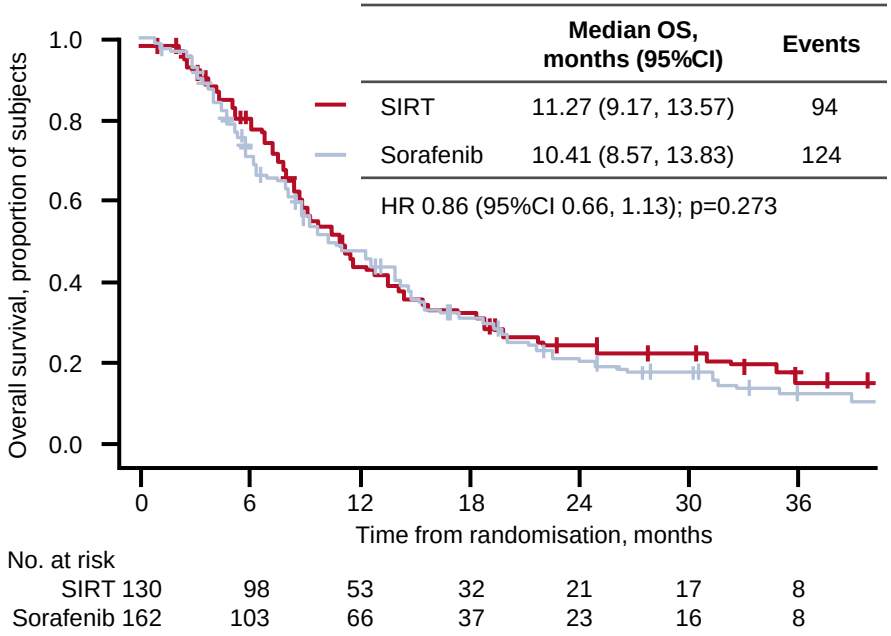
#### ITT population




No. at risk

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| SIRT 182 | 110 | 55 | 33 | 21 | 17 | 8 |
| Sorafenib 178 | 110 | 68 | 39 | 23 | 16 | 8 |

#### Treated population



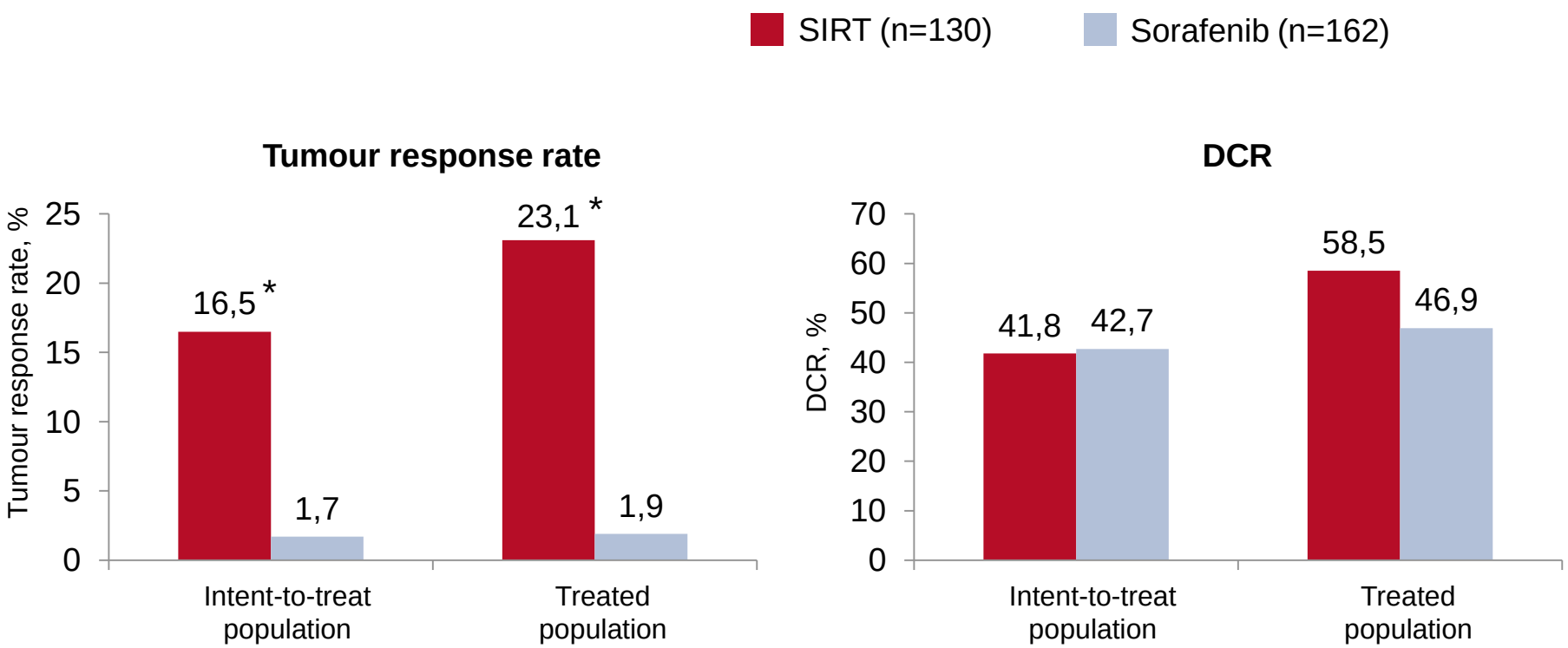

No. at risk

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| SIRT 130 | 98 | 53 | 32 | 21 | 17 | 8 |
| Sorafenib 162 | 103 | 66 | 37 | 23 | 16 | 8 |

Chow P, et al. J Clin Oncol 2017;35(Suppl):Abstr 4002

# 4002: Phase III multi-centre open-label randomized controlled trial of selective internal radiation therapy (SIRT) versus sorafenib in locally advanced hepatoceullar carcinoma: The SIRveNIB study – Chow P, et al

## Key results (cont.)

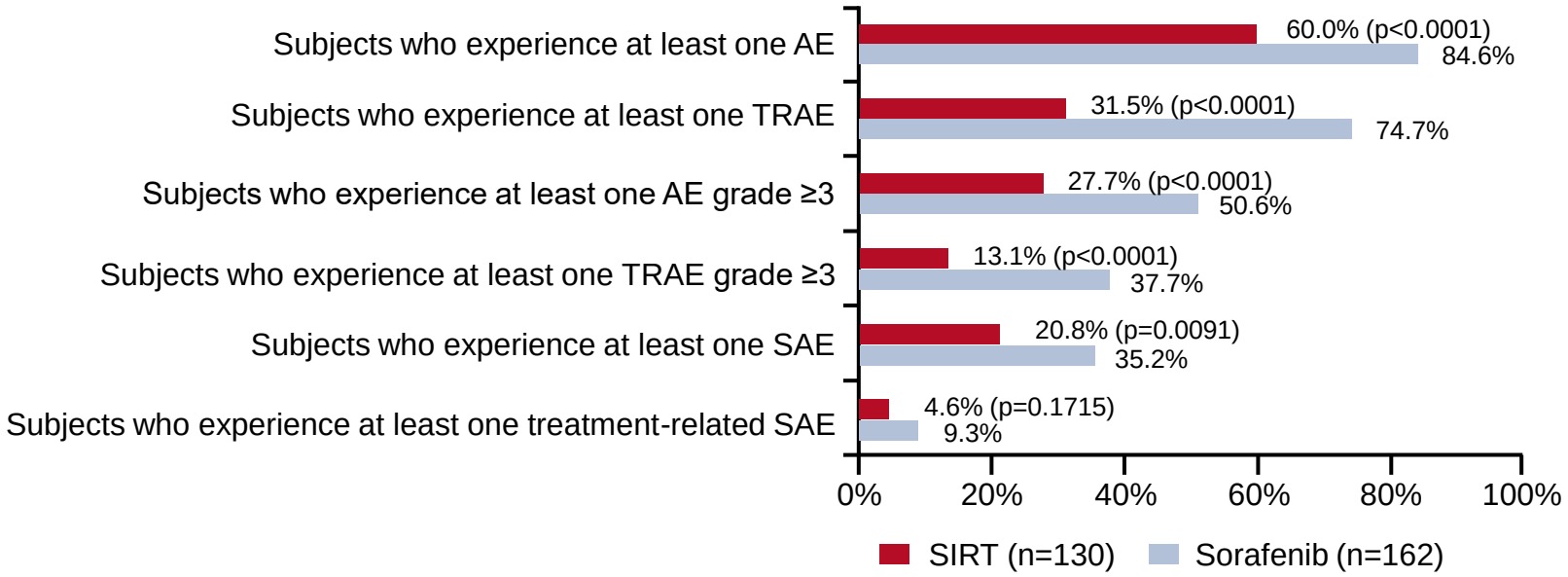



*p<0.001

Chow P, et al. J Clin Oncol 2017;35(Suppl):Abstr 4002

# 4002: Phase III multi-centre open-label randomized controlled trial of selective internal radiation therapy (SIRT) versus sorafenib in locally advanced hepatoceullar carcinoma: The SIRveNIB study – Chow P, et al

## Key results (cont.)




Includes AEs and SAEs with onset date on or after study treatment start date. TRAE or SAE defined as those with certain, probable, possible, or missing relationship to study treatment

Chow P, et al. J Clin Oncol 2017;35(Suppl):Abstr 4002

# 4002: Phase III multi-centre open-label randomized controlled trial of selective internal radiation therapy (SIRT) versus sorafenib in locally advanced hepatoceullar carcinoma: The SIRveNIB study – Chow P, et al

## Conclusions

- In patients with locally advanced HCC, SIRT was not shown to be superior to sorafenib with respect to OS
- Patients treated with SIRT had a significantly better tumour-response rate compared with sorafenib
- SIRT was associated with fewer AEs and SAEs compared with sorafenib

Chow P, et al. J Clin Oncol 2017;35(Suppl):Abstr 4002

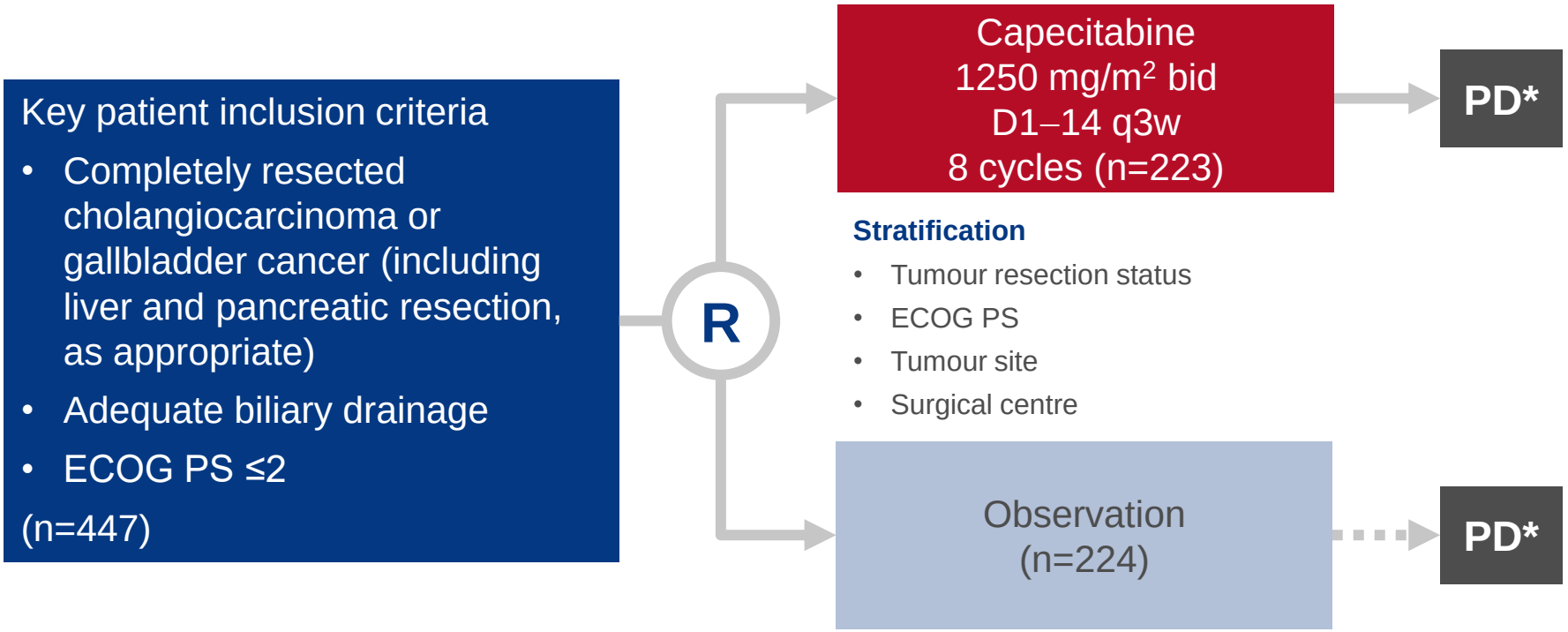
Cancers of the pancreas, small bowel and hepatobiliary tract

# BILIARY TRACT CANCER

# 4006: Adjuvant capecitabine for biliary tract cancer: The BILCAP randomized study – Primrose JN, et al

## Study objective

- To determine whether capecitabine improves OS compared with observation following radical surgery in cholangiocarcinoma or gallbladder cancer




### PRIMARY ENDPOINT

- OS

### SECONDARY ENDPOINTS

- RFS, TTP, toxicity, QoL

*Primary analysis after a minimum 2-year follow-up

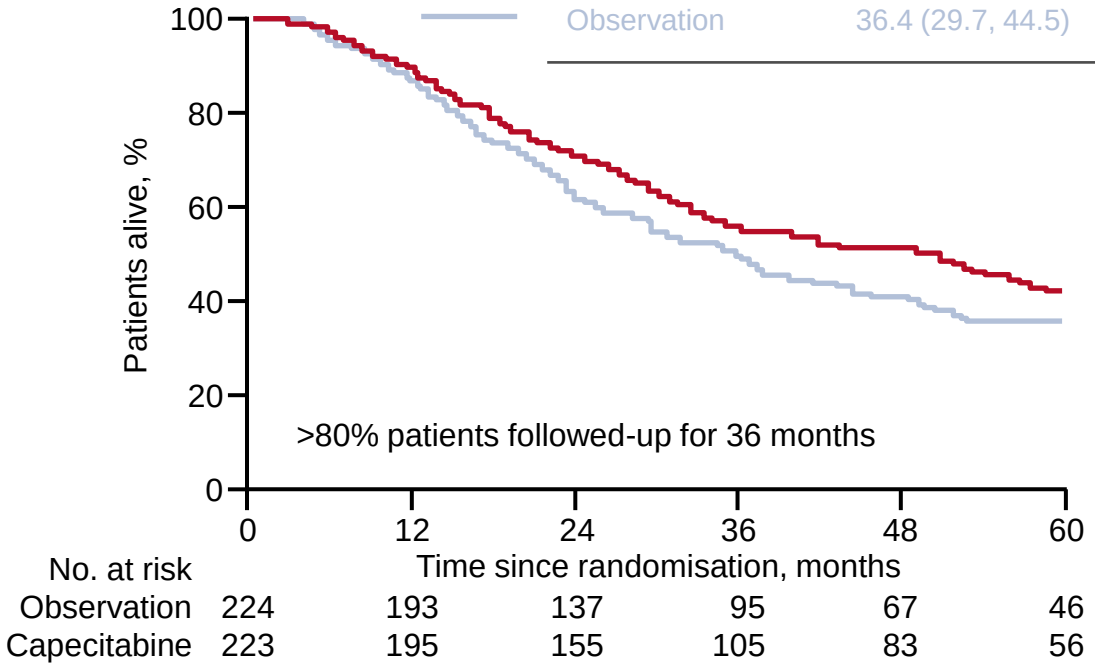
Primrose JN, et al. J Clin Oncol 2017;35(Suppl):Abstr 4006

# 4006: Adjuvant capecitabine for biliary tract cancer: The BILCAP randomized study – Primrose JN, et al

## Key results

### OS (ITT population)

| Treatment | Median OS, months (95%CI) | HR (95%CI) |
|---|---|---|
| Capecitabine | 51.1 (34.6, 59.1) | 0.81 (0.63, 1.04) p=0.097 |
| Observation | 36.4 (29.7, 44.5) | |




Sensitivity analyses

Adjusting for further prognostic factors (nodal status, disease grade, gender)

HR 0.70 (95%CI 0.55, 0.91); p=0.007

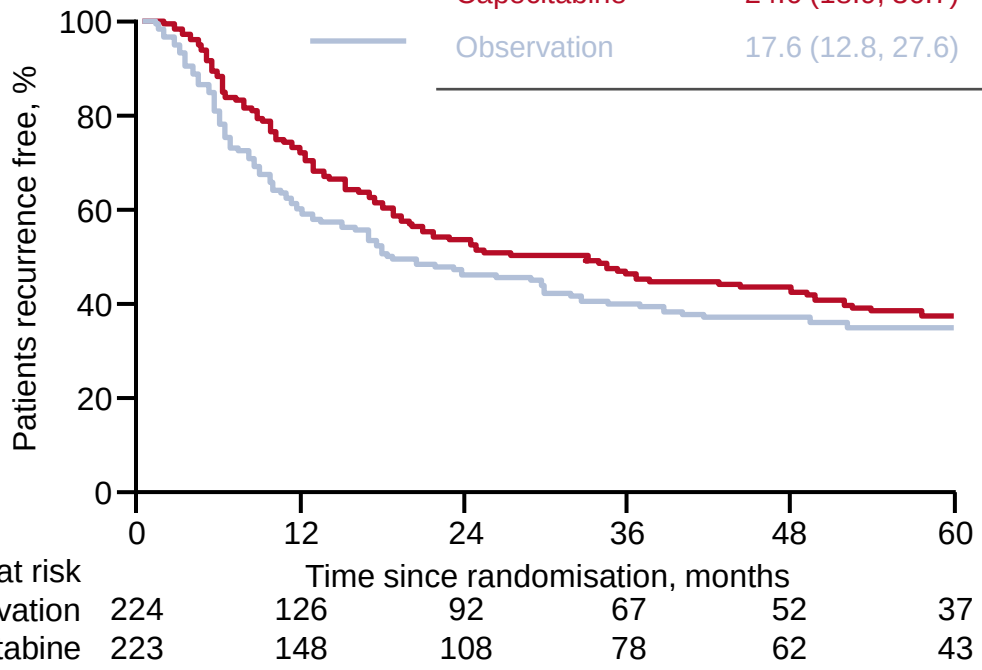
Primrose JN, et al. J Clin Oncol 2017;35(Suppl):Abstr 4006

# 4006: Adjuvant capecitabine for biliary tract cancer: The BILCAP randomized study – Primrose JN, et al

## Key results (cont.)

### RFS (ITT population)

| Treatment | Median OS, months (95%CI) | HR (95%CI) |
|---|---|---|
| Capecitabine | 24.6 (18.9, 36.7) | 0.76 (0.58, 0.99) p=0.039 |
| Observation | 17.6 (12.8, 27.6) | |




Primrose JN, et al. J Clin Oncol 2017;35(Suppl):Abstr 4006

# 4006: Adjuvant capecitabine for biliary tract cancer: The BILCAP randomized study – Primrose JN, et al

## Key results (cont.)

| AEs in patients receiving adjuvant capecitabine (n=213), n (%) | All grades | Grade 1/2 | Grade 3/4 |
|---|---|---|---|
| Fatigue | 175 (82) | 159 (75) | 16 (8) |
| Plantar palmar erythema | 174 (82) | 130 (61) | 44 (21) |
| Diarrhoea | 137 (64) | 121 (57) | 16 (8) |
| Nausea | 108 (51) | 106 (50) | 2 (1) |
| Mucositis/stomatitis | 96 (45) | 94 (44) | 2 (1) |
| Vomiting | 50 (24) | 49 (23) | 1 (0.5) |
| Neutropenia | 49 (23) | 45 (21) | 4 (2) |
| Bilirubin | 45 (21) | 42 (20) | 3 (1) |
| Thrombocytopenia | 26 (12) | 25 (12) | 1 (0.5) |
| Alopecia | 20 (9) | 20 (9) | 0 (0) |

Primrose JN, et al. J Clin Oncol 2017;35(Suppl):Abstr 4006

# 4006: Adjuvant capecitabine for biliary tract cancer: The BILCAP randomized study – Primrose JN, et al

## Conclusions

- In patients with resected biliary tract cancer, adjuvant capecitabine improved OS from 36 to 51 months and should become the standard of care in this patient population
- Capecitabine had modest toxicity and patient QoL was not reduced
- In future adjuvant studies of patients with biliary tract cancer, capecitabine should be used as the control arm

Primrose JN, et al. J Clin Oncol 2017;35(Suppl):Abstr 4006

# CANCERS OF THE COLON, RECTUM AND ANUS

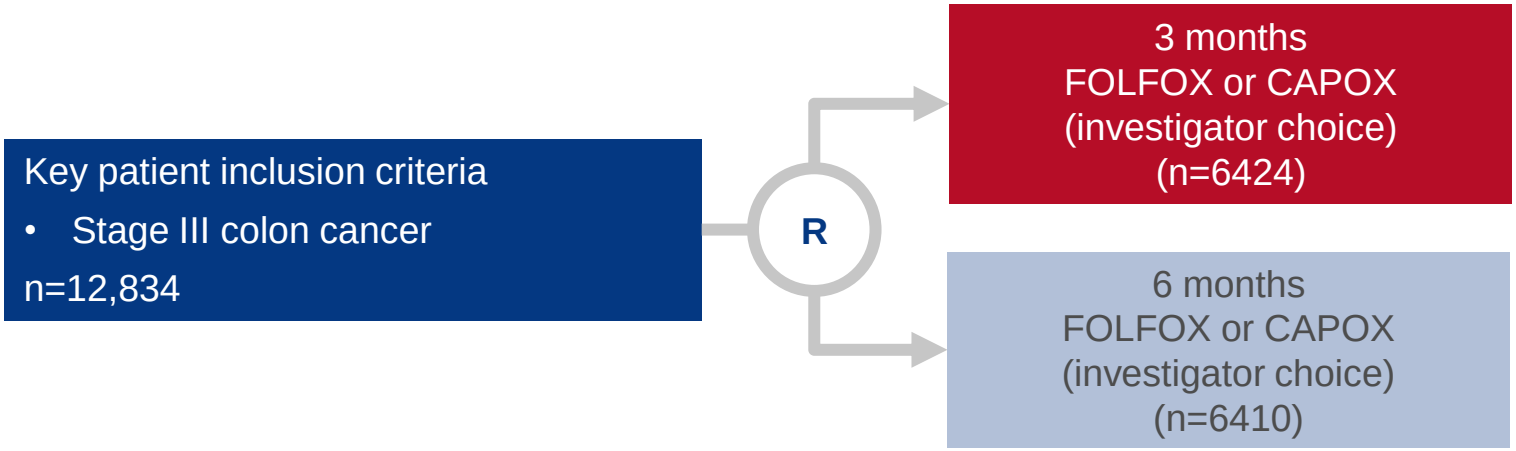
Cancers of the colon, rectum and anus

# COLORECTAL CANCER

# LBA1: Prospective pooled analysis of six phase III trials investigating duration of adjuvant (adjuv) oxaliplatin-based therapy (3 vs 6 months) for patients (pts) with stage III colon cancer (CC): The IDEA (International Duration Evaluation of Adjuvant chemotherapy) collaboration – Shi Q, et al

## Study objective

- To assess the non-inferiority of 3 months compared with 6 months of adjuvant oxaliplatin-based treatment in patients with stage III colon cancer (a pooled analysis of six phase 3 studies*)




### PRIMARY ENDPOINT

- DFS

### SECONDARY ENDPOINTS

- Pre-planned subgroup analyses by regimen and T/N stage

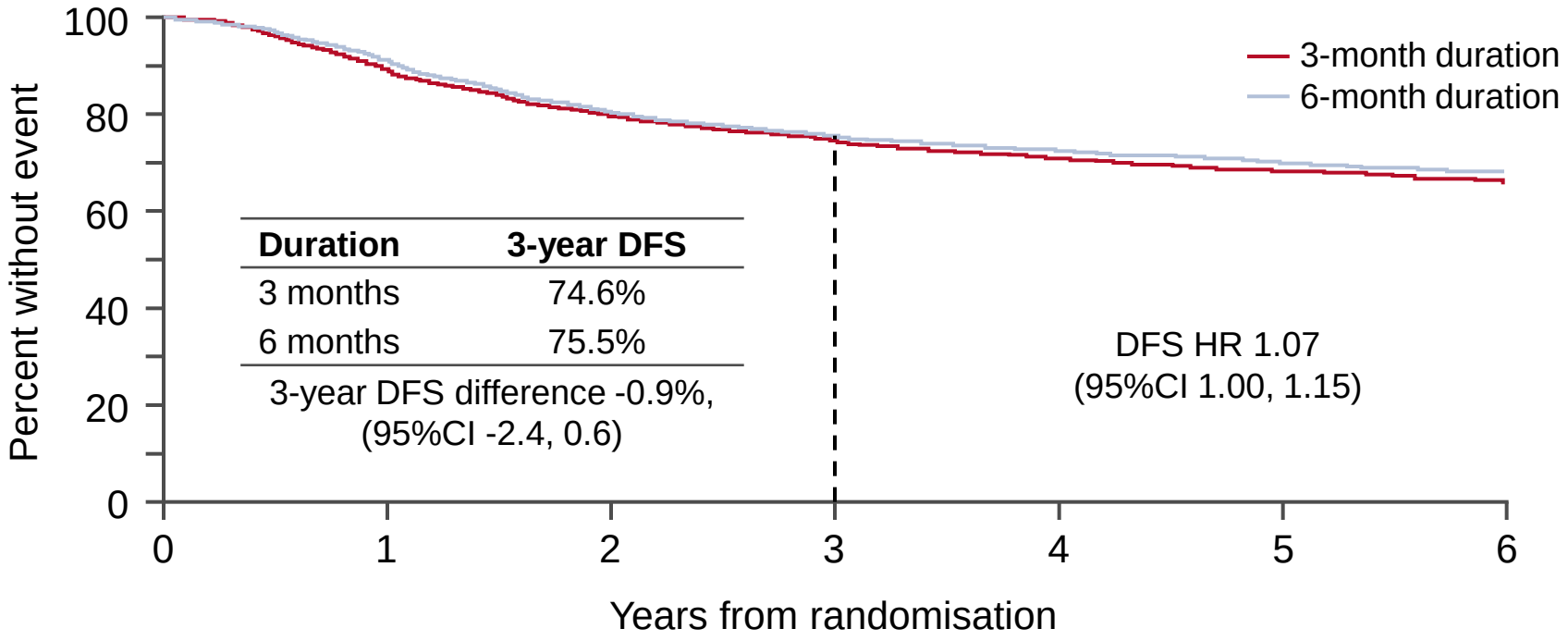
*SCOT, TOSCA, Alliance/SWOG 80702, IDEA France, ACHIEVE, HORG

Shi Q, et al. J Clin Oncol 2017;35(Suppl):Abstr LBA1

# LBA1: Prospective pooled analysis of six phase III trials investigating duration of adjuvant (adjuv) oxaliplatin-based therapy (3 vs 6 months) for patients (pts) with stage III colon cancer (CC): The IDEA (International Duration Evaluation of Adjuvant chemotherapy) collaboration – Shi Q, et al

## Key results

### Primary DFS analysis (mITT)



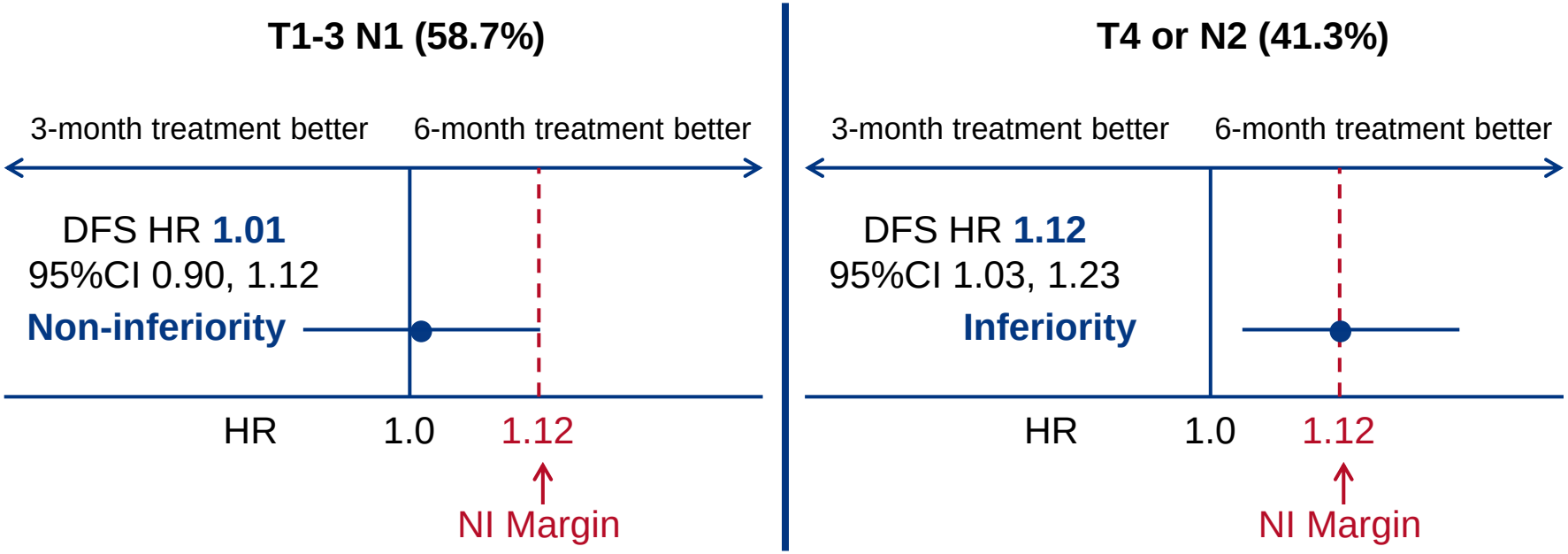

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| No. at risk | 6424 | 5446 | 4464 | 3000 | 1609 | 826 | 321 |
| | 6410 | 5530 | 4477 | 3065 | 1679 | 873 | 334 |

Shi Q, et al. J Clin Oncol 2017;35(Suppl):Abstr LBA1

# LBA1: Prospective pooled analysis of six phase III trials investigating duration of adjuvant (adjuv) oxaliplatin-based therapy (3 vs 6 months) for patients (pts) with stage III colon cancer (CC): The IDEA (International Duration Evaluation of Adjuvant chemotherapy) collaboration – Shi Q, et al

## Key results (cont.)

**DFS comparison by risk group**



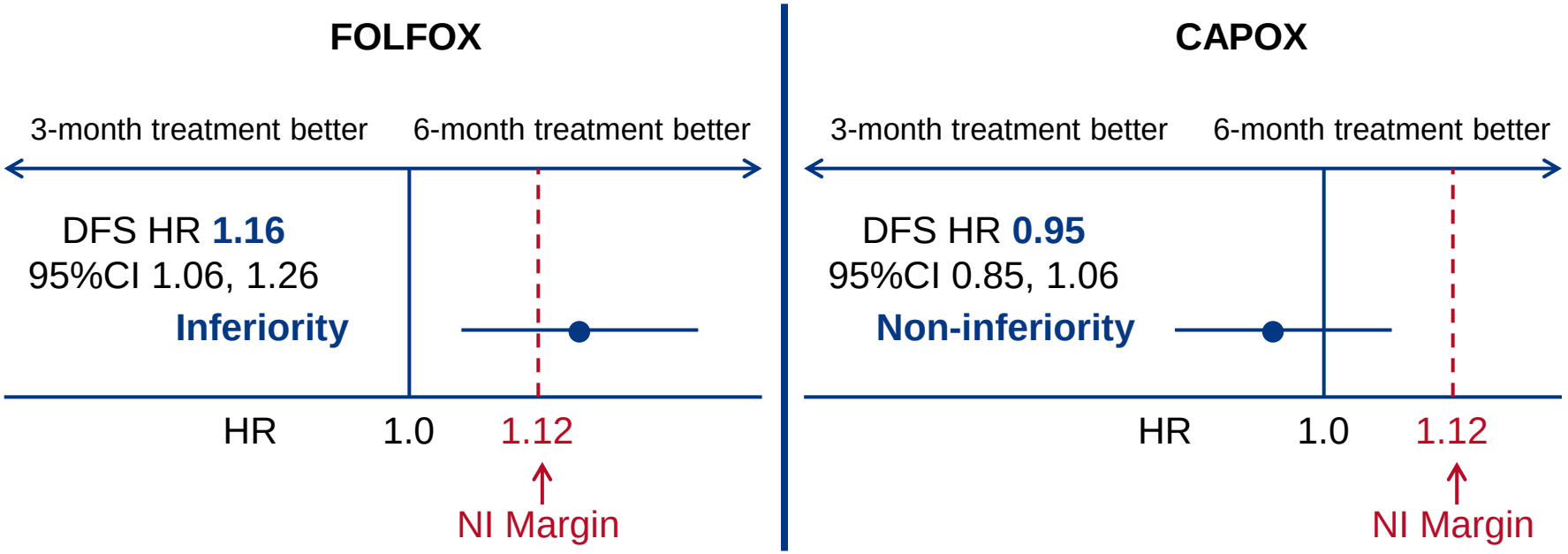

Interaction p-value = 0.11

Shi Q, et al. J Clin Oncol 2017;35(Suppl):Abstr LBA1

# LBA1: Prospective pooled analysis of six phase III trials investigating duration of adjuvant (adjuv) oxaliplatin-based therapy (3 vs 6 months) for patients (pts) with stage III colon cancer (CC): The IDEA (International Duration Evaluation of Adjuvant chemotherapy) collaboration – Shi Q, et al

## Key results (cont.)

**DFS comparison by regimen**



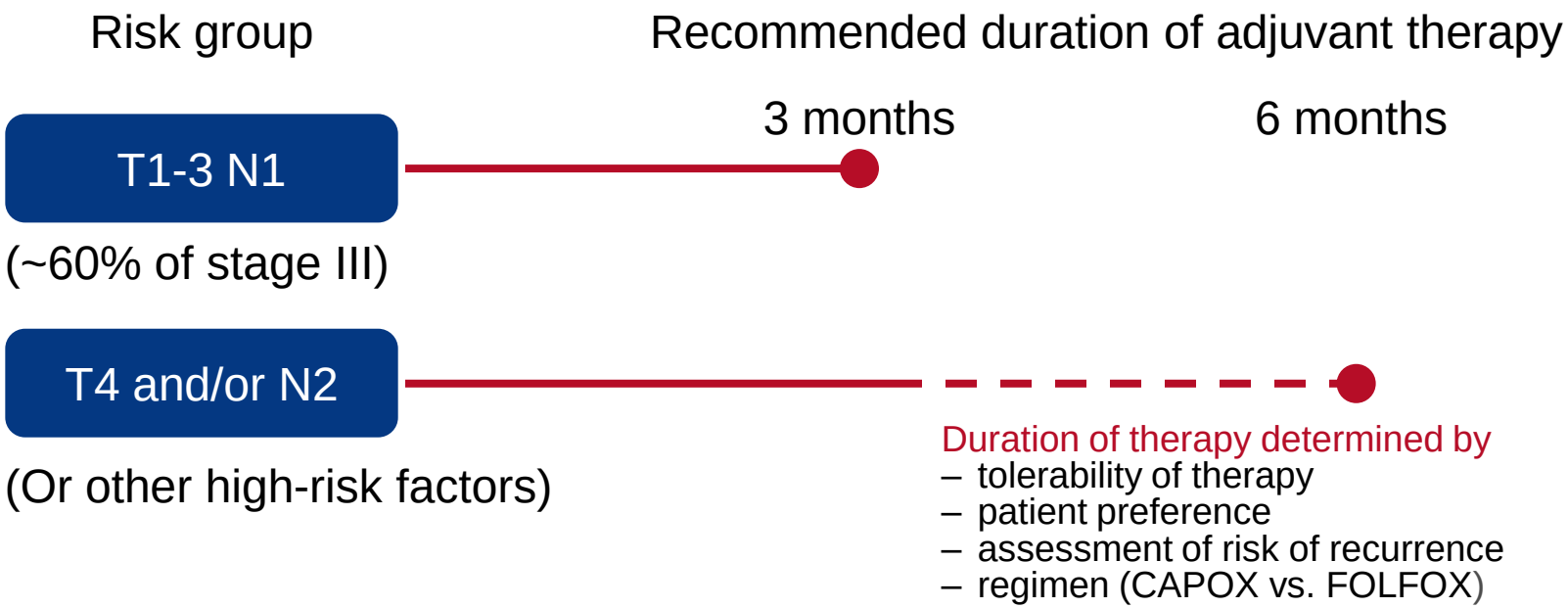

Interaction p-value = 0.0051

Shi Q, et al. J Clin Oncol 2017;35(Suppl):Abstr LBA1

# LBA1: Prospective pooled analysis of six phase III trials investigating duration of adjuvant (adjuv) oxaliplatin-based therapy (3 vs 6 months) for patients (pts) with stage III colon cancer (CC): The IDEA (International Duration Evaluation of Adjuvant chemotherapy) collaboration – Shi Q, et al

## Conclusions

- In overall stage III colon cancer, DFS non-inferiority of 3-month oxaliplatin-based adjuvant therapy was not established
- Data comparing DFS between 3 and 6 months of treatment appear dependent of risk group and regimen
- A risk-based approach to adjuvant chemotherapy in stage III colon cancer was proposed:

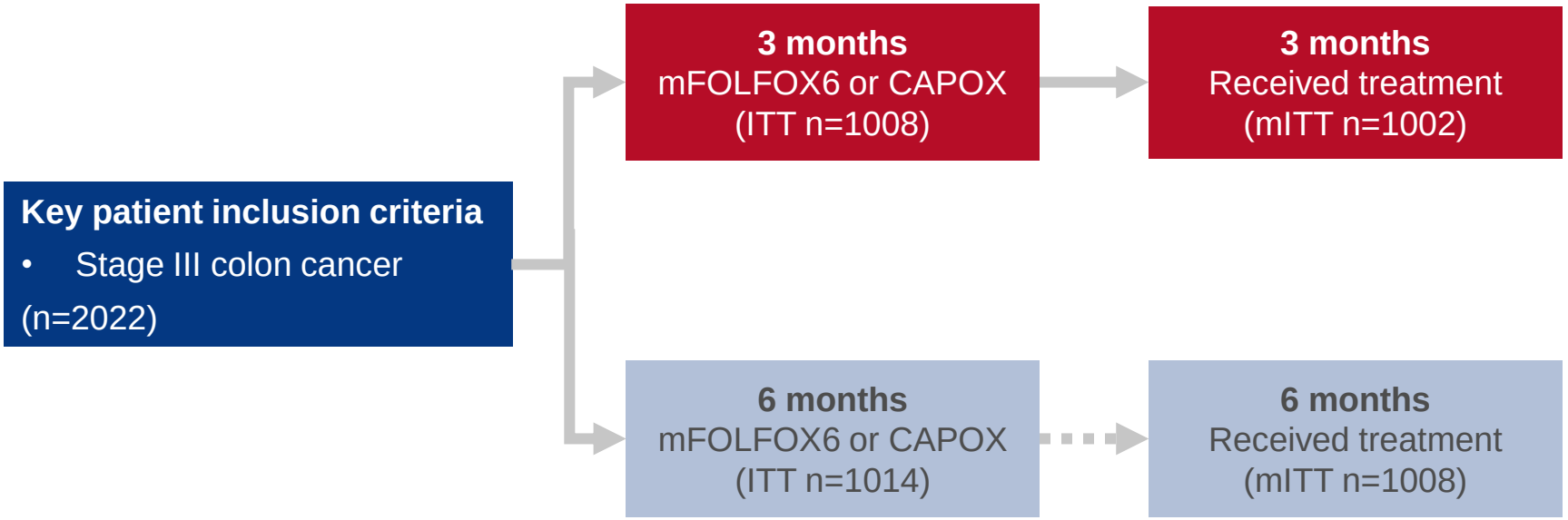



Shi Q, et al. J Clin Oncol 2017;35(Suppl):Abstr LBA1

# 3500: Oxaliplatin-based chemotherapy for patients with stage III colon cancer: Disease Free Survival results of the three versus six months adjuvant IDEA France Trial – André T, et al

## Study objective

- To evaluate the non-inferiority of 3- vs. 6-month treatment with mFOLFOX6 or CAPOX in patients with stage III colon cancer (French IDEA)



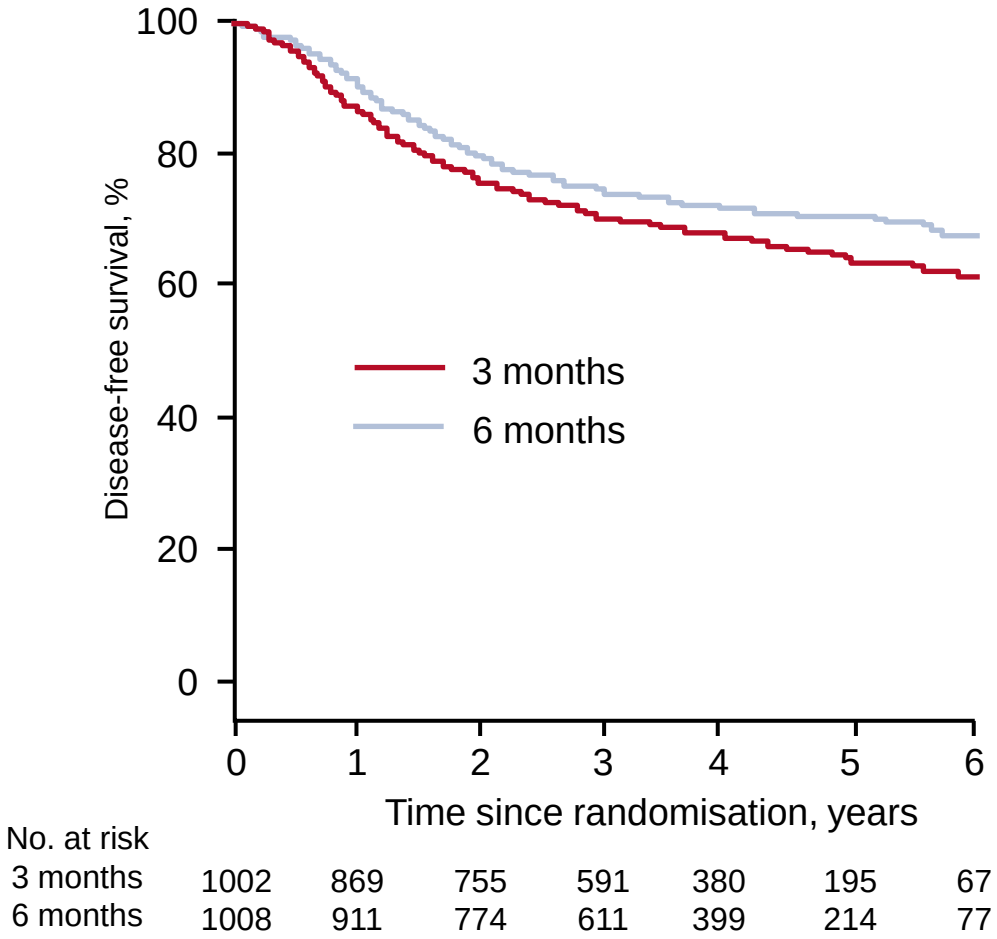

## PRIMARY ENDPOINT

- DFS

André T, et al. J Clin Oncol 2017;35(Suppl):Abstr 3500

# 3500: Oxaliplatin-based chemotherapy for patients with stage III colon cancer: Disease Free Survival results of the three versus six months adjuvant IDEA France Trial – André T, et al

## Key results




| | n | Events, n | 3-year rate, % (95%CI) |
|---|---|---|---|
| 3 months | 1002 | 314 | 72 (69, 75) |
| 6 months | 1008 | 264 | 76 (73, 78) |

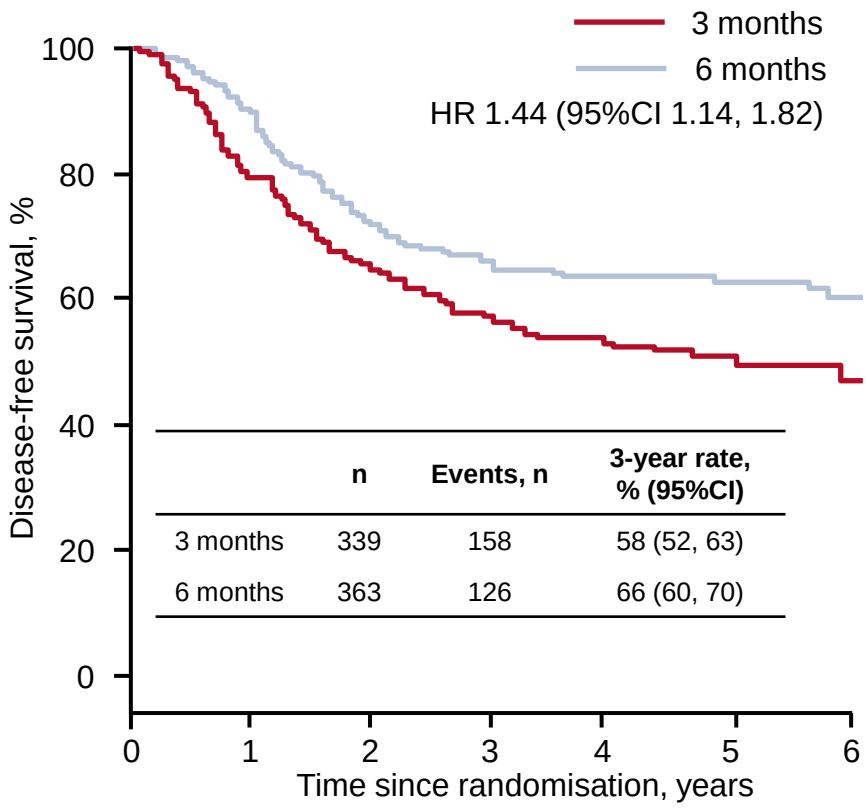
HR 1.24 (95%CI 1.05, 1.46)
p=0.011 (log-rank)

André T, et al. J Clin Oncol 2017;35(Suppl):Abstr 3500

# 3500: Oxaliplatin-based chemotherapy for patients with stage III colon cancer: Disease Free Survival results of the three versus six months adjuvant IDEA France Trial – André T, et al

## Key results (cont.)

### T4 and/or N2

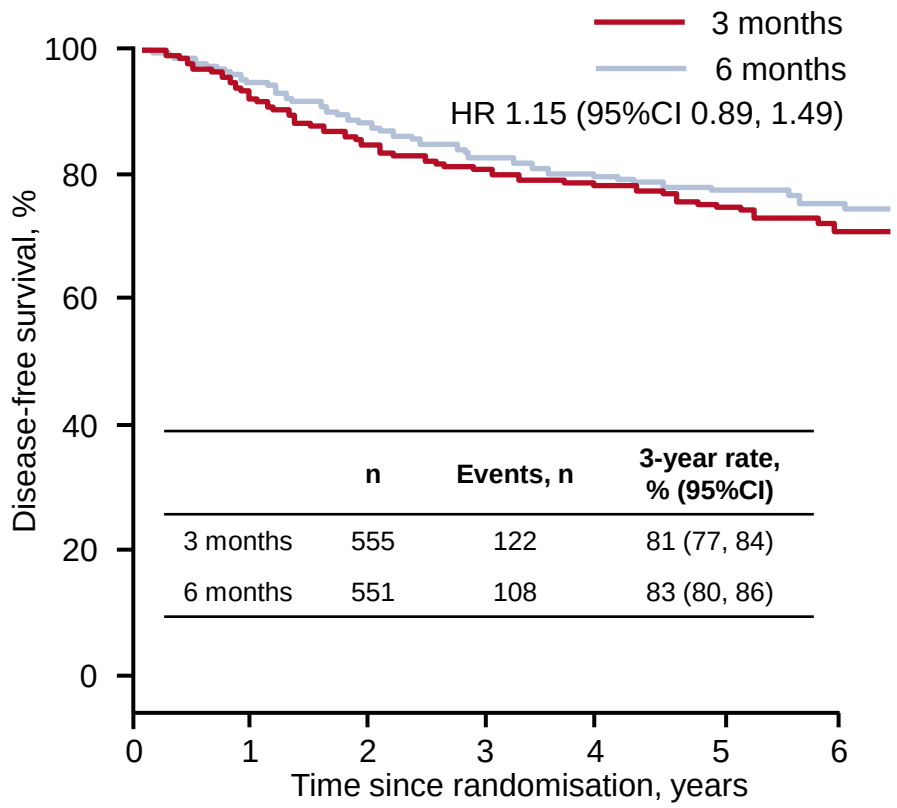



| | n | Events, n | 3-year rate, % (95%CI) |
|---|---|---|---|
| 3 months | 339 | 158 | 58 (52, 63) |
| 6 months | 363 | 126 | 66 (60, 70) |

No. at risk

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 3 months | 339 | 271 | 219 | 163 | 108 | 58 | 20 |
| 6 months | 363 | 317 | 246 | 193 | 134 | 80 | 30 |

### T1–3




| | n | Events, n | 3-year rate, % (95%CI) |
|---|---|---|---|
| 3 months | 555 | 122 | 81 (77, 84) |
| 6 months | 551 | 108 | 83 (80, 86) |

No. at risk

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 3 months | 555 | 502 | 453 | 366 | 232 | 120 | 46 |
| 6 months | 551 | 512 | 460 | 366 | 229 | 119 | 45 |

André T, et al. J Clin Oncol 2017;35(Suppl):Abstr 3500

# 3500: Oxaliplatin-based chemotherapy for patients with stage III colon cancer: Disease Free Survival results of the three versus six months adjuvant IDEA France Trial – André T, et al

## Key results (cont.)

| AEs, n (%) | 3 months (n=1002) | 6 months (n=1008) | p-value |
|---|---|---|---|
| All | 29.5 | 46.4 | **<0.001** |
| Neutropenia | 12.3 | 16.7 | **0.005** |
| Febrile neutropenia | 1.4 | 1.7 | 0.595 |
| Thrombocytopenia | 1.1 | 2.8 | **0.006** |
| Diarrhoea | 4.8 | 5.7 | 0.375 |
| Nausea | 1.7 | 2.3 | 0.343 |
| Vomiting | 2.3 | 1.9 | 0.524 |
| Fatigue | 2.6 | 5.2 | **0.003** |
| Oxaliplatin allergy (grade ≥2) | 1.7 | 4.6 | **<0.001** |
| Maximal neuropathy[a] | | | |
| During the first 7 months | | | |
| 2 | 23 | 39 | |
| 3–4 | 6 | 20 | **<0.001** |
| On-treatment and follow-up[b] | | | |
| 2 | 28 | 41 | |
| 3–4 | 8 | 25 | **<0.001** |
| Residual neuropathy at last follow-up visit | | | |
| 2 | 2 | 6 | |
| 3–4 | 0.5 | 2 | **<0.001** |

[a]Neuropathy grade ≥2
[b]Randomisation to last follow-up
Median (IQR) follow-up: 3.6 years (2.6–4.8)

André T, et al. J Clin Oncol 2017;35(Suppl):Abstr 3500

# 3500: Oxaliplatin-based chemotherapy for patients with stage III colon cancer: Disease Free Survival results of the three versus six months adjuvant IDEA France Trial – André T, et al

## Conclusions

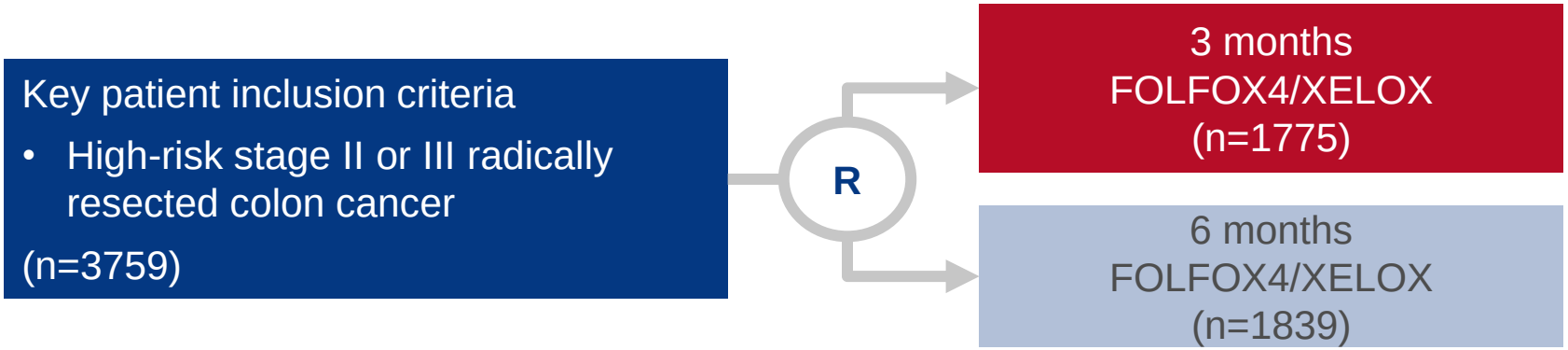
- Overall 6 months of adjuvant chemotherapy was superior to 3 months (3-year DFS: 72% vs. 76%; p=0.011) in this population, of which 90% were receiving mFOLFOX6
- In the 2% of patients with T1-3 N1, although there was a 3-year DFS advantage in the 6-month arm (83% vs. 81%) this needs to be balanced with a higher peripheral sensory neuropathy rate
- In the 8% of patients with T4 or N2, the 3-year DFS advantage in the 6-month arm (66% vs. 58%) would suggest that mFOLFOX6 be maintained for this duration but to stop oxaliplatin if grade ≥2 peripheral neuropathy occurred
- Data from this study should be considered together with the international IDEA data

André T, et al. J Clin Oncol 2017;35(Suppl):Abstr 3500

# 3501: FOLFOX4/XELOX in stage II–III colon cancer: Efficacy results of the Italian three or six colon adjuvant (TOSCA) trial – Sobrero AF, et al

## Study objective

- To assess the efficacy of 3 or 6 months of FOLFOX4/XELOX in patients with high-risk stage II or stage III radically resected colon cancer




### PRIMARY ENDPOINT

- RFS

### SECONDARY ENDPOINTS

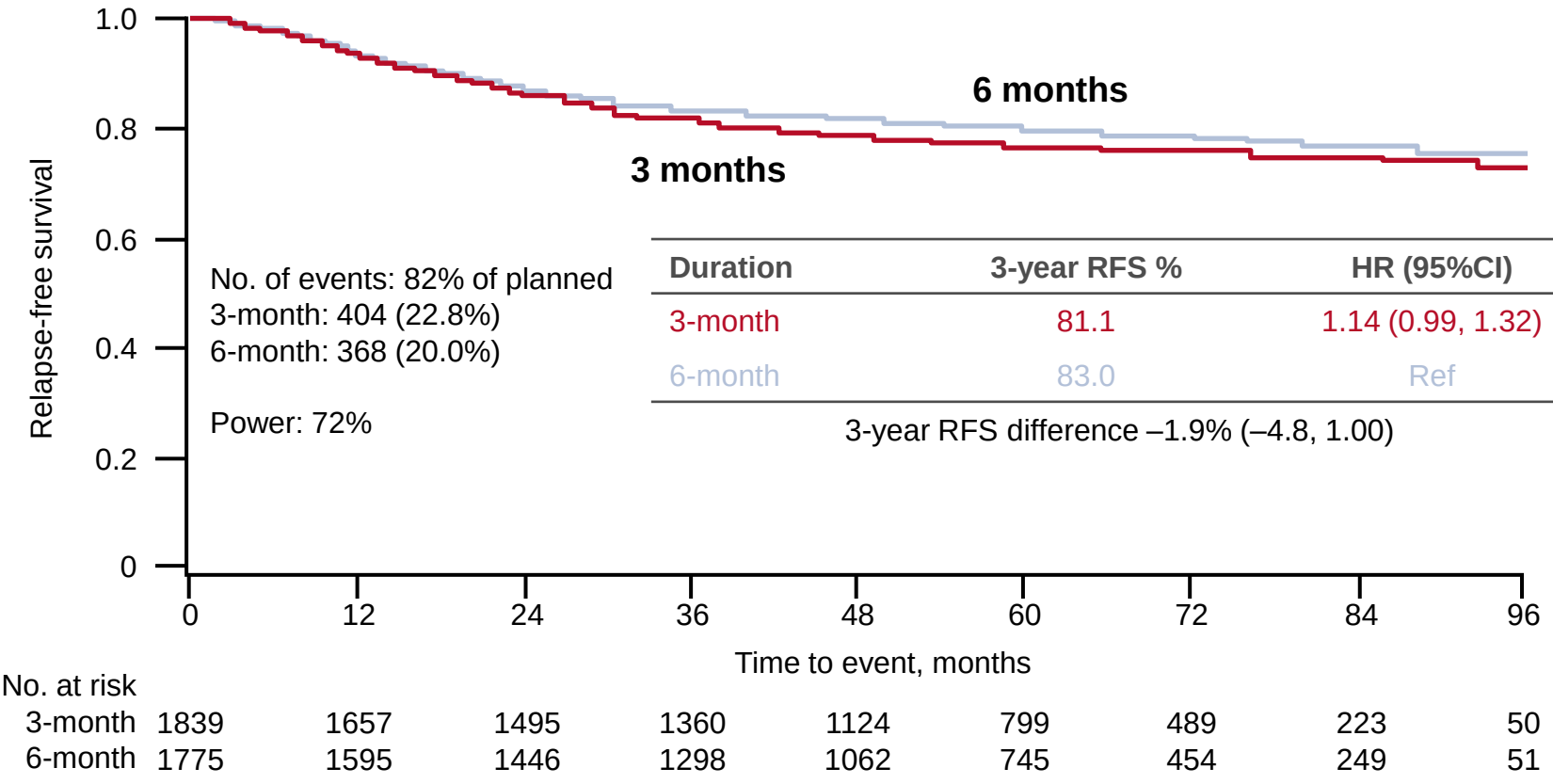
- Pre-planned subgroup analyses by stage

Sobrero AF, et al. J Clin Oncol 2017;35(Suppl):Abstr 3501

# 3501: FOLFOX4/XELOX in stage II–III colon cancer: Efficacy results of the Italian three or six colon adjuvant (TOSCA) trial – Sobrero AF, et al

## Key results

### RFS by treatment arm (Overall population)

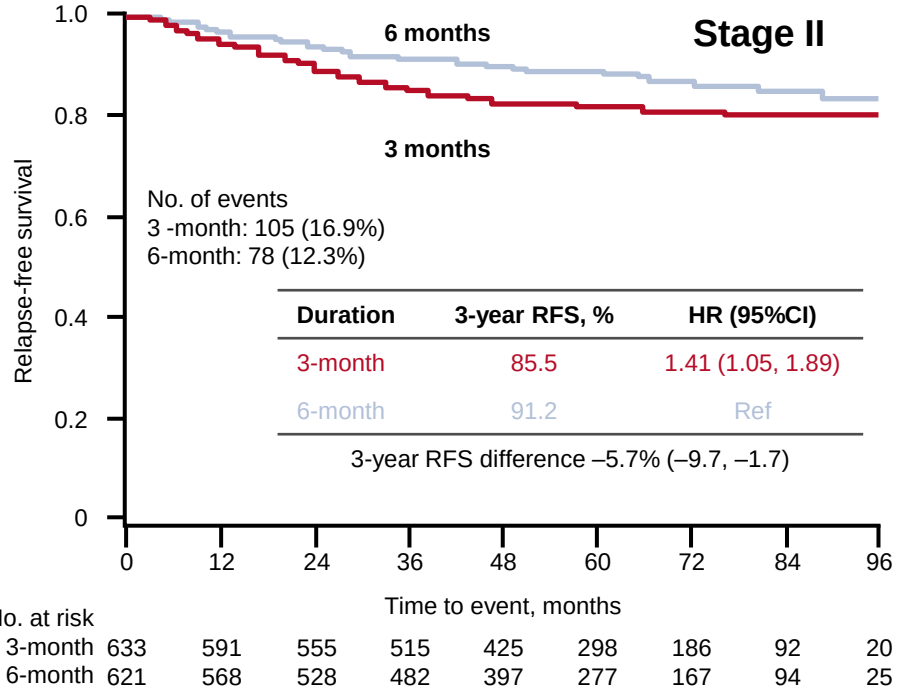


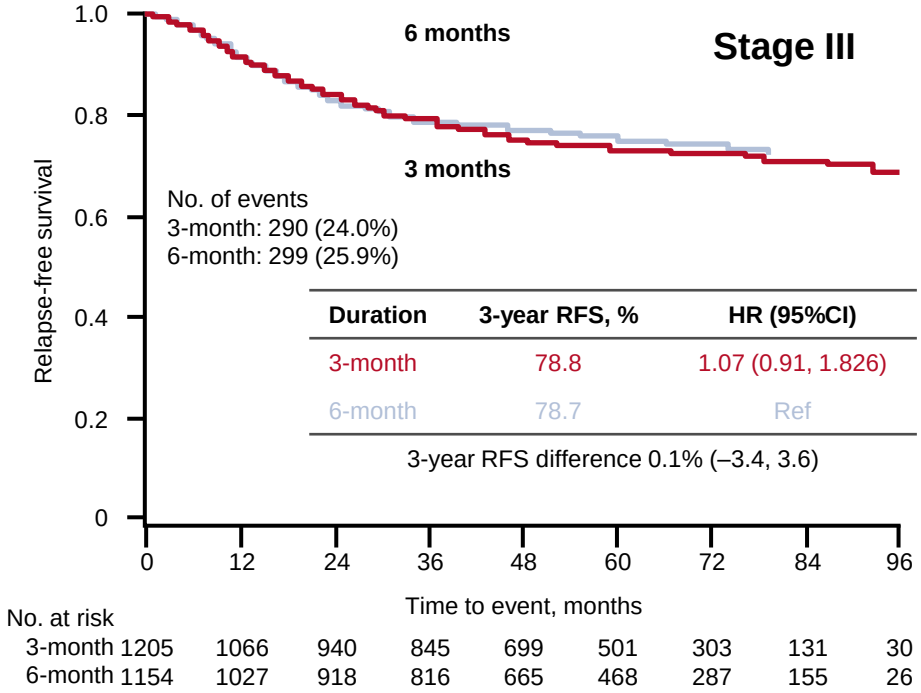

Sobrero AF, et al. J Clin Oncol 2017;35(Suppl):Abstr 3501

# 3501: FOLFOX4/XELOX in stage II–III colon cancer: Efficacy results of the Italian three or six colon adjuvant (TOSCA) trial – Sobrero AF, et al

## Key results (cont.)

### RFS by stage



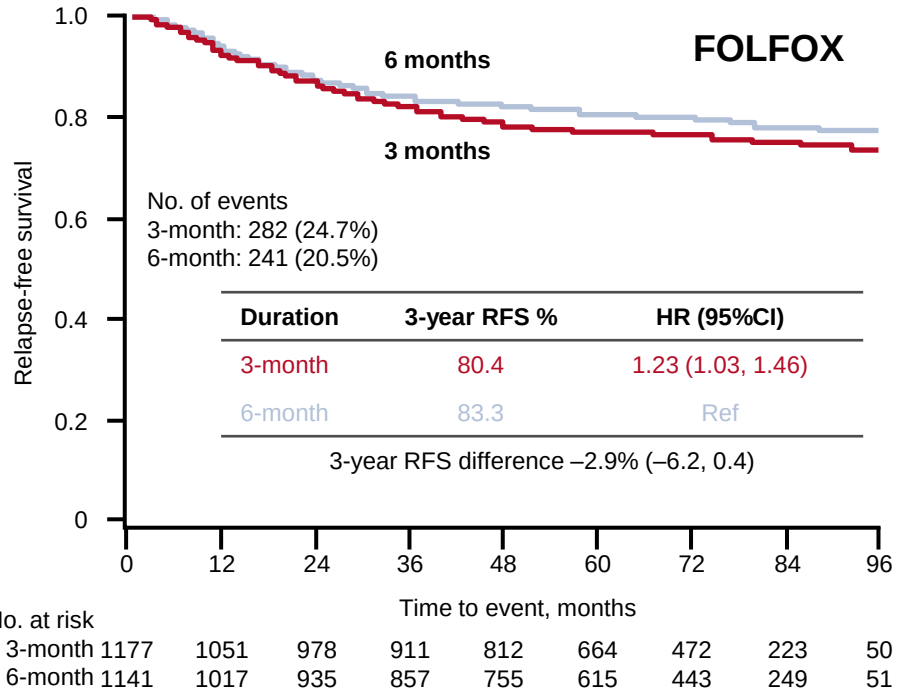

Interaction p-value = 0.108

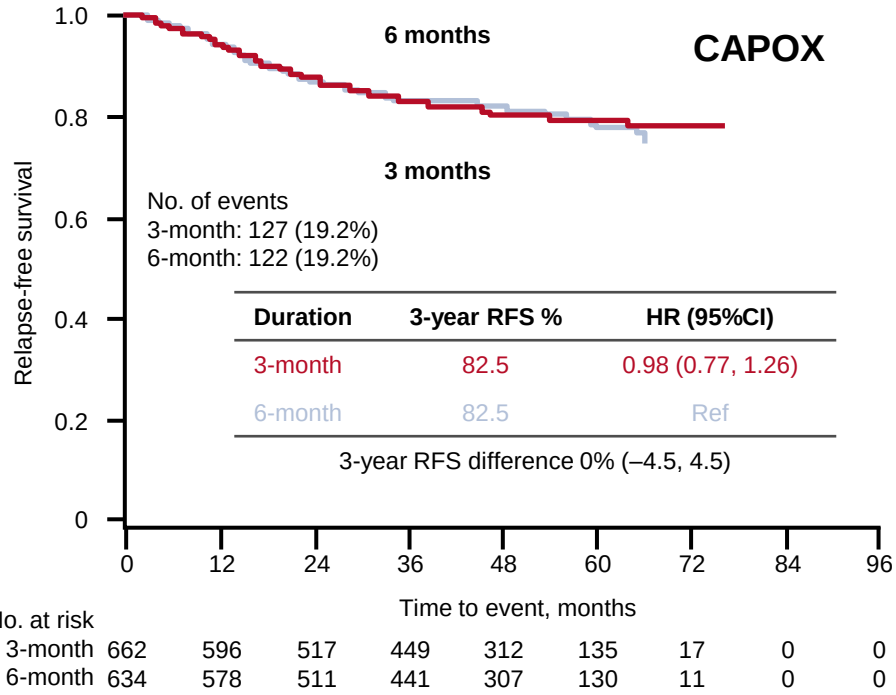
Sobrero AF, et al. J Clin Oncol 2017;35(Suppl):Abstr 3501

# 3501: FOLFOX4/XELOX in stage II–III colon cancer: Efficacy results of the Italian three or six colon adjuvant (TOSCA) trial – Sobrero AF, et al

## Key results (cont.)

### RFS by treatment




Interaction p-value = 0.140

Sobrero AF, et al. J Clin Oncol 2017;35(Suppl):Abstr 3501

# 3501: FOLFOX4/XELOX in stage II–III colon cancer: Efficacy results of the Italian three or six colon adjuvant (TOSCA) trial – Sobrero AF, et al

## Key results (cont.)

| AEs, % | Grade 1/2 | | Grade 3/4 | | p-value[1] |
|---|---|---|---|---|---|
| | 3-month | 6-month | 3-month | 6-month | |
| Neurological | 37.0 | 41.0 | 9.0* | 31.0* | <0.0001 |
| Febrile neutropenia | 1.7 | 3.5 | 1.4 | 2.7 | <0.0001 |
| Thrombocytopenia | 33.0 | 47.0 | 1.6 | 2.1 | <0.0001 |
| Diarrhoea | 29.0 | 35.0 | 5.1 | 6.4 | <0.0001 |
| Allergic reactions | 3.4 | 6.4 | 0.5 | 2.0 | <0.0001 |

## Conclusions

- **This study did not demonstrate that 3 months of oxaliplatin-based adjuvant treatment was as efficacious as 6 months of treatment**
- **However, because the absolute difference in RFS between the two treatment durations was small (<2% at 3 years), 3 months of oxaliplatin-based chemotherapy could be considered as another standard option for adjuvant treatment of resected colon cancer given the better tolerability profile**

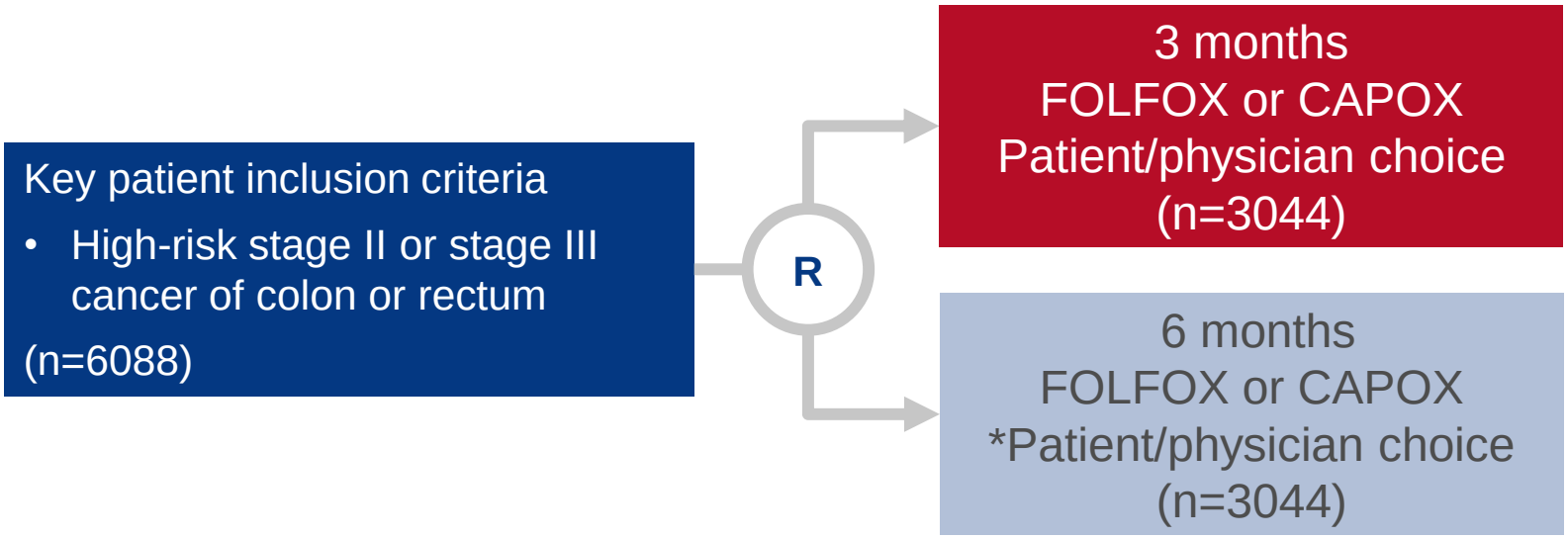
[1]Chi-squared test for trend
Total number of grade 5 events: 2 (“possible”)
*Clinically relevant neurological toxicity

Sobrero AF, et al. J Clin Oncol 2017;35(Suppl):Abstr 3501

# 3502: Final DFS results of the SCOT study: An international phase III randomised (1:1) non-inferiority trial comparing 3 versus 6 months of oxaliplatin based adjuvant chemotherapy for colorectal cancer – Iveson T, et al

## Study objective

- To evaluate whether 3 months of oxaliplatin-based adjuvant chemotherapy was as effective as 6 months of treatment in patients with high-risk stage II or stage III CRC




### PRIMARY ENDPOINT

- DFS

### SECONDARY ENDPOINTS

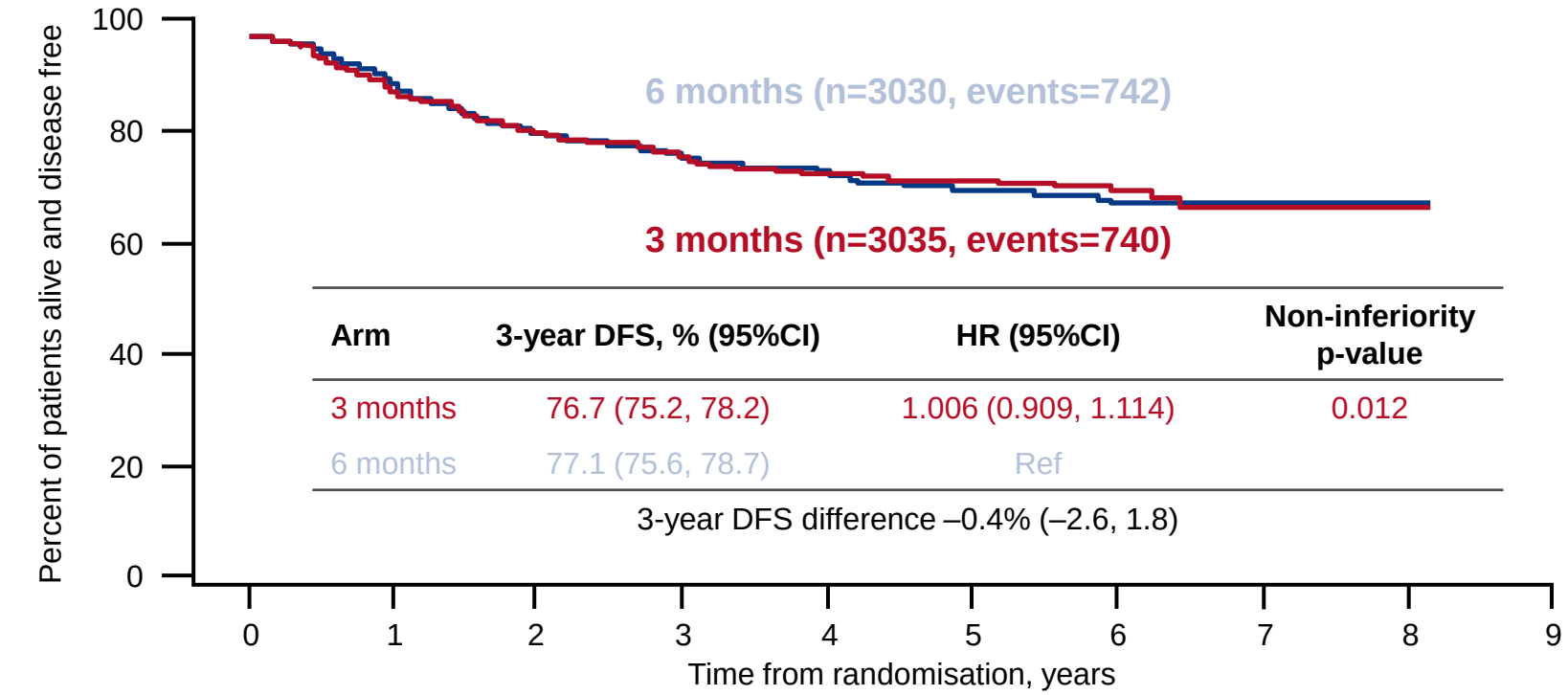
- Safety, QoL, health economics, OS

Iveson T, et al. J Clin Oncol 2017;35(Suppl):Abstr 3502

# 3502: Final DFS results of the SCOT study: An international phase III randomised (1:1) non-inferiority trial comparing 3 versus 6 months of oxaliplatin based adjuvant chemotherapy for colorectal cancer – Iveson T, et al

## Key results

### DFS (overall population)




| Arm | 3-year DFS, % (95%CI) | HR (95%CI) | Non-inferiority p-value |
|---|---|---|---|
| 3 months | 76.7 (75.2, 78.2) | 1.006 (0.909, 1.114) | 0.012 |
| 6 months | 77.1 (75.6, 78.7) | Ref | |

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

| No. at risk | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 3 months | 3035 | 2661 | 2329 | 1501 | 705 | 339 | 102 | 24 | 3 | 0 |
| 6 months | 3030 | 2697 | 2317 | 1541 | 758 | 346 | 113 | 28 | 4 | 0 |

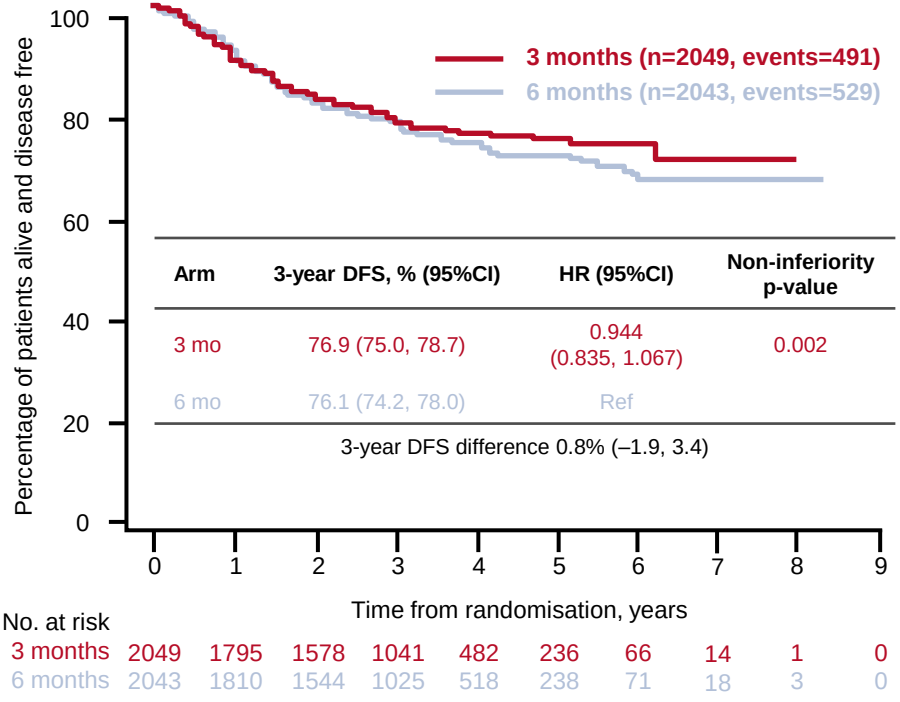
Iveson T, et al. J Clin Oncol 2017;35(Suppl):Abstr 3502

# 3502: Final DFS results of the SCOT study: An international phase III randomised (1:1) non-inferiority trial comparing 3 versus 6 months of oxaliplatin based adjuvant chemotherapy for colorectal cancer – Iveson T, et al

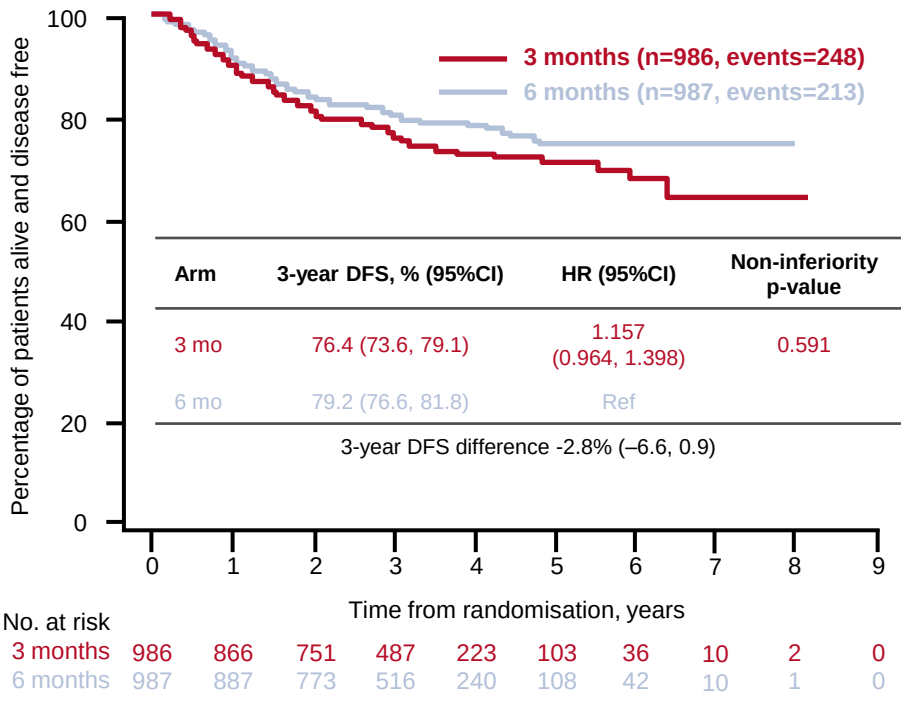
## Key results (cont.)

### DFS by regimen

#### CAPOX (n=4092)



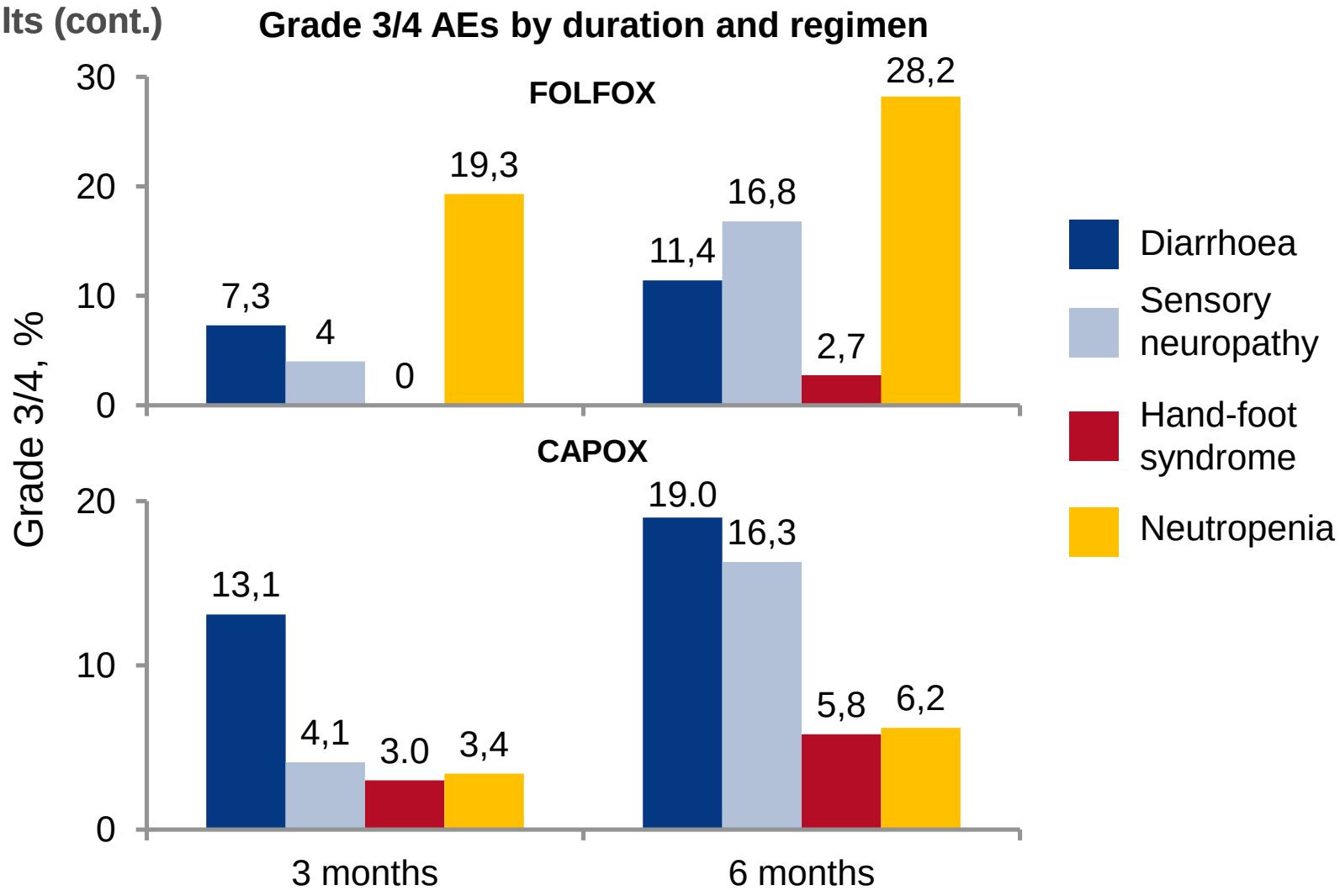

#### FOLFOX (n=1973)




Iveson T, et al. J Clin Oncol 2017;35(Suppl):Abstr 3502

# 3502: Final DFS results of the SCOT study: An international phase III randomised (1:1) non-inferiority trial comparing 3 versus 6 months of oxaliplatin based adjuvant chemotherapy for colorectal cancer – Iveson T, et al

**Key results (cont.)**




Iveson T, et al. J Clin Oncol 2017;35(Suppl):Abstr 3502

# 3502: Final DFS results of the SCOT study: An international phase III randomised (1:1) non-inferiority trial comparing 3 versus 6 months of oxaliplatin based adjuvant chemotherapy for colorectal cancer – Iveson T, et al

## Conclusion

- The SCOT study has shown that 3 months of oxaliplatin-based adjuvant chemotherapy (CAPOX) is not inferior to 6 months treatment and may be considered for some patients with low-risk stage III CRC

Iveson T, et al. J Clin Oncol 2017;35(Suppl):Abstr 3502

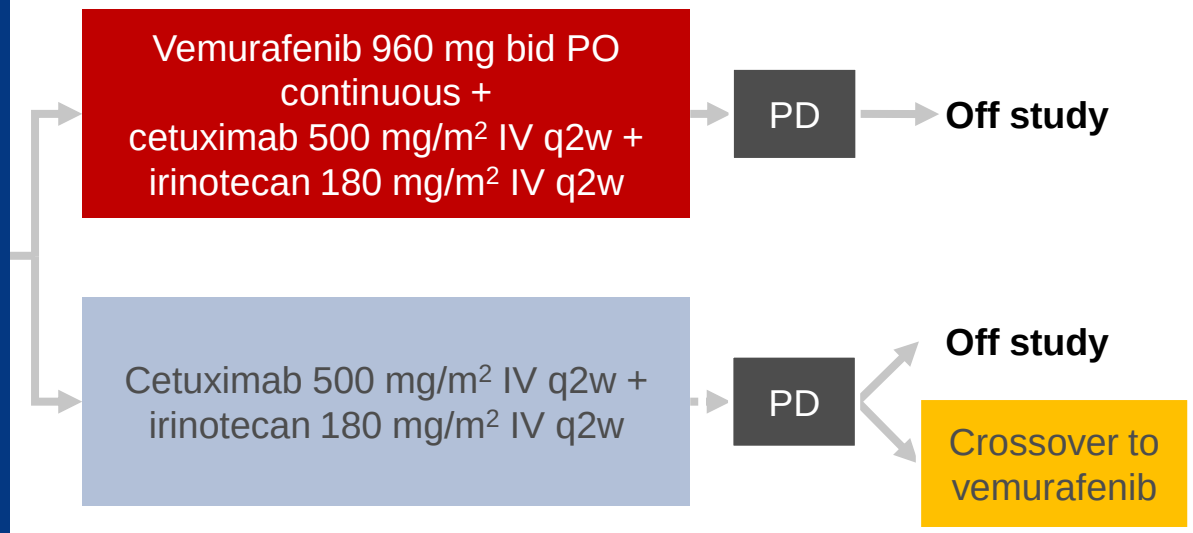
# 3505: Randomized trial of irinotecan and cetuximab with or without vemurafenib in BRAF-mutant metastatic colorectal cancer (SWOG S1406) – Kopetz S, et al

## Study objective

- To evaluate the safety and efficacy of cetuximab + irinotecan ± vemurafenib combination therapy in patients with BRAF V600 mutated and extended RAS wild-type metastatic CRC

**Key patient inclusion criteria**

- Measurable/non-measurable metastatic disease
- BRAF V600E mutation and tissue available for BRAF V600E testing
- Extended RAS wild-type
- PS 0–1
- 1—2 prior regimens of systemic chemotherapy for metastatic disease or locally advanced, unresectable disease




### PRIMARY ENDPOINT

- PFS

### SECONDARY ENDPOINTS

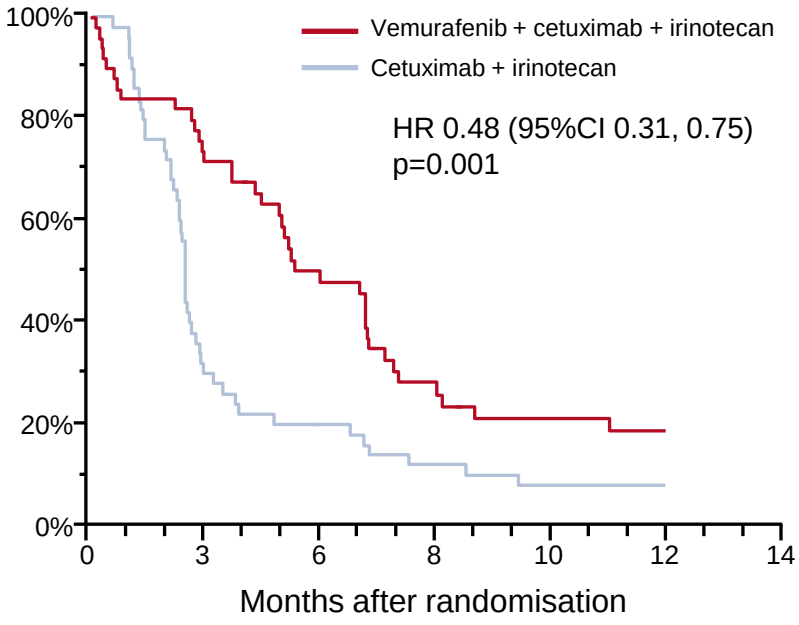
- Safety, OS, ORR

Kopetz S, et al. J Clin Oncol 2017;35(Suppl):Abstr 3505

# 3505: Randomized trial of irinotecan and cetuximab with or without vemurafenib in BRAF-mutant metastatic colorectal cancer (SWOG S1406) – Kopetz S, et al

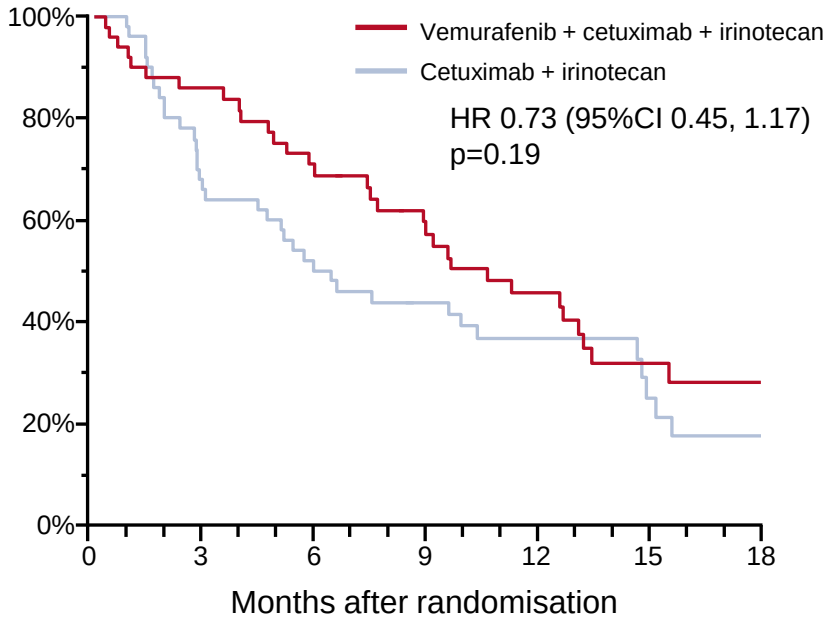
## Key results

### PFS




| | n | Events | Median, months (95%CI) |
|---|---|---|---|
| Vemurafenib + cetuximab + irinotecan | 49 | 40 | 4.3 (3.6, 5.7) |
| Cetuximab + irinotecan | 50 | 48 | 2.0 (1.8, 2.1) |

### OS




| | n | Events | Median, months (95%CI) |
|---|---|---|---|
| Vemurafenib + cetuximab + irinotecan | 49 | 32 | 9.6 (7.5, 13.1) |
| Cetuximab + irinotecan | 50 | 38 | 5.9 (3.0, 9.9) |

Kopetz S, et al. J Clin Oncol 2017;35(Suppl):Abstr 3505

# 3505: Randomized trial of irinotecan and cetuximab with or without vemurafenib in BRAF-mutant metastatic colorectal cancer (SWOG S1406) – Kopetz S, et al

## Key results (cont.)

| | Crossover to vemurafenib after progression (n=24) |
|---|---|
| mPFS, months (95%CI) | 5.8 (2.8, 6.1) |
| mOS, months (95%CI) | 12.1 (4.5, 12.5) |
| Response, %<br>PR<br>SD | <br>17<br>55 |
| DCR, % | 72 |

## Conclusions

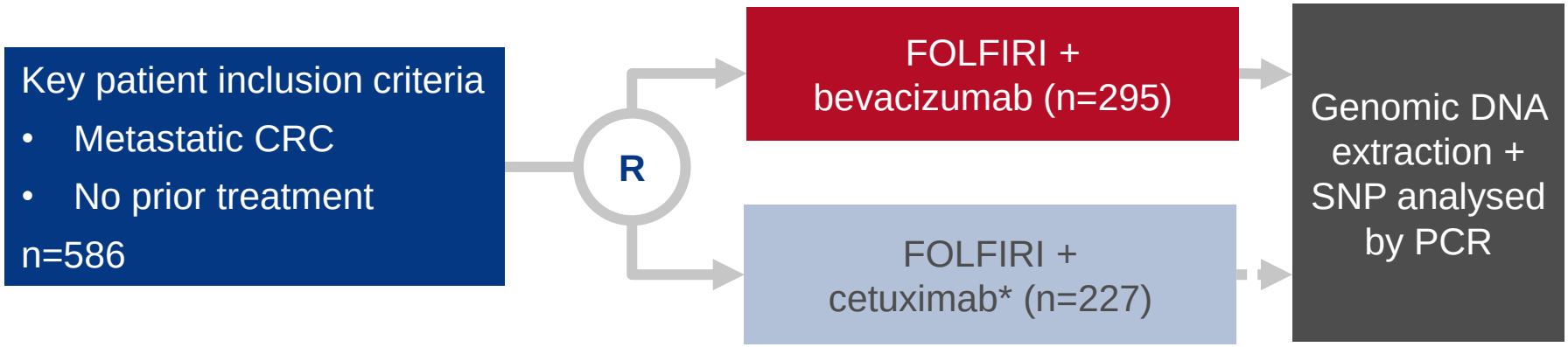
- **In patients with BRAF V600E CRC, vemurafenib plus cetuximab and irinotecan demonstrated improved PFS, even after progression on irinotecan + cetuximab**
- **The activity of the this combination did not differ by prior irinotecan, MSI status, PIK3CA mutations, or sidedness**

Kopetz S, et al. J Clin Oncol 2017;35(Suppl):Abstr 3505

# 11507: Genetic variations within the vitamin C transporter genes to predict outcome in metastatic colorectal cancer patients treated with first-line FOLFIRI and bevacizumab: Data from FIRE-3 trial – Berger MD, et al

**Study objective**

- To evaluate the impact of three functional SNP within the SVCT1, SVCT2 and Glut1 genes on outcome in patients with metastatic CRC treated with 1L FOLFIRI + bevacizumab in the randomized phase III FIRE-3 study



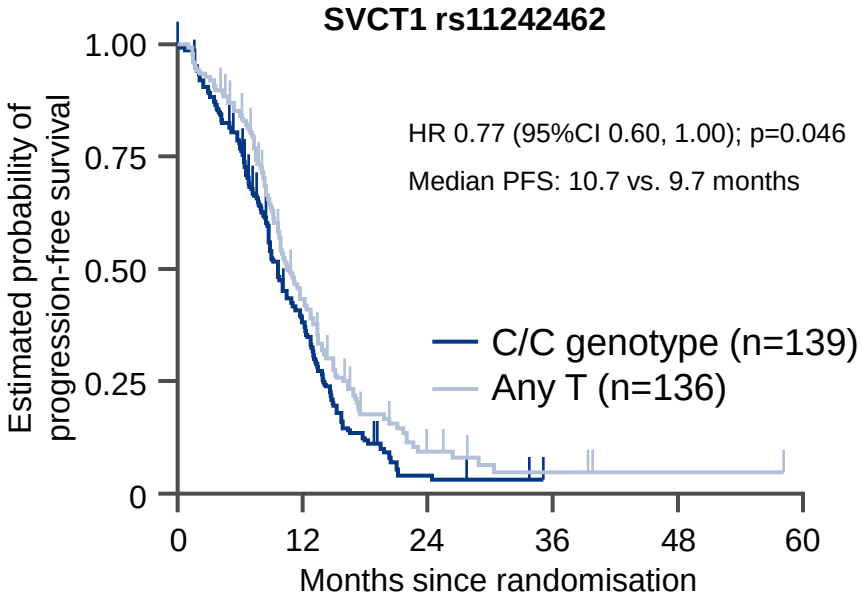

*Negative control

Berger MD, et al. J Clin Oncol 2017;35(Suppl):Abstr 11507

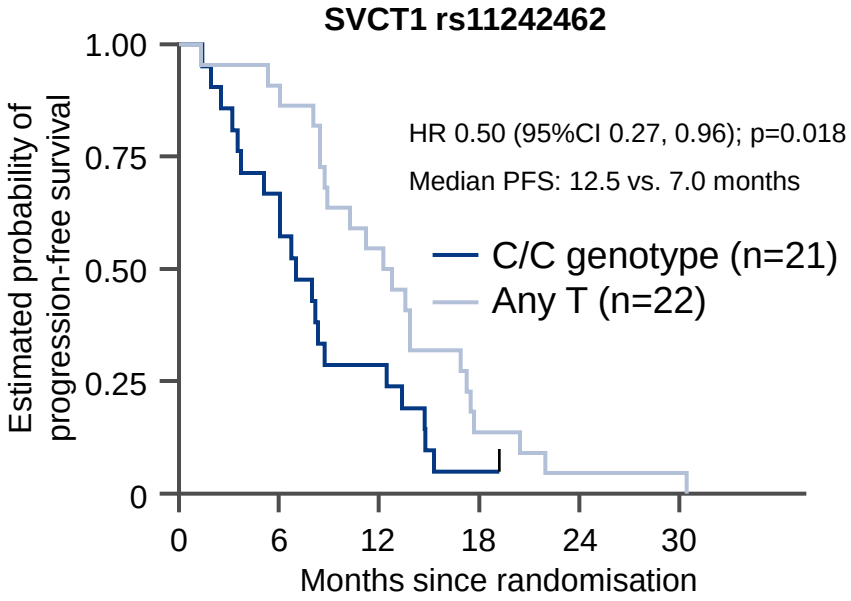
# 11507: Genetic variations within the vitamin C transporter genes to predict outcome in metastatic colorectal cancer patients treated with first-line FOLFIRI and bevacizumab: Data from FIRE-3 trial – Berger MD, et al

## Key results

**FIRE-3 FOLFIRI + bevacizumab arm**
**SVCT1 and PFS (all patients)**




**FIRE-3 FOLFIRI + bevacizumab arm**
**SVCT1 and PFS (*KRAS* mutant)**



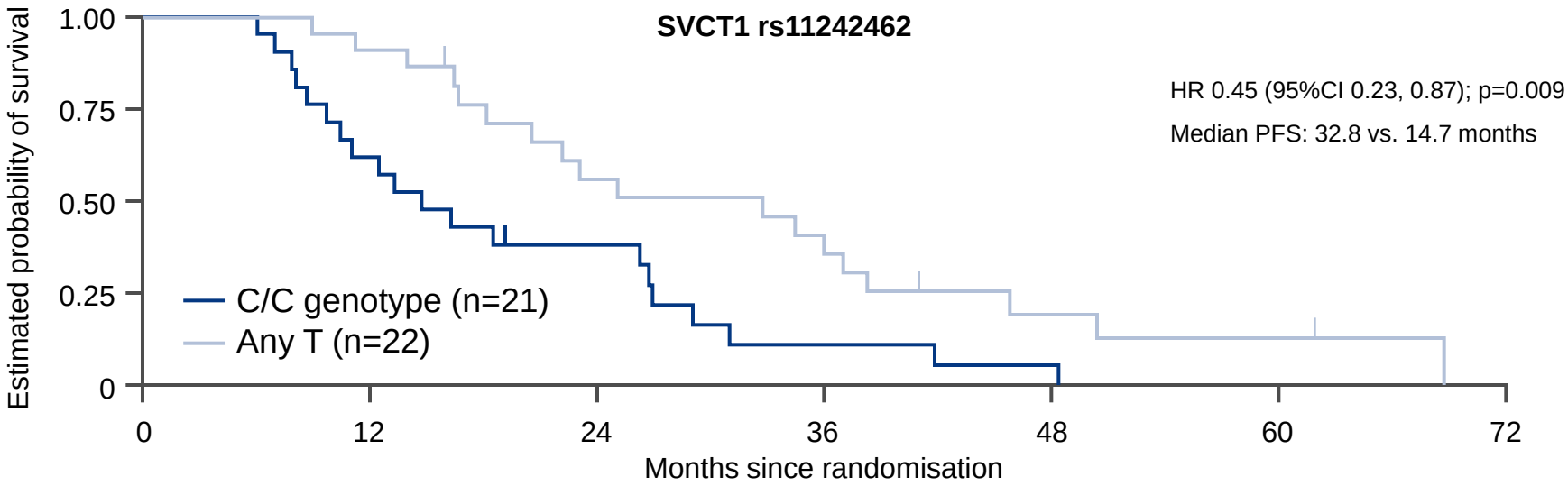

- The SVCT1 rs11242462 SNP showed significant association with PFS
- The effect on outcome was most significant among *KRAS* mutant patients

Berger MD, et al. J Clin Oncol 2017;35(Suppl):Abstr 11507

# 11507: Genetic variations within the vitamin C transporter genes to predict outcome in metastatic colorectal cancer patients treated with first-line FOLFIRI and bevacizumab: Data from FIRE-3 trial – Berger MD, et al

## Key results (cont.)

**FIRE-3 FOLFIRI + bevacizumab arm**
**SVCT1 and OS (*KRAS* mutant)**




## Conclusions

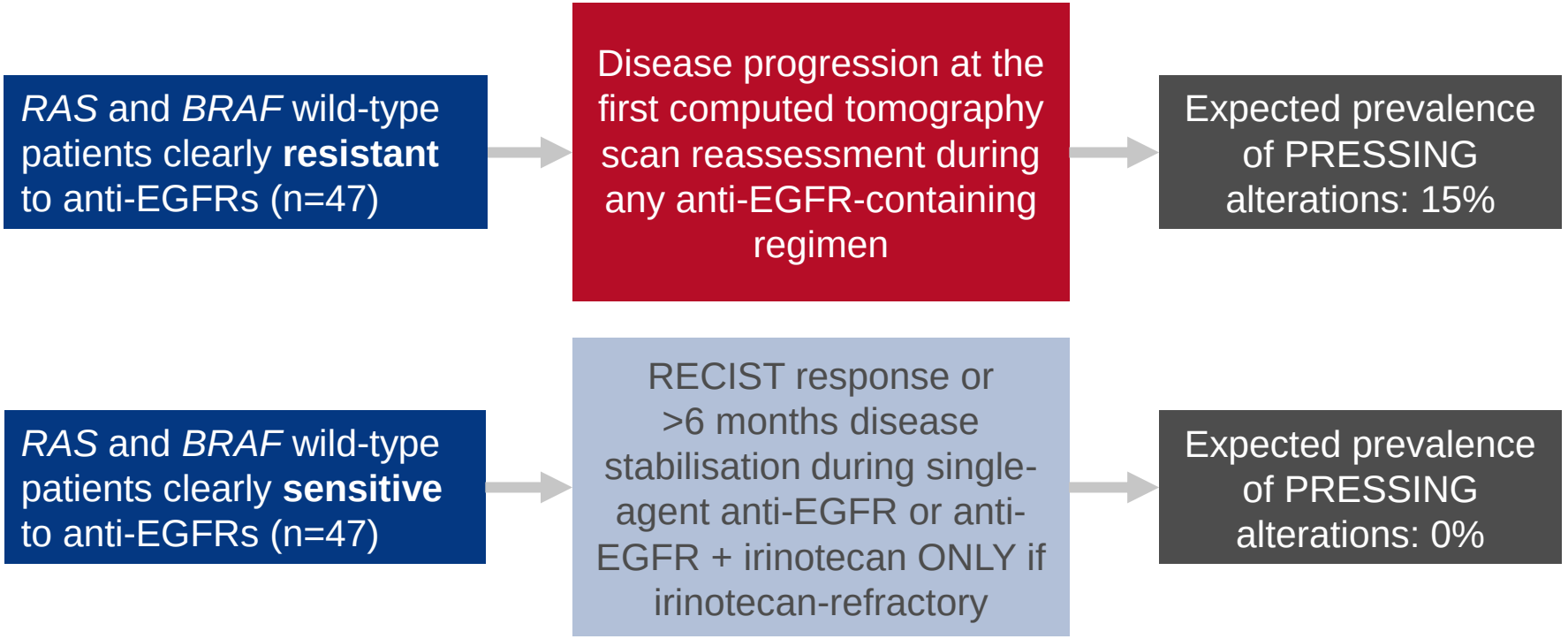
- **In patients with metastatic CRC receiving 1L-FOLFIRI + bevacizumab, the SVCT1 rs11242462 SNP appeared to be a predictive marker**
- **In comparison to CC carriers, patients harbouring any T allele showed a longer PFS**
- **Patients with *KRAS* mutations had the most favourable outcomes**

Berger MD, et al. J Clin Oncol 2017;35(Suppl):Abstr 11507

# 11508: Dissecting primary resistance to anti-EGFRs in RAS and BRAF wt metastatic colorectal cancer (mCRC): A case-control study – Cremolini C, et al

**Study objective**

- To evaluate the predictive role of primary tumour sidedness in PRESSING panel negative patients and the predictive role of microsatellite instability in patients with metastatic CRC

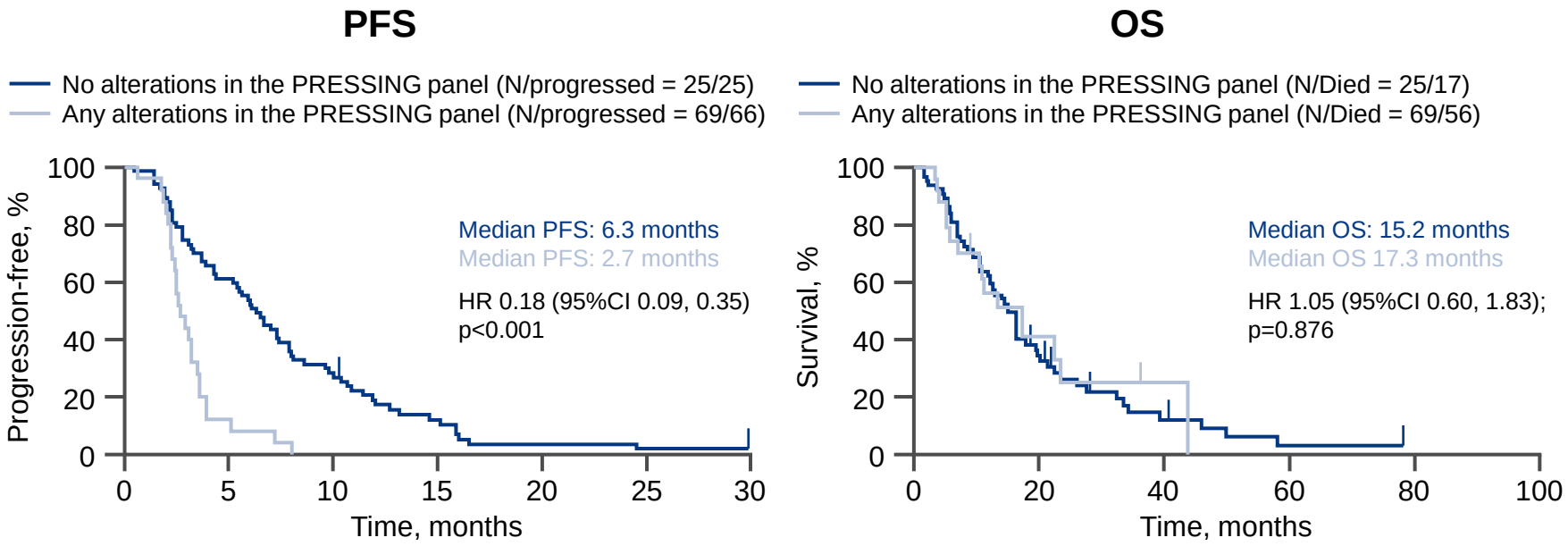



Cremolini C, et al. J Clin Oncol 2017;35(Suppl):Abstr 11508

# 11508: Dissecting primary resistance to anti-EGFRs in RAS and BRAF wt metastatic colorectal cancer (mCRC): A case-control study – Cremolini C, et al

## Key results

### Association of PRESSING panel alterations with survival

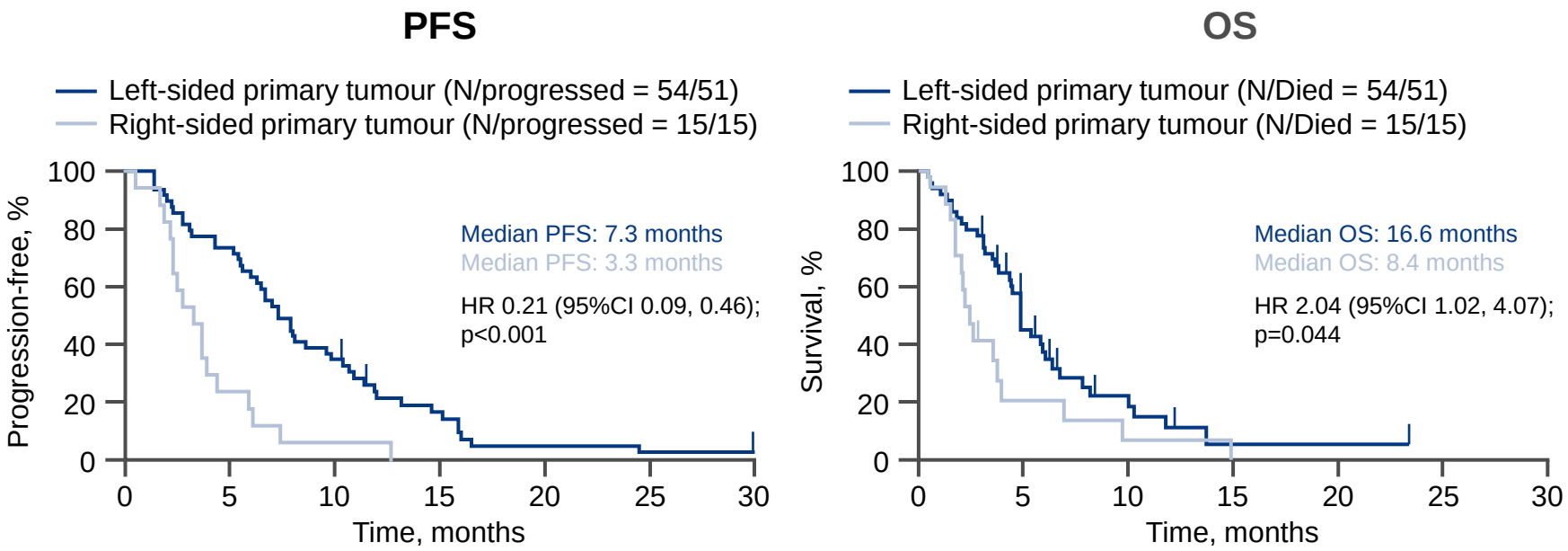



Cremolini C, et al. J Clin Oncol 2017;35(Suppl):Abstr 11508

# 11508: Dissecting primary resistance to anti-EGFRs in RAS and BRAF wt metastatic colorectal cancer (mCRC): A case-control study – Cremolini C, et al

## Key results (cont.)

### Association of primary sidedness with survival in hyper-selected patients




### Conclusions

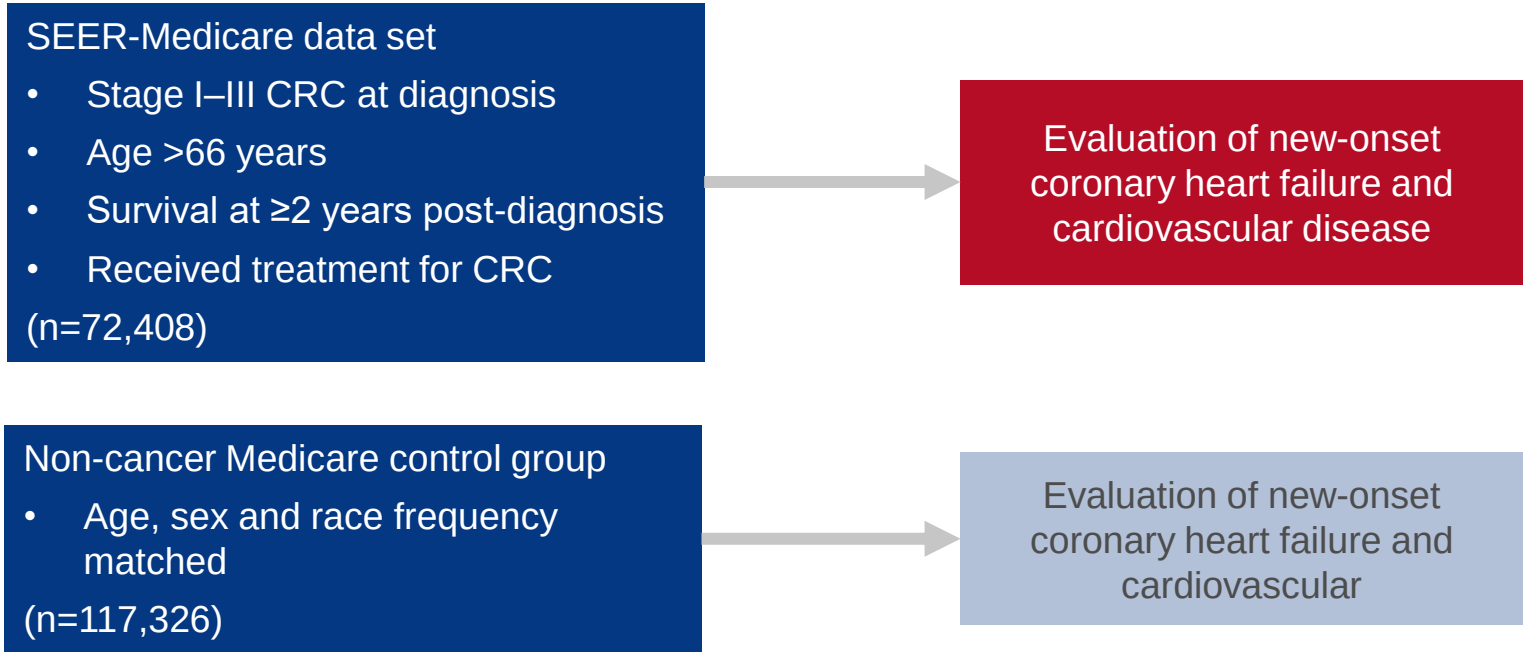
- **This study demonstrated the negative predictive impact of candidate alterations (PRESSING panel) with regards to anti-EGFRs**
- **Right-sidedness predicts resistance to anti-EGFRs in hyper-selected patients with metastatic CRC**

Cremolini C, et al. J Clin Oncol 2017;35(Suppl):Abstr 11508

# 10011: New-onset congestive heart failure (CHF) and cardiovascular disease (CVD) in older colorectal cancer (CRC) survivors: A population-based study – Kenzik K, et al

## Study objective

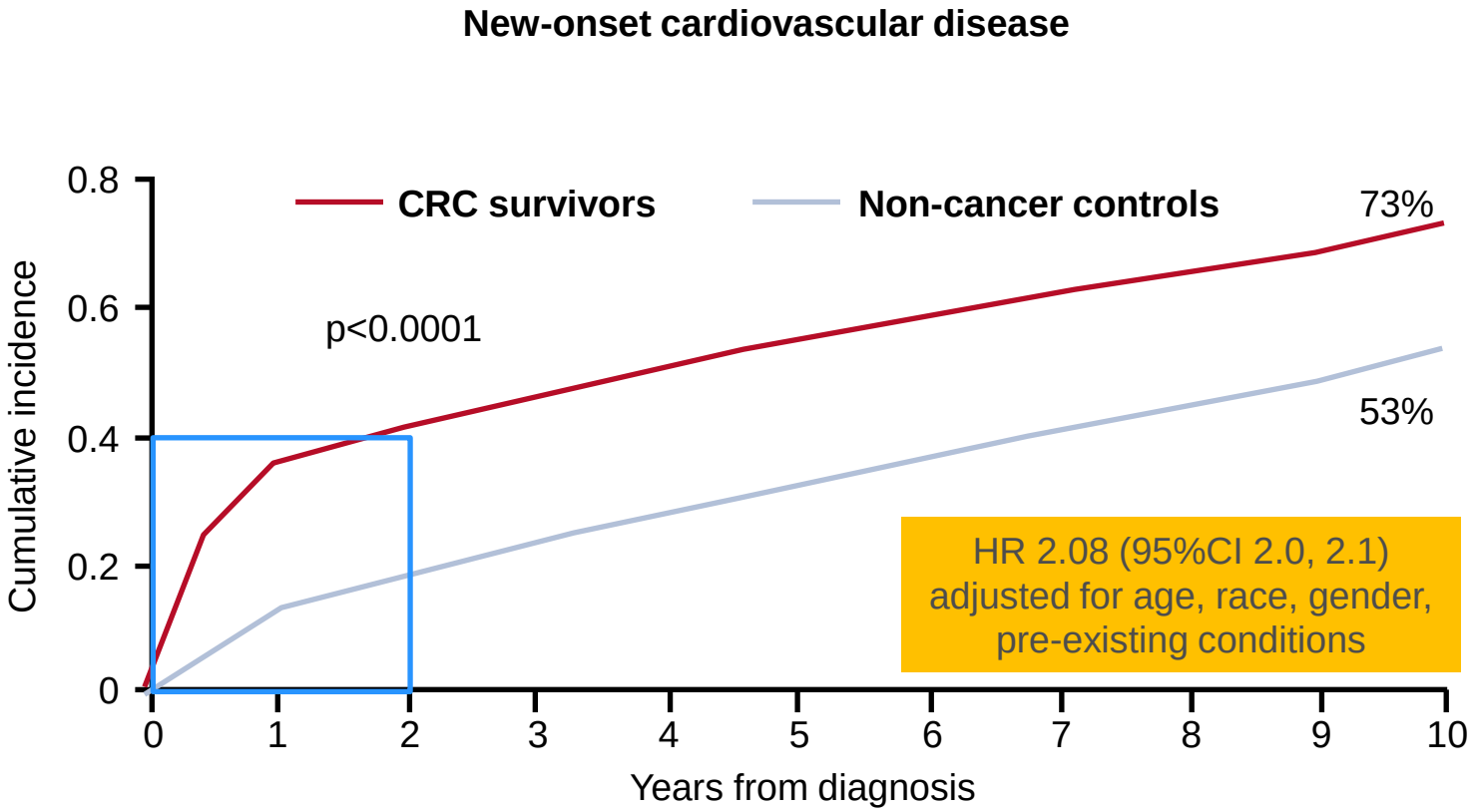
- To describe the magnitude of risk of new-onset cardiovascular morbidity in older individuals with CRC vs. those without CRC, to assess the impact of therapeutic exposures on the risk of new-onset morbidity and to understand the impact of pre-cancer comorbidity and sociodemographics on the risk of new-onset cardiovascular morbidity




Kenzik K, et al. J Clin Oncol 2017;35(Suppl):Abstr 10011

# 10011: New-onset congestive heart failure (CHF) and cardiovascular disease (CVD) in older colorectal cancer (CRC) survivors: A population-based study – Kenzik K, et al

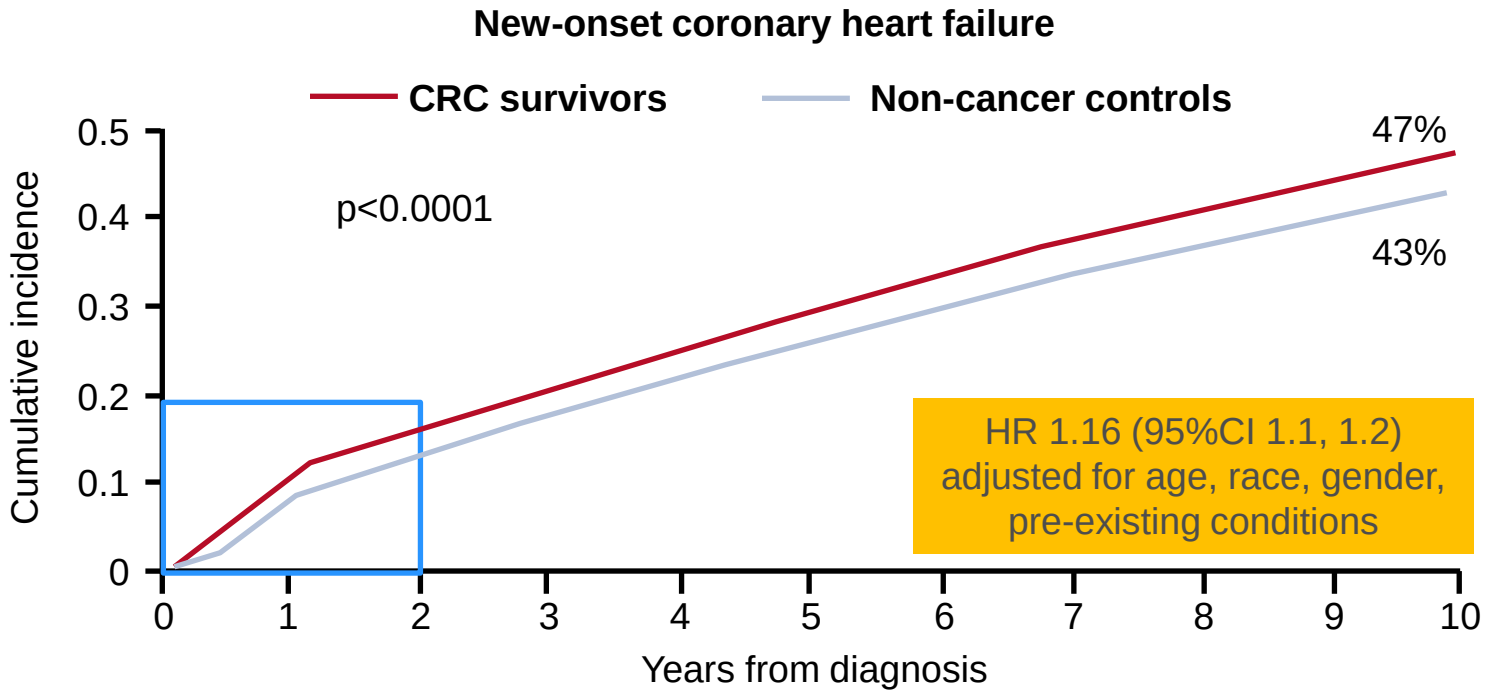
## Key results




Kenzik K, et al. J Clin Oncol 2017;35(Suppl):Abstr 10011

# 10011: New-onset congestive heart failure (CHF) and cardiovascular disease (CVD) in older colorectal cancer (CRC) survivors: A population-based study – Kenzik K, et al

## Key results (cont.)




## Conclusions

- In comparison with a non-cancer population, the 10-year incidence of new-onset cardiovascular morbidity is significantly greater in CRC survivors
- There appears to be a higher risk of cardiovascular morbidity within the first 2 years following CRC diagnosis

Kenzik K, et al. J Clin Oncol 2017;35(Suppl):Abstr 10011

# 3002: Phase Ia and Ib studies of the novel carcinoembryonic antigen (CEA) T-cell bispecific (CEA CD3 TCB) antibody as a single agent and in combination with atezolizumab: Preliminary efficacy and safety in patients with metastatic colorectal cancer (mCRC) – Tabernero J, et al

## Study objective

- To assess the efficacy and safety of CEA-TCB, a novel T-cell bi-specific antibody targeting CEA on tumour cells and CD3 on T cells, in patients with metastatic CRC

Key patient inclusion criteria

- Locally advanced metastatic CEA+ solid tumours
- ≥1 tumour lesion available for biopsy
- Progressed on or intolerant of standard therapy
- Measurable disease (RECIST v1.1)
- ECOG PS 0–1

(n=118)

**Study 1:**
CEA-TCB monotherapy IV qw
(0.5 to 600 mg)
(n=80, including 68 with mCRC)

**Study 2:**
CEA-TCB IV qw (5.0 to 160 mg) + atezolizumab 1200 mg IV q3w
(n=38, including 28 with mCRC)

### PRIMARY ENDPOINT

- Tumour response

### SECONDARY ENDPOINTS

- Safety, ORR, DoR, DCR, PFS

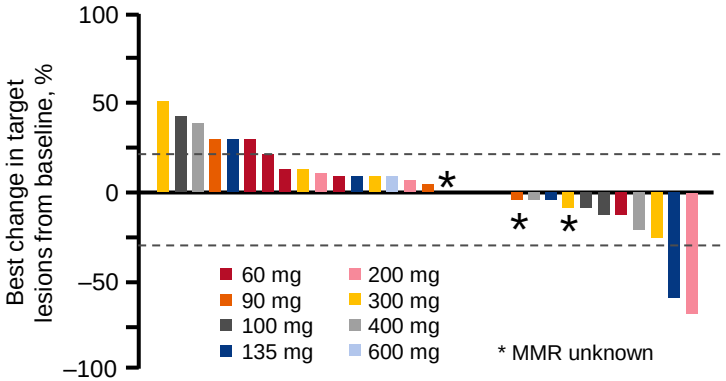
Tabernero J, et al. J Clin Oncol 2017;35(Suppl):Abstr 3002

# 3002: Phase Ia and Ib studies of the novel carcinoembryonic antigen (CEA) T-cell bispecific (CEA CD3 TCB) antibody as a single agent and in combination with atezolizumab: Preliminary efficacy and safety in patients with metastatic colorectal cancer (mCRC) – Tabernero J, et al

## Key results

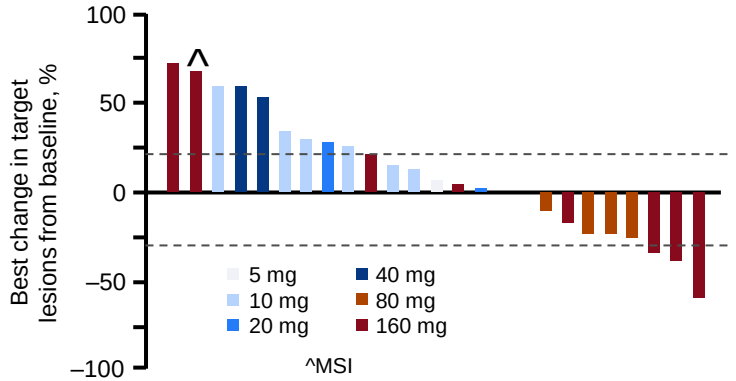
### CEA-TCB at doses ≥60 mg[a] demonstrated clinical activity in metastatic CRC as monotherapy and in combination with atezolizumab

**Study 1: CEA-TCB monotherapy N=31, 60–600 mg**




No clear correlation of CEA-TCB dose and response

**Study 2: CEA-TCB + atezolizumab N=25, 5–160 mg**




Correlation of CEA-TCB dose and response

Data reported by investigators, cut-off March 3, 2017
[a]Radiological signs of tumour inflammation seen at ≥60 mg (safety cut-off was ≥40 mg)

Tabernero J, et al. J Clin Oncol 2017;35(Suppl):Abstr 3002

# 3002: Phase Ia and Ib studies of the novel carcinoembryonic antigen (CEA) T-cell bispecific (CEA CD3 TCB) antibody as a single agent and in combination with atezolizumab: Preliminary efficacy and safety in patients with metastatic colorectal cancer (mCRC) – Tabernero J, et al

## Key results (cont.)

| Most common grade ≥3 TRAEs, % | Study 1: CEA-TCB monotherapy[a] | | Study 2: CEA-TCB + atezolizumab | |
|---|---|---|---|---|
| | All (n=80) | ≥40 mg (n=59)[b] | All (n=45) | ≥40 mg (n=33)[b] |
| Any | 28 | 37 | 31 | 39 |
| IRR | 18 | 24 | 11 | 12 |
| Diarrhoea | 5 | 7 | 13 | 18 |

## Conclusions

- **Ongoing phase 1 studies of CEA-TCB in heavily pre-treated patients with MSS metastatic CRC have demonstrated promising anti-tumour activity**
- **Clinical activity was shown with CEA-TCB both as monotherapy and in combination with atezolizumab, with a manageable safety profile**

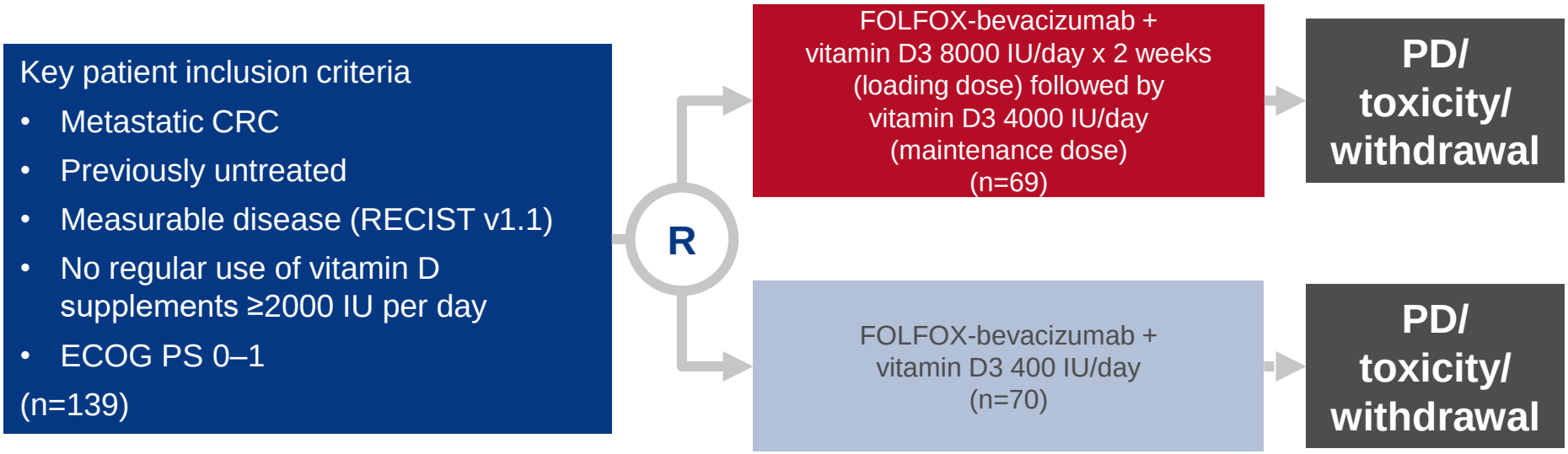
[a]Some patients were pre-treated with obinutuzumab
[b]Due to DLT at 40 mg in study 1 in a patient with NSCLC

Tabernero J, et al. J Clin Oncol 2017;35(Suppl):Abstr 3002

# 3506: SUNSHINE: Randomized double-blind phase II trial of vitamin D supplementation in patients with previously untreated metastatic colorectal cancer – Ng K, et al

## Study objective

- To assess the efficacy and safety of high-dose vitamin D supplementation vs. low-dose vitamin D in patients with previously untreated metastatic CRC




### PRIMARY ENDPOINT

- PFS

### SECONDARY ENDPOINTS

- ORR, OS, safety, incidence of vitamin D deficiency, association between plasma 25(OH)D levels and PFS and OS, time course of change in plasma 25(OH)D levels

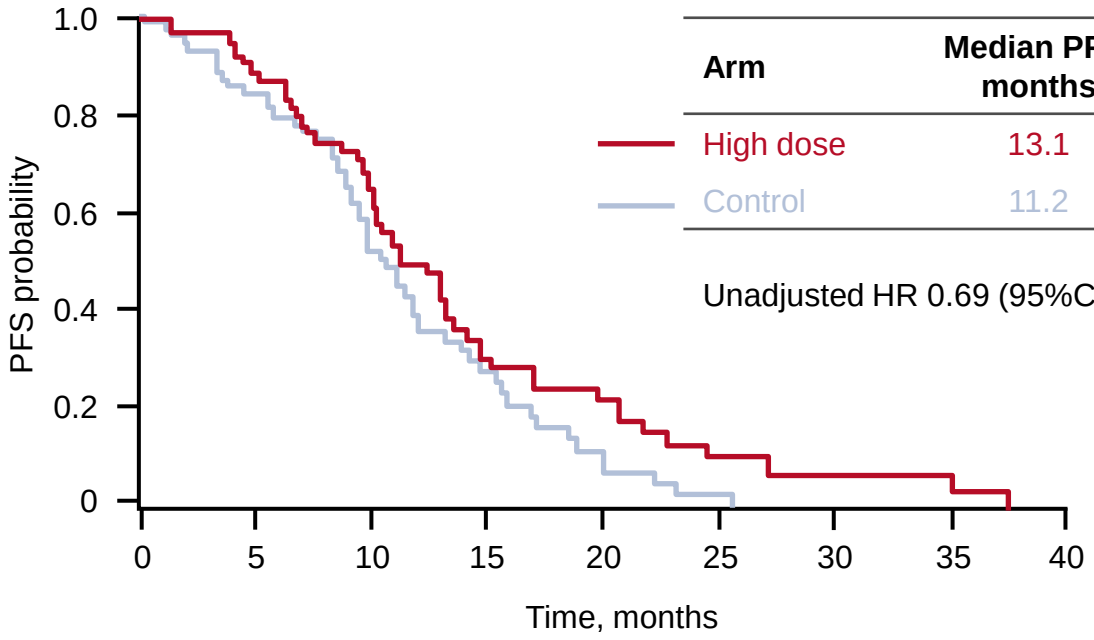
*Progression or unacceptable toxicity or withdrawal of consent

Ng K, et al. J Clin Oncol 2017;35(Suppl):Abstr 3506

# 3506: SUNSHINE: Randomized double-blind phase II trial of vitamin D supplementation in patients with previously untreated metastatic colorectal cancer – Ng K, et al

## Key results

### PFS




| Arm | Median PFS, months | 95%CI |
|---|---|---|
| High dose | 13.1 | 10.1, 14.7 |
| Control | 11.2 | 9.5, 14.2 |

Unadjusted HR 0.69 (95%CI 0.46, 1.02); p=0.04

Data lock April 25, 2017

Ng K, et al. J Clin Oncol 2017;35(Suppl):Abstr 3506

# 3506: SUNSHINE: Randomized double-blind phase II trial of vitamin D supplementation in patients with previously untreated metastatic colorectal cancer – Ng K, et al

## Key results (cont.)

| Grade 3/4 AEs reported in ≥5% of patients, n (%) | High-dose (n=68) | Control (n=67) | p-value |
|---|---|---|---|
| Neutropenia | 30 (44) | 25 (37) | 0.53 |
| Hypertension | 13 (19) | 13 (19) | 0.97 |
| Peripheral neuropathy | 5 (7) | 5 (7) | 0.98 |
| Fatigue | 4 (6) | 5 (7) | 0.74 |
| Thromboembolic event | 5 (7) | 4 (6) | 1.00 |
| Diarrhoea | 1 (1) | 8 (12) | 0.02 |
| Vomiting | 2 (3) | 6 (9) | 0.16 |
| Anaemia | 2 (3) | 5 (7) | 0.27 |
| Hyperglycaemia | 5 (7) | 3 (5) | 0.72 |
| Hypokalaemia | 4 (6) | 3 (5) | 1.00 |

## Conclusions

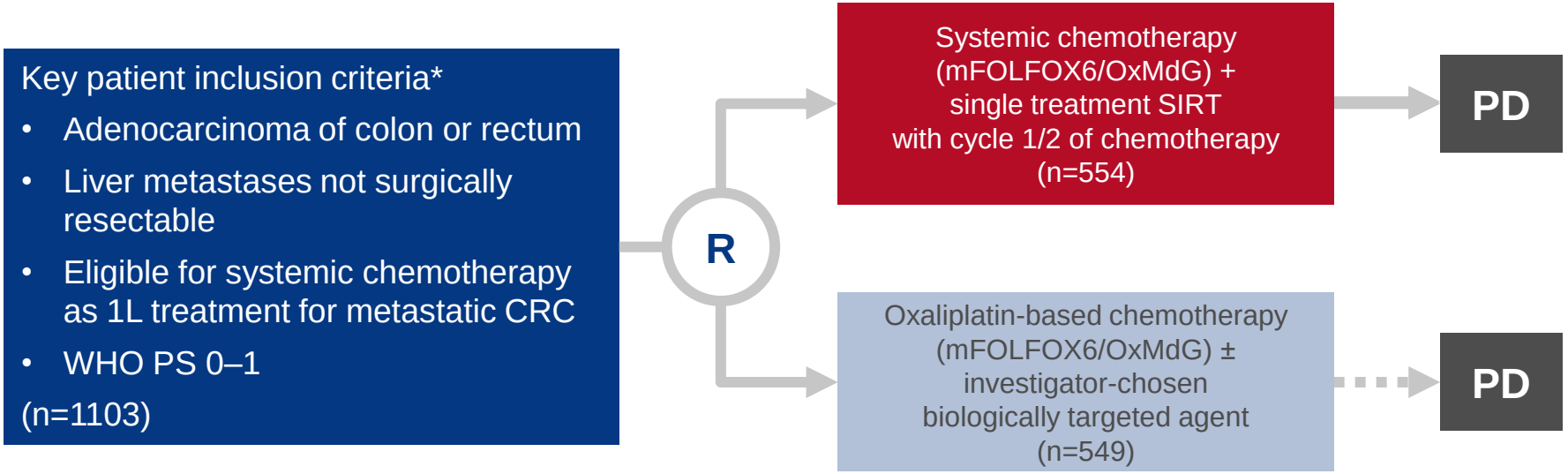
- **High-dose vitamin D3 in combination with 1L chemotherapy significantly improved PFS in patients with metastatic CRC**
- **Use of high-dose vitamin D3 resulted in significantly less grade 3/4 diarrhoea**

Ng K, et al. J Clin Oncol 2017;35(Suppl):Abstr 3506

# 3507: Overall survival analysis of the FOXFIRE prospective randomized studies of first-line selective internal radiotherapy (SIRT) in patients with liver metastases from colorectal cancer – Sharma RA, et al

## Study objective

- To evaluate efficacy and safety of 1L SIRT in patients with liver metastases from CRC




### PRIMARY ENDPOINT

- OS

### SECONDARY ENDPOINTS

- PFS at any site, liver-specific PFS, objective tumour response rate, hepatic resection rate, safety, HRQoL

*Patients from FOXFIRE, SIRFLOX, and FOXFIRE-Global studies

Sharma RA, et al. J Clin Oncol 2017;35(Suppl):Abstr 3507

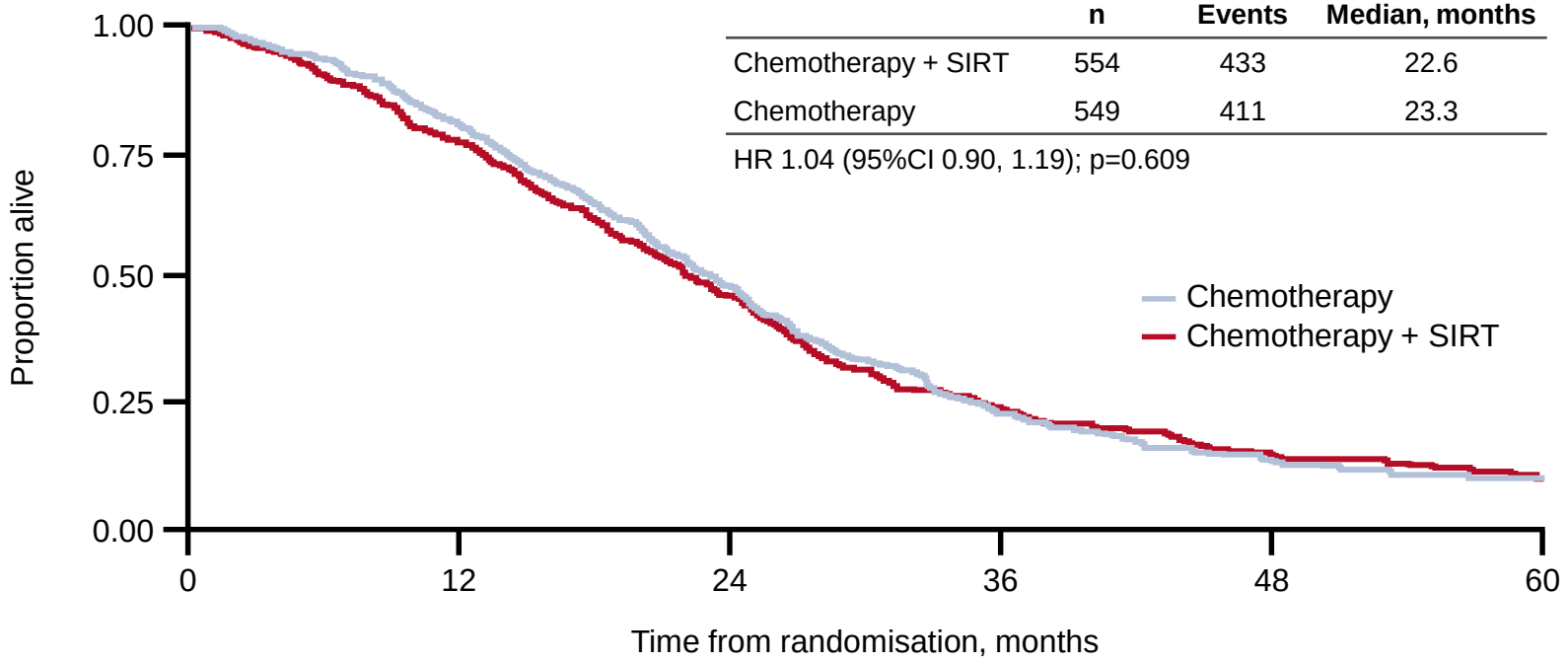
# 3507: Overall survival analysis of the FOXFIRE prospective randomized studies of first-line selective internal radiotherapy (SIRT) in patients with liver metastases from colorectal cancer – Sharma RA, et al

## Key results (cont.)

### OS

| | n | Events | Median, months |
|---|---|---|---|
| Chemotherapy + SIRT | 554 | 433 | 22.6 |
| Chemotherapy | 549 | 411 | 23.3 |

HR 1.04 (95%CI 0.90, 1.19); p=0.609




| No. at risk | | | | | | |
|---|---|---|---|---|---|---|
| Chemotherapy | 549 | 419 | 242 | 88 | 33 | 12 |
| Chemotherapy + SIRT | 554 | 417 | 247 | 91 | 35 | 17 |

Sharma RA, et al. J Clin Oncol 2017;35(Suppl):Abstr 3507

# 3507: Overall survival analysis of the FOXFIRE prospective randomized studies of first-line selective internal radiotherapy (SIRT) in patients with liver metastases from colorectal cancer – Sharma RA, et al

## Key results (cont.)

| AEs reported in ≥5% of patients, % | Chemotherapy + SIRT (n=507) | Chemotherapy (n=571) |
|---|---|---|
| Any grade | 99.8 | 99.6 |
| Grade ≥3 | 74.0 | 66.5 |
| Haematological (grade ≥3) | | |
| Neutropenia | 36.7 | 24.2 |
| Febrile neutropenia | 6.5 | 2.8 |
| Thrombocytopenia | 7.7 | 1.2 |
| Leukopenia | 5.9 | 2.3 |
| Non-haematological (grade ≥3) | | |
| Fatigue | 8.5 | 4.9 |
| Abdominal pain | 6.1 | 2.3 |
| Diarrhoea | 6.7 | 6.5 |
| Peripheral neuropathy | 3.6 | 5.8 |

## Conclusion

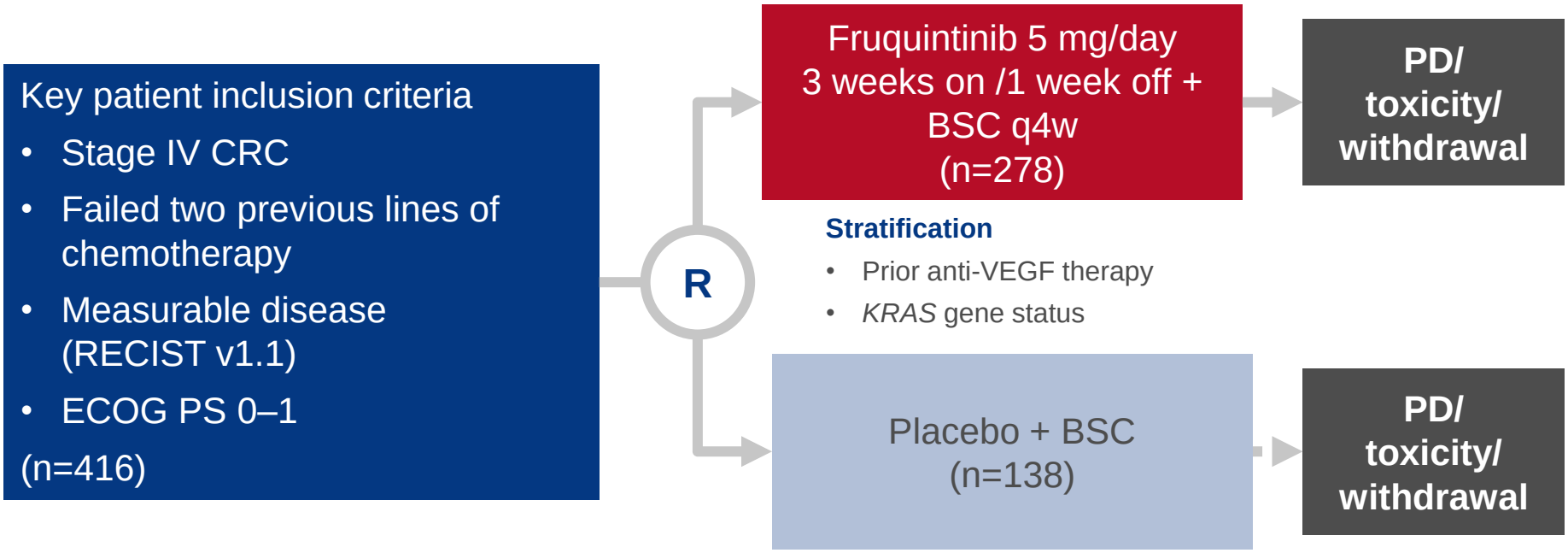
- **In patients with liver-only and liver-dominant metastatic CRC, the addition of SIRT to 1L oxaliplatin-fluorouracil chemotherapy did not improve OS or PFS**

Sharma RA, et al. J Clin Oncol 2017;35(Suppl):Abstr 3507

# 3508: A randomized, double-blind, placebo-controlled, multi-centered phase 3 trial comparing fruquintinib versus placebo plus best supportive care in Chinese patients with metastatic colorectal cancer (FRESCO) – Li J, et al

## Study objective

- To assess fruquintinib + BSC vs. placebo + BSC in Chinese patients with metastatic CRC




### PRIMARY ENDPOINT

- OS

### SECONDARY ENDPOINTS

- PFS, ORR, DCR

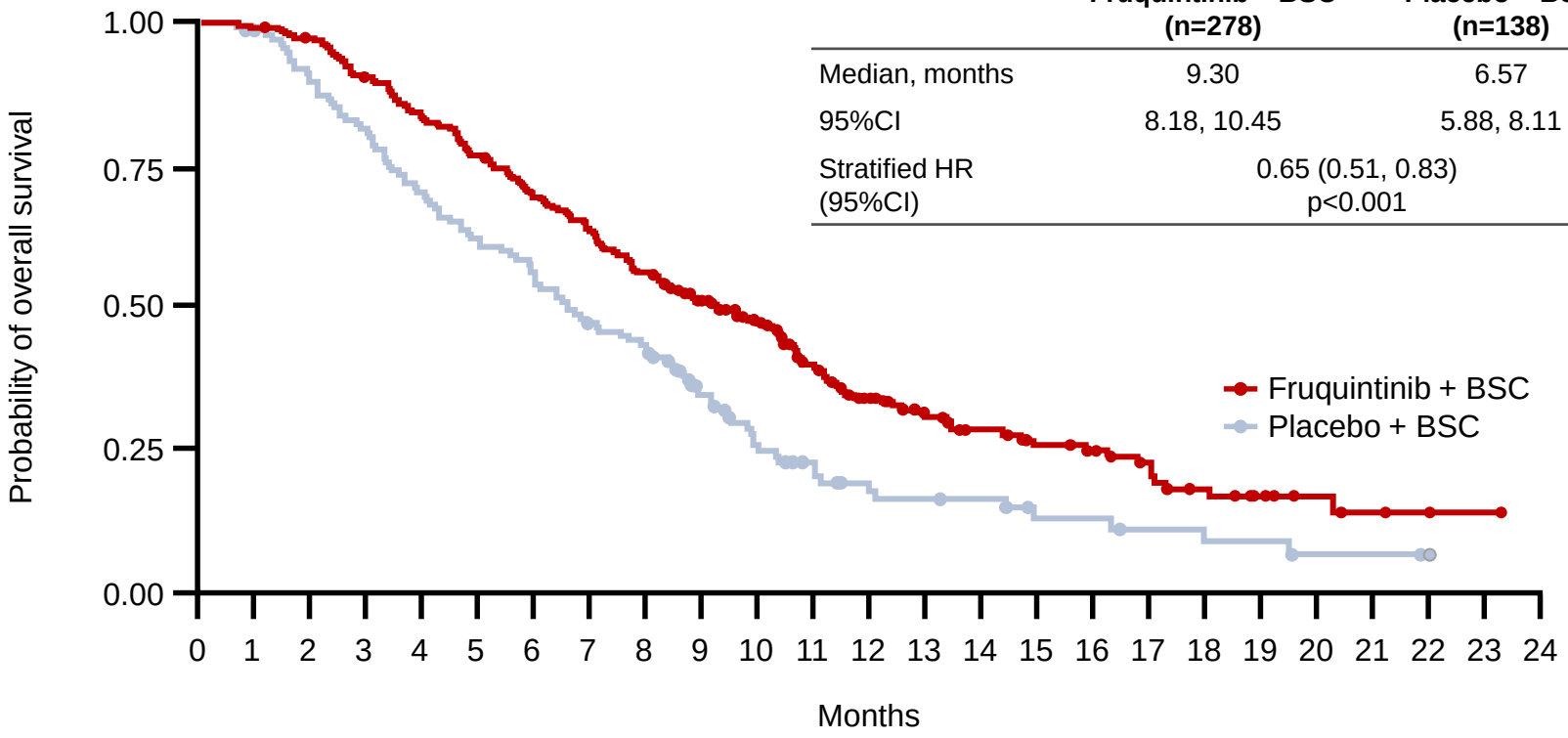
Li J, et al. J Clin Oncol 2017;35(Suppl):Abstr 3508

# 3508: A randomized, double-blind, placebo-controlled, multi-centered phase 3 trial comparing fruquintinib versus placebo plus best supportive care in Chinese patients with metastatic colorectal cancer (FRESCO) – Li J, et al

## Key results

### OS

| | Fruquintinib + BSC (n=278) | Placebo + BSC (n=138) |
|---|---|---|
| Median, months | 9.30 | 6.57 |
| 95%CI | 8.18, 10.45 | 5.88, 8.11 |
| Stratified HR (95%CI) | 0.65 (0.51, 0.83) p<0.001 | |



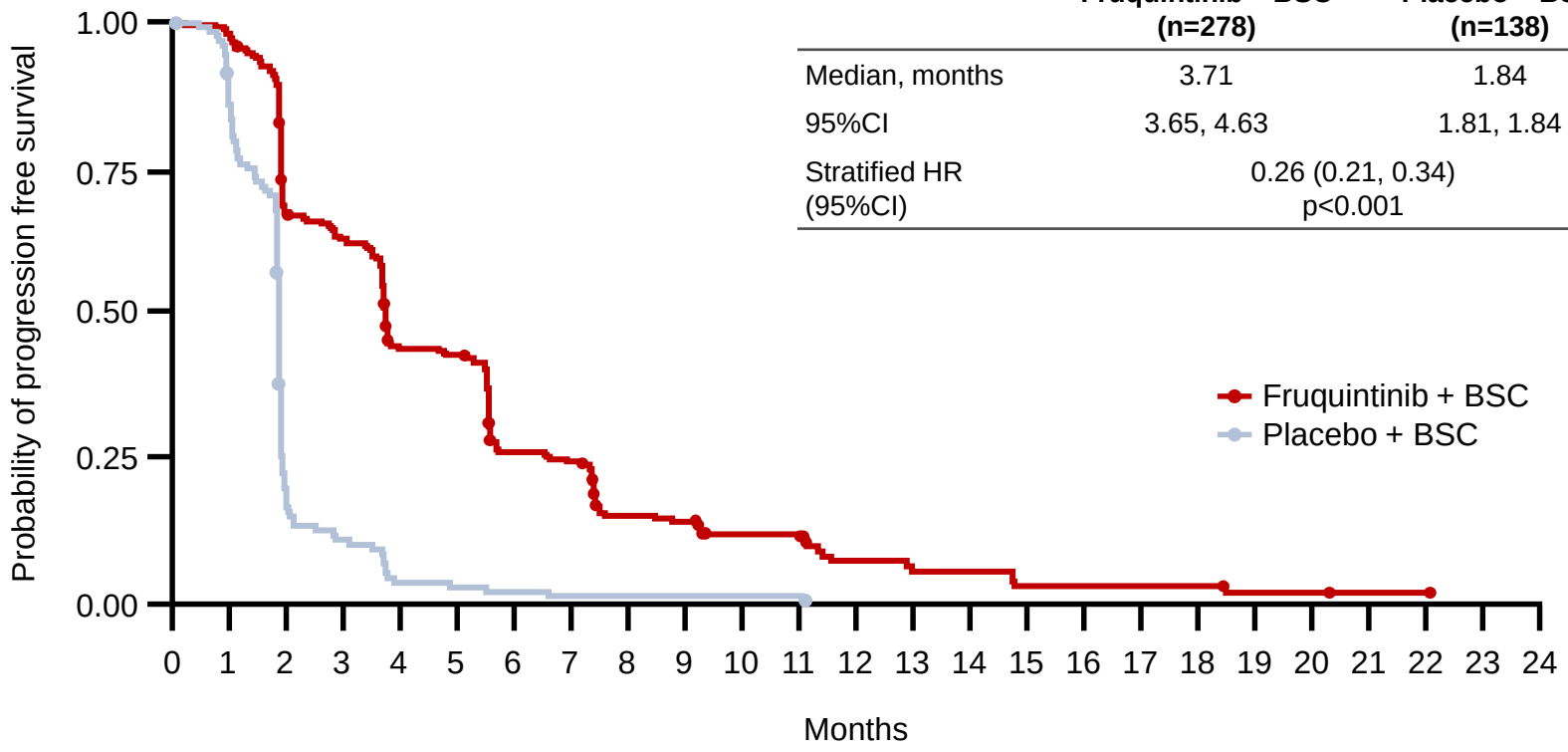

Li J, et al. J Clin Oncol 2017;35(Suppl):Abstr 3508

# 3508: A randomized, double-blind, placebo-controlled, multi-centered phase 3 trial comparing fruquintinib versus placebo plus best supportive care in Chinese patients with metastatic colorectal cancer (FRESCO) – Li J, et al

## Key results (cont.)

### PFS

| | Fruquintinib + BSC (n=278) | Placebo + BSC (n=138) |
|---|---|---|
| Median, months | 3.71 | 1.84 |
| 95%CI | 3.65, 4.63 | 1.81, 1.84 |
| Stratified HR (95%CI) | 0.26 (0.21, 0.34) p<0.001 | |




Li J, et al. J Clin Oncol 2017;35(Suppl):Abstr 3508

# 3508: A randomized, double-blind, placebo-controlled, multi-centered phase 3 trial comparing fruquintinib versus placebo plus best supportive care in Chinese patients with metastatic colorectal cancer (FRESCO) – Li J, et al

## Key results (cont.)

| TRAEs occurring in >15% patients, n (%) | Fruquintinib + BSC (n=278) | | Placebo + BSC (n=137) | |
|---|---|---|---|---|
| | All grades | Grade 3/4 | All grades | Grade 3/4 |
| Hypertension | 154 (55.4) | 59 (21.2) | 21 (15.3) | 3 (2.2) |
| PPE (or HFSR) | 137 (49.3) | 30 (10.8) | 4 (2.9) | 0 |
| Proteinuria | 117 (42.1) | 9 (3.2) | 34 (24.8) | 0 |
| Dysphonia | 100 (36.0) | 0 | 2 (1.5) | 0 |
| TSH increased | 69 (24.8) | 0 | 3 (2.2) | 0 |
| AST increased | 64 (23.0) | 1 (0.4) | 14 (10.2) | 1 (0.7) |
| Weight decreased | 59 (21.2) | 4 (1.4) | 12 (8.8) | 0 |
| Bilirubin increased | 56 (20.1) | 4 (1.4) | 10 (7.3) | 2 (1.5) |
| Diarrhoea | 56 (20.1) | 8 (2.9) | 3 (2.2) | 0 |
| ALT increased | 50 (18.0) | 2 (0.7) | 12 (8.8) | 2 (1.5) |
| Stomatitis | 47 (16.9) | 1 (0.4) | 0 | 0 |
| Decreased appetite | 45 (16.2) | 3 (1.1) | 11 (8.0) | 0 |
| Hypothyroidism | 43 (15.5) | 0 | 3 (2.2) | 0 |

Li J, et al. J Clin Oncol 2017;35(Suppl):Abstr 3508

# 3508: A randomized, double-blind, placebo-controlled, multi-centered phase 3 trial comparing fruquintinib versus placebo plus best supportive care in Chinese patients with metastatic colorectal cancer (FRESCO) – Li J, et al

## Conclusions

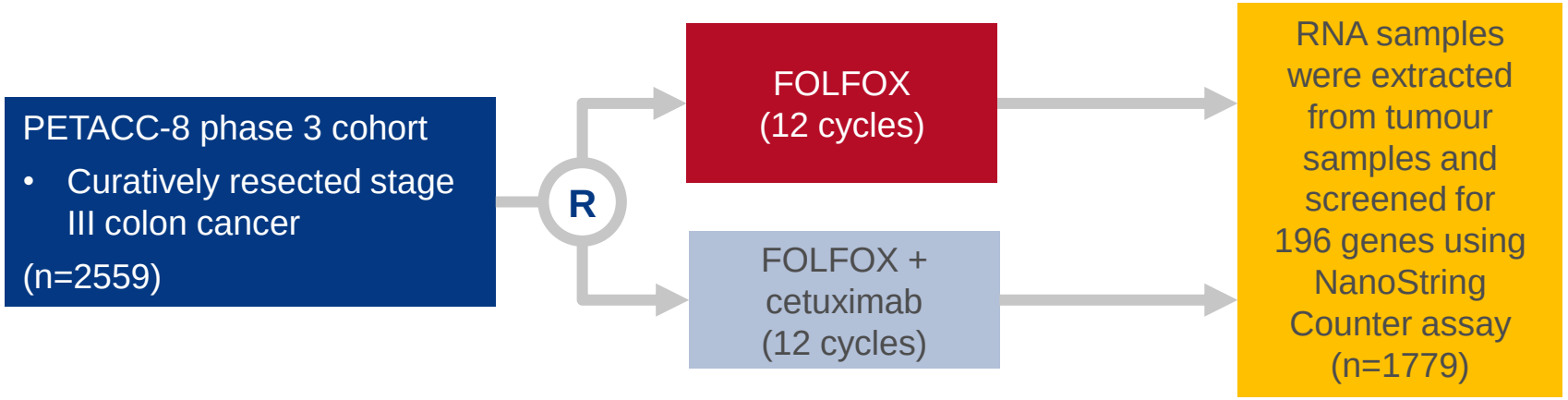
- In patients with metastatic CRC who had previously failed ≥2 lines of systemic therapy, fruquintinib significantly extended survival time
- Clinically meaningful and significant benefits were also observed in PFS, ORR and DCR
- Fruquintinib was well tolerated with a safety profile consistent with that previously reported in other studies

Li J, et al. J Clin Oncol 2017;35(Suppl):Abstr 3508

# 3509: Clinical utility of colon cancer molecular subtypes: Validation of two main colorectal molecular classifications on the PETACC-8 phase III trial cohort – Marisa L, et al

## Study objective

- To evaluate the clinical utility of colon cancer molecular subtypes in patients with curatively resected stage III colon cancer



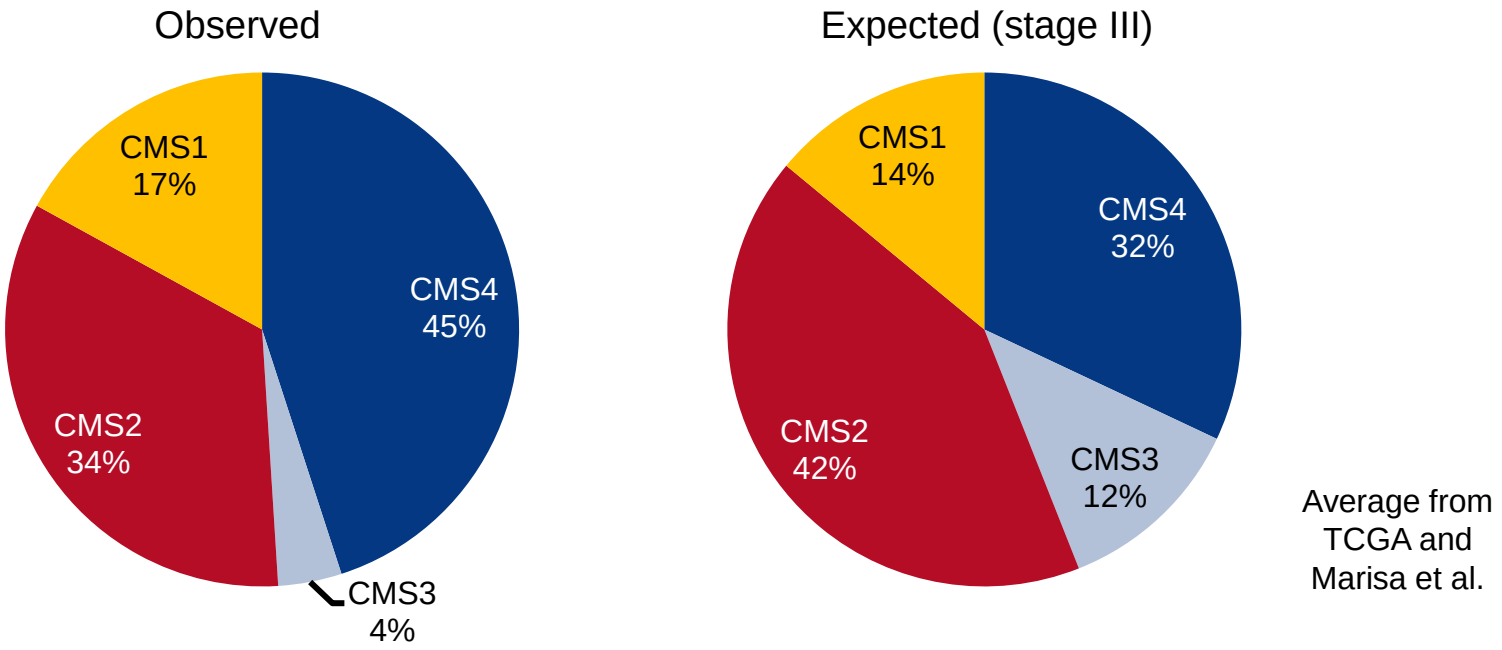

Marisa L, et al. J Clin Oncol 2017;35(Suppl):Abstr 3509

# 3509: Clinical utility of colon cancer molecular subtypes: Validation of two main colorectal molecular classifications on the PETACC-8 phase III trial cohort – Marisa L, et al

## Key results

**PETACC-8 CMS subtyping***

**CMS† prediction**




Average from TCGA and Marisa et al.

*Among 2043 patients, 1779 RNA samples were extracted from tumour samples and screened by NanoString assay
†CMS1, MSI immune; CMS2, canonical; CMS3, metabolic; CMS4, mesenchymal (4 subtypes based on Guinney et al.)

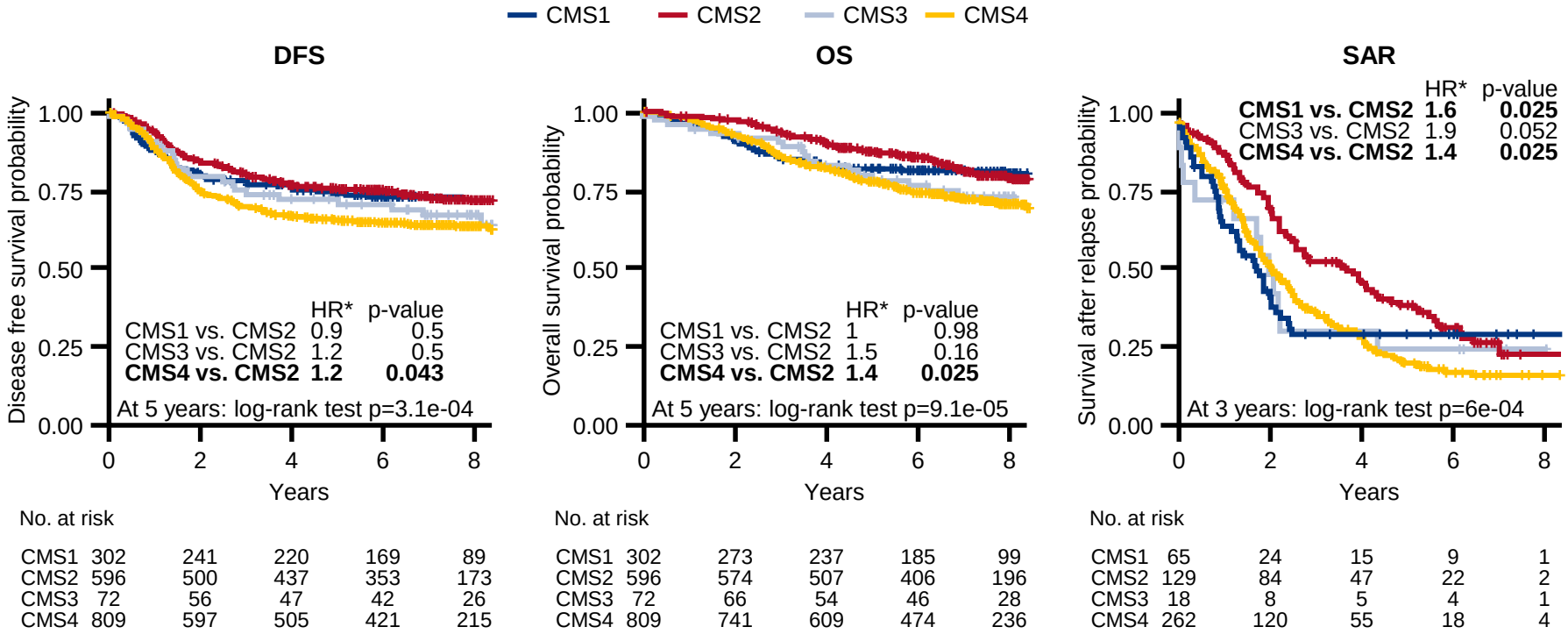
Marisa L, et al. J Clin Oncol 2017;35(Suppl):Abstr 3509

# 3509: Clinical utility of colon cancer molecular subtypes: Validation of two main colorectal molecular classifications on the PETACC-8 phase III trial cohort – Marisa L, et al

## Key results (cont.)

### Characteristics of predicted CMS in PETACC-8

#### Prognostic value




*Adjusted on age, T, N, differentiation, bowel perforation or obstruction, tumour location, performance status, treatment arm

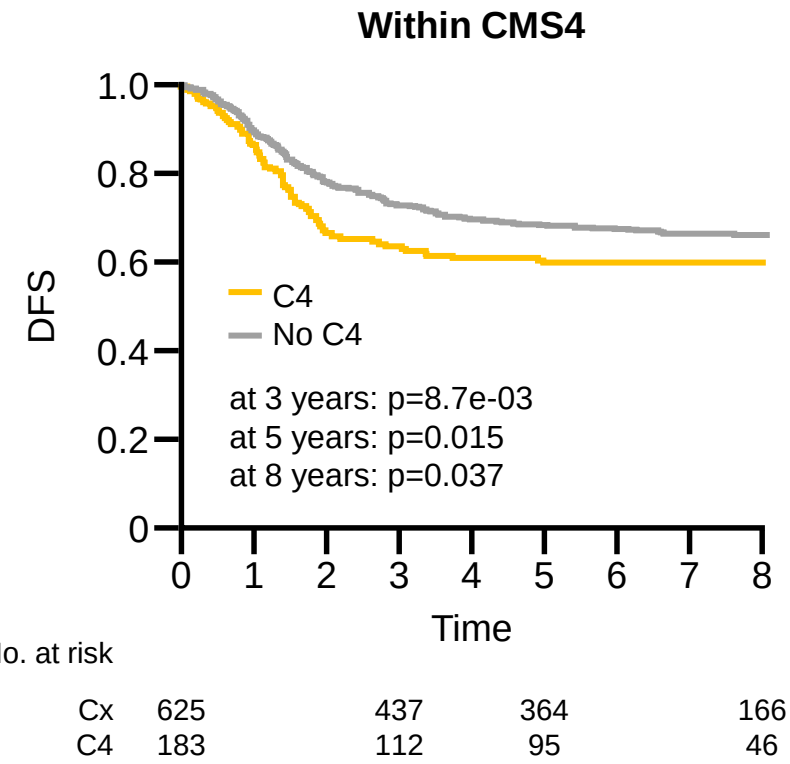
Marisa L, et al. J Clin Oncol 2017;35(Suppl):Abstr 3509

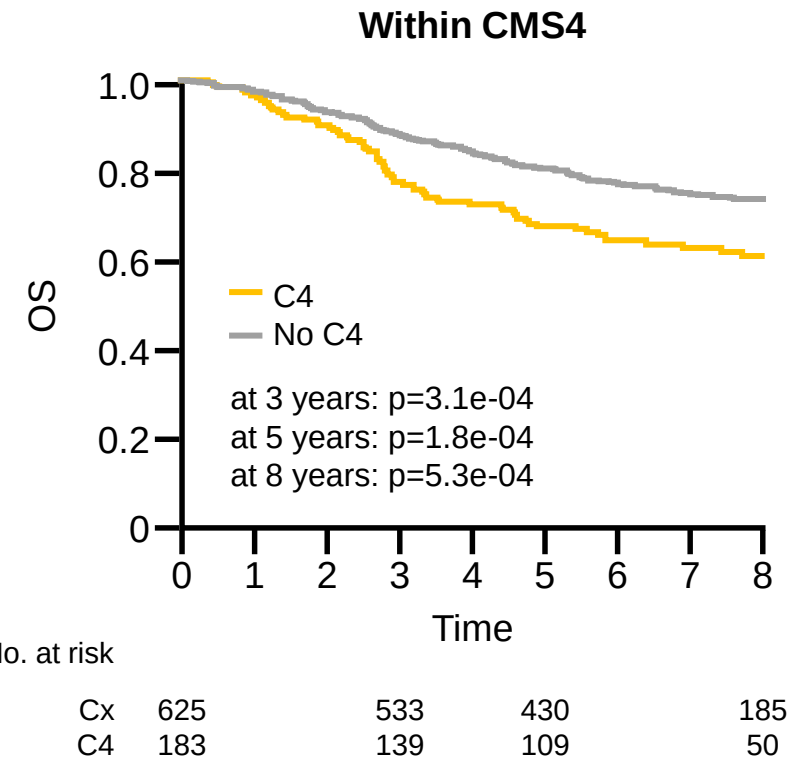
# 3509: Clinical utility of colon cancer molecular subtypes: Validation of two main colorectal molecular classifications on the PETACC-8 phase III trial cohort – Marisa L, et al

## Key results (cont.)

### CMS vs. Marisa subtypes*

### C4 prognostic value within CMS4 tumours




*Marisa subtypes: C1, immune down; C2, MSI; C3, KRASm; C4, stem cell; C5, Wnt up; C6, Norm-L

Marisa L, et al. J Clin Oncol 2017;35(Suppl):Abstr 3509

# 3509: Clinical utility of colon cancer molecular subtypes: Validation of two main colorectal molecular classifications on the PETACC-8 phase III trial cohort – Marisa L, et al

## Conclusions

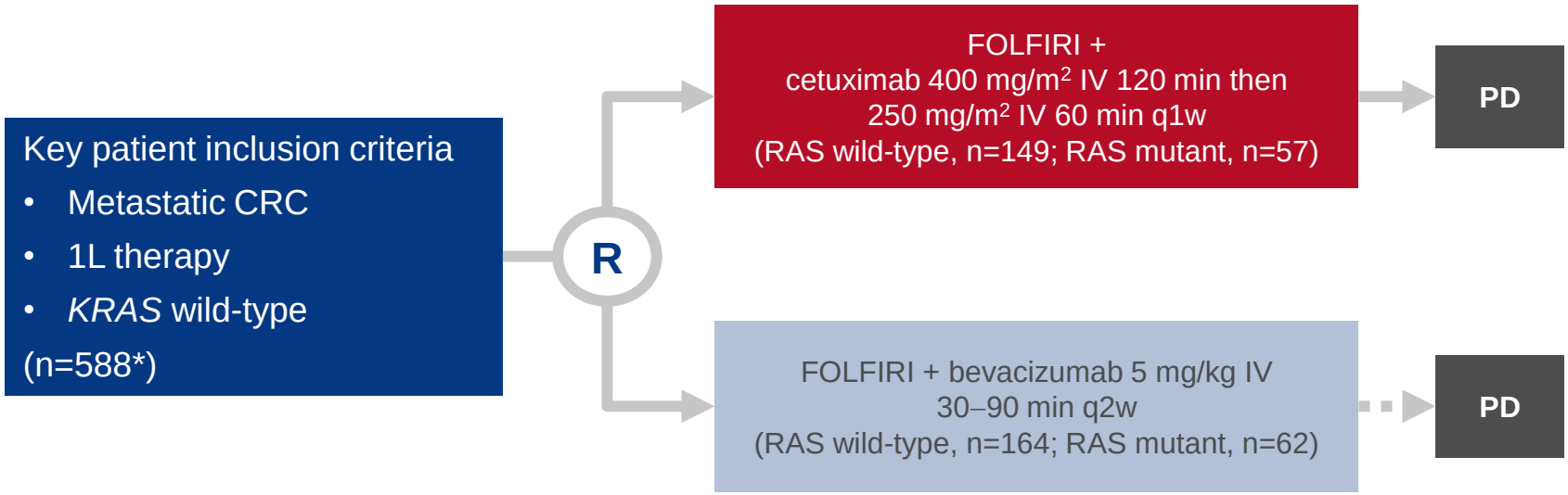
- The CMS predicted classes displayed expected clinical and molecular characteristics
- In stage III colon cancer, CMS4 was predicted with a higher prevalence than expected
- The predictor used confirmed the poor prognosis of CMS4 in a homogeneous colon cancer series, and the Marisa C4 subtype within CMS4 offers an additional prognostic value

Marisa L, et al. J Clin Oncol 2017;35(Suppl):Abstr 3509

# 3510: Consensus molecular subgroups (CMS) of colorectal cancer (CRC) and first-line efficacy of FOLFIRI plus cetuximab or bevacizumab in the FIRE3 (AIO KRK-0306) trial – Stintzing S, et al

## Study objective

- To determine the impact of CMS on 1L FOLFIRI + cetuximab or bevacizumab in patients with *KRAS* wild-type metastatic CRC enrolled in the FIRE3 study




### PRIMARY ENDPOINT

- Tumour response

### SECONDARY ENDPOINTS

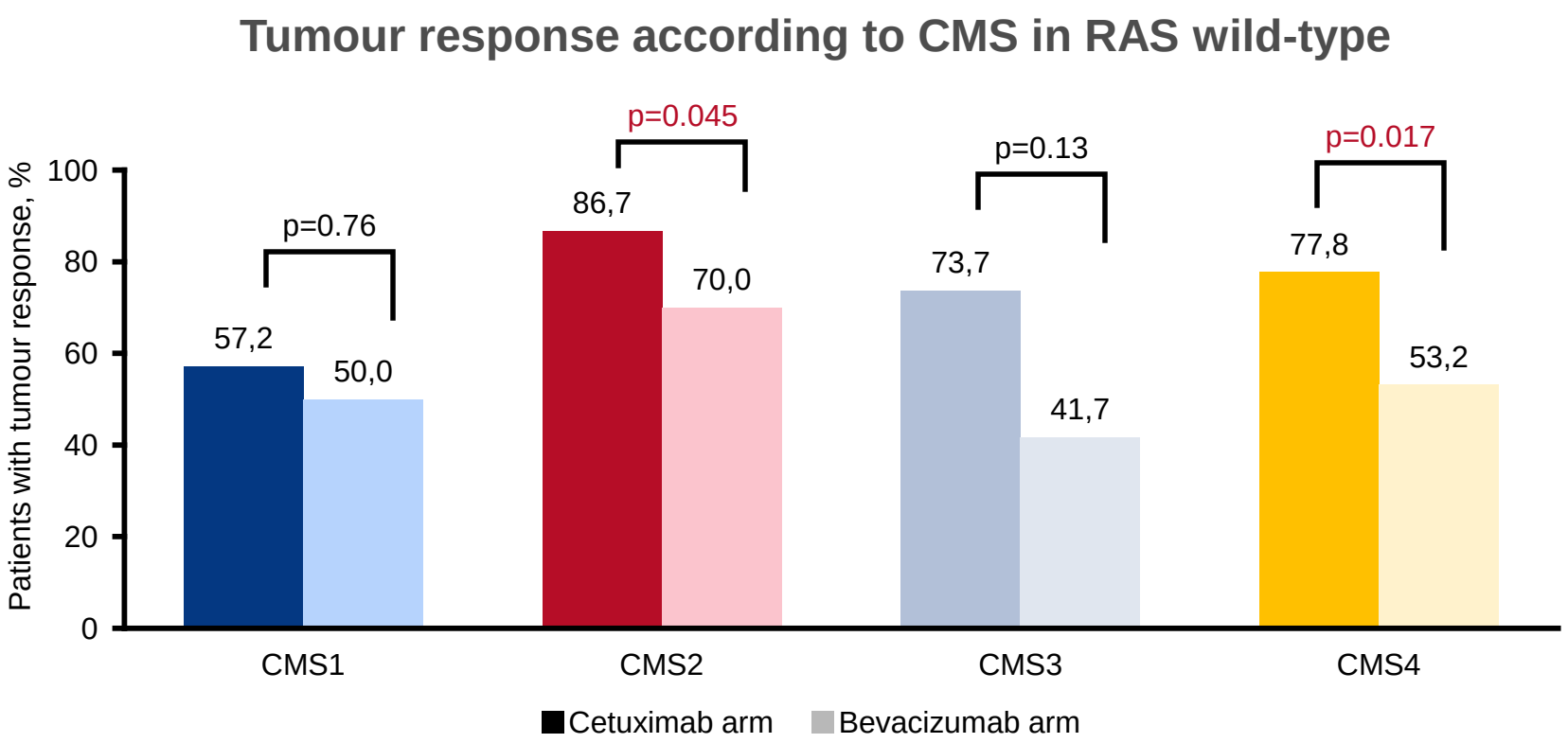
- OS, PFS

Patients were grouped according to tumour CRC-CMS
*Patients were not included where tumour material was unavailable or if gene expression analysis failed

Stintzing S, et al. J Clin Oncol 2017;35(Suppl):Abstr 3510

# 3510: Consensus molecular subgroups (CMS) of colorectal cancer (CRC) and first-line efficacy of FOLFIRI plus cetuximab or bevacizumab in the FIRE3 (AIO KRK-0306) trial – Stintzing S, et al

## Key results




Stintzing S, et al. J Clin Oncol 2017;35(Suppl):Abstr 3510

# 3510: Consensus molecular subgroups (CMS) of colorectal cancer (CRC) and first-line efficacy of FOLFIRI plus cetuximab or bevacizumab in the FIRE3 (AIO KRK-0306) trial – Stintzing S, et al

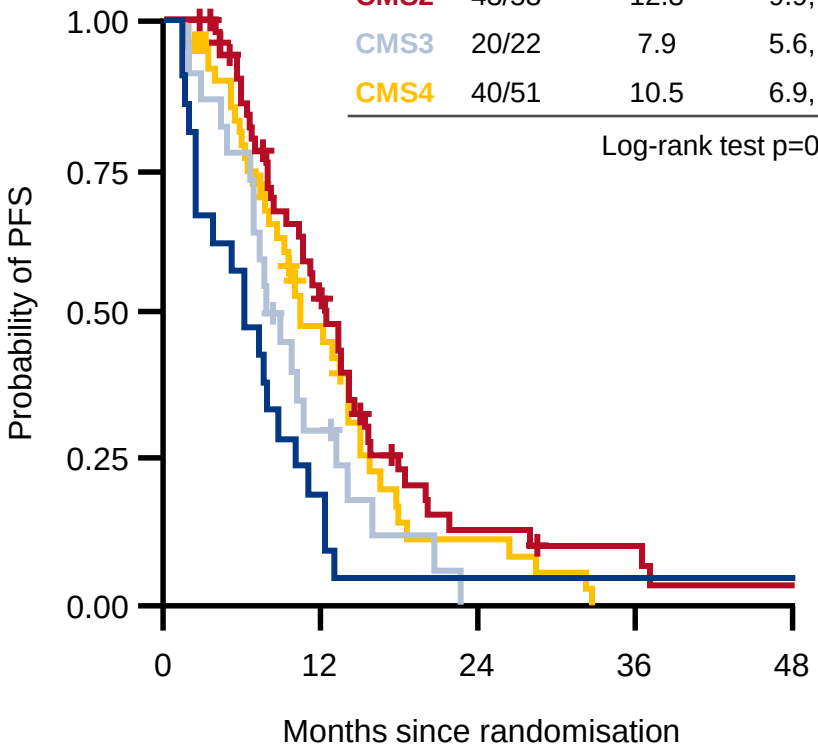
## Key results (cont.)

### PFS in RAS wild-type

**FOLFIRI cetuximab arm**

| | n/N | Median PFS, months | 95%CI |
|---|---|---|---|
| CMS1 | 20/23 | 6.1 | 3.0, 9.3 |
| CMS2 | 43/53 | 12.3 | 9.9, 14.7 |
| CMS3 | 20/22 | 7.9 | 5.6, 10.1 |
| CMS4 | 40/51 | 10.5 | 6.9, 14.2 |

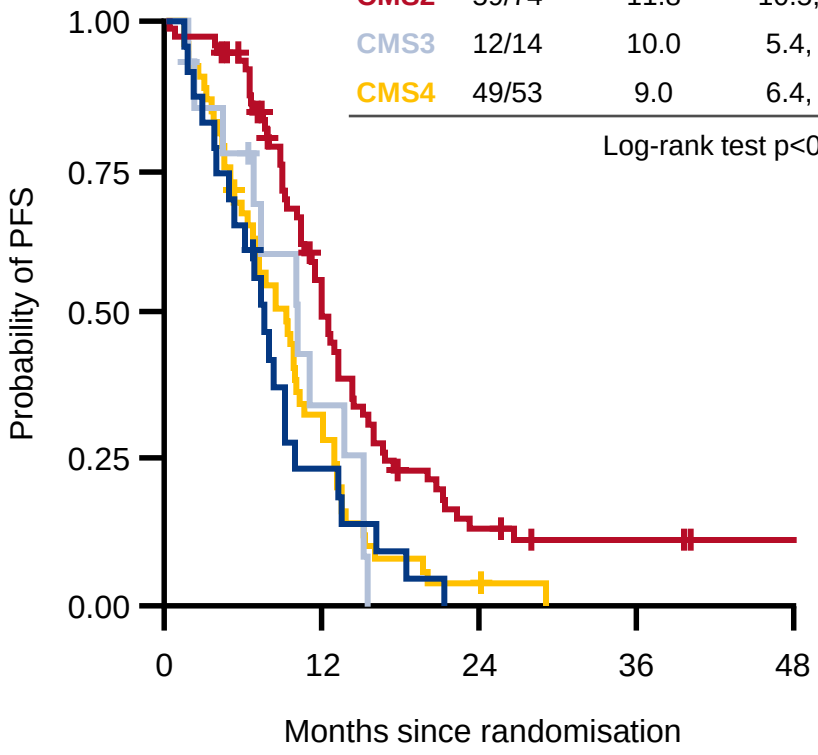
Log-rank test p=0.006




**FOLFIRI bevacizumab arm**

| | n/N | Median PFS, months | 95%CI |
|---|---|---|---|
| CMS1 | 22/23 | 7.4 | 5.7, 9.1 |
| CMS2 | 59/74 | 11.8 | 10.5, 13.2 |
| CMS3 | 12/14 | 10.0 | 5.4, 14.5 |
| CMS4 | 49/53 | 9.0 | 6.4, 11.8 |

Log-rank test p<0.001




Stintzing S, et al. J Clin Oncol 2017;35(Suppl):Abstr 3510

# 3510: Consensus molecular subgroups (CMS) of colorectal cancer (CRC) and first-line efficacy of FOLFIRI plus cetuximab or bevacizumab in the FIRE3 (AIO KRK-0306) trial – Stintzing S, et al

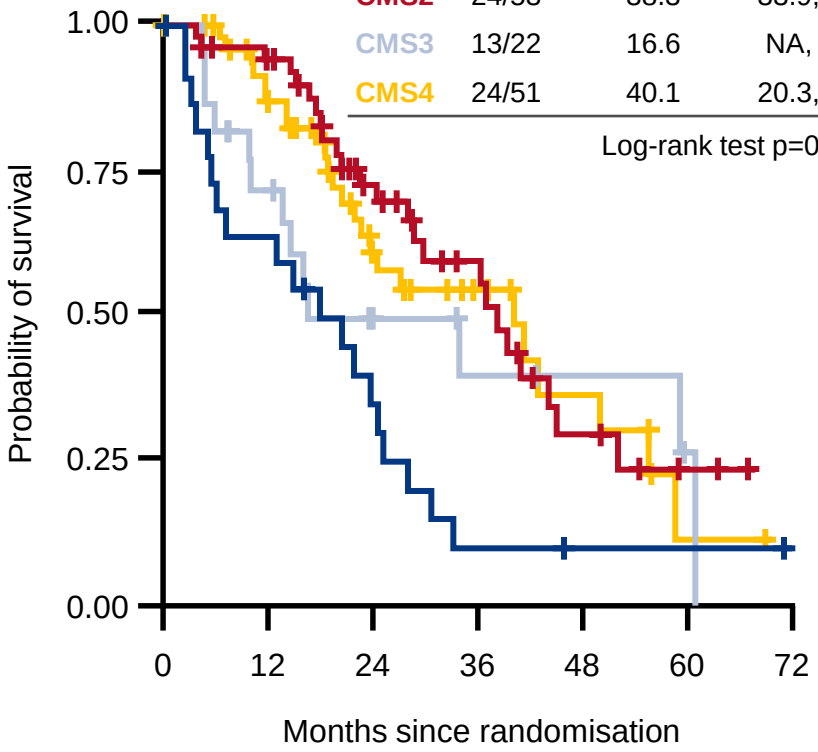
## Key results (cont.)

### OS in RAS wild-type

**FOLFIRI cetuximab arm**

| | n/N | Median OS, months | 95%CI |
|---|---|---|---|
| CMS1 | 19/23 | 17.9 | 7.1, 28.7 |
| CMS2 | 24/53 | 38.3 | 33.9, 42.8 |
| CMS3 | 13/22 | 16.6 | NA, 42.3 |
| CMS4 | 24/51 | 40.1 | 20.3, 59.9 |

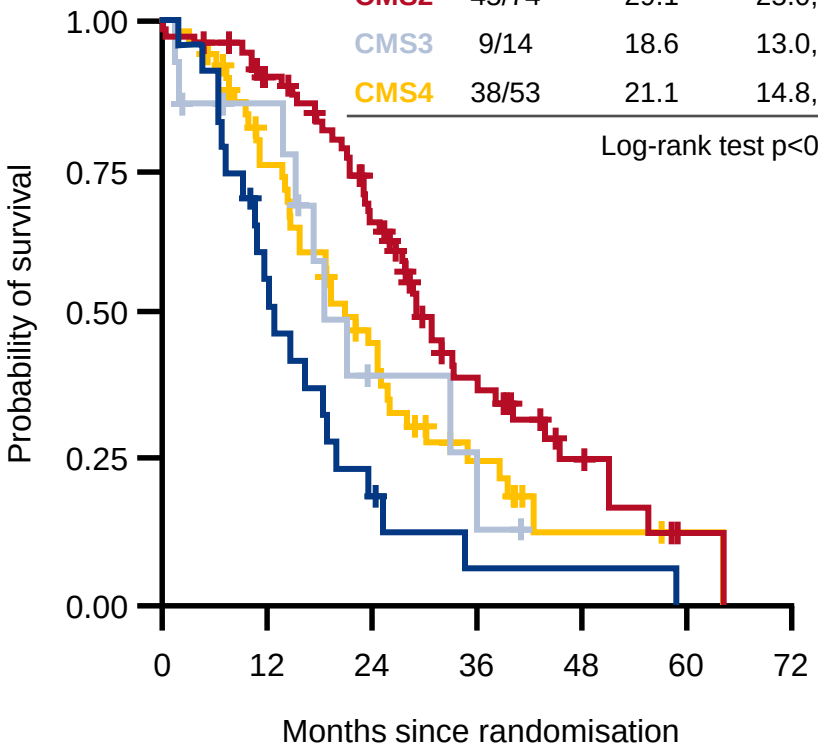
Log-rank test p=0.004




**FOLFIRI bevacizumab arm**

| | n/N | Median OS, months | 95%CI |
|---|---|---|---|
| CMS1 | 21/23 | 13.1 | 8.5, 17.6 |
| CMS2 | 45/74 | 29.1 | 25.0, 33.3 |
| CMS3 | 9/14 | 18.6 | 13.0, 24.3 |
| CMS4 | 38/53 | 21.1 | 14.8, 27.3 |

Log-rank test p<0.001

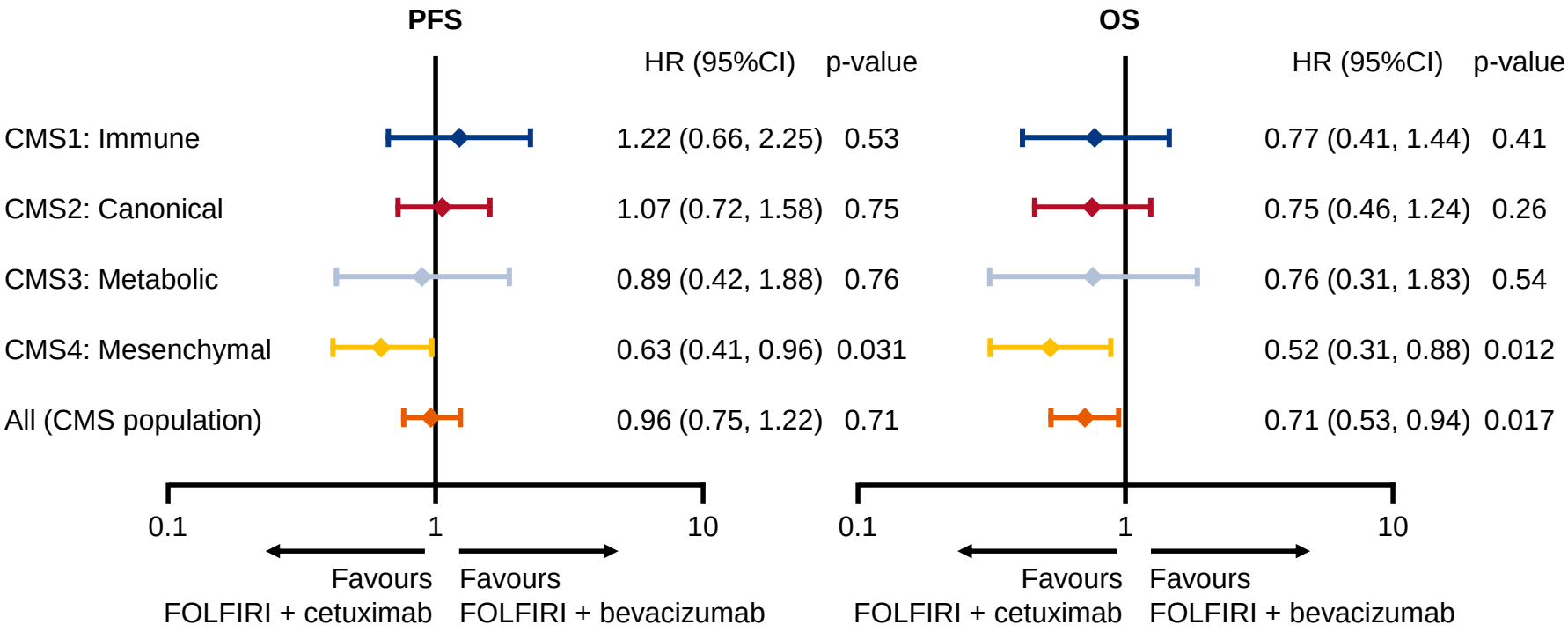



Stintzing S, et al. J Clin Oncol 2017;35(Suppl):Abstr 3510

# 3510: Consensus molecular subgroups (CMS) of colorectal cancer (CRC) and first-line efficacy of FOLFIRI plus cetuximab or bevacizumab in the FIRE3 (AIO KRK-0306) trial – Stintzing S, et al

## Key results (cont.)

### FOLFIRI + cetuximab vs. FOLFIRI + bevacizumab




Stintzing S, et al. J Clin Oncol 2017;35(Suppl):Abstr 3510

# 3510: Consensus molecular subgroups (CMS) of colorectal cancer (CRC) and first-line efficacy of FOLFIRI plus cetuximab or bevacizumab in the FIRE3 (AIO KRK-0306) trial – Stintzing S, et al

## Conclusions

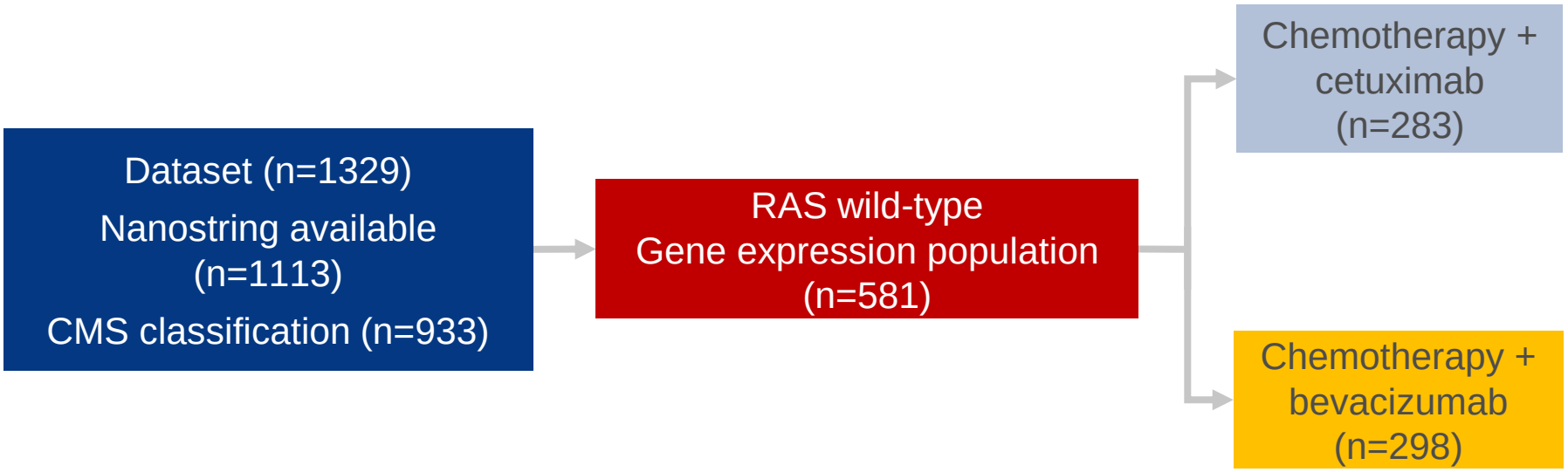
- CMS classification appears to be prognostic for metastatic CRC
- For all CMS groups in the RAS wild-type population, ORR was in favour of FOLFIRI + cetuximab vs. FOLFIRI + bevacizumab
- The survival benefit in RAS wild-type for FOLFIRI + cetuximab vs. FOLFIRI + bevacizumab seems to be driven by CMS4 followed by CMS2

Stintzing S, et al. J Clin Oncol 2017;35(Suppl):Abstr 3510

# 3511: Impact of consensus molecular subtyping (CMS) on overall survival (OS) and progression free survival (PFS) in patients (pts) with metastatic colorectal cancer (mCRC): analysis of CALGB/SWOG 80405 (Alliance) – Lenz H-J, et al

## Study objective

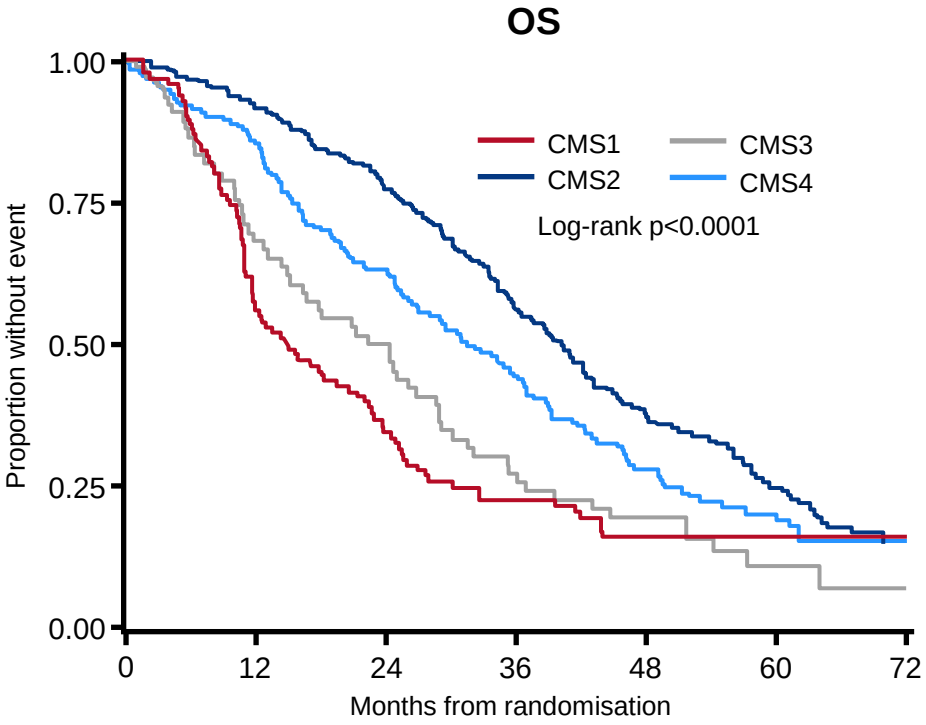
- To determine the CMS classification of KRAS wild-type (codon 12 and 13) primary tumours and the correlation between CMS class and OS and PFS in patients enrolled in the CALGB/SWOG 80405 (Alliance) study



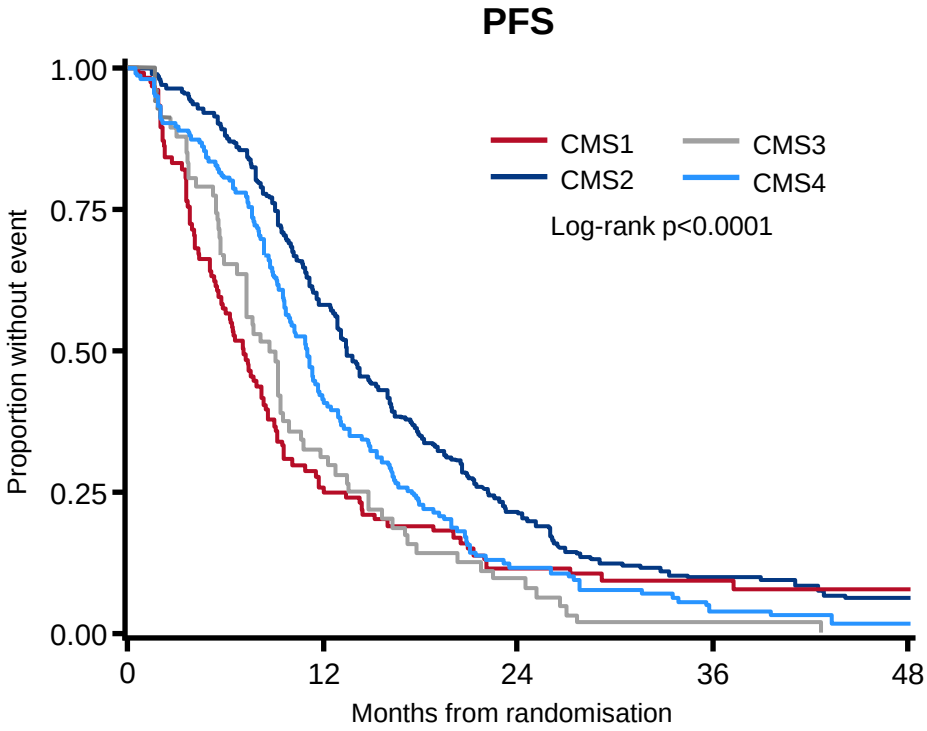

Lenz H-J, et al. J Clin Oncol 2017;35(Suppl):Abstr 3511

# 3511: Impact of consensus molecular subtyping (CMS) on overall survival (OS) and progression free survival (PFS) in patients (pts) with metastatic colorectal cancer (mCRC): analysis of CALGB/SWOG 80405 (Alliance) – Lenz H-J, et al

## Key results




| | Events/total | mOS, months (95%CI) |
|---|---|---|
| CMS1 | 85/104 | 15.0 (11.7, 22.4) |
| CMS2 | 173/242 | 40.3 (36.1, 43.1) |
| CMS3 | 58/68 | 24.3 (16.4, 29.0) |
| CMS4 | 127/167 | 31.4 (26.3, 36.9) |



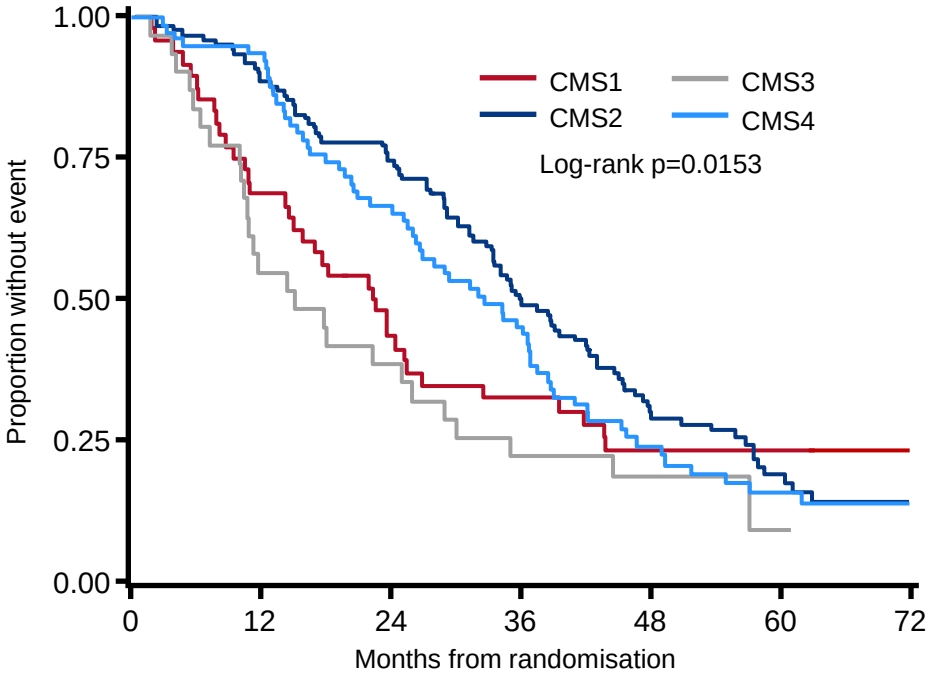

| | Events/total | mPFS, months (95%CI) |
|---|---|---|
| CMS1 | 92/104 | 7.1 (5.7, 8.6) |
| CMS2 | 224/242 | 13.4 (12.8, 15.4) |
| CMS3 | 65/68 | 8.7 (7.2, 9.8) |
| CMS4 | 152/167 | 11.0 (9.7, 12.0) |

Lenz H-J, et al. J Clin Oncol 2017;35(Suppl):Abstr 3511

# 3511: Impact of consensus molecular subtyping (CMS) on overall survival (OS) and progression free survival (PFS) in patients (pts) with metastatic colorectal cancer (mCRC): analysis of CALGB/SWOG 80405 (Alliance) – Lenz H-J, et al

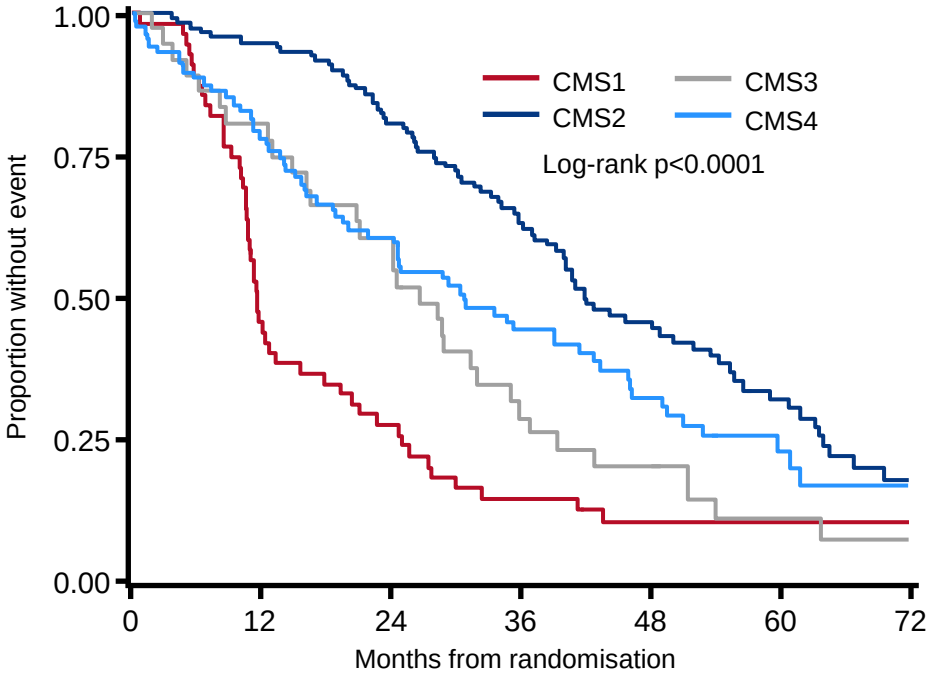
## Key results (cont.)

### OS with bevacizumab




| | Events/total | mOS, months (95%CI) |
|---|---|---|
| CMS1 | 39/49 | 22.5 (15.9, 32.6) |
| CMS2 | 94/123 | 36.0 (33.5, 42.3) |
| CMS3 | 26/31 | 15.1 (10.8, 30.1) |
| CMS4 | 65/80 | 32.7 (26.3, 37.5) |

### OS with cetuximab



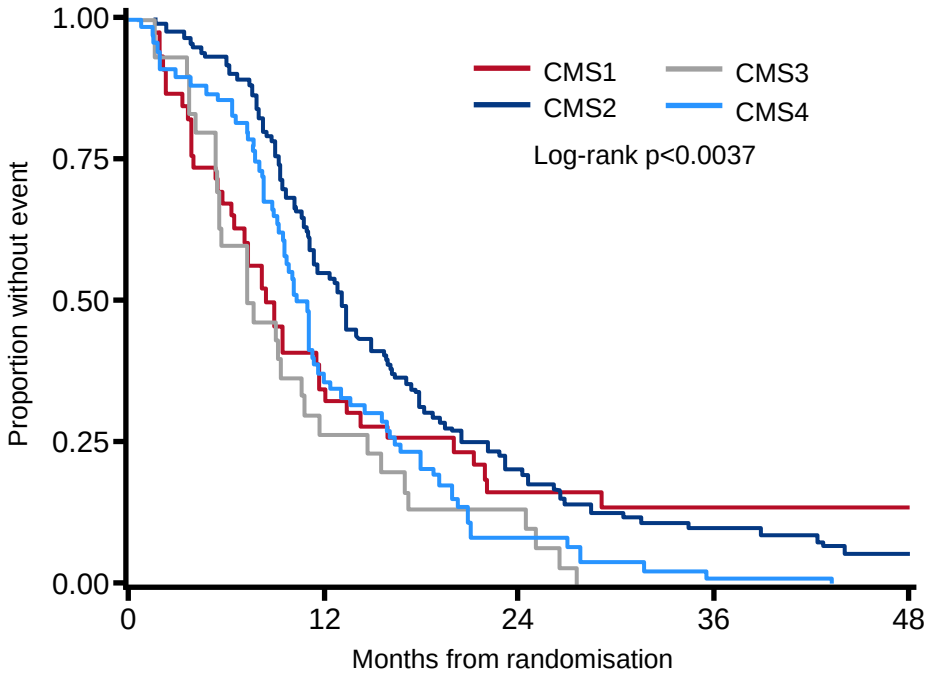

| | Events/total | mOS, months (95%CI) |
|---|---|---|
| CMS1 | 49/55 | 11.7 (10.9, 18.0) |
| CMS2 | 79/119 | 42.0 (39.3, 54.4) |
| CMS3 | 32/37 | 26.8 (20.9, 36.0) |
| CMS4 | 62/87 | 30.8 (24.4, 43.5) |

Lenz H-J, et al. J Clin Oncol 2017;35(Suppl):Abstr 3511

# 3511: Impact of consensus molecular subtyping (CMS) on overall survival (OS) and progression free survival (PFS) in patients (pts) with metastatic colorectal cancer (mCRC): analysis of CALGB/SWOG 80405 (Alliance) – Lenz H-J, et al

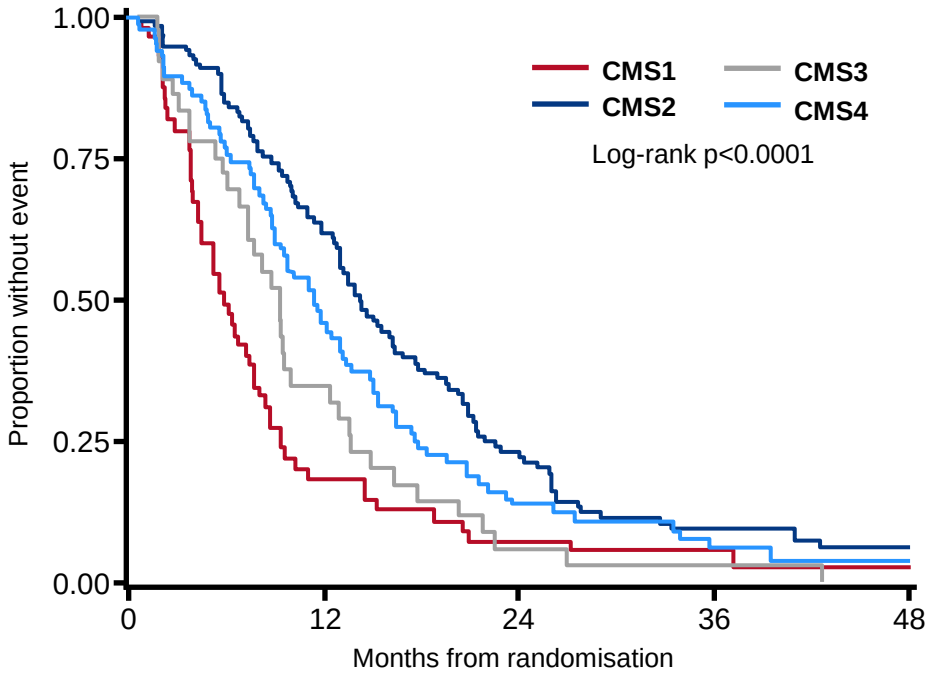
## Key results (cont.)

### PFS with bevacizumab




| | Events/total | mPFS, months (95%CI) |
|---|---|---|
| CMS1 | 39/49 | 8.7 (7.1, 12.0) |
| CMS2 | 116/123 | 13.1 (11.4, 15.8) |
| CMS3 | 30/31 | 7.7 (5.7, 11.7) |
| CMS4 | 73/80 | 10.3 (9.6, 12.0) |

### PFS with cetuximab




| | Events/total | mPFS, months (95%CI) |
|---|---|---|
| CMS1 | 53/55 | 5.7 (4.4, 7.7) |
| CMS2 | 108/119 | 14.1 (12.8, 16.7) |
| CMS3 | 35/37 | 9.2 (7.3, 12.7) |
| CMS4 | 79/87 | 11.3 (9.2, 13.6) |

Lenz H-J, et al. J Clin Oncol 2017;35(Suppl):Abstr 3511

# 3511: Impact of consensus molecular subtyping (CMS) on overall survival (OS) and progression free survival (PFS) in patients (pts) with metastatic colorectal cancer (mCRC): analysis of CALGB/SWOG 80405 (Alliance) – Lenz H-J, et al

**Conclusions**

- **CMS classification appears to be highly prognostic and may also be predictive which warrants further exploration**
- **In pathway driven prospective clinical studies and stratification in clinical studies, this new CMS classification may be useful**

Lenz H-J, et al. J Clin Oncol 2017;35(Suppl):Abstr 3511

# ROUTINE CANCER CARE

# LBA2: Overall survival results of a randomized trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment – Basch EM, et al

## Study objective

- To evaluate OS in patients receiving chemotherapy for metastatic solid tumours self-reporting symptoms vs. 'standard' symptom monitoring

**Key patient inclusion criteria**

- Patients receiving routine outpatient chemotherapy for metastatic solid tumours at Memorial Sloan Kettering Cancer Center, USA

(n=766)

R*

Patient self-report (12 common symptoms)

- Prior to/between visits (via tablet computer)
- Weekly email reminders to patients
- Alerts to nurse (by email)
- Reports to oncologists (at visits)

(n=441)

**Stratification**

- Prior computer use

'Standard' symptom monitoring
(n=325)

### PRIMARY ENDPOINT

- OS

### SECONDARY ENDPOINTS

- QoL
- Emergency room visits

*Randomized 2:1 for those without prior computer use

Basch EM, et al. J Clin Oncol 2017;35(Suppl):Abstr LBA2

# LBA2: Overall survival results of a randomized trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment – Basch EM, et al

**Key results**

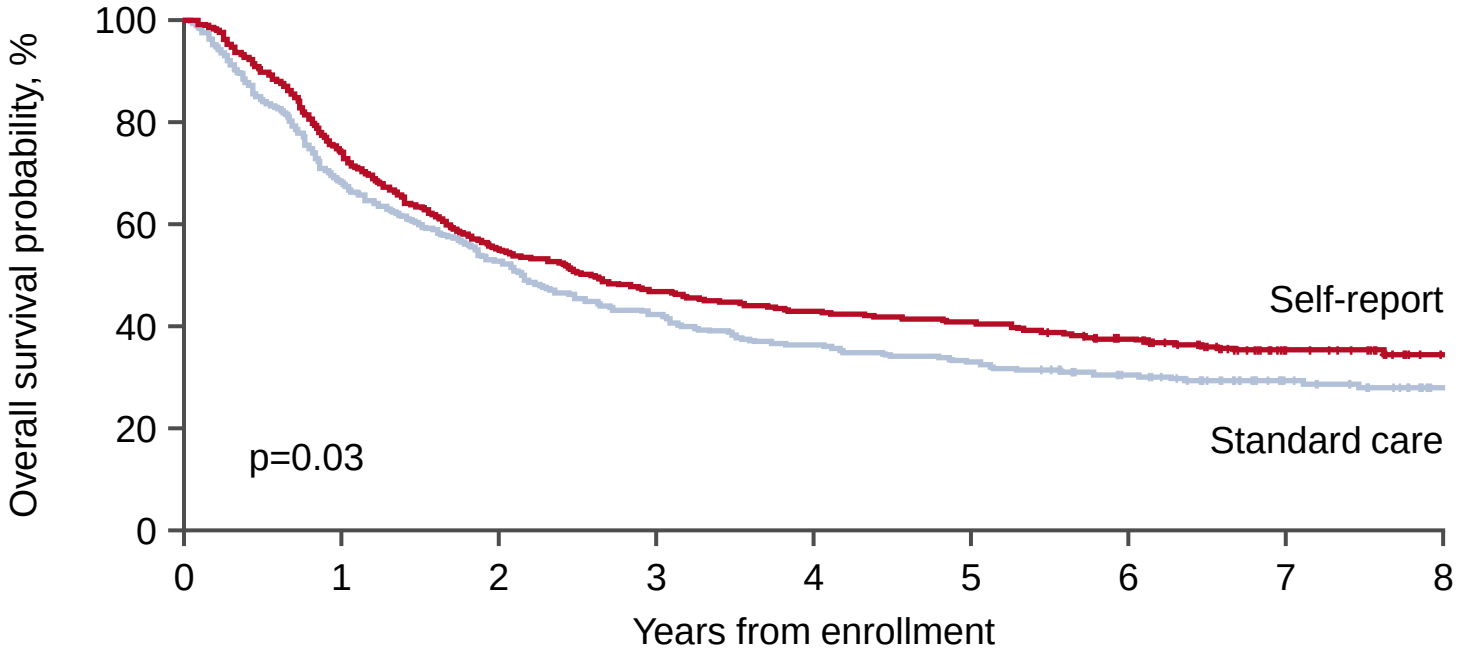
- 766 patients enrolled between June 2007 and January 2011
- OS analysis in June 2016
  - Median follow-up of 7 years
  - 517/766 (67%) participants had died

Basch EM, et al. J Clin Oncol 2017;35(Suppl):Abstr LBA2

# LBA2: Overall survival results of a randomized trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment – Basch EM, et al

## Key results (cont.)

- Median OS was 5 months longer among patients in the self-reporting arm vs. standard care (31.2 vs. 26 months; p=0.03)




| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Total | 766 | 554 | 415 | 344 | 308 | 288 | 237 | 115 | 60 |
| Self-report | 441 | 331 | 244 | 207 | 190 | 181 | 148 | 65 | 33 |
| Standard | 325 | 223 | 171 | 137 | 118 | 107 | 89 | 50 | 27 |

*Remained significant in multivariable analysis: adjusted HR 0.832 (95%CI 0.696, 0.995)

Basch EM, et al. J Clin Oncol 2017;35(Suppl):Abstr LBA2

# LBA2: Overall survival results of a randomized trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment – Basch EM, et al

## Conclusions

- Systematic symptom monitoring during outpatient chemotherapy using web-based patient-reported outcomes improves OS
- It is suggested that this approach be included as a part of standard symptom management
- Implementation strategies for integrating self-reporting into electronic health records and into workflow of oncology practice should be considered

Basch EM, et al. J Clin Oncol 2017;35(Suppl):Abstr LBA2