# GI SLIDE DECK 2021

## Selected abstracts from:



esdo european society of digestive oncology

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# Letter from ESDO

**DEAR COLLEAGUES**

It is our pleasure to present this ESDO slide set which has been designed to highlight and summarize key findings in digestive cancers from the major congresses in 2021. This slide set specifically focuses on the **ESMO World Congress on Gastrointestinal Cancer 2021 Virtual Meeting** and **ESMO Congress 2021** and is available in English and Japanese.

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

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

Yours sincerely,

**Eric Van Cutsem**
**Thomas Seufferlein**
**Côme Lepage**

**Tamara Matysiak-Budnik**
**Jaroslaw Regula**
**Thomas Gruenberger**

**Jean-Luc Van Laethem**
**Ana-Maria Bucalau** (Young Group)
**Pieter-Jan Cuyle** (Young Group)

(ESDO Governing Board)

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european society of digestive oncology

# ESDO Medical Oncology Slide Deck
## Editors 2021

### COLORECTAL CANCERS



| | |
|---|---|
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### PANCREATIC CANCER AND HEPATOBILIARY TUMOURS



| | |
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| **Prof Thomas Seufferlein** | Clinic of Internal Medicine I, University of Ulm, Ulm, Germany |
| **Dr Ann-Maria Bucalau** | Digestive Oncology, Erasme University Hospital, Brussels, Belgium |

### GASTRO-OESOPHAGEAL AND NEUROENDOCRINE TUMOURS



| | |
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### BIOMARKERS



| | |
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| **Prof Eric Van Cutsem** | Digestive Oncology, University Hospitals, Leuven, Belgium |
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esdo

# Glossary

| | |
|---|---|
| 1L | first-line |
| 2L | second-line |
| 5FU | 5-fluouracil |
| AE | adverse event |
| ALT | alanine aminotransferase |
| AST | aspartate aminotransferase |
| Bev | bevacizumab |
| BICR | blinded-independent central review |
| bid | twice daily |
| Bini | binimetinib |
| BCLC | Barcelona Clinic Liver Cancer |
| BOR | best overall response |
| BRAF | v-raf murine sarcoma viral oncogene homolog B1 |
| BW | body weight |
| CA19-9 | carbohydrate antigen 19-9 |
| CAPOX | capecitabine + oxaliplatin |
| CCR | completeness of cytoreduction |
| Cet | cetuximab |
| cfDNA | cell free DNA |
| Chemo | chemotherapy |
| CI | confidence interval |
| Cis | cisplatin |
| combos | combination therapies |
| CPS | combined positive score |
| CR | complete response |
| CRC | colorectal cancer |
| CRS | cytoreductive surgery |
| CT | computed tomography |
| ctDNA | circulating tumour DNA |
| D | day |
| DCR | disease control rate |
| ddPCR | droplet digital polymerase chain reaction |
| DFS | disease-free survival |
| DMC | data monitoring committee |
| DMFS | distant metastases-free survival |
| dMMR | deficient mismatch repair |
| (m)DoR | (median) duration of response |
| ECOG | Eastern Cooperative Oncology Group |
| EGFR | epidermal growth factor receptor |
| Enco | encorafenib |
| ESCC | esophageal squamous cell carcinoma |
| EU | European |
| FAS | full analysis set |
| FDR | false discovery rate-adjusted |
| FFPE | formalin-fixed, paraffin-embedded |
| FOLFIRI | folinic acid + 5-fluouracil + irinotecan |
| FP | 5-fluouracil + cisplatin |
| Fpy | fluoropyrimidine |
| (m)FOLFIRINOX | (modified) oxaliplatin + irinotecan + leucovorin + 5FU |
| (m)FOLFOX | (modified) leucovorin + 5-fluorouracil + oxaliplatin |
| FOLFOXIRI | oxaliplatin + irinotecan + leucovorin + 5FU |
| GEJ | gastro-esophageal junction |
| Gem | gemcitabine |
| GGT | gamma0glutamyltransferase |
| GI | gastrointestinal |
| Gy | Gray |
| HCC | hepatocellular carcinoma |
| HER2 | human epidermal growth factor receptor 2 |
| HIPEC | hyperthermic intraperitoneal chemotherapy |
| HR | hazard ratio |
| HRQoL | health-related quality of life |
| ICR | independent committee review |
| IHC | immunohistochemistry |
| Ip | intraperitoneal |
| IPI | ipilimumab |
| irAE | immune-related adverse event |
| ISH | in-situ hybridisation |
| (m)ITT | (modified) intent-to-treat |
| iv | intravenous |
| KRAS | Ki-ras2 Kirsten rat sarcoma viral oncogene homolog |
| LN | lymph node |
| LV | leucovorin |
| MAF | mutant allele fraction |
| mCRC | metastatic colorectal cancer |
| MEK | mitogen-activated protein kinase |
| mo | months |
| mono | monotherapy |
| MSI-H | high microsatellite instability |
| MSS | microsatellite stability |
| NA | not available |
| nab-P | nab-paclitaxel |
| Nal-IRI | nal-irinotecan |
| NCCN | National Comprehensive Cancer Network |
| NE | not evaluable/estimable |
| NET | neuroendocrine tumour |
| NGS | next generation sequencing |
| NIVO | nivolumab |
| NR | not reached |
| ORR | overall/objective response rate |
| OR | odds ratio |
| (m)OS | (median) overall survival |
| pCR | pathological complete response |
| PCI | peritoneal cancer index |
| PD | progressive disease |
| PDAC | pancreatic ductal adenocarcinoma |
| PD-(L)1 | programmed death-(ligand) 1 |
| Pembro | pembrolizumab |
| (m)PFS | (median) progression-free survival |
| PK | pharmacokinetics |
| PP | per protocol |
| PR | partial response |
| PS | performance status |
| q(2/3/4/8)w | every (2/3/4/8) week(s) |
| QoL | quality of life |
| R | randomized |
| R0/1 | resection 0/1 |
| RAF | rapidly accelerated fibrosarcoma |
| RECIST | Response Evaluation Criteria In Solid Tumors |
| RP2D | recommended phase 2 dose |
| RoW | rest of world |
| RT | radiotherapy |
| SBA | small bowel adenocarcinoma |
| SD | stable disease |
| SoC | standard of care |
| SSI | surgical site infection |
| TACE | transarterial chemoembolization |
| TARE | transarterial radioembolization |
| T-DXd | trastuzumab deruxtecan |
| TEAE | treatment-emergent adverse event |
| TMB | tumour mutational burden |
| Torip | toripalimab |
| TPS | tumour proportion score |
| Trast | trastuzumab |
| TRAE | treatment-related adverse event |
| TRG | tumour regression grade |
| TTFields | tumour treating fields |
| (m)TTP | (median) time to progression |
| TTR | time to response |
| ULN | upper limit of normal |
| Vem | vemurafenib |
| WBC | white blood cell |
| WT | wild type |
| XELOX | oxaliplatin + capecitabine |

# Contents



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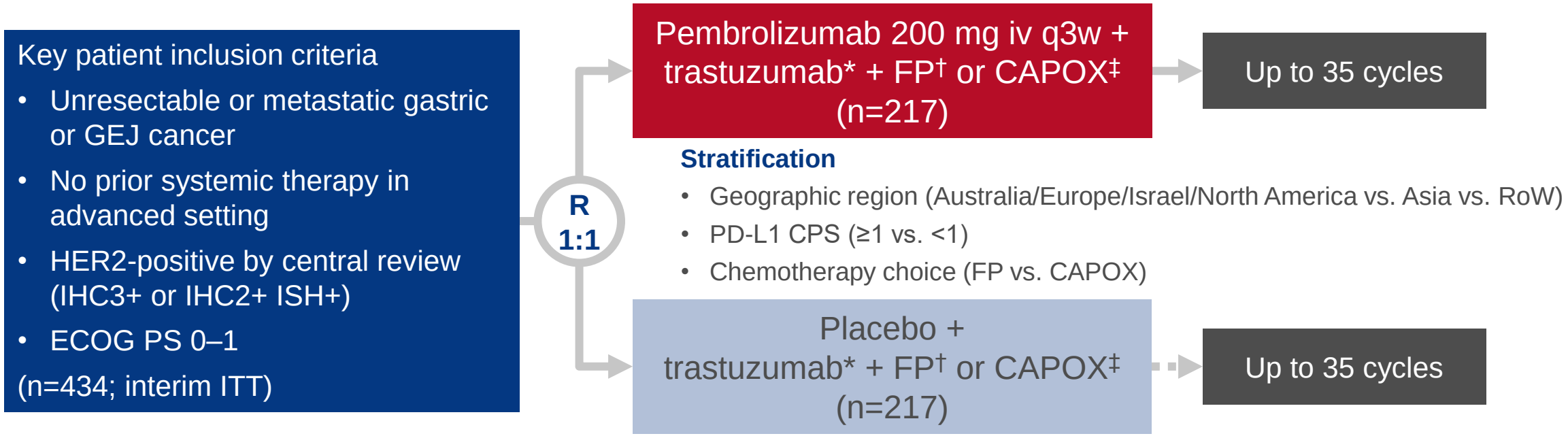
# CANCERS OF THE OESOPHAGUS AND STOMACH

# LBA-4: Initial data from the phase 3 KEYNOTE-811 study of trastuzumab and chemotherapy with or without pembrolizumab for HER2-positive metastatic gastric or gastroesophageal junction (G/GEJ) cancer – Janjigian YY, et al

## Study objective

- To evaluate the efficacy and safety of trastuzumab + chemotherapy with or without pembrolizumab in patients with HER2-positive metastatic gastric or GEJ cancer at an interim analysis of the KEYNOTE-811 study




**CO-PRIMARY ENDPOINTS**

- OS, PFS (RECIST v1.1, BICR)

**SECONDARY ENDPOINTS**

- ORR, DoR, safety

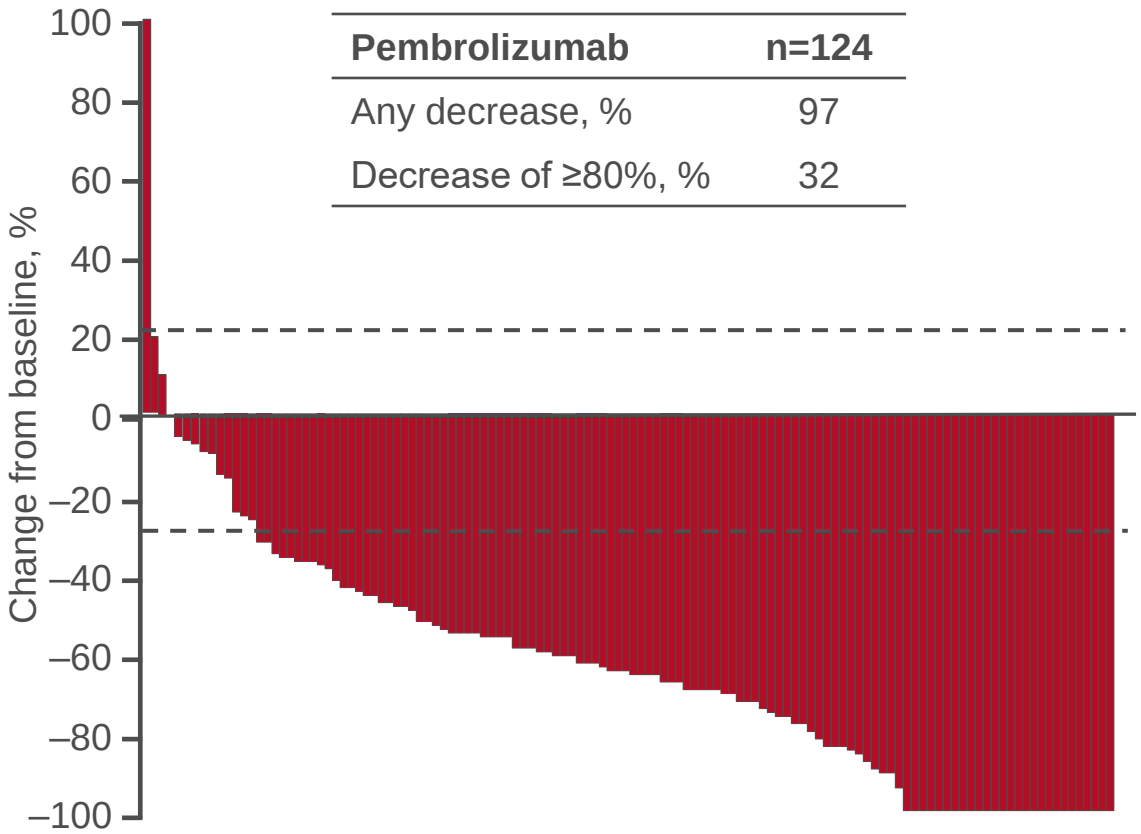
*Trastuzumab 6 mg/kg iv q3w following an 8 mg/kg loading dose; †5FU 800 mg/m$^2$ iv D1–5 q3w + cisplatin 80 mg/m$^2$ iv q3w; ‡capecitabine 1000 mg/m$^2$ bid D1–14 q3w + oxaliplatin 130 mg/m$^2$ iv q3w

Janjigian YY, et al. Ann Oncol 2021;32(suppl):abstr LBA-4

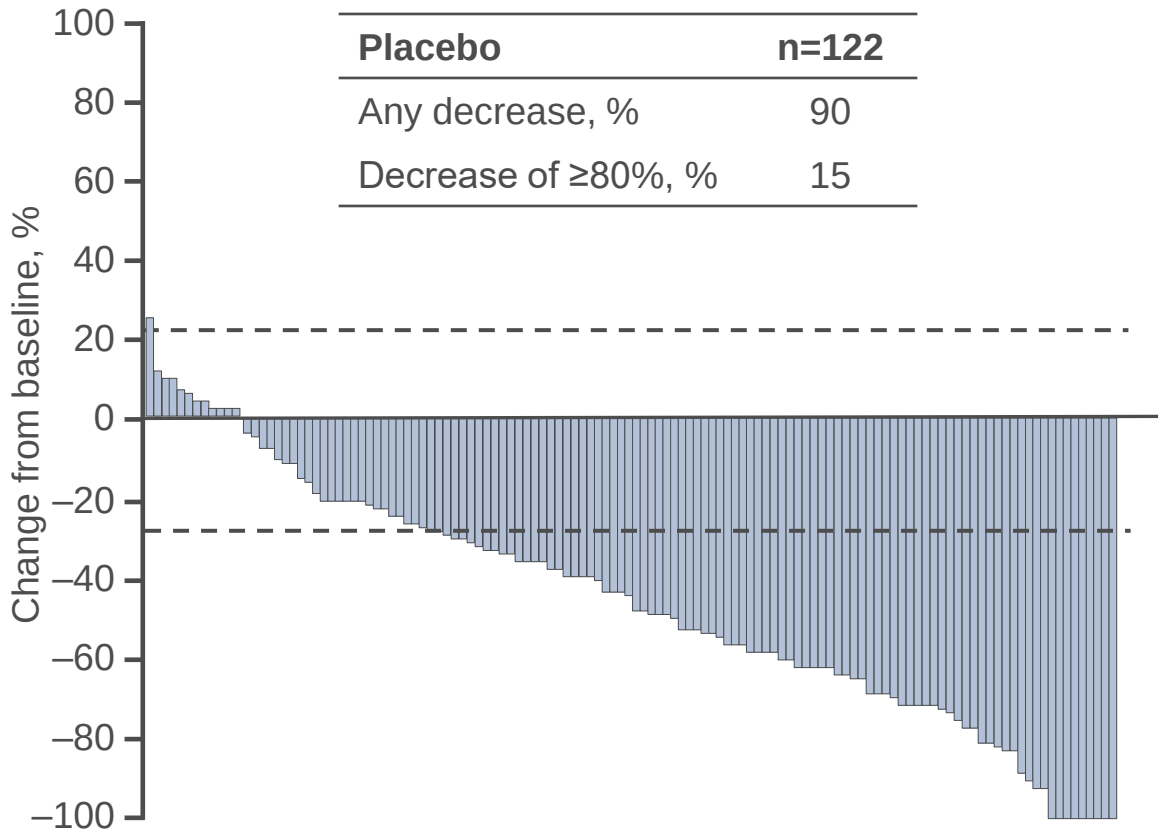
# LBA-4: Initial data from the phase 3 KEYNOTE-811 study of trastuzumab and chemotherapy with or without pembrolizumab for HER2-positive metastatic gastric or gastroesophageal junction (G/GEJ) cancer – Janjigian YY, et al

## Key results

### Best % change in target lesion size




| Pembrolizumab | n=124 |
|---|---|
| Any decrease, % | 97 |
| Decrease of ≥80%, % | 32 |




| Placebo | n=122 |
|---|---|
| Any decrease, % | 90 |
| Decrease of ≥80%, % | 15 |

Janjigian YY, et al. Ann Oncol 2021;32(suppl):abstr LBA-4

# LBA-4: Initial data from the phase 3 KEYNOTE-811 study of trastuzumab and chemotherapy with or without pembrolizumab for HER2-positive metastatic gastric or gastroesophageal junction (G/GEJ) cancer – Janjigian YY, et al

## Key results (cont.)

| | Pembrolizumab (n=133) | Placebo (n=131) |
|---|---|---|
| ORR, % (95%CI) | 74.4 (66.2, 81.6) | 51.9 (43.0, 60.7) |
| ORR difference, % (95%CI); p-value | 22.7 (11.2, 33.7); 0.00006 | |
| DCR, % (95%CI) | 96.2 (91.4, 98.8) | 89.3 (82.7, 94.0) |
| Median DoR, mo (range) | 10.6 (1.1+ to 16.5+) | 9.5 (1.4+ to 15.4+) |
| DoR ≥6 months, % | 70 | 61 |
| BOR, n (%) | | |
| CR | 15 (11) | 4 (3) |
| PR | 84 (63) | 64 (49) |
| SD | 29 (22) | 49 (37) |
| PD | 5 (4) | 7 (5) |
| NE | 0 | 2 (2) |
| NA | 0 | 5 (4) |

| | All-cause AEs | |
|---|---|---|
| | Pembrolizumab (n=217) | Placebo (n=216) |
| Any grade | 211 (97) | 212 (98) |
| Grade 3–5 | 124 (57) | 124 (57) |
| Serious | 68 (31) | 83 (38) |
| Led to discontinuation | 53 (24) | 56 (26) |
| Led to death | 7 (3) | 10 (5) |

## Conclusions

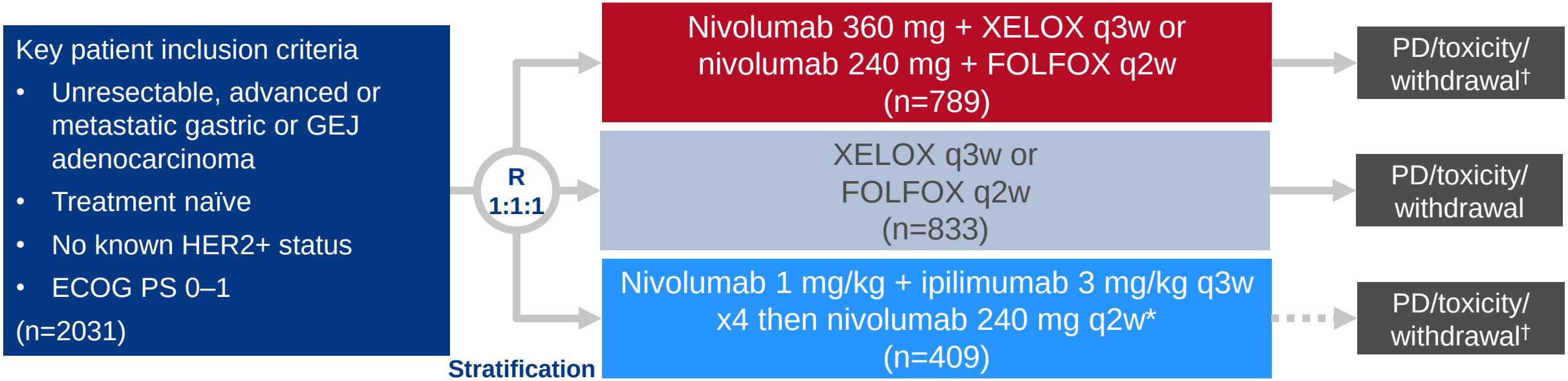
- **In patients with HER2-positive metastatic gastric or GEJ cancer, at interim analysis, pembrolizumab + trastuzumab + chemotherapy demonstrated promising and durable clinical responses and was generally well-tolerated**

Janjigian YY, et al. Ann Oncol 2021;32(suppl):abstr LBA-4

# LBA7: Nivolumab (NIVO) plus chemotherapy (chemo) or ipilimumab (IPI) vs chemo as first-line (1L) treatment for advanced gastric cancer/gastroesophageal junction cancer/ esophageal adenocarcinoma (GC/GEJC/EAC): CheckMate 649 study – Janjigian YY, et al

## Study objective

- To evaluate the efficacy and safety of 1L nivolumab + chemotherapy or ipilimumab in patients with advanced gastric or GEJ adenocarcinoma in the CheckMate 649 study




**Stratification**

- Tumour cell PD-L1 expression, region, ECOG PS, chemotherapy

### CO-PRIMARY ENDPOINTS

- OS, PFS (BICR, PD-L1 CPS ≥5)

### SECONDARY ENDPOINTS (HIERACHICAL)

- OS (PD-L1 CPS ≥1, all randomized patients)

XELOX: oxaliplatin 130 mg/m$^2$ iv D1 + capecitabine 1000 mg/m$^2$ bid D1–14
FOLFOX: oxaliplatin 85 mg/m$^2$ + leucovorin 400 mg/m$^2$ + FU 400 mg/m$^2$ iv D1 & FU 1200 mg/m$^2$ iv D1–2
*Unless consented to treatment beyond progression for nivolumab + chemotherapy or ipilimumab;
†nivolumab + ipilimumab arm stopped early based on DMC recommendation

Janjigian YY, et al. Ann Oncol 2021;32(suppl):abstr LBA7

# LBA7: Nivolumab (NIVO) plus chemotherapy (chemo) or ipilimumab (IPI) vs chemo as first-line (1L) treatment for advanced gastric cancer/gastroesophageal junction cancer/ esophageal adenocarcinoma (GC/GEJC/EAC): CheckMate 649 study – Janjigian YY, et al

## Key results

| | Nivolumab + chemotherapy | Chemotherapy |
|---|---|---|
| **PD-L1 CPS ≥5, n** | 473 | 482 |
| mOS, mo (95%CI) | 14.4 (13.1, 16.2) | 11.1 (10.0, 12.1) |
| HR (95%CI) | 0.70 (0.61, 0.81) | |
| mPFS, mo (95%CI) | 8.1 (7.0, 9.2) | 6.1 (5.6, 6.9) |
| HR (95%CI) | 0.70 (0.60, 0.81) | |
| mDoR, mo (95%CI) | 9.7 (8.2, 12.4) | 7.0 (5.6, 7.9) |
| **All randomized, n** | 789 | 792 |
| mOS, mo (95%CI) | 13.8 (12.4, 14.5) | 11.6 (10.9, 12.5) |
| HR (95%CI) | 0.79 (0.71, 0.88) | |
| mPFS, mo (95%CI) | 7.7 (7.1, 8.6) | 6.9 (6.7, 7.2) |
| HR (95%CI) | 0.79 (0.70, 0.89) | |
| mDoR, mo (95%CI) | 8.5 (7.7, 10.2) | 6.9 (5.8, 7.2) |

| | Nivolumab + ipilimumab | Chemotherapy |
|---|---|---|
| **PD-L1 CPS ≥5, n** | 234 | 239 |
| mOS, mo (95%CI) | 11.2 (9.2, 13.4) | 11.6 (10.1, 12.7) |
| HR (95%CI) | 0.89 (0.71, 1.10); p=0.2302 | |
| mPFS, mo (95%CI) | 2.8 (2.6, 4.0) | 6.3 (5.6, 7.1) |
| HR (95%CI) | 1.42 (1.14, 1.76) | |
| mDoR, mo (95%CI) | 13.2 (8.3, 18.3) | 6.9 (5.2, 7.6) |
| **All randomized, n** | 409 | 404 |
| mOS, mo (95%CI) | 11.7 (9.6, 13.5) | 11.8 (11.0, 12.7) |
| HR (95%CI) | 0.91 (0.77, 1.07) | |
| mPFS, mo (95%CI) | 2.8 (2.6, 3.6) | 7.1 (6.9, 8.2) |
| HR (95%CI) | 1.66 (1.40, 1.95) | |
| mDoR, mo (95%CI) | 13.8 (9.4, 17.7) | 6.8 (5.6, 7.2) |

Janjigian YY, et al. Ann Oncol 2021;32(suppl):abstr LBA7

# LBA7: Nivolumab (NIVO) plus chemotherapy (chemo) or ipilimumab (IPI) vs chemo as first-line (1L) treatment for advanced gastric cancer/gastroesophageal junction cancer/ esophageal adenocarcinoma (GC/GEJC/EAC): CheckMate 649 study – Janjigian YY, et al

## Key results (cont.)

| Grade 3/4 TRAEs, n (%) | Nivolumab + chemotherapy (n=782) | Chemotherapy (n=767) | Nivolumab + ipilimumab (n=403) | Chemotherapy (n=389) |
|---|---|---|---|---|
| Any | 471 (60) | 344 (45) | 155 (38) | 180 (46) |
| Serious | 133 (17) | 77 (10) | 93 (23) | 45 (12) |
| Led to discontinuation | 141 (18) | 70 (9) | 68 (17) | 37 (10) |
| Led to death | 16 (2) | 4 (<1) | 10 (2) | 3 (<1) |

## Conclusions

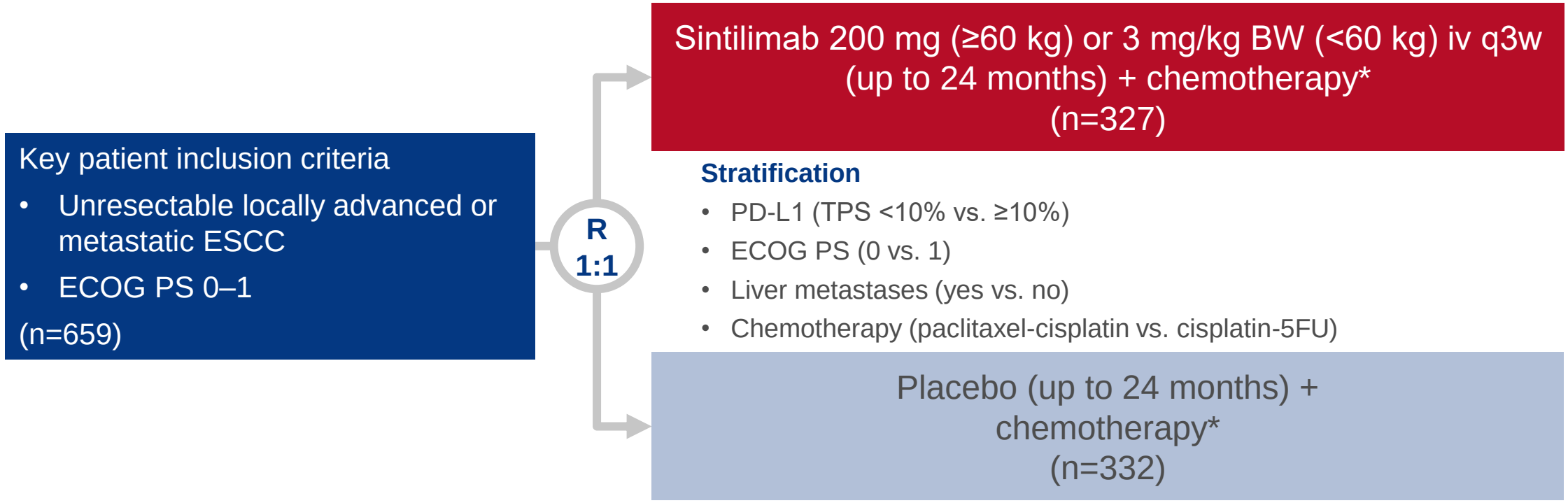
- **In patients advanced gastric or GEJ adenocarcinoma, 1L nivolumab + chemotherapy continued to provide improvements in survival and other outcomes compared with chemotherapy alone and no new safety signals were reported**

Janjigian YY, et al. Ann Oncol 2021;32(suppl):abstr LBA7

# LBA52: Sintilimab plus chemotherapy versus chemotherapy as first-line therapy in patients with advanced or metastatic esophageal squamous cell cancer: first results of the phase 3 ORIENT-15 study – Shen L, et al

## Study objective

- To evaluate the efficacy and safety of 1L sintilimab + chemotherapy in patients with advanced or metastatic ESCC in the ORIENT-15 study




**CO-PRIMARY ENDPOINTS**

- OS in CPS ≥10 and all randomized patients

**SECONDARY ENDPOINTS**

- PFS, ORR, DCR, DoR, safety

*Paclitaxel 175 mg/m$^2$ + cisplatin 75 mg/m$^2$ or cisplatin 75 mg/m$^2$ + 5FU 800 mg/m$^2$ D1–5 for a maximum of 6 cycles

Shen L, et al. Ann Oncol 2021;32(suppl):abstr LBA52

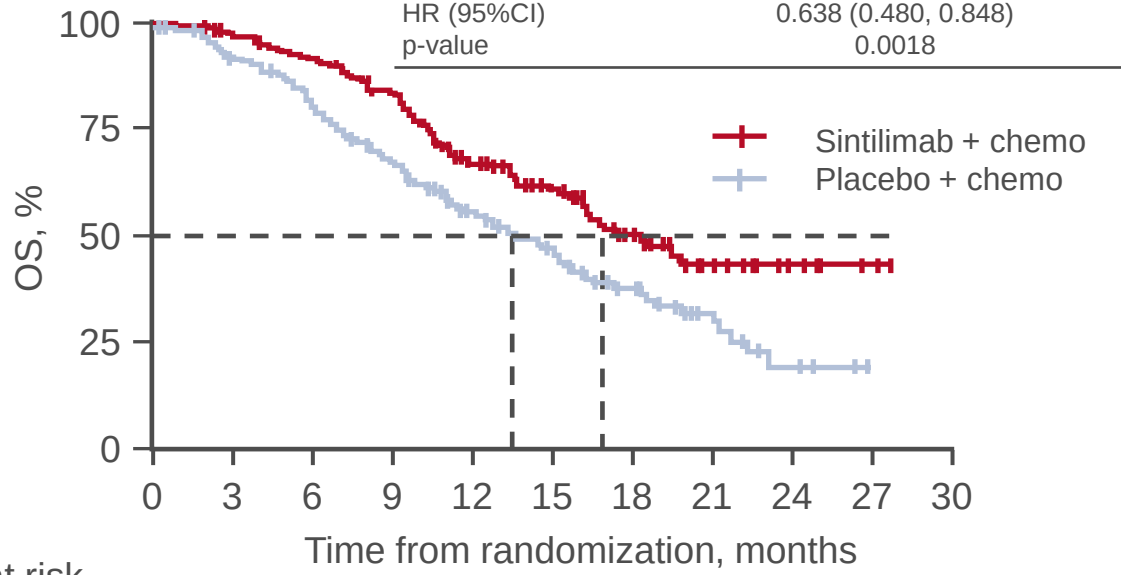
# LBA52: Sintilimab plus chemotherapy versus chemotherapy as first-line therapy in patients with advanced or metastatic esophageal squamous cell cancer: first results of the phase 3 ORIENT-15 study – Shen L, et al

## Key results

### Overall survival

#### PD-L1 CPS ≥10

| | Sintilimab + chemo (n=188) | Placebo + chemo (n=193) |
|---|---|---|
| mOS, mo (95%CI) | 17.2 (15.5, NC) | 13.6 (11.3, 15.7) |
| HR (95%CI) | 0.638 (0.480, 0.848) | |
| p-value | 0.0018 | |

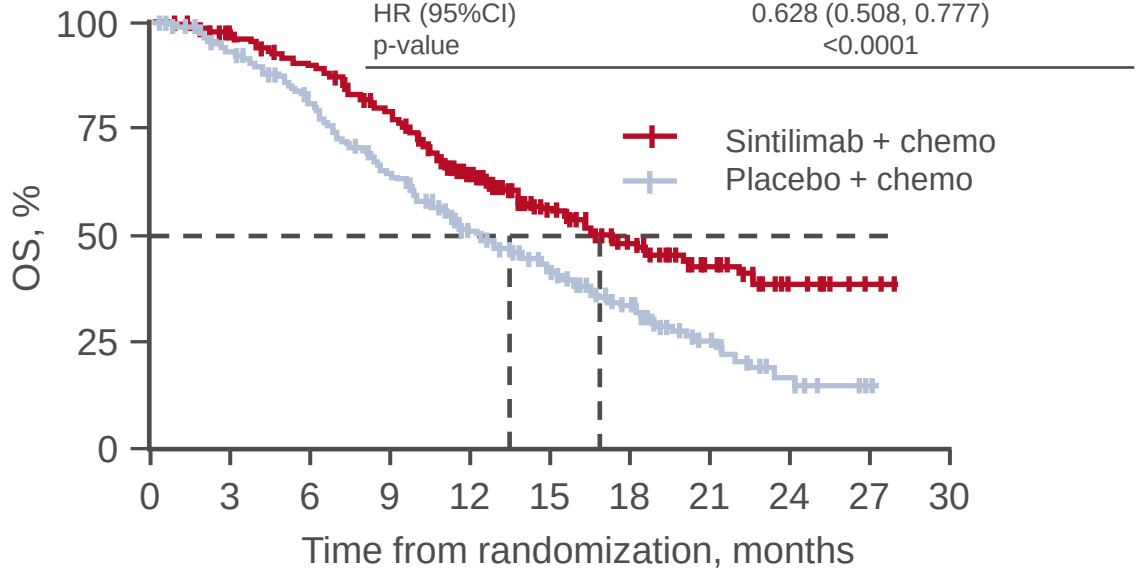



No. at risk

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Sintilimab + chemo | 188 | 178 | 167 | 146 | 96 | 65 | 33 | 14 | 6 | 1 | 0 |
| Placebo + chemo | 193 | 174 | 151 | 122 | 82 | 57 | 31 | 13 | 5 | 0 | 0 |

#### All patients

| | Sintilimab + chemo (n=327) | Placebo + chemo (n=332) |
|---|---|---|
| mOS, mo (95%CI) | 16.7 (14.8, 21.7) | 12.5 (11.0, 14.5) |
| HR (95%CI) | 0.628 (0.508, 0.777) | |
| p-value | <0.0001 | |




| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Sintilimab + chemo | 327 | 305 | 283 | 240 | 161 | 105 | 52 | 25 | 11 | 2 | 0 |
| Placebo + chemo | 332 | 300 | 258 | 202 | 127 | 88 | 45 | 17 | 6 | 0 | 0 |

Shen L, et al. Ann Oncol 2021;32(suppl):abstr LBA52

# LBA52: Sintilimab plus chemotherapy versus chemotherapy as first-line therapy in patients with advanced or metastatic esophageal squamous cell cancer: first results of the phase 3 ORIENT-15 study – Shen L, et al

## Key results (cont.)

| | Sintilimab + chemo | Placebo + chemo |
|---|---|---|
| PD-L1 CPS ≥10, n | 188 | 193 |
| mPFS, mo (95%CI) | 8.3 (6.9, 12.4) | 6.4 (5.5, 6.9) |
| HR (95%CI); p-value | 0.580 (0.449, 0.749); <0.0001 | |
| All patients, n | 327 | 332 |
| mPFS, mo (95%CI) | 7.2 (7.0, 9.6) | 5.7 (5.5, 6.8) |
| HR (95%CI); p-value | 0.558 (0.461, 0.676); <0.0001 | |
| ORR, n/N (%) | 216/327 (66.1) | 151/332 (45.5) |
| Difference (95%CI); p-value | 20.2 (12.9, 27.6); <0.0001 | |
| Response, n | 216 | 151 |
| mDoR, mo (95%CI) | 9.7 (7.1, 13.7) | 6.9 (5.6, 7.2) |
| HR (95%CI) | 0.616 (0.473, 0.803) | |

| TRAEs, n (%) | Sintilimab + chemo (n=327) | Placebo + chemo (n=332) |
|---|---|---|
| Any | 321 (98.2) | 326 (98.2) |
| Grade ≥3 | 196 (59.9) | 181 (54.5) |
| Serious | 90 (27.5) | 68 (20.5) |
| Led to discontinuation | 68 (20.8) | 41 (12.3) |
| Led to death | 9 (2.8) | 6 (1.8) |

## Conclusions

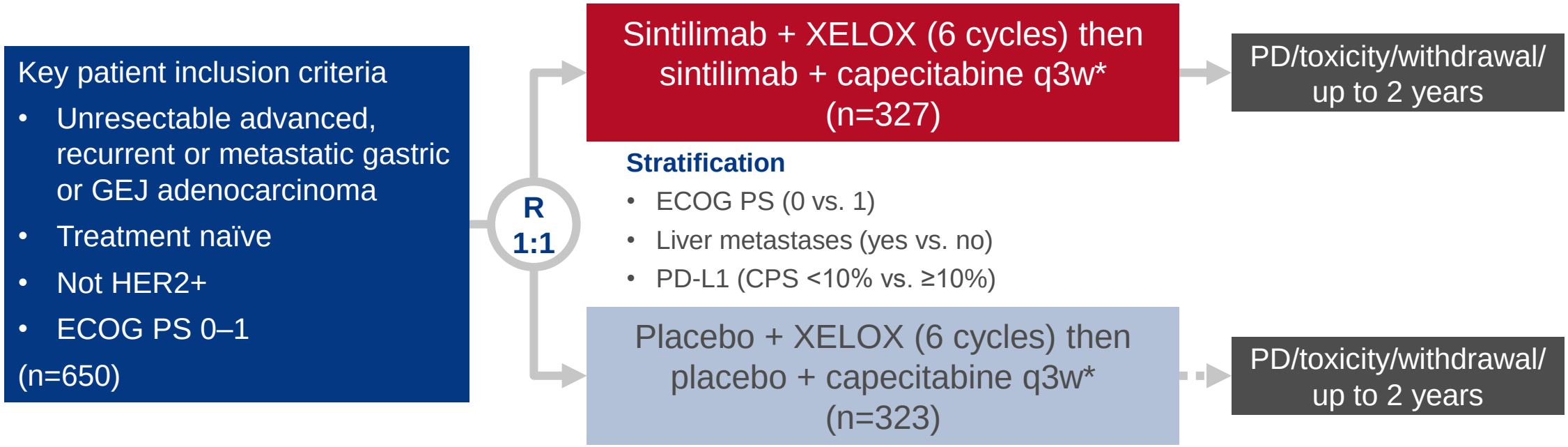
- **In patients with advanced or metastatic ESCC, 1L sintilimab + chemotherapy demonstrated significant survival benefit over chemotherapy alone regardless of PD-L1 expression level and no new safety signals were observed**

Shen L, et al. Ann Oncol 2021;32(suppl):abstr LBA52

# LBA53: Sintilimab plus chemotherapy (chemo) versus chemo as first-line treatment for advanced gastric or gastroesophageal junction (G/GEJ) adenocarcinoma (ORIENT-16): first results of a randomized, double-blind, phase 3 study – Xu J, et al

## Study objective

- To evaluate the efficacy and safety of 1L sintilimab + chemotherapy in patients with gastric or GEJ adenocarcinoma in the ORIENT-16 study




### CO-PRIMARY ENDPOINTS

- OS in CPS ≥10 and all randomized patients

### SECONDARY ENDPOINTS

- PFS, ORR, DCR, DoR, safety

*Sintilimab 3 mg/kg BW <60 kg or 200 mg ≥60 kg; oxaliplatin 130 mg/m$^2$; capecitabine 1000 mg/m$^2$ bid D1–14

Xu J, et al. Ann Oncol 2021;32(suppl):abstr LBA53

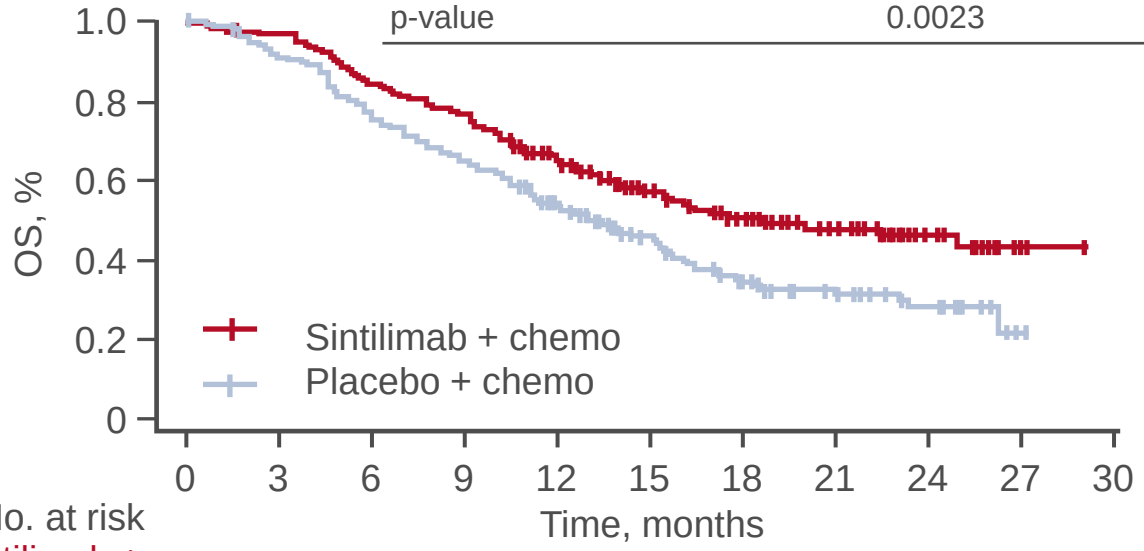
# LBA53: Sintilimab plus chemotherapy (chemo) versus chemo as first-line treatment for advanced gastric or gastroesophageal junction (G/GEJ) adenocarcinoma (ORIENT-16): first results of a randomized, double-blind, phase 3 study – Xu J, et al

## Key results

### Overall survival

#### PD-L1 CPS ≥5

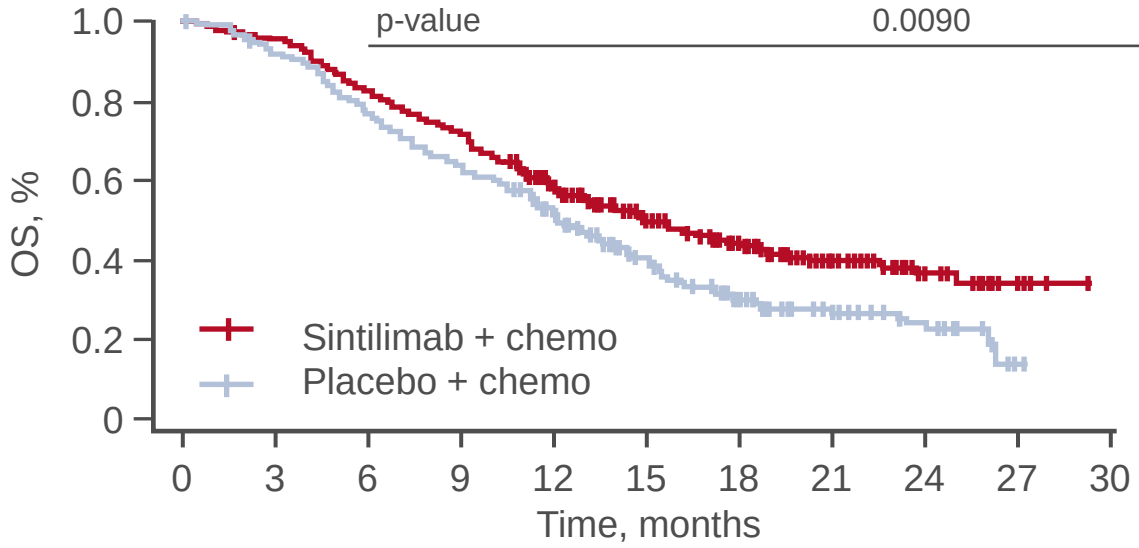
| | Sintilimab + chemo (n=197) | Placebo + chemo (n=200) |
|---|---|---|
| mOS, mo (95%CI) | 18.4 (14.6, NC) | 12.9 (11.1, 15.4) |
| HR (95%CI) | 0.660 (0.505, 0.864) | |
| p-value | 0.0023 | |




| No. at risk | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Sintilimab + chemo | 197 | 191 | 166 | 151 | 106 | 79 | 61 | 39 | 18 | 2 | 0 |
| Placebo + chemo | 200 | 181 | 150 | 128 | 91 | 60 | 39 | 26 | 16 | 1 | 0 |

#### All randomized

| | Sintilimab + chemo (n=327) | Placebo + chemo (n=323) |
|---|---|---|
| mOS, mo (95%CI) | 15.2 (12.9, 18.4) | 12.3 (11.3, 13.8) |
| HR (95%CI) | 0.766 (0.626, 0.936) | |
| p-value | 0.0090 | |




| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Sintilimab + chemo | 327 | 311 | 269 | 234 | 163 | 115 | 86 | 47 | 19 | 3 | 0 |
| Placebo + chemo | 323 | 295 | 246 | 205 | 142 | 88 | 51 | 31 | 19 | 1 | 0 |

Xu J, et al. Ann Oncol 2021;32(suppl):abstr LBA53

# LBA53: Sintilimab plus chemotherapy (chemo) versus chemo as first-line treatment for advanced gastric or gastroesophageal junction (G/GEJ) adenocarcinoma (ORIENT-16): first results of a randomized, double-blind, phase 3 study – Xu J, et al

## Key results (cont.)

| | Sintilimab + chemo | Placebo + chemo |
|---|---|---|
| PD-L1 CPS ≥10, n | 197 | 200 |
| mPFS, mo (95%CI) | 7.7 (6.9, 9.7) | 5.8 (5.5, 6.9) |
| HR (95%CI); p-value | 0.628 (0.489, 0.805); 0.0002 | |
| All patients, n | 327 | 323 |
| mPFS, mo (95%CI) | 7.1 (6.9, 8.5) | 5.7 (5.5, 6.9) |
| HR (95%CI); p-value | 0.636 (0.525, 0.771); <0.0001 | |
| ORR, % (95%CI) | 58.2 (52.3, 64.2) | 48.4 (42.3, 54.6) |
| Response, n | 152 | 123 |
| Events, n (%) | 75 (49.3) | 93 (75.6) |
| mDoR, mo (95%CI) | 9.8 (8.3, 17.4) | 7.0 (5.5, 8.3) |

| TRAEs, n (%) | Sintilimab + chemo (n=328) | Placebo + chemo (n=320) |
|---|---|---|
| Any | 319 (97.3) | 308 (96.3) |
| Grade ≥3 | 196 (59.8) | 168 (52.5) |
| Serious | 86 (26.2) | 70 (21.9) |
| Led to discontinuation | 38 (11.6) | 25 (7.8) |
| Led to interruption | 245 (74.7) | 223 (69.7) |
| Led to death | 6 (1.8) | 2 (0.6) |

## Conclusions

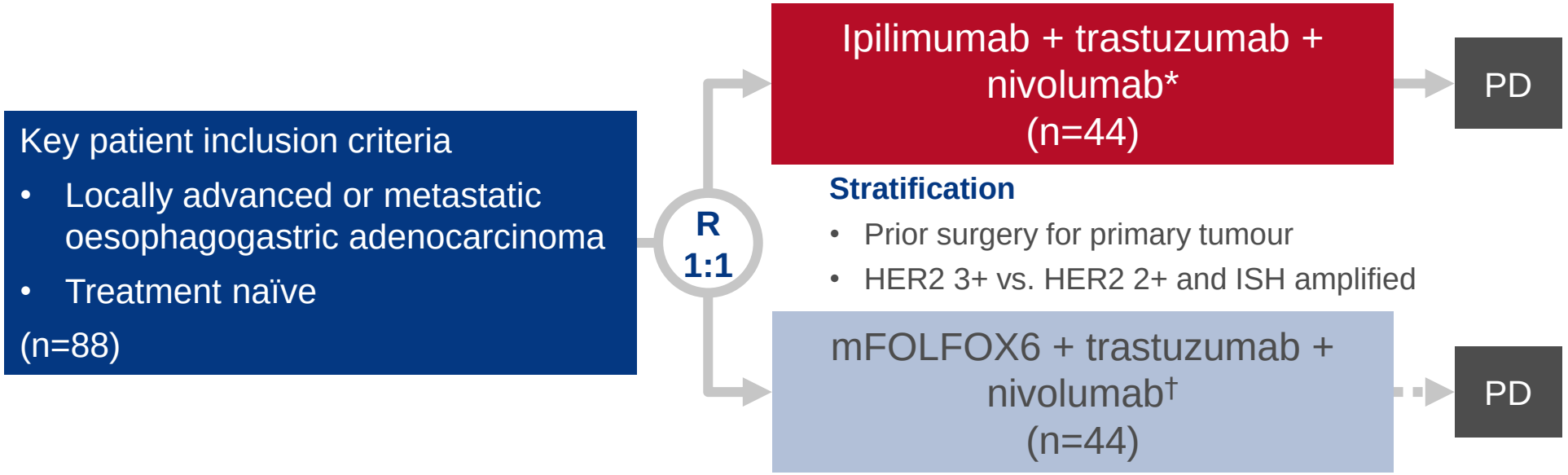
- **In patients with advanced gastric or GEJ adenocarcinoma, 1L sintilimab + chemotherapy demonstrated significant survival benefit over chemotherapy alone and had a manageable safety profile**

Xu J, et al. Ann Oncol 2021;32(suppl):abstr LBA53

# LBA54: Ipilimumab or FOLFOX in combination with nivolumab and trastuzumab in previously untreated HER2 positive locally advanced or metastatic esophagogastric adenocarcinoma (EGA) – results of the randomized phase 2 INTEGA trial (AIO STO 0217) – Stein A, et al

## Study objective

- To evaluate the efficacy and safety of 1L ipilimumab or mFOLFOX6 combined with trastuzumab + nivolumab in patients with HER2+ locally advanced or metastatic oesophagogastric adenocarcinoma in the INTEGA study




**PRIMARY ENDPOINT**

- 12-month OS rate

**SECONDARY ENDPOINTS**

- PFS, ORR, DoR, QoL, safety

*Ipilimumab 3 mg/kg + trastuzumab 6 mg/kg (loading dose 8 mg/kg) + nivolumab 1 mg/kg q3w (weeks 1–12) then trastuzumab 4 mg/kg + nivolumab 240 mg q2w; †oxaliplatin 85 mg/m$^2$ + 5FU 400 mg/m$^2$ iv bolus + folinic acid 400 mg/m$^2$ + 5FU 2400 mg/m$^2$ 46 h iv + trastuzumab 4 mg/kg (loading dose 6 mg/kg) + nivolumab 240 mg q2w

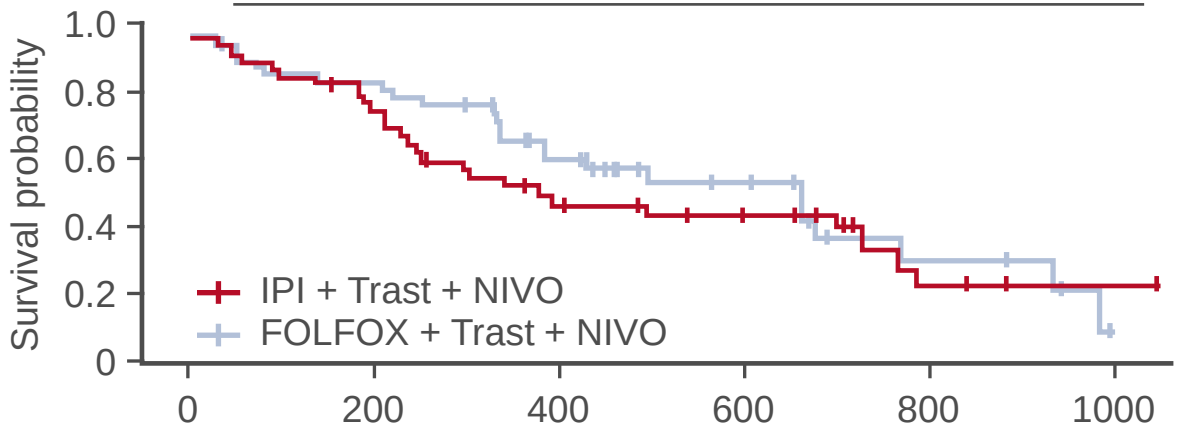
Stein A, et al. Ann Oncol 2021;32(suppl):abstr LBA54

# LBA54: Ipilimumab or FOLFOX in combination with nivolumab and trastuzumab in previously untreated HER2 positive locally advanced or metastatic esophagogastric adenocarcinoma (EGA) – results of the randomized phase 2 INTEGA trial (AIO STO 0217) – Stein A, et al

## Key results

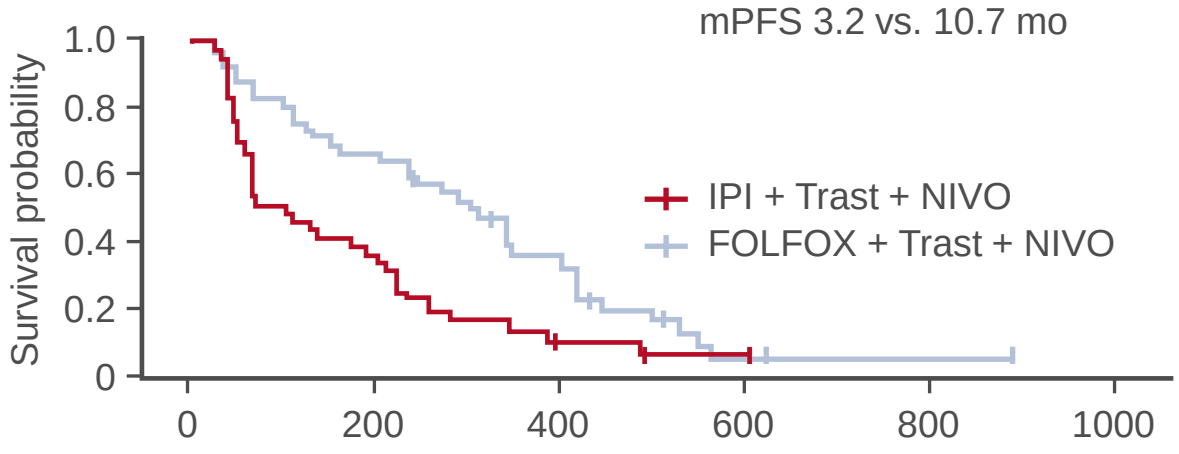
### Overall survival

| | 12-mo OS rate, % | mO, mo |
|---|---|---|
| IPI + Trast + NIVO | 57% | 16.4 |
| FOLFOX + Trast + NIVO | 70% | 21.8 |




| No. at risk | | | | | | |
|---|---|---|---|---|---|---|
| IPI + Trast + NIVO | 44 | 33 | 19 | 14 | 5 | 1 |
| FOLFOX + Trast + NIVO | 44 | 38 | 24 | 13 | 6 | 1 |

### Progression free survival




| No. at risk | | | | | | |
|---|---|---|---|---|---|---|
| IPI + Trast + NIVO | 42 | 13 | 3 | 1 | 0 | |
| FOLFOX + Trast + NIVO | 43 | 29 | 12 | 2 | 1 | 0 |

Stein A, et al. Ann Oncol 2021;32(suppl):abstr LBA54

# LBA54: Ipilimumab or FOLFOX in combination with nivolumab and trastuzumab in previously untreated HER2 positive locally advanced or metastatic esophagogastric adenocarcinoma (EGA) – results of the randomized phase 2 INTEGA trial (AIO STO 0217) – Stein A, et al

## Key results (cont.)

| | ITT | | CPS ≥1 | | CPS ≥5 | | HER2+ central | |
|---|---|---|---|---|---|---|---|---|
| | IPI (n=44) | FOLFOX (n=44) | IPI (n=31) | FOLFOX (n=28) | IPI (n=24) | FOLFOX (n=22) | IPI (n=40) | FOLFOX (n=36) |
| ORR, % | 32 | 56 | 36 | 63 | 33 | 67 | 35 | 63 |
| mPFS, mo | 3.2 | 10.7 | 2.2 | 10.7 | 2.2 | 11.0 | 3.4 | 10.7 |
| 12-mo PFS rate, % | 15 | 37 | 14 | 33 | 7 | 38 | 17 | 36 |
| mDoR, mo | 5.8 | 9.2 | - | - | - | - | - | - |
| mOS, mo | 16.4 | 21.8 | 16.4 | 21.6 | 12.5 | 21.6 | 16.4 | 22.4 |
| 12-mo OS rate, % | 57 | 70 | 54 | 71 | 53 | 72 | 58 | 74 |

| Grade ≥3 TRAEs occurring in ≥10%, n (%) | Ipilimumab + Trast + NIVO (n=44) | FOLFOX + Trast + NIVO (n=43) |
|---|---|---|
| Any | 20 (46) | 29 (67) |
| Diarrhoea | 6 (14) | 2 (5) |
| Anaemia | 5 (11) | 3 (7) |
| Infection | 5 (11) | 7 (16) |
| Fatigue | 3 (7) | 6 (14) |
| Leukopenia | 2 (5) | 10 (23) |
| Neuropathy | 0 | 5 (11) |

## Conclusions

- **In patients with HER2+ locally advanced or metastatic oesophagogastric adenocarcinoma, both 1L ipilimumab or FOLFOX combined with trastuzumab + nivolumab were feasible, although the FOLFOX arm demonstrated a higher 12-month OS rate than the ipilimumab arm**

Stein A, et al. Ann Oncol 2021;32(suppl):abstr LBA54

# LBA55: Primary analysis of a phase 2 single-arm trial of trastuzumab deruxtecan (T-DXd) in Western patients (pts) with HER2-positive (HER2+) unresectable or metastatic gastric or gastroesophageal junction (GEJ) cancer who progressed on or after a trastuzumab-containing regimen – Van Cutsem E, et al

## Study objective

- To evaluate the efficacy and safety of trastuzumab deruxtecan in patients with HER2+ unresectable or metastatic gastric or GEJ cancer who had progressed on or after a trastuzumab-containing regimen in the DESTINY-Gastric02 study

Key patient inclusion criteria

- Unresectable or metastatic gastric or GEJ cancer
- HER2+ (IHC3+ or IHC2+/ISH+) after progression on 1L trastuzumab-containing regimen
- ECOG PS 0–1

(n=79)

→ T-DXd 6.4 mg/kg q3w

**PRIMARY ENDPOINT**

- ORR (ICR)

**SECONDARY ENDPOINTS**

- PFS, OS, DoR, safety

Van Cutsem E, et al. Ann Oncol 2021;32(suppl):abstr LBA55

# LBA55: Primary analysis of a phase 2 single-arm trial of trastuzumab deruxtecan (T-DXd) in Western patients (pts) with HER2-positive (HER2+) unresectable or metastatic gastric or gastroesophageal junction (GEJ) cancer who progressed on or after a trastuzumab-containing regimen – Van Cutsem E, et al

## Key results

| | n=79 |
|---|---|
| ORR, n (%) [95%CI] | 30 (38) [27.3, 49.6] |
| BOR, n (%) | |
| CR | 3 (3.8) |
| PR | 27 (34.2) |
| SD | 34 (43.0) |
| PD | 13 (16.5) |
| NE | 2 (2.5) |
| mDoR, mo (95%CI) | 8.1 (4.1, NE) |
| DCR, n (%) [95%CI] | 64 (81.0) [70.6, 89.0] |
| mTTR, mo (95%CI) | 1.4 (1.4, 2.6) |
| mPFS, mo (95%CI) | 5.5 (4.2, 7.3) |
| Median follow-up, mo (range) | 5.7 (0.7–15.2) |

| TRAEs, n (%) | n=79 |
|---|---|
| Any | 74 (93.7) |
| Grade ≥3 | 21 (26.6) |
| Serious | 8 (10.1) |
| Led to discontinuation | 7 (8.9) |
| Led to dose reduction | 15 (19.0) |
| Led to death | 1 (1.3) |

## Conclusions

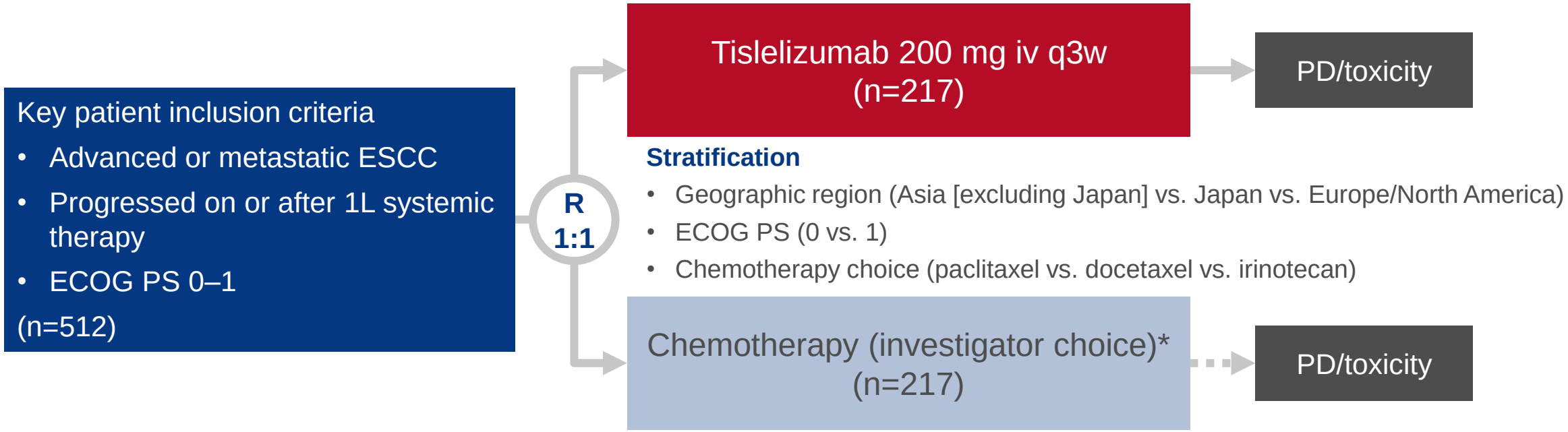
- **In patients with HER2+ unresectable or metastatic gastric or GEJ cancer, 2L trastuzumab deruxtecan demonstrated encouraging activity with durable responses and a safety profile comparable with previous findings**

Van Cutsem E, et al. Ann Oncol 2021;32(suppl):abstr LBA55

# O-15: Randomized, phase 3 study of second-line tislelizumab vs chemotherapy in advanced or metastatic esophageal squamous cell carcinoma (RATIONALE 302) in the overall population and Europe/North America subgroup – Ajani J, et al

## Study objective

- To evaluate the efficacy and safety of 2L tislelizumab, an anti-PD-1, in patients with advanced or metastatic oesophageal squamous cell carcinoma in the RATIONALE 302 study




**PRIMARY ENDPOINT**

- OS

**SECONDARY ENDPOINTS**

- PFS, ORR, DoR, HRQoL, safety

*Paclitaxel 135–175 mg/m$^2$ iv q3w or 80–100 mg/m$^2$ iv qw; docetaxel 75 mg/m$^2$ iv q3w; irinotecan 125 mg/m$^2$ D1, 8 q3w

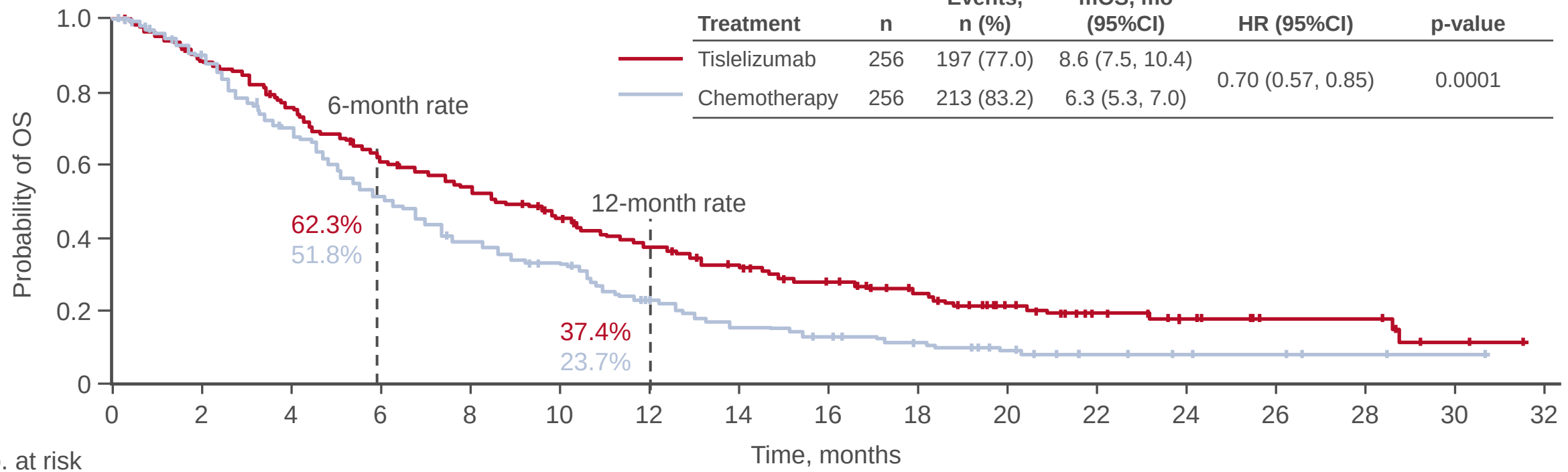
Ajani J, et al. Ann Oncol 2021;32(suppl):abstr O-15

# O-15: Randomized, phase 3 study of second-line tislelizumab vs chemotherapy in advanced or metastatic esophageal squamous cell carcinoma (RATIONALE 302) in the overall population and Europe/North America subgroup – Ajani J, et al

## Key results

### Overall survival

| Treatment | n | Events, n (%) | mOS, mo (95%CI) | HR (95%CI) | p-value |
|---|---|---|---|---|---|
| Tislelizumab | 256 | 197 (77.0) | 8.6 (7.5, 10.4) | 0.70 (0.57, 0.85) | 0.0001 |
| Chemotherapy | 256 | 213 (83.2) | 6.3 (5.3, 7.0) | | |




No. at risk

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Tislelizumab | 256 | 245 | 226 | 214 | 191 | 172 | 157 | 144 | 134 | 122 | 110 | 96 | 88 | 81 | 73 | 63 | 59 | 52 | 44 | 35 | 30 | 25 | 20 | 18 | 13 | 11 | 8 | 8 | 8 | 3 | 2 | 1 | 0 |
| Chemo | 256 | 235 | 219 | 191 | 167 | 143 | 124 | 105 | 93 | 83 | 77 | 59 | 51 | 42 | 36 | 34 | 29 | 26 | 21 | 19 | 15 | 11 | 7 | 6 | 5 | 4 | 4 | 2 | 2 | 1 | 1 | 0 | 0 |

Ajani J, et al. Ann Oncol 2021;32(suppl):abstr O-15

# O-15: Randomized, phase 3 study of second-line tislelizumab vs chemotherapy in advanced or metastatic esophageal squamous cell carcinoma (RATIONALE 302) in the overall population and Europe/North America subgroup – Ajani J, et al

## Key results (cont.)

| | Overall population | | EU/N American population | |
|---|---|---|---|---|
| | Tislelizumab (n=256) | Chemotherapy (n=256) | Tislelizumab (n=55) | Chemotherapy (n=53) |
| mOS, mo (95%CI) | 8.6 (7.5, 10.4) | 6. (5.3, 7.0) | 11.2 (5.9, 14.8) | 6.3 (4.6, 7.7) |
| HR (95%CI) | 0.70 (0.57, 0.85) | | 0.55 (0.35, 0.87) | |
| mPFS, mo (95%CI) | 1.6 (1.4, 2.7) | 2.1 (1.5, 1.7) | - | - |
| HR (95%CI) | 0.83 (0.67, 1.01) | | 0.97 (0.64, 1.47) | |
| ORR, n (%) [95%CI] | 52 (20.3) [15.6, 25.8] | 25 (9.8) [6.4, 14.1] | 11 (20) [10.4, 33.0] | 6 (11.3) [4.3, 23.0] |
| OR (95%CI) | 2.4 (1.4, 4.0) | | 2 (0.7, 5.8) | |
| BOR, n (%) | | | | |
| CR | 5 (2.0) | 1 (0.4) | 2 (3.6) | 0 |
| PR | 47 (18.4) | 24 (9.4) | 9 (16.4) | 6 (11.3) |
| SD | 68 (26.6) | 82 (32.0) | 17 (30.9) | 20 (37.7) |
| PD | 116 (45.3) | 86 (33.6) | 23 (41.8) | 16 (30.2) |
| mDoR, mo (95%CI) | 7.1 (4.1, 11.3) | 4.0 (2.1, 8.2) | 5.1 (1.6, NE) | 2.1 (1.3, 6.3) |

| AEs, n (%) | Overall population | |
|---|---|---|
| | Tislelizumab (n=255) | Chemotherapy (n=240) |
| ≥1 TEAE | 244 (95.7) | 236 (98.3) |
| Grade 3–5 | 118 (46.3) | 163 (67.9) |
| Serious | 105 (41.2) | 105 (43.8) |
| Led to discontinuation | 49 (19.2) | 64 (26.7) |
| Led to death | 14 (5.5) | 14 (5.8) |
| TRAEs occuring in ≥20% | | |
| Anaemia | 28 (11.0) | 83 (34.6) |
| Appetite decreased | 16 (6.3) | 75 (31.3) |
| Diarrhoea | 14 (5.5) | 66 (27.5) |
| Nausea | 7 (2.7) | 66 (27.5) |
| WBC count decresed | 5 (2.0) | 98 (40.8) |
| Neutrophil count decreased | 3 (1.2) | 94 (39.2) |

## Conclusions

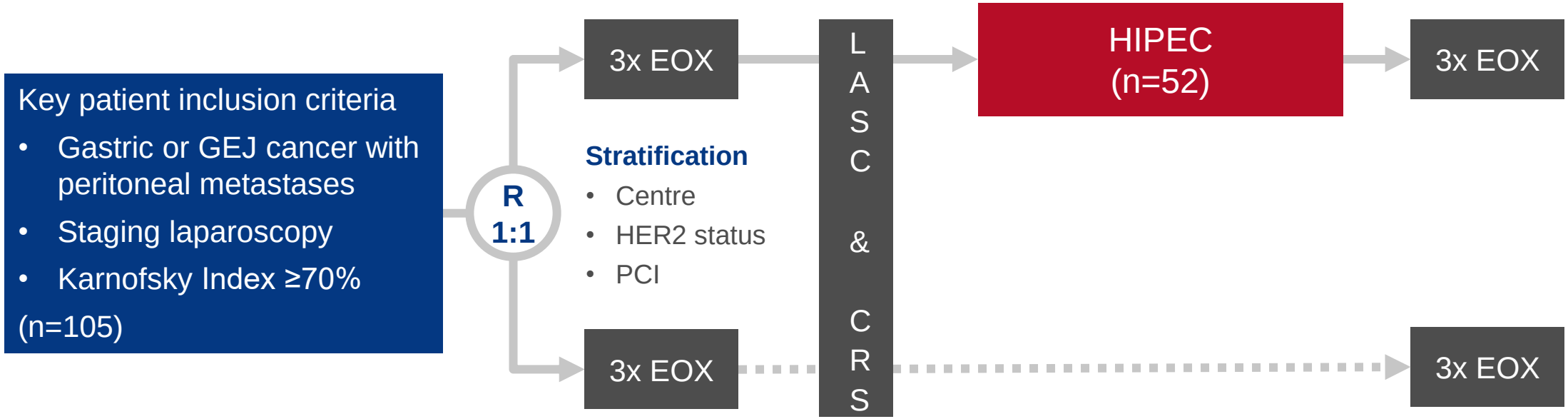
- **In patients with advanced or metastatic ESCC, 2L tislelizumab demonstrated significant improvement in OS compared with chemotherapy in the overall and EU/North American populations with a manageable safety profile**

Ajani J, et al. Ann Oncol 2021;32(suppl):abstr O-15

# 1376O: The effect of hyperthermic intraperitoneal chemotherapy (HIPEC) upon cytoreductive surgery (CRS) in gastric cancer (GC) with synchronous peritoneal metastasis (PM): a randomized multicentre phase III trial (GASTRIPEC-I-trial) – Rau B, et al

## Study objective

- To evaluate the impact of HIPEC upon CRS in patients with gastric cancer and synchronous peritoneal metastases in the GASTRIPEC-I study*




### PRIMARY ENDPOINT

- OS

### SECONDARY ENDPOINTS

- PFS, DFS, QoL, safety

HER2-, epirubicin 50 mg/m$^2$ + oxaliplatin 130 mg/m$^2$ + capecitabine 635 mg/m$^2$ q3w
HER2+, cisplatin 80 mgm$^2$ + capecitabine 1000 mg/m$^2$ + trastuzumab 8, 6, 6 mg/kg (3 cycles) q3w
HIPEC, cisplatin 75 mg/m$^2$ ip + mitomycin 15 mg/m$^2$ ip, 60 min >41°C
*Study was terminated early due to slow accrual

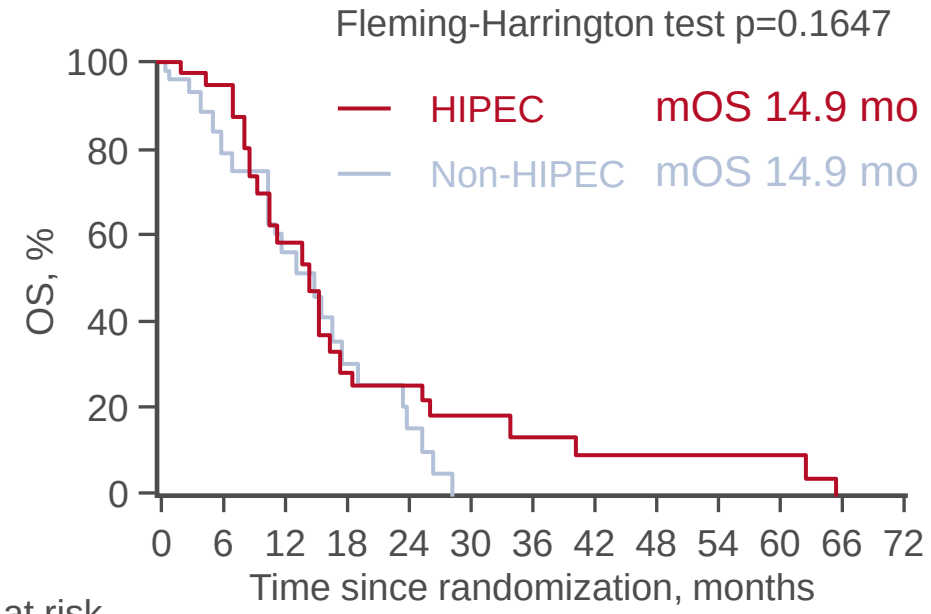
Rau B, et al. Ann Oncol 2021;32(suppl):abstr 1376O

# 1376O: The effect of hyperthermic intraperitoneal chemotherapy (HIPEC) upon cytoreductive surgery (CRS) in gastric cancer (GC) with synchronous peritoneal metastasis (PM): a randomized multicentre phase III trial (GASTRIPEC-I-trial) – Rau B, et al

## Key results

### Overall survival

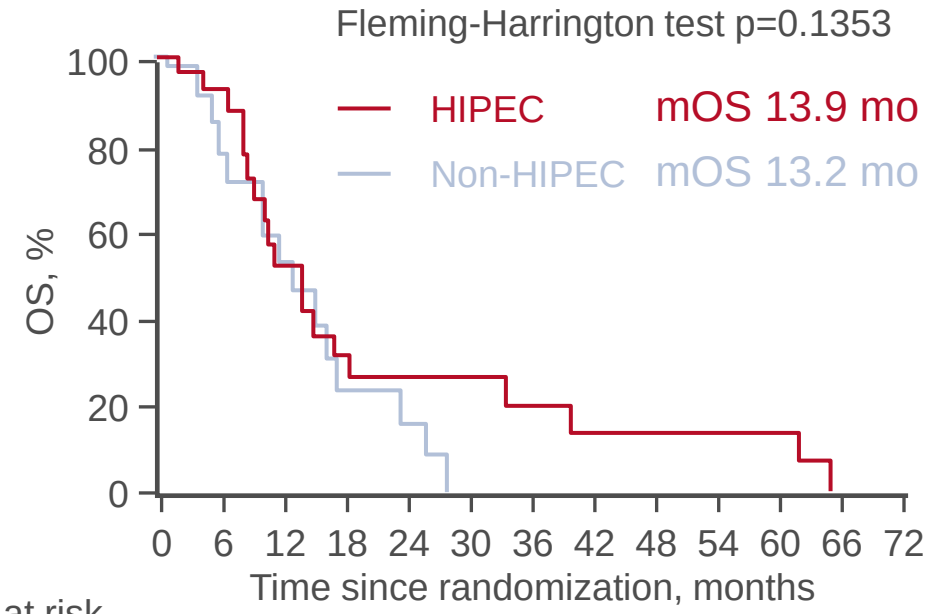
#### FAS




No. at risk

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| HIPEC | 52 | 27 | 16 | 8 | 7 | 4 | 3 | 2 | 2 | 2 | 2 | 0 |
| Non-HIPEC | 53 | 18 | 13 | 6 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

#### PP




No. at risk

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| HIPEC | 36 | 19 | 10 | 6 | 5 | 4 | 3 | 2 | 2 | 2 | 2 | 0 |
| Non-HIPEC | 39 | 13 | 9 | 3 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Rau B, et al. Ann Oncol 2021;32(suppl):abstr 1376O

# 1376O: The effect of hyperthermic intraperitoneal chemotherapy (HIPEC) upon cytoreductive surgery (CRS) in gastric cancer (GC) with synchronous peritoneal metastasis (PM): a randomized multicentre phase III trial (GASTRIPEC-I-trial) – Rau B, et al

## Key results (cont.)

| Resectability, n (%) | HIPEC (n=41) | Non-HIPEC (n=35) |
|---|---|---|
| Non-resectable | 11 (26.8) | 13 (37.1) |
| CCR 0 | 20 (48.8) | 16 (45.7) |
| CCR 1 | 10 (24.3) | 4 (11.4) |
| CCR ≥2 | 0 | 2 (5.7) |

| | HIPEC | Non-HIPEC |
|---|---|---|
| mOS, mo | | |
| CCR 0 | 15.4 | 16.6 |
| CCR ≥1 | 14.8 | 6.5 |
| mPFS, mo | | |
| FAS | 7.1 | 3.5 |
| PP | 7.1 | 3.5 |

| Post-operative complications | | HIPEC (CRS+HIPEC n=28; HIPEX n=13) | Non-HIPEC (CRS n=22) |
|---|---|---|---|
| Hospitalization | Mean, days (range) | 13.5 (7.0–29.1) | 15.1 (8.4–26.4) |
| Grade 3/4 complication, n/N (%) | Anastomotic insufficiency | 3/28 (10.7) | 1/19 (5.3) |
| | Fistula | 2/39 (5.1) | 1/19 (5.3) |
| | Re-operation | 2/41 (5.1) | 3/21 (15.8) |
| | SSI with intervention | 1/39 (2.6) | 2/19 (10.5) |
| | Bleeding requiring transfusion | 1/39 (2.6) | 0 |
| Death, n (%) | | 1 (2.6) | 0 |

| Grade 3/4 AEs, n/N (%) | HIPEC | Non-HIPEC | p-value |
|---|---|---|---|
| Pre-op chemo | 23/50 (46.0) | 31/50 (62.0) | 0.454 |
| Due to surgery | 17/39 (43.6) | 8/21 (38.1) | 0.786 |
| Post-op chemo | 10/23 (43.5) | 10/13 (76.9) | 0.083 |

## Conclusions

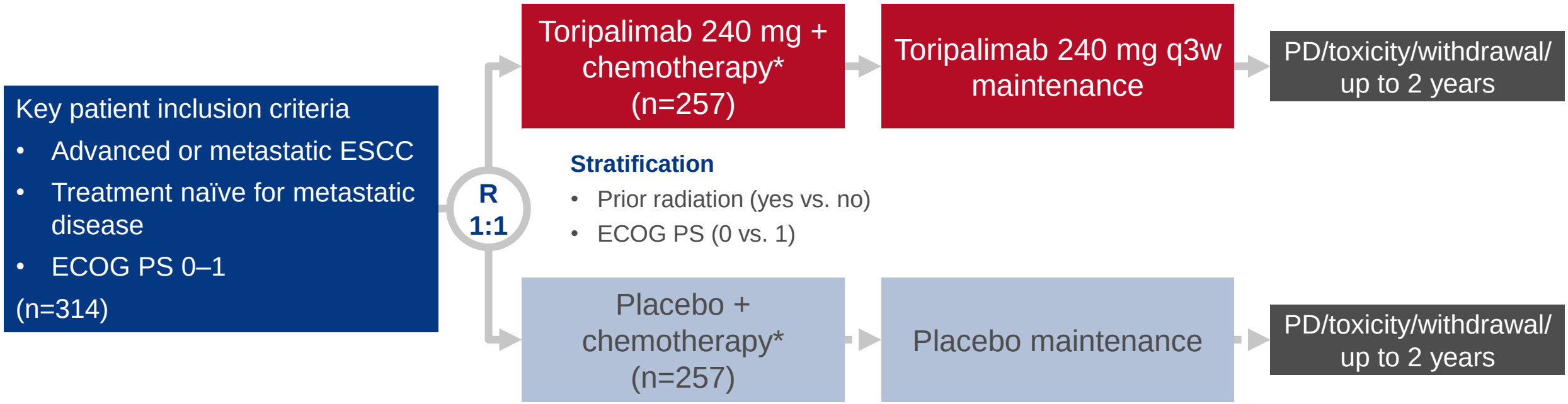
- **In patients with gastric cancer and peritoneal metastases, HIPEC demonstrated a significant improvement in PFS with no impact on morbidity or mortality, but only provided a significant improvement in OS for those who had complete CRS**

Rau B, et al. Ann Oncol 2021;32(suppl):abstr 1376O

# 1373MO: JUPITER-06: a randomized, double-blind, phase 3 study of toripalimab versus placebo in combination with first-line chemotherapy for treatment naive advanced or metastatic esophageal squamous cell carcinoma (ESCC) – Xu RH, et al

## Study objective

- To evaluate the efficacy and safety of 1L toripalimab + chemotherapy in patients with advanced or metastatic ESCC in the JUPITER-06 study




### CO-PRIMARY ENDPOINTS

- PFS (BICR, RECIST v1.1), OS

### SECONDARY ENDPOINTS

- ORR, DoR, DCR, HRQoL, safety

*Paclitaxel 175 mg/m$^2$ + cisplatin 75 mg/m$^2$ q3w up to 6 cycles

Xu RH, et al. Ann Oncol 2021;32(suppl):abstr 1373MO

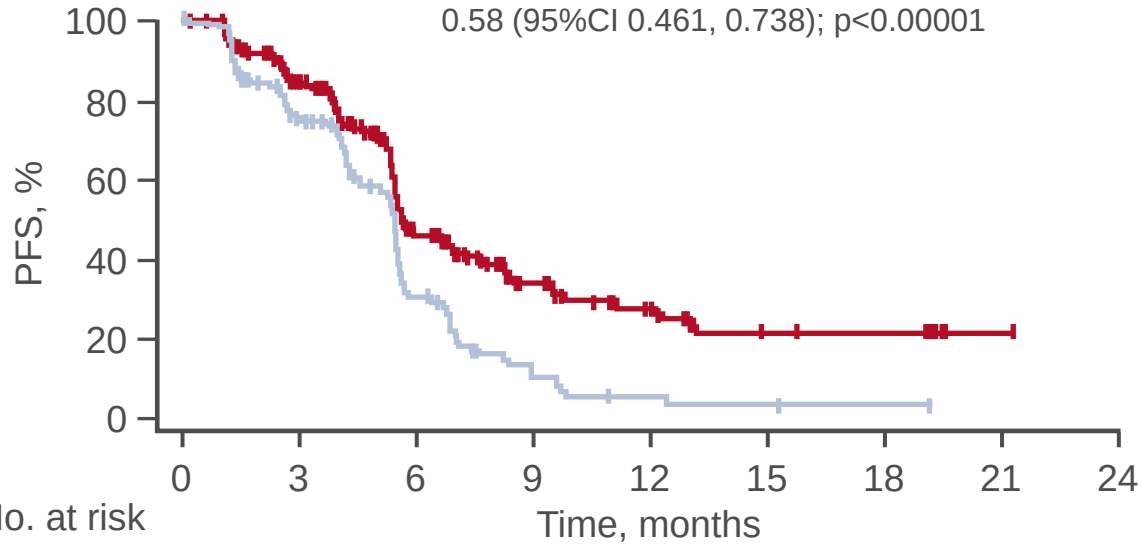
# 1373MO: JUPITER-06: a randomized, double-blind, phase 3 study of toripalimab versus placebo in combination with first-line chemotherapy for treatment naive advanced or metastatic esophageal squamous cell carcinoma (ESCC) – Xu RH, et al

## Key results

### Progression-free survival

| | Events, n/ pts, n | mPFS, mo (95%CI) | 1-yr PFS rate, % (95%CI) |
|---|---|---|---|
| Toripalimab + chemo | 132/257 | 5.7 (5.6, 7.0) | 27.8 (20.4, 35.8) |
| Placebo + chemo | 164/257 | 5.5 (5.2, 5.6) | 6.1 (2.2, 12.6) |

Stratified HR for disease progression or death
0.58 (95%CI 0.461, 0.738); p<0.00001

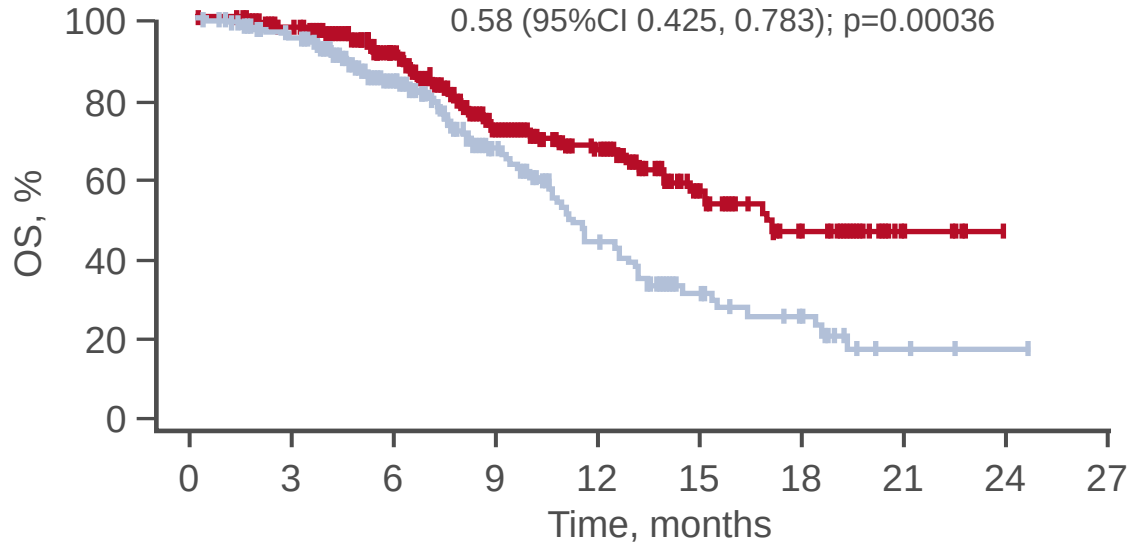



| No. at risk | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Torip + chemo | 257 | 189 | 70 | 36 | 19 | 9 | 7 | 1 | 0 |
| Placebo + chemo | 257 | 170 | 42 | 9 | 3 | 2 | 1 | 0 | 0 |

### Overall survival

| Events, n/ pts, n | mOS, mo (95%CI) | 1-yr OS rate, % (95%CI) | 2-yr OS rate, % (95%CI) |
|---|---|---|---|
| 70/257 | 17.0 (14.0, NE) | 66.0 (57.5, 73.2) | NE (NE, NE) |
| 103/257 | 11.0 (10.4, 12.6) | 43.7 (34.4, 52.6) | 17.5 (8.7, 28.9) |

Stratified HR for death
0.58 (95%CI 0.425, 0.783); p=0.00036




| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Torip + chemo | 257 | 246 | 171 | 86 | 52 | 31 | 18 | 4 | 0 | 0 |
| Placebo + chemo | 257 | 242 | 166 | 79 | 33 | 18 | 11 | 3 | 1 | 0 |

Xu RH, et al. Ann Oncol 2021;32(suppl):abstr 1373MO

# 1373MO: JUPITER-06: a randomized, double-blind, phase 3 study of toripalimab versus placebo in combination with first-line chemotherapy for treatment naive advanced or metastatic esophageal squamous cell carcinoma (ESCC) – Xu RH, et al

## Key results (cont.)

| PD-L1 expression | Toripalimab + chemotherapy | Placebo + chemotherapy | HR (95%CI) |
|---|---|---|---|
| mPFS, mo | | | |
| CPS ≥1 | 5.7 | 5.5 | 0.58 (0.444, 0.751) |
| CPS <1 | 5.7 | 5.6 | 0.66 (0.370, 1.189) |
| mOS, mo | | | |
| CPS ≥1 | 15.2 | 10.9 | 0.61 (0.435, 0.870) |
| CPS <1 | NE | 11.6 | 0.61 (0.297, 1.247) |

| Grade ≥3 TRAEs, n (%) | Toripalimab + chemotherapy (n=257) | Placebo + chemotherapy (n=257) |
|---|---|---|
| Any | 166 (64.6) | 144 (56.0) |
| irAEs | 18 (7.0) | 4 (1.6) |
| Infusion reactions | 2 (0.8) | 0 |
| Led to discontinuation | 7 (2.7) | 1 (0.4) |
| Led to death | 1 (0.4) | 3 (1.2) |

## Conclusions

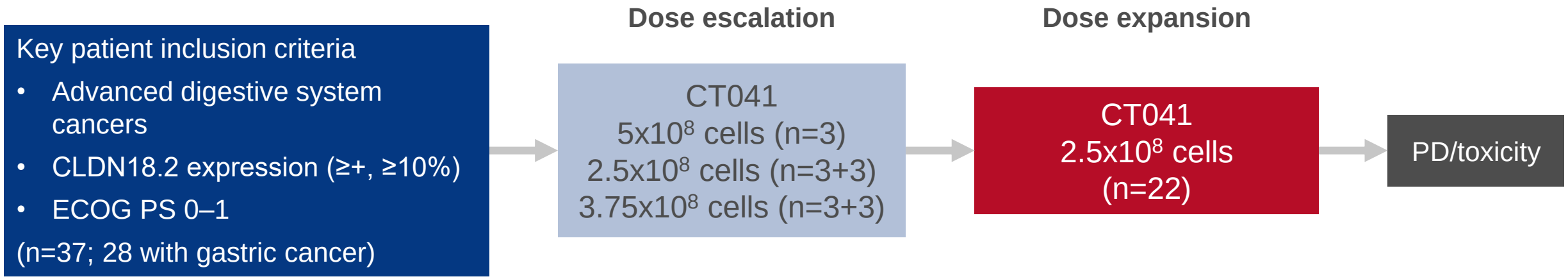
- **In patients with advanced or metastatic ESCC, 1L toripalimab + chemotherapy demonstrated significant improvement in survival over chemotherapy alone and no new safety signals were observed**

Xu RH, et al. Ann Oncol 2021;32(suppl):abstr 1373MO

# 1372O: CLDN 18.2-targeted CAR-T cell therapy in patients with cancers of the digestive system – Qi C, et al

**Study objective**

- To evaluate the efficacy and safety of CT041, a Claudin18.2-redirected CAR-T cell therapy, in patients with digestive system cancers including gastric cancer




**PRIMARY ENDPOINT**

- Safety

**SECONDARY ENDPOINTS**

- Efficacy, pharmacokinetics

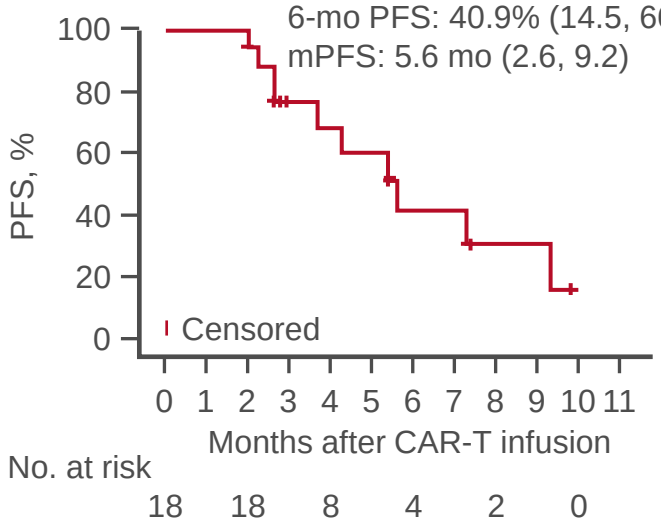
Qi C, et al. Ann Oncol 2021;32(suppl):abstr 1372O

# 1372O: CLDN 18.2-targeted CAR-T cell therapy in patients with cancers of the digestive system – Qi C, et al

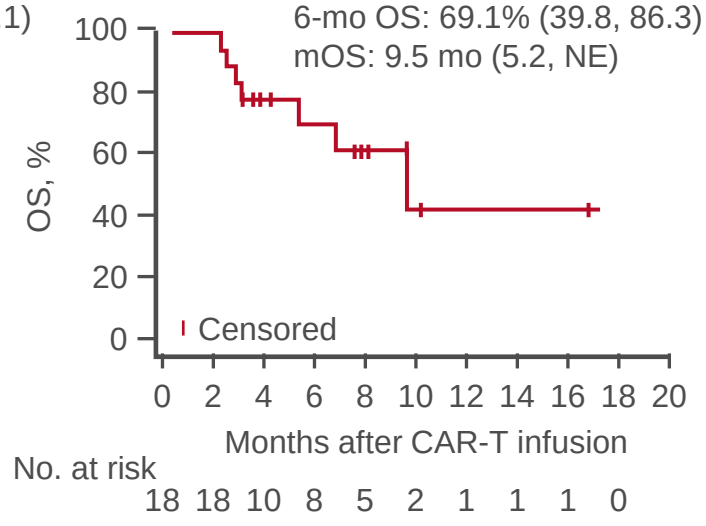
## Key results

| Patients with gastric cancer ≥2L with 2.5x10$^8$ cells | n=18 |
|---|---|
| BOR, n (%) | |
| CR | 0 |
| PR | 11 (61.1) |
| SD | 4 (22.2) |
| PD | 3 (16.7) |
| ORR, n (%) [95%CI] | 11 (61.1) [35.75, 82.70] |
| DCR, n (%) [95%CI] | 15 (83.3) [58.58, 96.42] |
| mPFS, mo (95%CI) | 5.6 (2.6, 9.2) |
| mOS, mo (95%CI) | 9.5 (5.2, NE) |
| mDoR, mo (95%CI) | 6.4 (2.7, NE) |

### Progression-free survival




### Overall survival




Qi C, et al. Ann Oncol 2021;32(suppl):abstr 1372O

# 1372O: CLDN 18.2-targeted CAR-T cell therapy in patients with cancers of the digestive system – Qi C, et al

## Key results (cont.)

| AEs, n (%) | Dose escalation | | Dose expansion | | |
|---|---|---|---|---|---|
| | $2.5x10^8$ (n=6) | $3.75x10^8$ (n=6) | $5x10^8$ (n=3) | $2.5x10^8$ (n=22) | Total (n=37) |
| Any | 6 (100) | 6 (100) | 3 (100) | 22 (100) | 37 (100) |
| Dose-limiting toxicity | 0 | 0 | 1 (33.3) | 0 | 1 (2.7) |
| Led to discontinuation | 0 | 0 | 1 (33.3) | 0 | 1 (2.7) |
| Treatment-related SAEs | 0 | 0 | 1 (33.3) | 2 (9.1) | 3 (8.1) |
| TRAEs | 6 (100) | 6 (100) | 3 (100) | 22 (100) | 37 (100) |

## Conclusions

- **In previously treated patients with CLDN18.2-positive gastric or GEJ cancer, CT041 demonstrated encouraging activity and was generally well-tolerated**

Qi C, et al. Ann Oncol 2021;32(suppl):abstr 1372O

# CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT

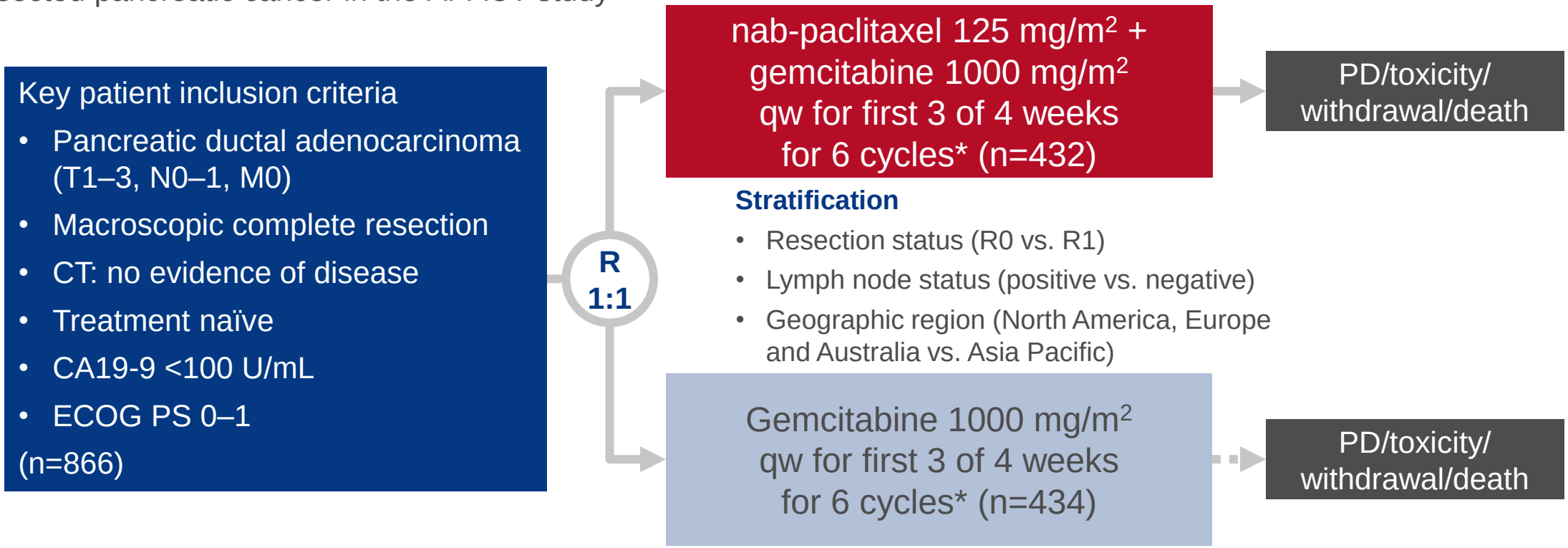
Cancers of the pancreas, small bowel and hepatobiliary tract

# PANCREATIC CANCER

# LBA-1: Phase 3 APACT trial of adjuvant nab-paclitaxel plus gemcitabine (nab-P + Gem) vs gemcitabine (Gem) alone in patients with resected pancreatic cancer (PC): updated 5-year overall survival – Tempero MA, et al

## Study objective

- To present the 5-year OS data of nab-paclitaxel + gemcitabine compared with gemcitabine in patients with surgically resected pancreatic cancer in the APACT study




**PRIMARY ENDPOINT**

- DFS (ICR)

**SECONDARY ENDPOINTS**

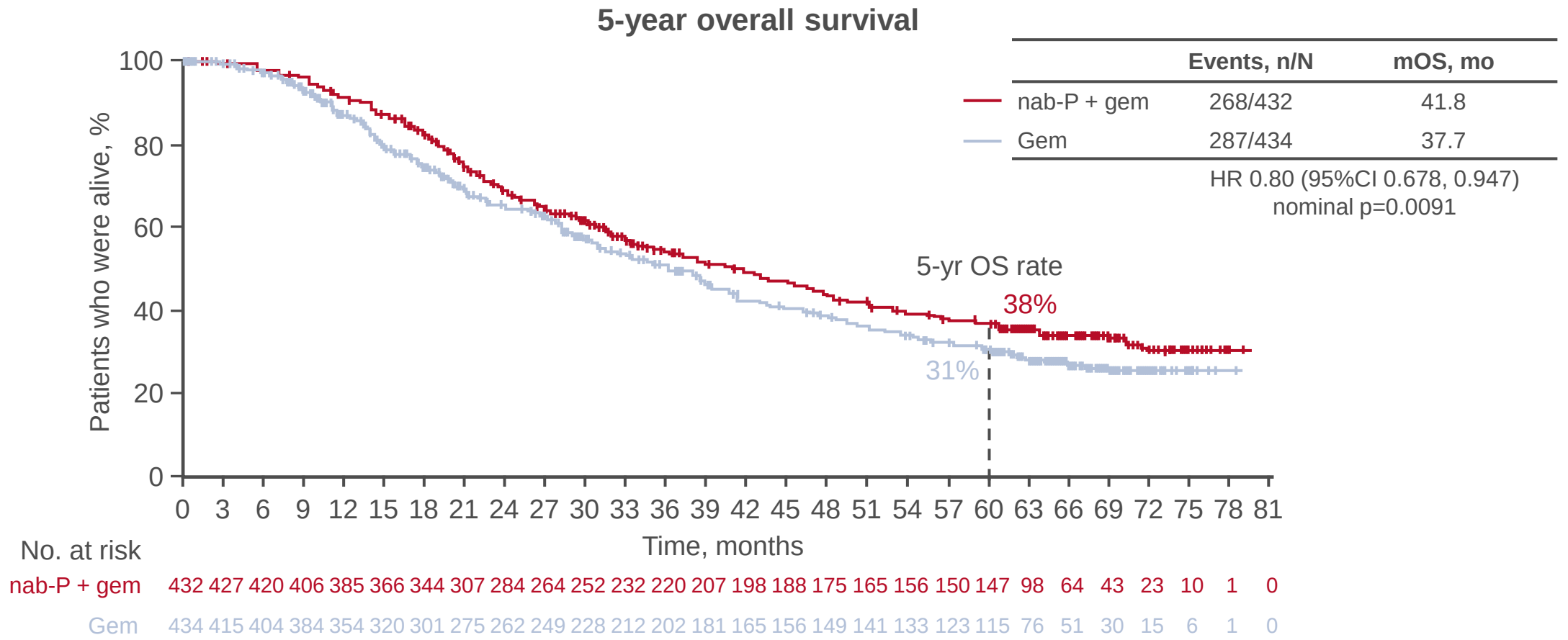
- OS, safety

*Treatment initiated ≤12 weeks post-surgery

Tempero MA, et al. Ann Oncol 2021;32(suppl):abstr LBA-1

# LBA-1: Phase 3 APACT trial of adjuvant nab-paclitaxel plus gemcitabine (nab-P + Gem) vs gemcitabine (Gem) alone in patients with resected pancreatic cancer (PC): updated 5-year overall survival – Tempero MA, et al

## Key results



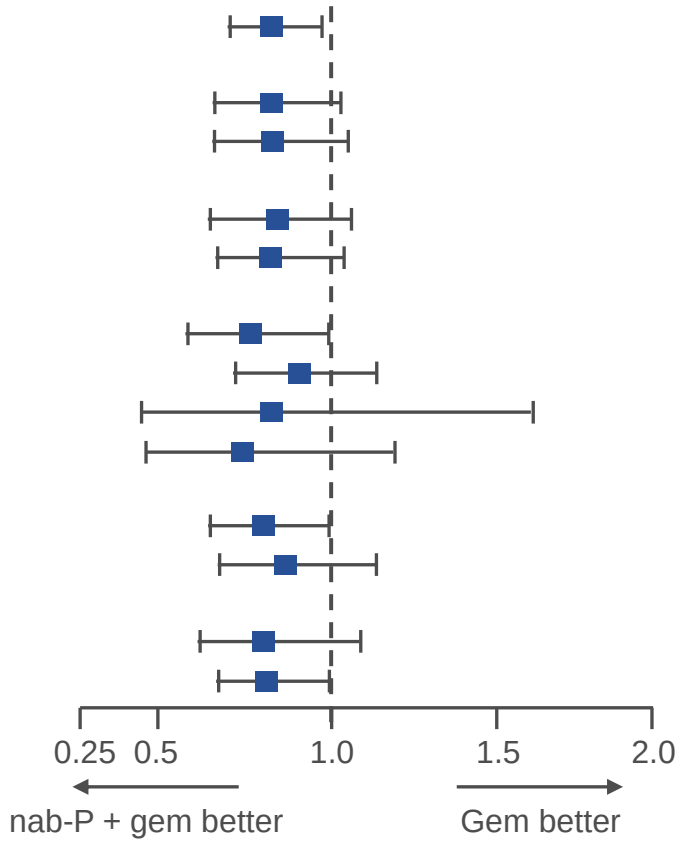

Tempero MA, et al. Ann Oncol 2021;32(suppl):abstr LBA-1

# LBA-1: Phase 3 APACT trial of adjuvant nab-paclitaxel plus gemcitabine (nab-P + Gem) vs gemcitabine (Gem) alone in patients with resected pancreatic cancer (PC): updated 5-year overall survival – Tempero MA, et al

## Key results (cont.)

### Overall survival in pre-specified subgroups

| Subgroup | No. of events/patients nab-P + gem | Gem | HR for death (95%CI) |
|---|---|---|---|
| **All patients** | 268/432 | 287/434 | 0.83 (0.705, 0.983) |
| **Age** | | | |
| <65 years | 143/221 | 151/225 | 0.83 (0.658, 1.040) |
| ≥65 years | 125/211 | 136/209 | 0.83 (0.654, 1.065) |
| **Sex** | | | |
| Female | 125/204 | 119/181 | 0.84 (0.653, 1.078) |
| Male | 143/228 | 168/253 | 0.83 (0.667, 1.041) |
| **Geographic region** | | | |
| North America | 85/144 | 100/156 | 0.75 (0.559, 0.998) |
| Europe | 132/203 | 136/205 | 0.92 (0.721, 1.164) |
| Australia | 21/30 | 15/20 | 0.84 (0.431, 1.625) |
| Asia Pacific | 30/55 | 36/53 | 0.73 (0.453, 1.194) |
| **Baseline ECOG PS** | | | |
| 0 | 151/252 | 182/268 | 0.80 (0.645, 0.994) |
| 1 | 117/180 | 105/166 | 0.88 (0.674, 1.142) |
| **Distance from tumour to the closest margin** | | | |
| <1mm | 83/114 | 83/112 | 0.82 (0.602, 1.107) |
| ≥1mm | 163/287 | 185/292 | 0.80 (0.648, 0.988) |



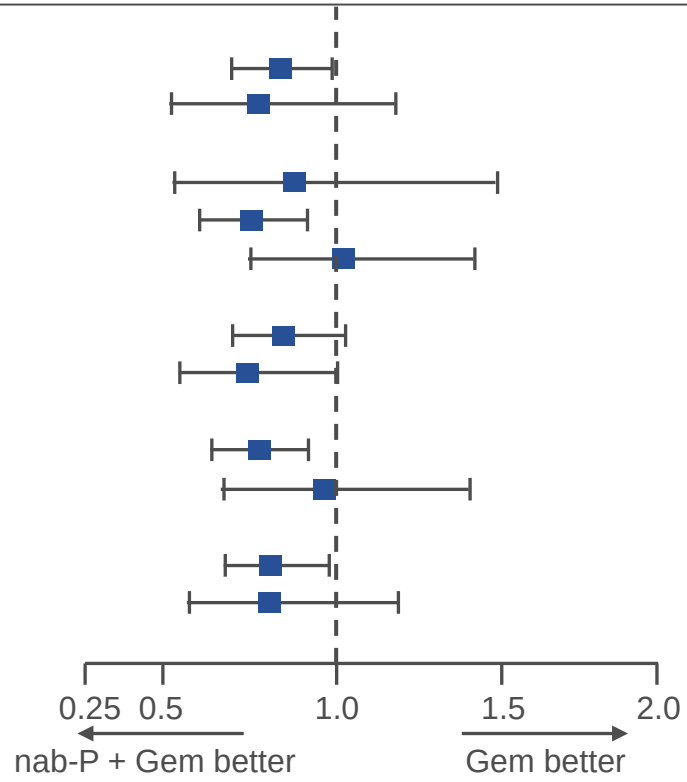

Tempero MA, et al. Ann Oncol 2021;32(suppl):abstr LBA-1

# LBA-1: Phase 3 APACT trial of adjuvant nab-paclitaxel plus gemcitabine (nab-P + Gem) vs gemcitabine (Gem) alone in patients with resected pancreatic cancer (PC): updated 5-year overall survival – Tempero MA, et al

## Key results (cont.)

### Overall survival in pre-specified subgroups

| Subgroup | No. of events/patients: nab-P + Gem | No. of events/patients: Gem | HR for death (95%CI) |
|---|---|---|---|
| **Pancreatic cancer primary location** | | | |
| Head | 229/354 | 238/347 | 0.84 (0.697, 1.003) |
| Other | 39/78 | 49/87 | 0.78 (0.509, 1.181) |
| **Tumour grade** | | | |
| Well differentiated | 25/49 | 31/55 | 0.88 (0.519, 1.490) |
| Moderately differentiated | 164/264 | 172/241 | 0.74 (0.601, 0.922) |
| Poorly differentiated | 70/101 | 72/115 | 1.04 (0.746, 1.442) |
| **Resection status** | | | |
| R0 | 190/327 | 210/334 | 0.85 (0.698, 1.034) |
| R1 | 78/105 | 77/100 | 0.73 (0.534, 1.003) |
| **Nodal status** | | | |
| LN positive | 215/311 | 231/312 | 0.77 (0.636, 0.922) |
| LN negative | 53/121 | 56/122 | 0.97 (0.667, 1.415) |
| **Level of CA19-9 at baseline** | | | |
| WNL | 208/351 | 226/345 | 0.82 (0.675, 0.984) |
| ULN <100 U/mL | 51/70 | 59/81 | 0.82 (0.561, 1.188) |
| ≥100 U/mL | 2/2 | 2/3 | – |




## Conclusions

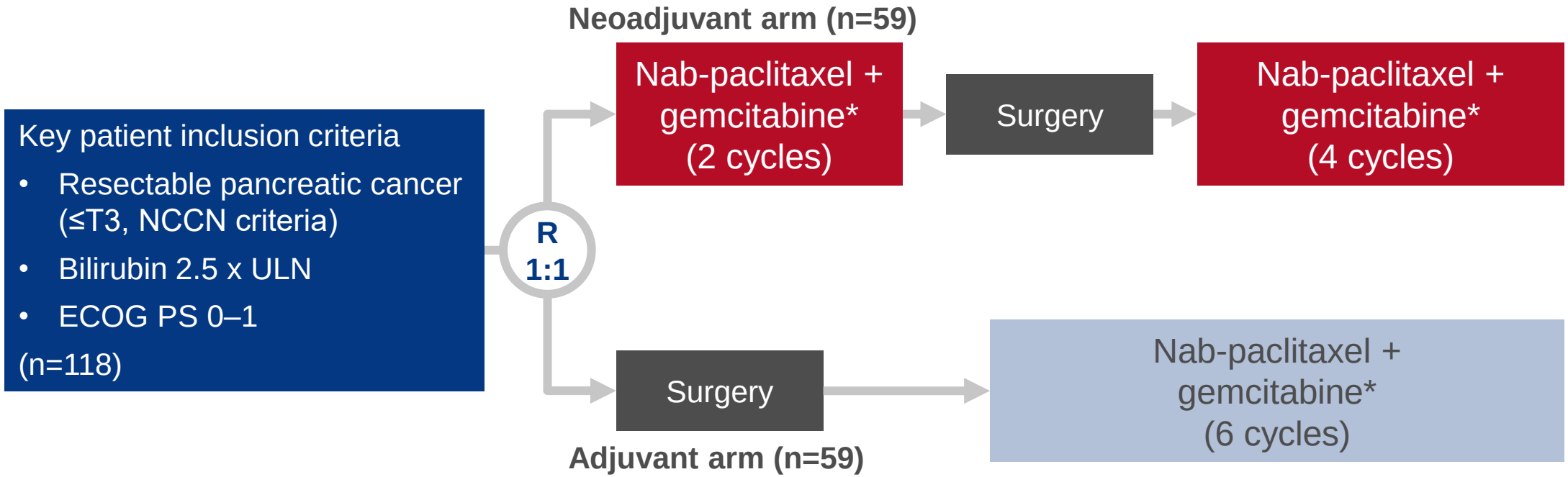
- **In patients with resected pancreatic cancer, this long-term follow-up of the APACT trial showed consistently longer OS with nab-paclitaxel + gemcitabine compared with gemcitabine alone across the majority of pre-specified subgroups**

Tempero MA, et al. Ann Oncol 2021;32(suppl):abstr LBA-1

# LBA56: Perioperative or only adjuvant nab-paclitaxel plus gemcitabine for resectable pancreatic cancer - results of the NEONAX trial, a randomized phase II AIO study – Seufferlein T, et al

## Study objective

- To evaluate the efficacy and safety of perioperative or adjuvant nab-paclitaxel + gemcitabine in patients with resectable pancreatic cancer in the NEONAX study




### PRIMARY ENDPOINT

- 18-month DFS rate

### SECONDARY ENDPOINTS

- OS, R0 resection rate, ORR, QoL, safety

*Nab-paclitaxel 125 mg/m$^2$ iv qw + gemcitabine 1000 mg/m$^2$ iv qw 3/4 weeks

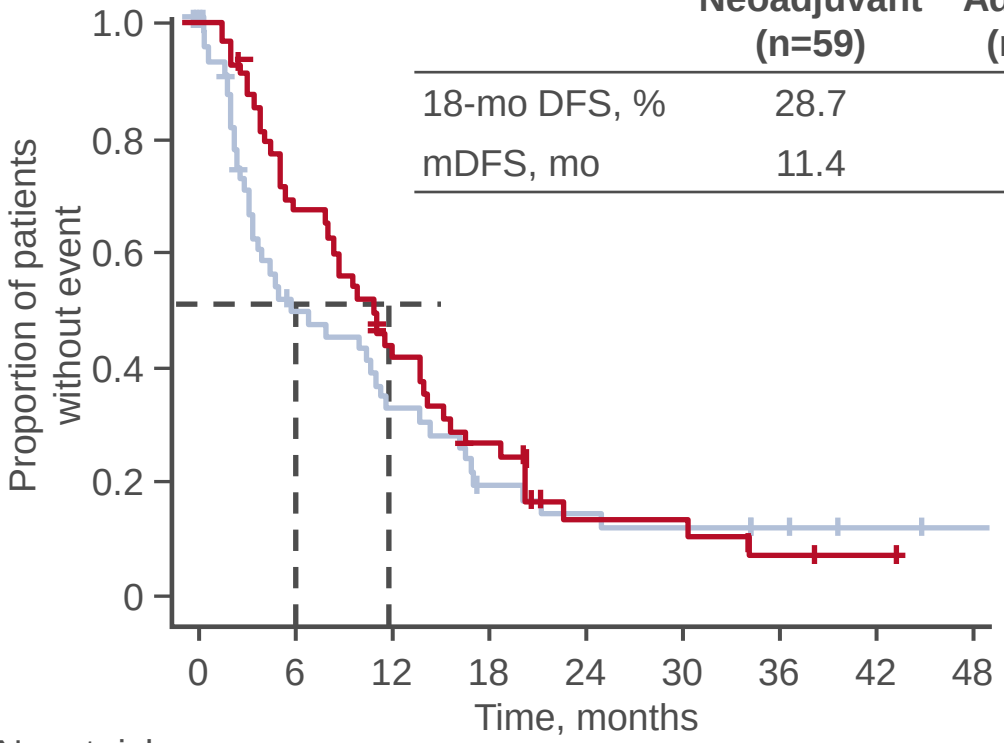
Seufferlein T, et al. Ann Oncol 2021;32(suppl):abstr LBA56

# LBA56: Perioperative or only adjuvant nab-paclitaxel plus gemcitabine for resectable pancreatic cancer - results of the NEONAX trial, a randomized phase II AIO study – Seufferlein T, et al

## Key results

### Disease-free survival – ITT population

| | Neoadjuvant (n=59) | Adjuvant (n=59) |
|---|---|---|
| 18-mo DFS, % | 28.7 | 19.3 |
| mDFS, mo | 11.4 | 5.9 |




| Response, n (%) | Neoadjuvant (n=45) | Adjuvant (n=59) |
|---|---|---|
| DCR | 42 (93.3) | - |
| ORR | 13 (28.9) | - |
| BOR<br>CR<br>PR<br>SD<br>PD | <br>0<br>13 (28.9)<br>29 (64.4)<br>3 (6.7) | - |
| Resection rate<br>R0<br>R1<br>R2 | 41 (69.5)<br>36 (87.8)<br>3 (7.3)<br>2 (4.9) | 46 (78.0)<br>31 (67.4)<br>13 (28.3)<br>2 (4.3) |
| mITT population, n | 39 | 25 |
| 18-month DFS rate, % | 32.2 | 41.4 |
| mDFS, mo | 14.1 | 17.0 |

Seufferlein T, et al. Ann Oncol 2021;32(suppl):abstr LBA56

# LBA56: Perioperative or only adjuvant nab-paclitaxel plus gemcitabine for resectable pancreatic cancer - results of the NEONAX trial, a randomized phase II AIO study – Seufferlein T, et al

## Conclusions

- In patients with resectable pancreatic cancer, neither perioperative nor adjuvant nab-paclitaxel + gemcitabine demonstrated the prespecified improvement in 18-month DFS rate, although the median DFS was higher in those who received chemotherapy prior to surgery

Seufferlein T, et al. Ann Oncol 2021;32(suppl):abstr LBA56

# SO-3: Treatment sequences and prognostic factors in metastatic pancreatic ductal adenocarcinoma: univariate and multivariate analyses of a real-world study in Europe – Taieb J, et al

## Study objective

- To evaluate the treatment patterns and impact of treatment sequencing on survival outcomes as well as identifying prognostic factors in patients with metastatic PDAC in a real-world setting across 5 European countries

## Methods

- Data from online patient reports (n=6000) were reviewed from 5 European countries (France, Germany, Italy, Spain and the UK) to find patients diagnosed with metastatic PDAC (n=3432) between January and October 2016 who had received 1L or 2L treatment (n=1218)
- Data were collected from date of diagnosis until 5 years or death
- Cox regression was used to determine prognostic factors from patients with 1L and 2L treatment data (n=915

## Key results

| Most common 1L treatments, n (%) | |
|---|---|
| (m)FOLFIRINOX | 974 (28.4) |
| Gem + nab-P | 961 (28.0) |
| Gem mono | 790 (23.0) |
| Other gem-based | 369 (10.8) |
| Fluoropyrimidines + oxaliplatin | 188 (5.5) |
| Other | 150 (4.3) |

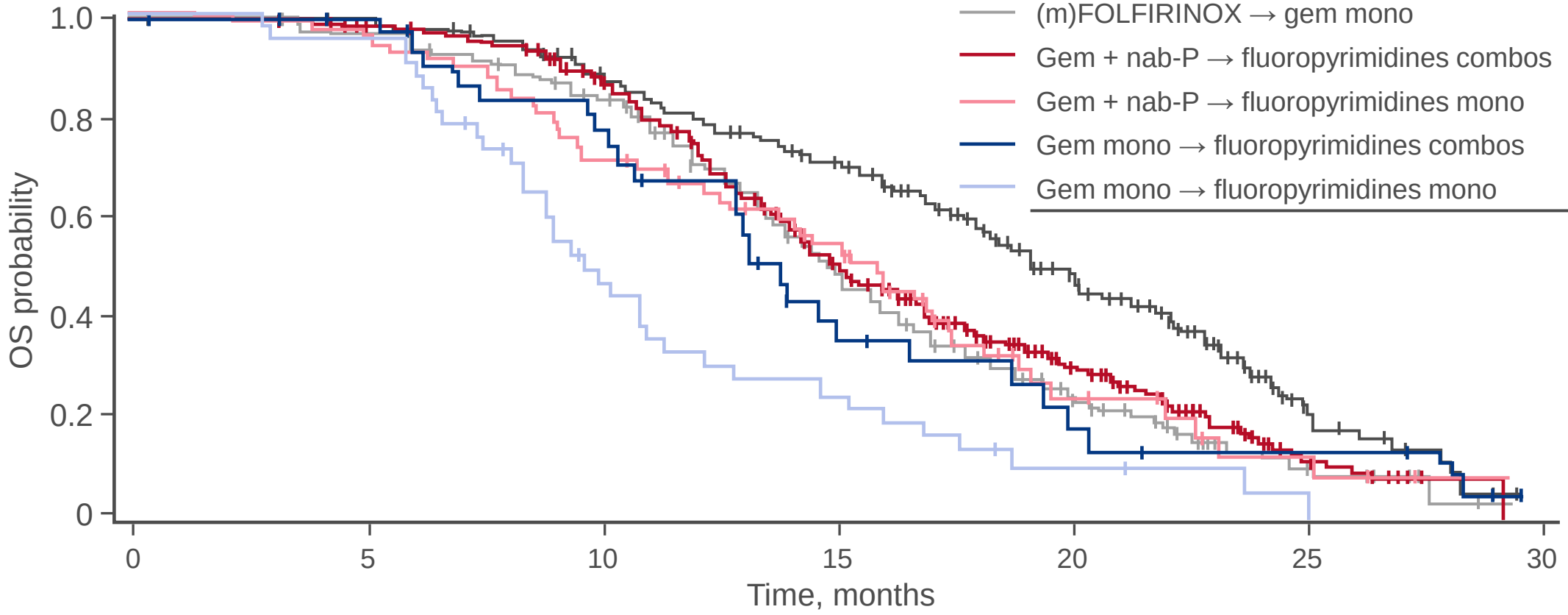
| Most common treatment sequences (1L → 2L), n (%) | |
|---|---|
| Gem + nab-P → fluoropyrimidines | 286 (24) |
| (m)FOLFIRINOX → gem combos | 263 (22) |
| (m)FOLFIRINOX → gem mono | 228 (19) |
| Gem + nab-P → fluoropyrimidines mono | 65 (5) |
| Gem mono → fluoropyrimidines mono | 41 (3) |
| Gem mono → fluoropyrimidines combos | 32 (3) |

Taieb J, et al. Ann Oncol 2021;32(suppl):abstr SO-3

# SO-3: Treatment sequences and prognostic factors in metastatic pancreatic ductal adenocarcinoma: univariate and multivariate analyses of a real-world study in Europe – Taieb J, et al

## Key results

### Overall survival




| Treatment sequence (1L → 2L) | PS 0/1 | PS ≥2 |
|---|---|---|
| (m)FOLFIRINOX → gem combos | 20.0 | 12.6 |
| (m)FOLFIRINOX → gem mono | 14.8 | 15.0 |
| Gem + nab-P → fluoropyrimidines combos | 15.6 | 12.7 |
| Gem + nab-P → fluoropyrimidines mono | 15.9 | 8.3 |
| Gem mono → fluoropyrimidines combos | 15.0 | 12.8 |
| Gem mono → fluoropyrimidines mono | 10.2 | 8.8 |

Taieb J, et al. Ann Oncol 2021;32(suppl):abstr SO-3

# SO-3: Treatment sequences and prognostic factors in metastatic pancreatic ductal adenocarcinoma: univariate and multivariate analyses of a real-world study in Europe – Taieb J, et al

## Key results (cont.)

| Prognostic factors for survival | HR | p-value |
|---|---|---|
| No liver metastases | 0.397 | <0.0001 |
| ECOG PS 0–1 | 0.448 | <0.0001 |
| CA19-9 <400 U/mL | 0.747 | 0.0004 |
| No lung metastases | 0.789 | 0.0049 |
| Male | 0.828 | 0.0228 |

| Treatments prognostic for survival (vs. gem mono → fluoropyrimidine mono) | HR (95%CI) | p-value |
|---|---|---|
| (m)FOLFIRINOX → gem combos | 0.424 (0.293, 0.615) | <0.0001 |
| Gem + nab-P → fluoropyrimidines combos | 0.601 (0.418, 0.865) | <0.0001 |
| Gem + nab-P → fluoropyrimidines mono | 0.645 (0.413, 1.007) | <0.0001 |
| (m)FOLFIRINOX → gem mono | 0.665 (0.461, 0.958) | <0.0001 |
| Gem mono → fluoropyrimidines combos | 0.787 (0.465, 1.332) | <0.0001 |

## Conclusions

- **In patients with metastatic PDAC, liver metastases, treatment type, ECOG PS, CA19-9 level and lung metastases were all found to be independent prognostic factors of OS and patients who received (m)FOLFIRINOX followed by gemcitabine combinations demonstrated the longest OS**

Taieb J, et al. Ann Oncol 2021;32(suppl):abstr SO-3

Cancers of the pancreas, small bowel and hepatobiliary tract

# HEPATOCELLULAR CARCINOMA

# LBA37: IMMUTACE: A biomarker-orientated, multi center phase II AIO study of transarterial chemoembolization (TACE) in combination with nivolumab performed for intermediate stage hepatocellular carcinoma (HCC) – Vogel A, et al

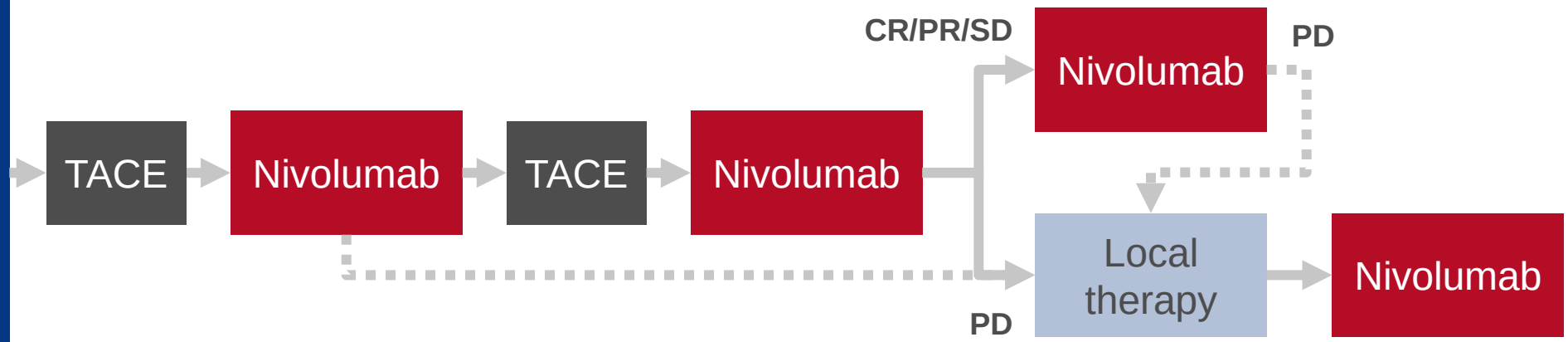
**Study objective**

- To evaluate the efficacy and safety of TACE combined with nivolumab in patients with intermediate stage HCC in the IMMUTACE study

Key patient inclusion criteria

- Intermediate stage HCC
- Limited metastatic disease permitted
- Child-Pugh A
- ECOG PS ≤2

(n=49)




**PRIMARY ENDPOINT**

- ORR

**SECONDARY ENDPOINTS**

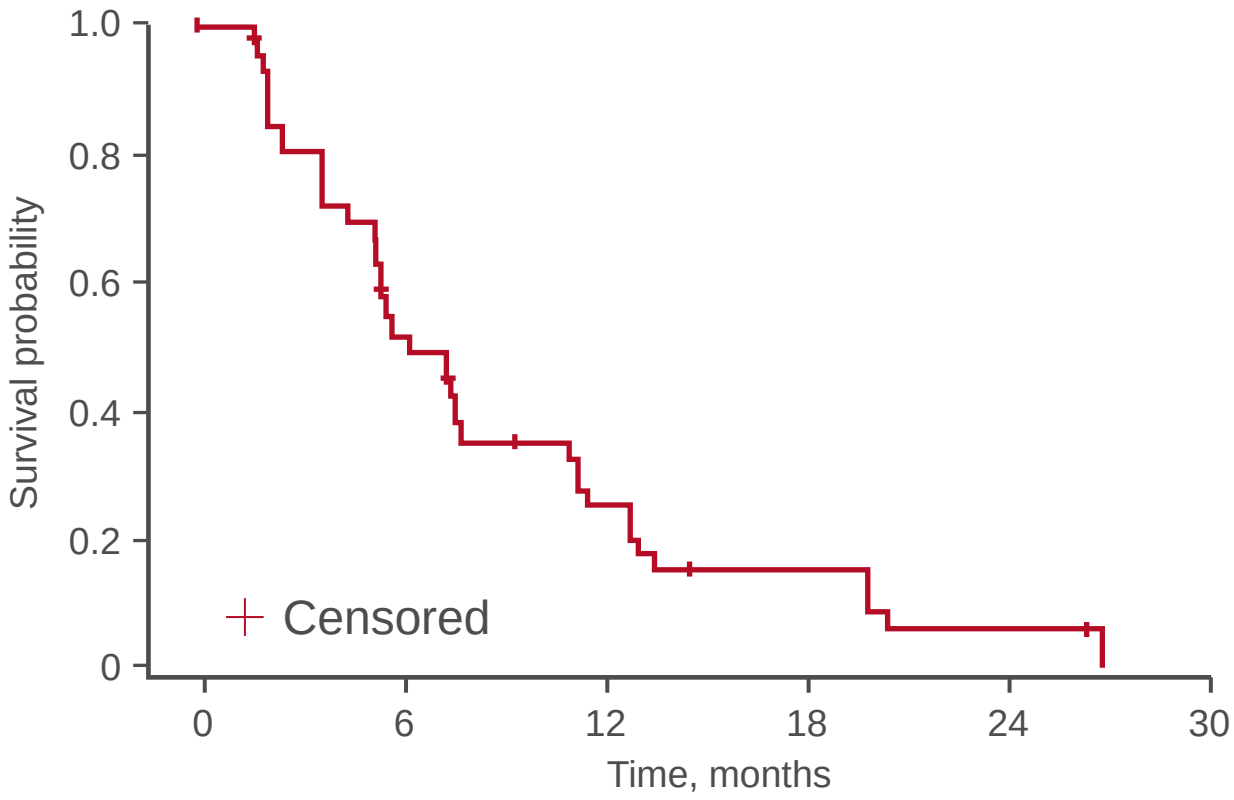
- PFS, OS, QoL, safety

Vogel A, et al. Ann Oncol 2021;32(suppl):abstr LBA37

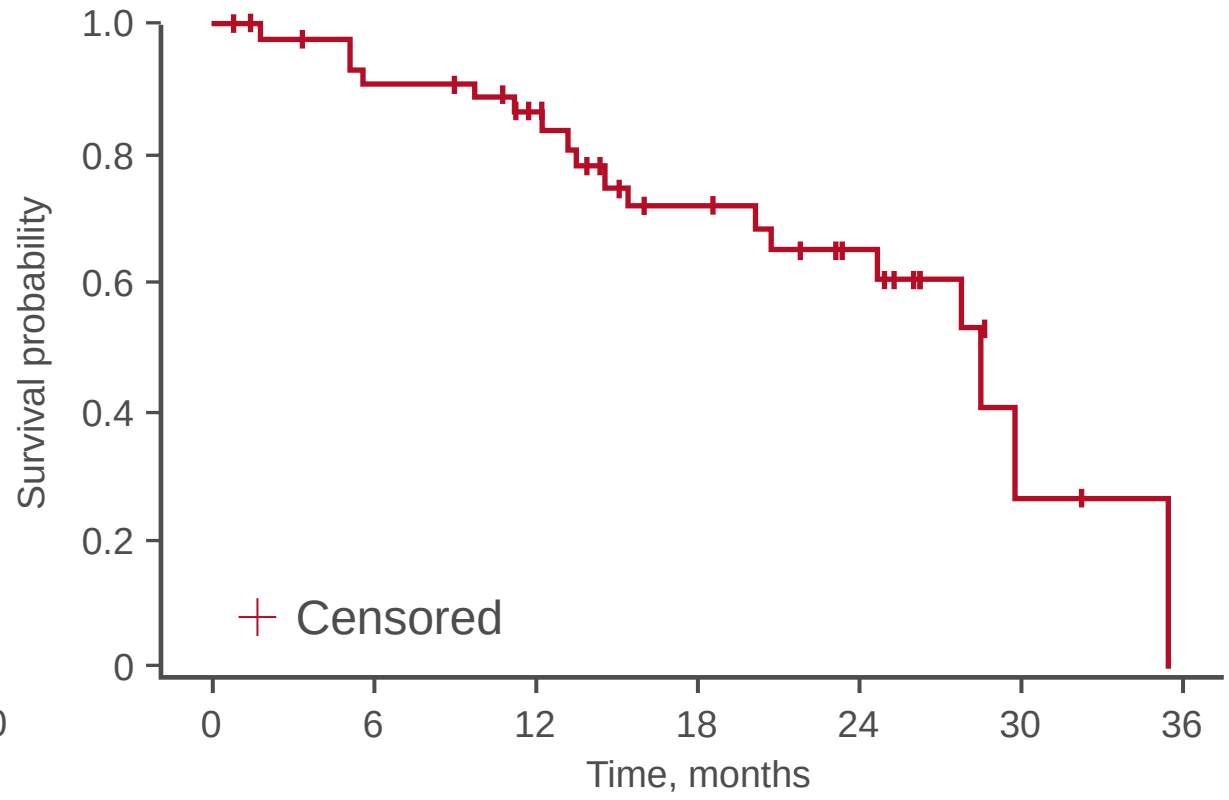
# LBA37: IMMUTACE: A biomarker-orientated, multi center phase II AIO study of transarterial chemoembolization (TACE) in combination with nivolumab performed for intermediate stage hepatocellular carcinoma (HCC) – Vogel A, et al

## Key results

### Progression-free survival




### Overall survival




Vogel A, et al. Ann Oncol 2021;32(suppl):abstr LBA37

# LBA37: IMMUTACE: A biomarker-orientated, multi center phase II AIO study of transarterial chemoembolization (TACE) in combination with nivolumab performed for intermediate stage hepatocellular carcinoma (HCC) – Vogel A, et al

## Key results (cont.)

| | n=49 |
|---|---|
| ORR, % (95%CI) | 71.4 (56.8, 83.4) |
| BOR, n (%) | |
| CR | 8 (16.3) |
| PR | 27 (55.1) |
| SD | 2 (4.1) |
| PD | 7 (14.3) |
| NE | 5 (10.2) |

| Grade ≥3 AEs, n (%) | n=49 |
|---|---|
| AST increased | 7 (14.3) |
| GGT increased | 5 (10.2) |
| ALT increased | 4 (8.2) |
| Pain | 3 (6.1) |
| Fever | 1 (2.0) |
| Pruritus | 1 (2.0) |
| Thrombotic thrombocytopenic purpura | 1 (2.0) |

## Conclusions

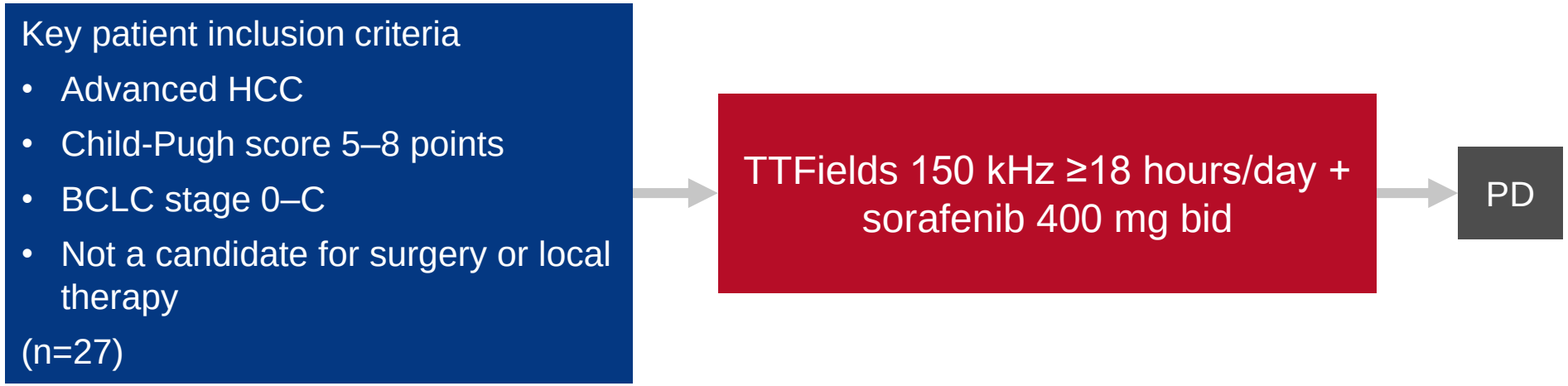
- **In patients with intermediate stage HCC, TACE combined with nivolumab demonstrated promising activity with no new safety signals reported**

Vogel A, et al. Ann Oncol 2021;32(suppl):abstr LBA37

# O-16: HEPANOVA: final efficacy and safety results from a phase 2 study of Tumor Treating Fields (TTFields, 150 kHz) concomitant with sorafenib in advanced hepatocellular carcinoma (HCC) – Grosu AL, et al

**Study objective**

- To evaluate the efficacy and safety of TTFields concomitant with sorafenib in patients with advanced HCC in the HEPANOVA study




**PRIMARY ENDPOINT**

- ORR (RECIST v1.1, investigator-assessed)

**SECONDARY ENDPOINTS**

- PFS, OS, DMFS, safety

Presented by Eleni Gkika

Grosu AL, et al. Ann Oncol 2021;32(suppl):abstr O-16

# O-16: HEPANOVA: final efficacy and safety results from a phase 2 study of Tumor Treating Fields (TTFields, 150 kHz) concomitant with sorafenib in advanced hepatocellular carcinoma (HCC) – Grosu AL, et al

## Key results

| | TTFields ≥12 weeks + sorafenib (n=11) | TTFields + sorafenib (n=11) |
|---|---|---|
| ORR, % | 18 | 9.5 (p=0.24) |
| BOR, % | | |
| CR | 0 | 0 |
| PR | 18 | 9.5 |
| SD | 73 | 66.5 |
| DCR, % | 91 | 76 |

| | TTFields + sorafenib (n=27) |
|---|---|
| 1-year in-field control rate, % | 9.5 |
| mPFS, mo (95%CI) | 5.8 (3.0, 8.9) |
| mTTP, mo (95%CI) | 8.9 (3.1, NR) |
| 1-year PFS rate, % (95%CI) | 23 (7, 45) |
| 1-year OS rate, % (95%CI) | 30 (11, 52) |
| 1-year DMFS rate, % (95%CI) | 26 (8, 49) |

Presented by Eleni Gkika

Grosu AL, et al. Ann Oncol 2021;32(suppl):abstr O-16

# O-16: HEPANOVA: final efficacy and safety results from a phase 2 study of Tumor Treating Fields (TTFields, 150 kHz) concomitant with sorafenib in advanced hepatocellular carcinoma (HCC) – Grosu AL, et al

## Key results (cont.)

| Grade 3/4 AEs occurring in ≥10%, n (%) | TTFields + sorafenib (n=27) |
|---|---|
| Gastrointestinal | 7 (26) |
| Metabolism | 5 (19) |
| General disorders/administation site | 4 (15) |
| Laboratory investigations | 4 (15) |
| Respiratory | 4 (15) |
| Musculoskeletal | 3 (11) |
| Vascular | 3 (11) |

## Conclusions

- **In patients with advanced HCC, TTFields concomitant with sorafenib demonstrated promising activity and was generally well-tolerated**

Presented by Eleni Gkika

Grosu AL, et al. Ann Oncol 2021;32(suppl):abstr O-16

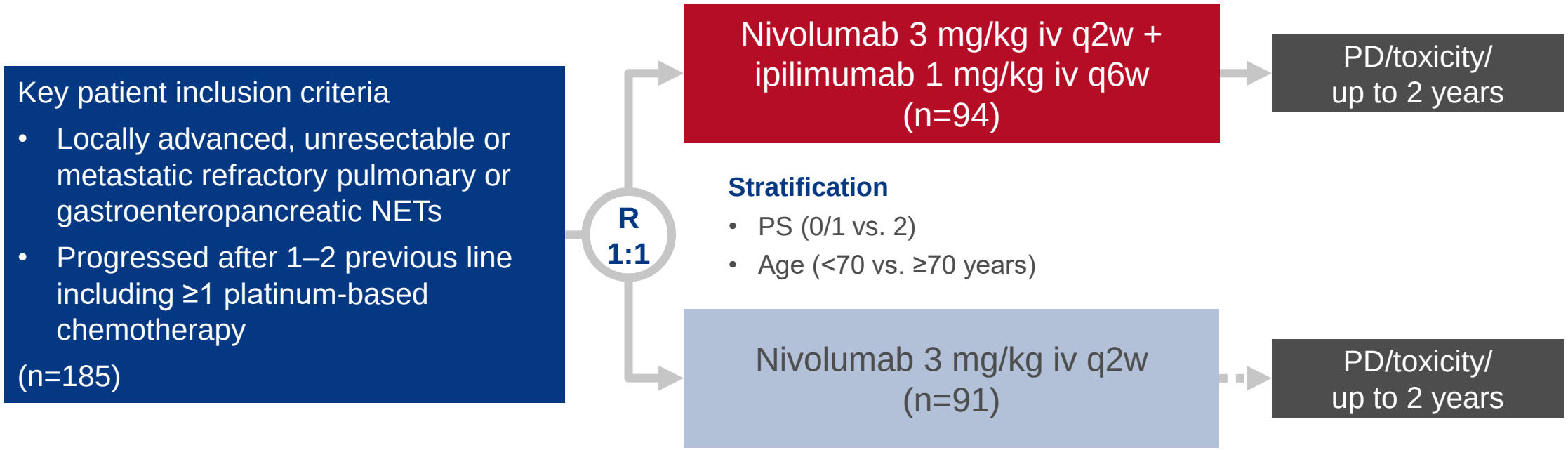
Cancers of the pancreas, small bowel and hepatobiliary tract

# NEUROENDOCRINE TUMOUR

# LBA41: Nivolumab (nivo) ± ipilimumab (ipi) in pre-treated patients with advanced, refractory pulmonary or gastroenteropancreatic poorly differentiated neuroendocrine tumors (NECs) (GCO-001 NIPINEC) – Girard N, et al

## Study objective

- To evaluate the efficacy and safety of nivolumab with or without ipilimumab in previously treated patients with advanced, refractory pulmonary or gastroenteropancreatic poorly differentiated NETs in the NIPINEC study




**PRIMARY ENDPOINT**

- 8-week ORR rate

**SECONDARY ENDPOINTS**

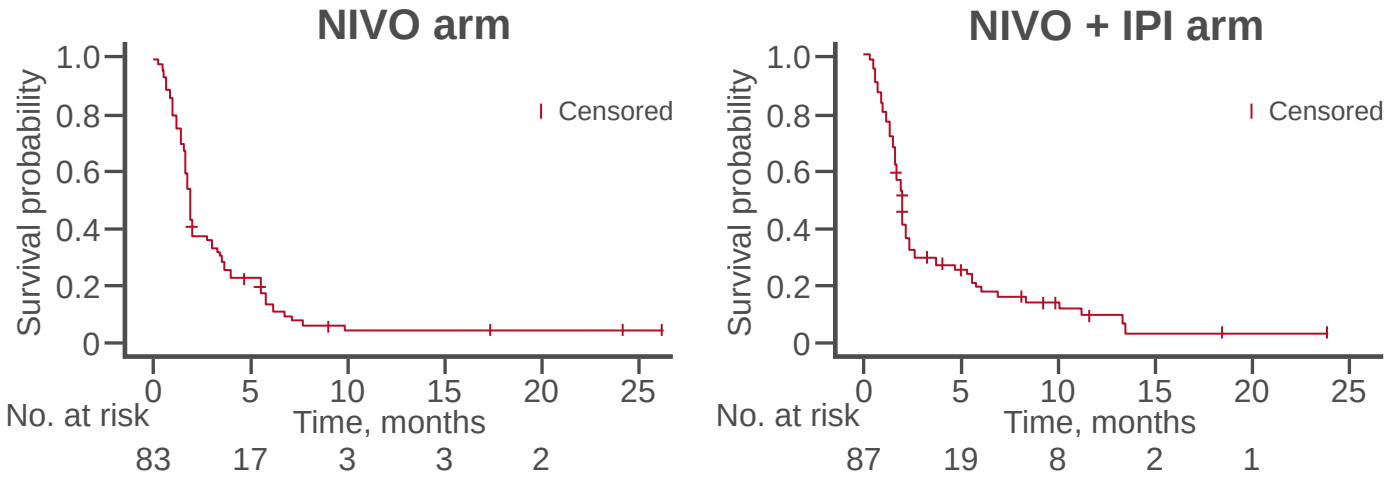
- DCR, DoR, PFS, OS, safety

Girard N, et al. Ann Oncol 2021;32(suppl):abstr LBA41

# LBA41: Nivolumab (nivo) ± ipilimumab (ipi) in pre-treated patients with advanced, refractory pulmonary or gastroenteropancreatic poorly differentiated neuroendocrine tumors (NECs) (GCO-001 NIPINEC) – Girard N, et al

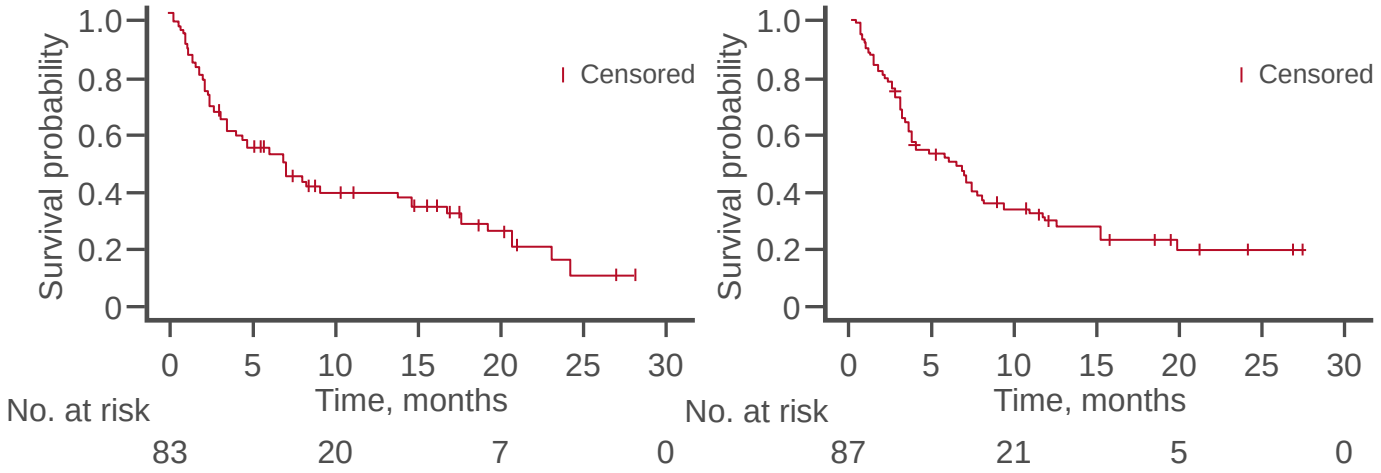
## Key results

### Progression-free survival




| | NIVO (n=83) | NIVO + IPI (n=87) |
|---|---|---|
| Events, n (%) | 73 (88.0) | 72 (82.8) |
| mPFS, mo (95%CI) | 1.8 (1.7, 2.0) | 1.9 (1.6, 2.1) |
| 6-mo PFS, % (95%CI) | 15.1 (8.1, 24.2) | 20.2 (12.0, 29.9) |

### Overall survival




| | NIVO (n=83) | NIVO + IPI (n=87) |
|---|---|---|
| Events, n (%) | 54 (65.1) | 58 (66.7) |
| mOS, mo (95%CI) | 7.2 (3.7, 14.1) | 5.8 (3.4, 7.6) |
| 6-mo OS, % (95%CI) | 53.8 (42.2, 64.1) | 50.0 (38.6, 60.3) |

Girard N, et al. Ann Oncol 2021;32(suppl):abstr LBA41

# LBA41: Nivolumab (nivo) ± ipilimumab (ipi) in pre-treated patients with advanced, refractory pulmonary or gastroenteropancreatic poorly differentiated neuroendocrine tumors (NECs) (GCO-001 NIPINEC) – Girard N, et al

## Key results (cont.)

| Gastroenteropancreatic NETs response, n (%) [95%CI] | Nivolumab + ipilimumab (n=43) | Nivolumab (n=42) |
|---|---|---|
| ORR | 5 (11.6) [3.9, 25.1] | 3 (7.1) [1.5, 19.5] |
| SD | 6 (14.0) [5.3, 27.9] | 9 (21.4) [10.3, 36.8] |
| Disease control | 11 (25.6) [13.5, 41.2] | 12 (28.6) [15.7, 44.6] |
| PD | 23 (53.5) [37.7, 68.8] | 25 (59.5) [43.3, 74.4] |
| NE | 9 (20.9) [10.0, 36.0] | 5 (11.9) [4.0, 25.6] |

| Overall TRAEs, n (%) | Nivolumab + ipilimumab (n=90) | Nivolumab (n=91) |
|---|---|---|
| Any | 62 (68.9) | 55 (60.4) |
| Grade 3 | 9 (10.0) | 6 (6.6) |
| Grade 4 | 7 (7.8) | 4 (4.4) |
| Serious | 9 (10.0) | 7 (7.7) |
| Led to discontinuation | 7 (7.8) | 3 (3.4) |
| Led to death | 0 | 2 (2.2)* |

## Conclusions

- **In previously treated patients with advanced, refractory pulmonary or gastroenteropancreatic poorly differentiated NETs, nivolumab + ipilimumab, but not nivolumab alone, met the ORR primary endpoint and the safety profile in both arms was comparable to that previously reported**

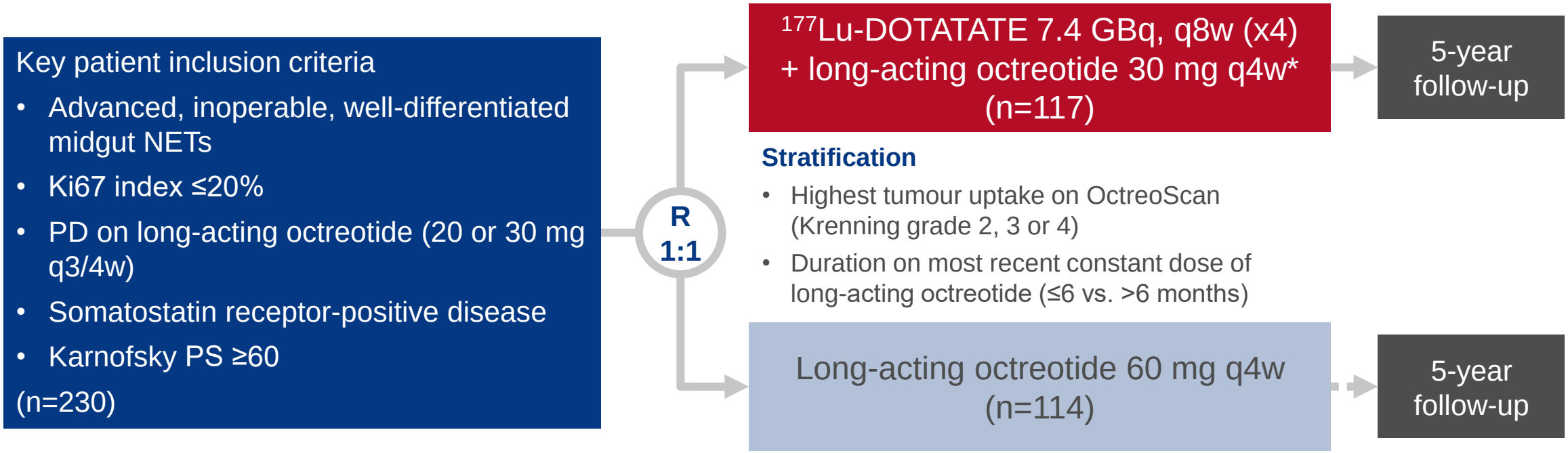
*Encephalitis pneumonitis

Girard N, et al. Ann Oncol 2021;32(suppl):abstr LBA41

# O-2: Final overall survival in the phase 3 NETTER-1 study of lutetium-177-DOTATATE in patients with midgut neuroendocrine tumors – Strosberg JR, et al

## Study objective

- To present the final OS and safety data of $^{177}$Lu-DOTATATE compared with long-acting octreotide in patients with advanced, progressive somatostatin receptor-positive midgut NETs




**PRIMARY ENDPOINT**

- PFS (RECIST v1.1, BICR)

**SECONDARY ENDPOINTS**

- ORR, OS, TTP, QoL, safety

*Dosed q8w during $^{177}$Lu-DOTATATE

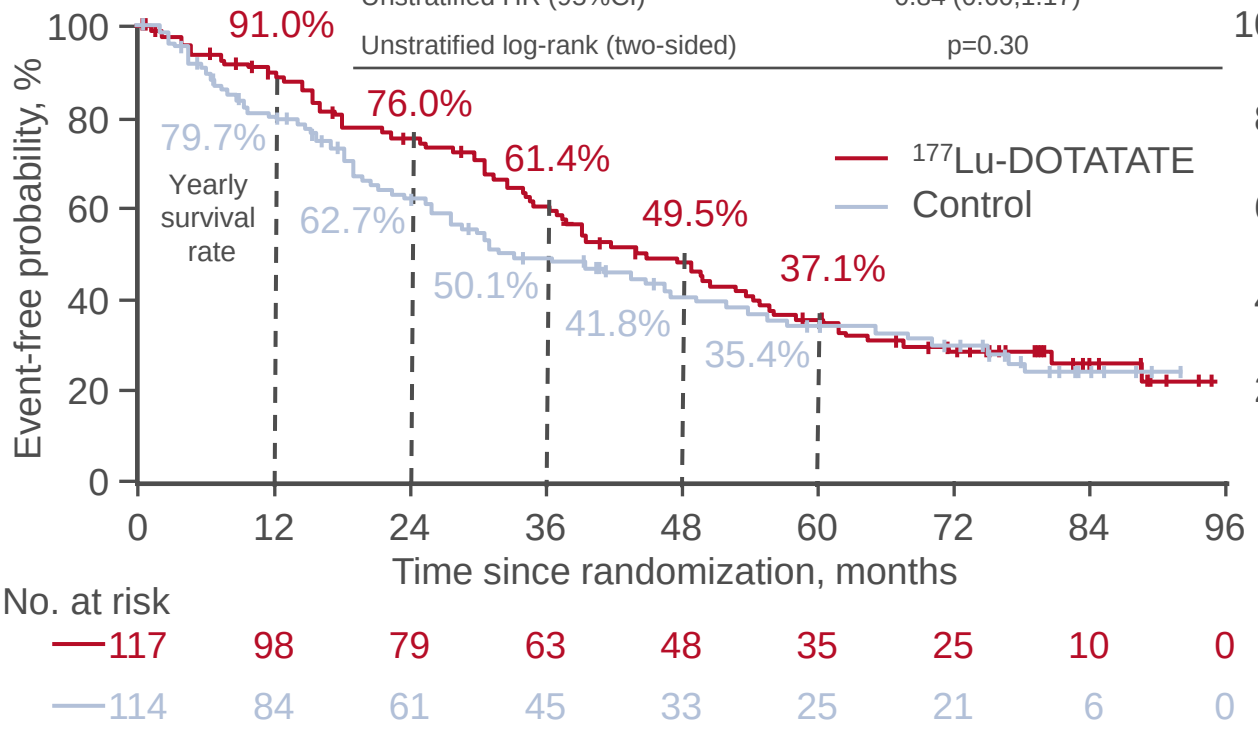
Strosberg JR, et al. Ann Oncol 2021;32(suppl):abstr O-2

# O-2: Final overall survival in the phase 3 NETTER-1 study of lutetium-177-DOTATATE in patients with midgut neuroendocrine tumors – Strosberg JR, et al

## Key results

### Overall survival (ITT)

| | $^{177}$Lu-DOTATATE | Control |
|---|---|---|
| mOS, mo (95%CI) | 48.0 (37.4, 55.2) | 36.3 (25.9, 51.7) |
| Unstratified HR (95%CI) | 0.84 (0.60,1.17) | |
| Unstratified log-rank (two-sided) | p=0.30 | |

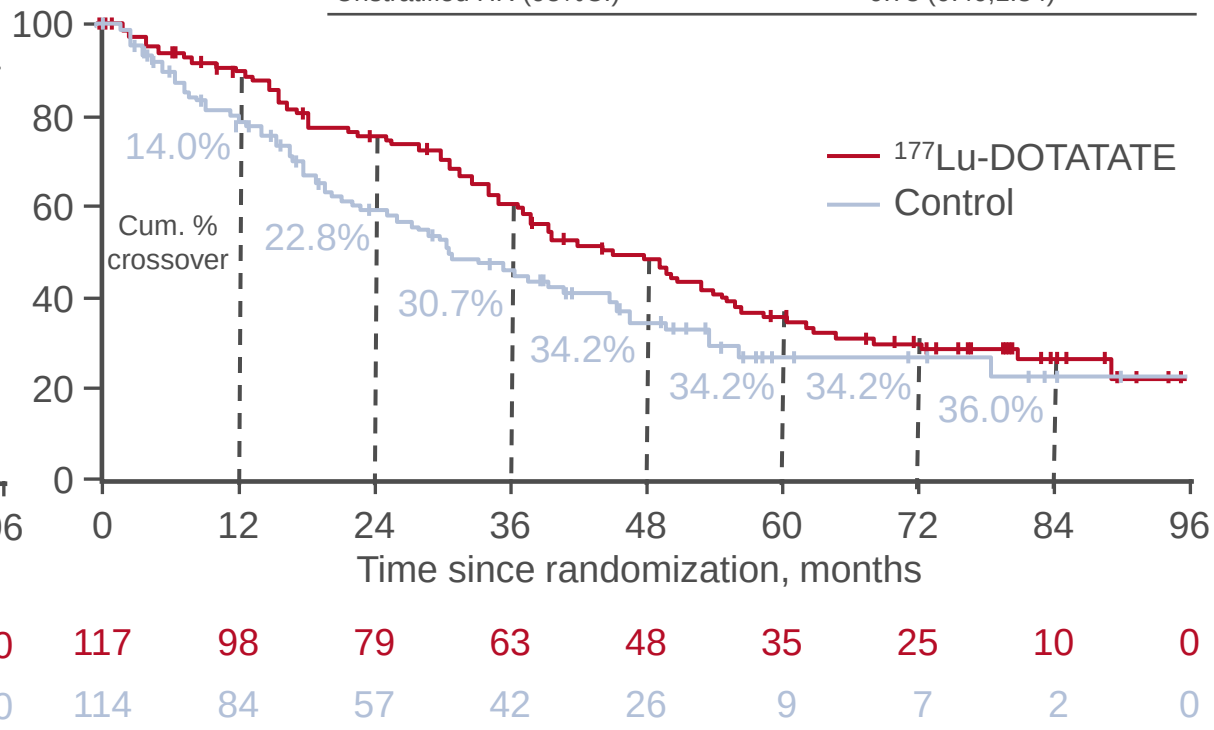



No. at risk

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| $^{177}$Lu-DOTATATE | 117 | 98 | 79 | 63 | 48 | 35 | 25 | 10 | 0 |
| Control | 114 | 84 | 61 | 45 | 33 | 25 | 21 | 6 | 0 |

### Overall survival (accounting for crossover in control arm)

| | $^{177}$Lu-DOTATATE | Control |
|---|---|---|
| mOS, mo | 48.0 | 30.9 |
| Unstratified HR (95%CI) | 0.73 (0.40,1.34) | |




| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| $^{177}$Lu-DOTATATE | 117 | 98 | 79 | 63 | 48 | 35 | 25 | 10 | 0 |
| Control | 114 | 84 | 57 | 42 | 26 | 9 | 7 | 2 | 0 |

Strosberg JR, et al. Ann Oncol 2021;32(suppl):abstr O-2

# O-2: Final overall survival in the phase 3 NETTER-1 study of lutetium-177-DOTATATE in patients with midgut neuroendocrine tumors – Strosberg JR, et al

## Key results (cont.)

| Subsequent treatment, % | $^{177}$Lu-DOTATATE (n=117) | Control (n=114) |
|---|---|---|
| Anti-neoplastic agent | 21.4 | 26.3 |
| Radioligand therapy | 12.0 | 36.0 |

| Select AEs, n (%) | $^{177}$Lu-DOTATATE (n=111) | Control (n=112) |
|---|---|---|
| Myelodysplastic syndrome | 2 (1.8) | - |
| Grade ≥3 nephrotoxicity | 6 (5.4) | 4 (3.6) |

## Conclusions

- **In patients with midgut NETs, $^{177}$Lu-DOTATATE did not demonstrate a statistically significant improvement in OS possibly because of a number of confounding factors such as crossover from the control arm (36%); there were no new safety signals observed**

Strosberg JR, et al. Ann Oncol 2021;32(suppl):abstr O-2

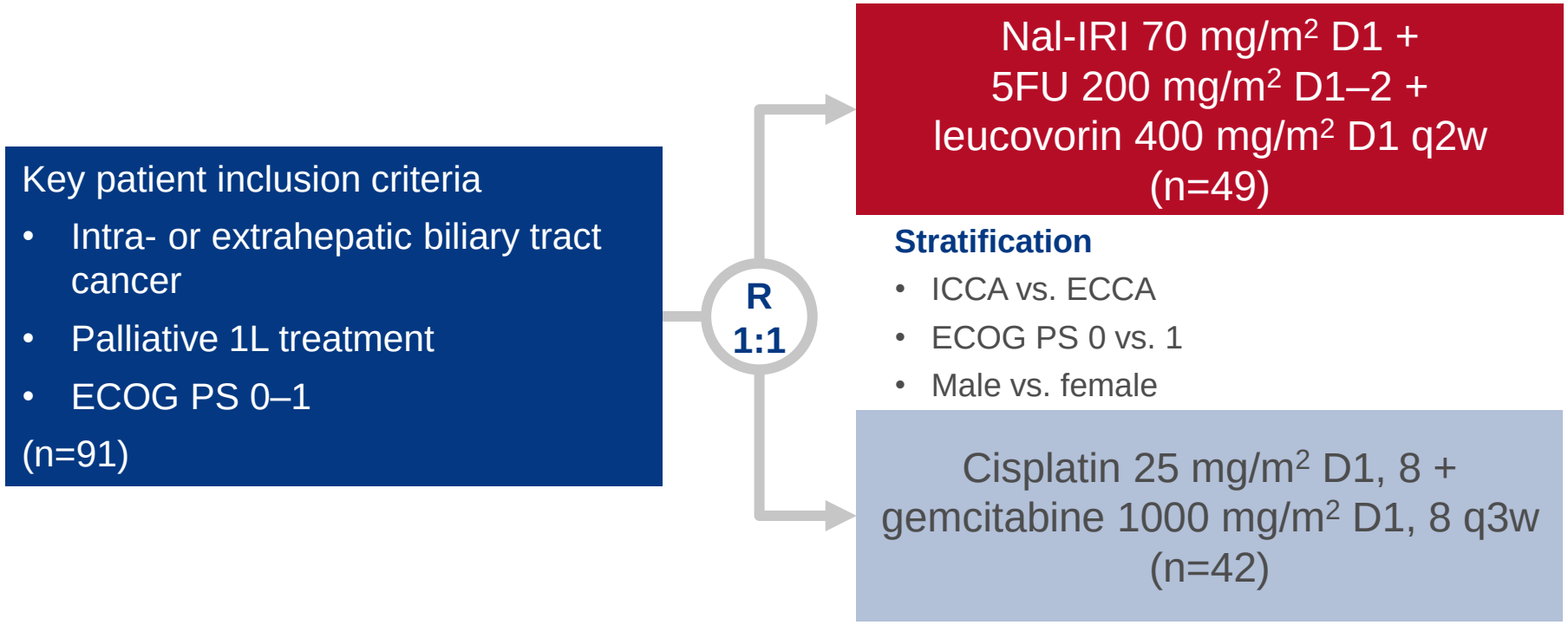
Cancers of the pancreas, small bowel and hepatobiliary tract

# BILIARY TRACT CANCER

# LBA10: Nal-IRI with 5-fluorouracil (5-FU) and leucovorin or gemcitabine plus cisplatin in advanced biliary tract cancer – final results of the NIFE-trial (AIO-YMO HEP-0315) - a randomized phase II study of the AIO biliary tract cancer group – Perkhofer L, et al

## Study objective

- To evaluate the efficacy and safety of Nal-IRI combined with 5FU + leucovorin compared with gemcitabine + cisplatin in patients with advanced biliary tract cancer in the NIFE study




### PRIMARY ENDPOINT

- 4-month PFS rate

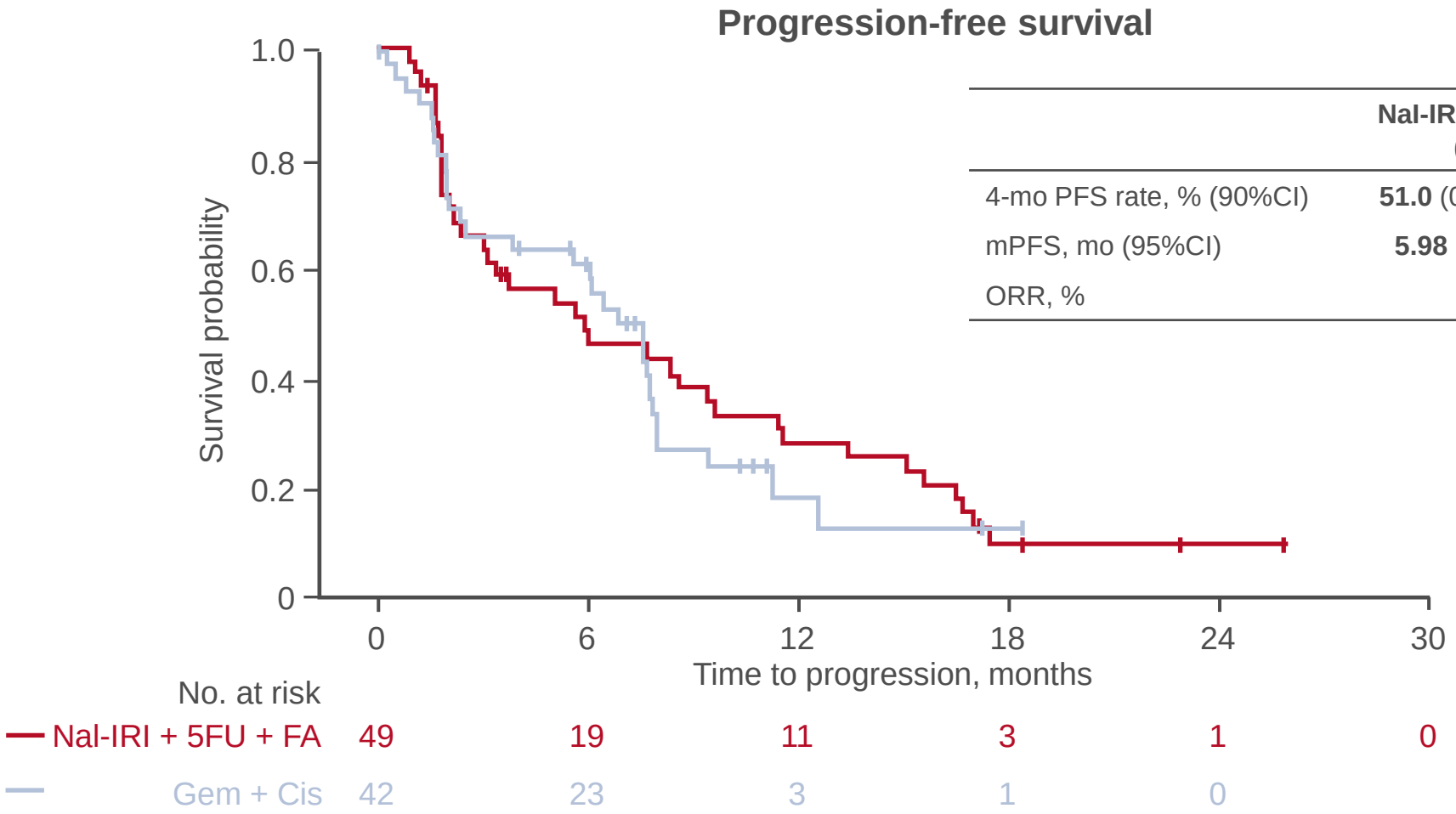
### SECONDARY ENDPOINTS

- PFS, OS, ORR, PROs, safety

Perkhofer L, et al. Ann Oncol 2021;32(suppl):abstr LBA10

# LBA10: Nal-IRI with 5-fluorouracil (5-FU) and leucovorin or gemcitabine plus cisplatin in advanced biliary tract cancer – final results of the NIFE-trial (AIO-YMO HEP-0315) - a randomized phase II study of the AIO biliary tract cancer group – Perkhofer L, et al

## Key results




| | Nal-IRI + 5FU + FA (n=49) | Gem + Cis (n=42) |
|---|---|---|
| 4-mo PFS rate, % (90%CI) | **51.0** (0.415, 0.605) | **59.5** |
| mPFS, mo (95%CI) | **5.98** (2.37, 9.59) | **6.87** (2.46, 7.82) |
| ORR, % | 24.5 | 11.9 |

Perkhofer L, et al. Ann Oncol 2021;32(suppl):abstr LBA10

# LBA10: Nal-IRI with 5-fluorouracil (5-FU) and leucovorin or gemcitabine plus cisplatin in advanced biliary tract cancer – final results of the NIFE-trial (AIO-YMO HEP-0315) - a randomized phase II study of the AIO biliary tract cancer group – Perkhofer L, et al

## Key results (cont.)

| | Nal-IRI + 5FU + LV | Gem + Cis |
|---|---|---|
| ICCA, n | 34 | 32 |
| mPFS, mo (95%CI) | 3.45 (2.10, 6.05) | 7.72 (6.05, 9.46) |
| mOS, mo (95%CI) | 14.19 (7.69, 21.85) | 16.36 (7.46, 19.91) |
| ECCA, n | 15 | 10 |
| mPFS, mo (95%CI) | 9.59 (1.94, 15.67) | 1.76 (0.16, 6.87) |
| mOS, mo (95%CI) | 18.23 (8.67, 30.95) | 6.34 (0.16, NE) |

| Grade 3/4 AEs, % | Nal-IRI + 5FU + LV (n=49) | Gem + Cis (n=42) |
|---|---|---|
| Diarrhea | 22.4 | 2.4 |
| Nausea | 12.2 | 0 |
| Neutropenia | 10.2 | 21.4 |
| Anemia | 4.1 | 26.2 |
| Fatigue | 4.1 | 2.4 |
| Thrombocytopenia | 2.0 | 9.5 |
| Mucositis | 2.0 | 0 |

## Conclusions

- **In patients with advanced biliary tract cancer, Nal-IRI + 5FU + leucovorin demonstrated encouraging clinical activity meeting the primary endpoint and with a safety profile similar to previous findings**

Perkhofer L, et al. Ann Oncol 2021;32(suppl):abstr LBA10

# CANCERS OF THE COLON, RECTUM AND ANUS

# LBA-3: Integrated analysis of cell free DNA (cfDNA) BRAF mutant allele fraction (MAF) and whole exome sequencing in BRAFV600E metastatic colorectal cancer (mCRC) treated with BRAF-antiEFGR +/- MEK inhibitors – Elez E, et al

## Study objective

- To evaluate the prognostic value of BRAF MAF and identify potential predictive biomarkers in patients with BRAF V600E mCRC

## Methods

- Data from 282 patients with BRAF V600E mCRC were assessed, of whom 86 had received targeted treatment with a BRAF/EGFR inhibitor with or without MEK inhibitor (encorafenib-cetuximab ± binimetinib), 74 had full clinical/pathological data available and 23 had FFPE/plasma samples available
- ddPCR was used to determine the baseline BRAF MAF and stratified as high (≥5%; n=14) or low (<5%; n=10) and wild-type (n=16)
- Univariate and multivariate Cox models were used to correlate BRAF MAF with OS
- Somatic mutations and copy number alterations were assessed using whole-exome sequencing (20,000 genes) and ctDNA quantification and copy number alterations were assessed using shallow whole-genome sequencing

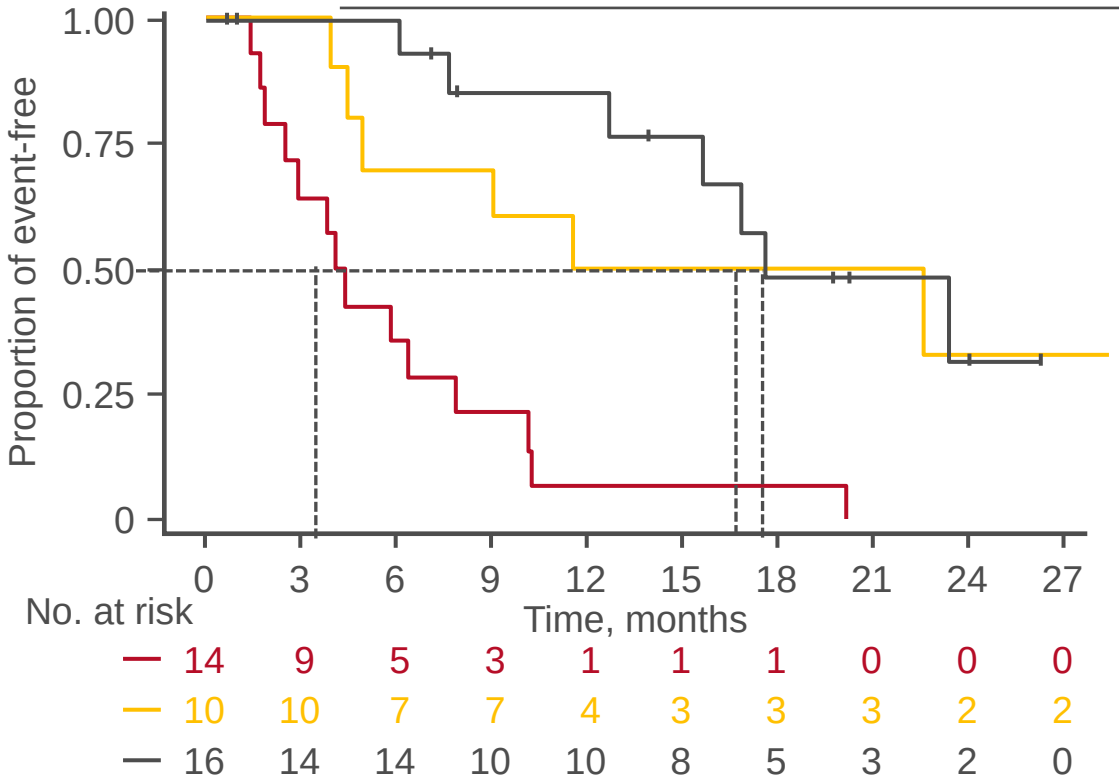
Elez E, et al. Ann Oncol 2021;32(suppl):abstr LBA-3

# LBA-3: Integrated analysis of cell free DNA (cfDNA) BRAF mutant allele fraction (MAF) and whole exome sequencing in BRAFV600E metastatic colorectal cancer (mCRC) treated with BRAF-antiEFGR +/- MEK inhibitors – Elez E, et al

## Key results

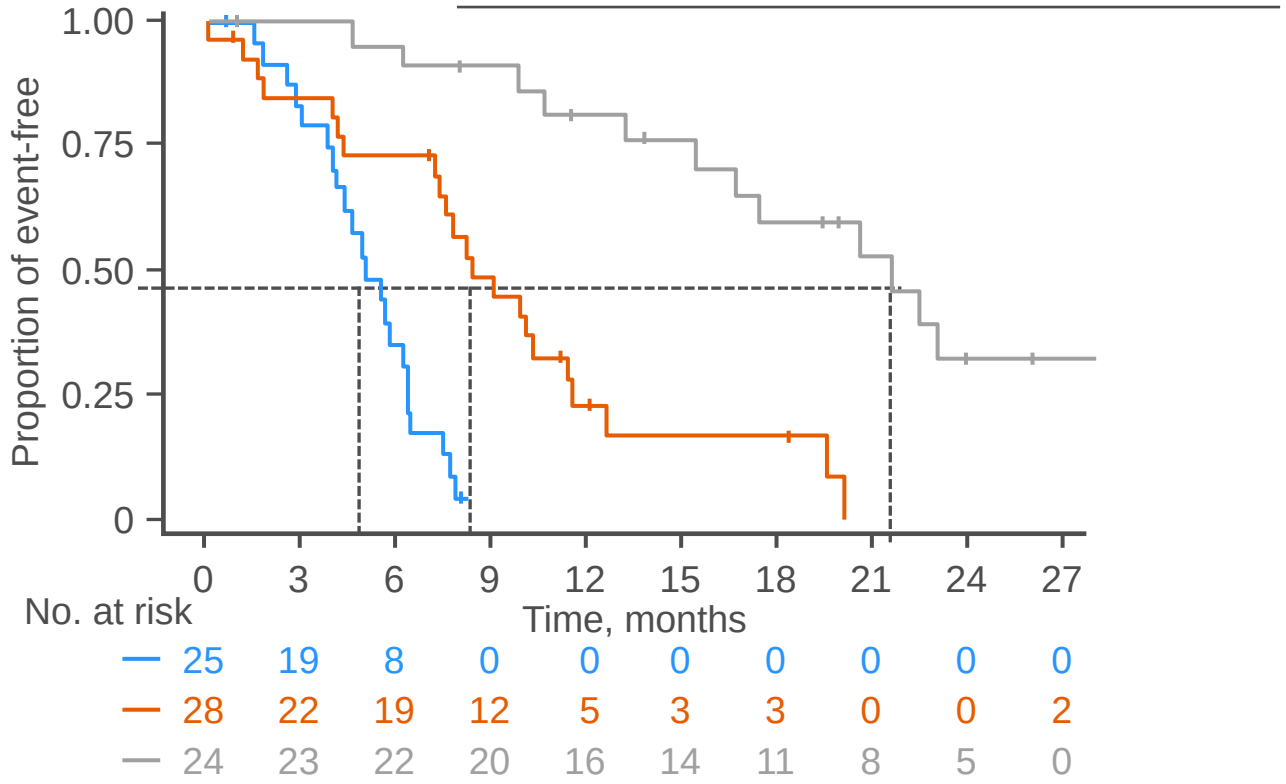
### OS by baseline MAF BRAF (univariate analysis)

| Baseline BRAF MAF | n | mOS, mo | HR (95%CI) | p-value |
|---|---|---|---|---|
| High (>5%) | 14 | 4.2 | Ref | |
| Low (<5%) | 10 | 17.1 | 0.21 (0.08, 0.59) | <0.001 |
| Undetectable | 16 | 17.5 | 0.15 (0.06, 0.40) | <0.001 |




### OS by risk group (multivariate model)

| Risk group | n | mOS, mo | HR (95%CI) | p-value |
|---|---|---|---|---|
| High risk | 25 | 5.1 | Ref | |
| Intermediate risk | 28 | 8.4 | 0.26 (0.12, 0.54) | <0.001 |
| Low risk | 24 | 21.8 | 0.05 (0.02, 0.13) | <0.001 |

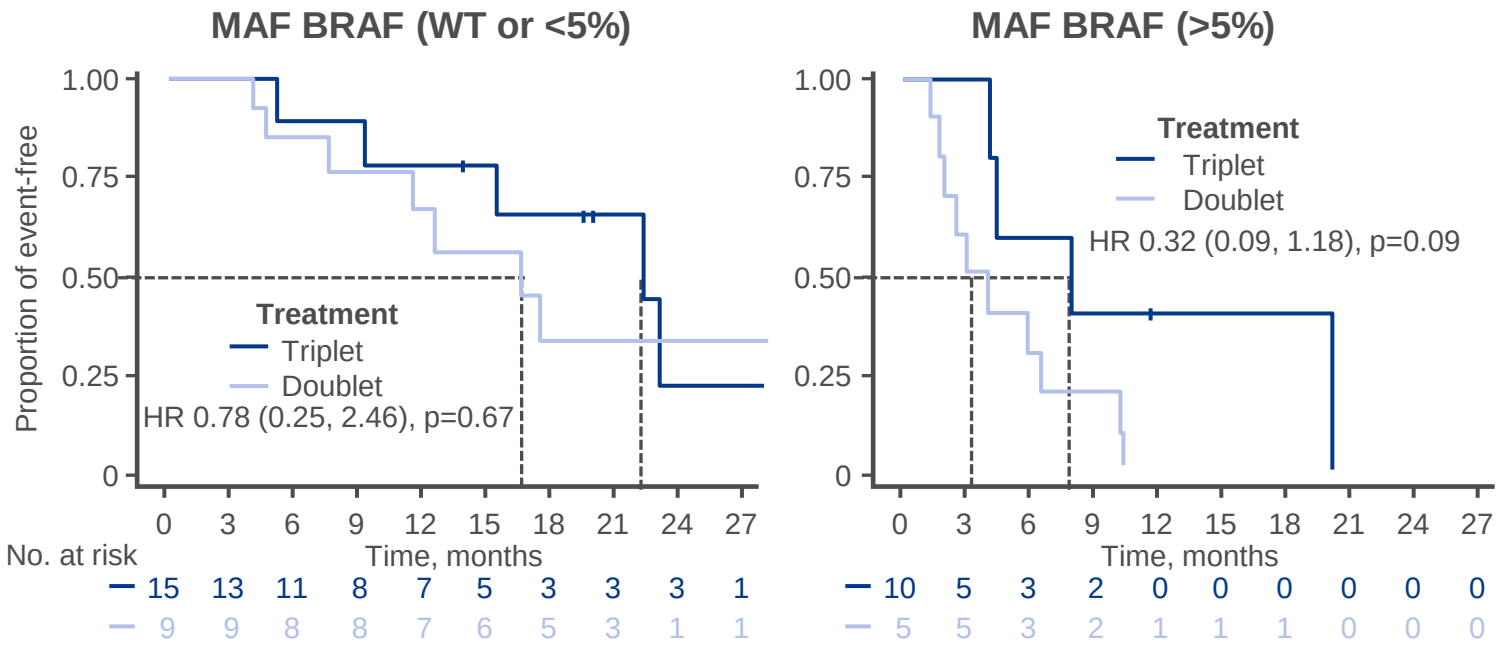


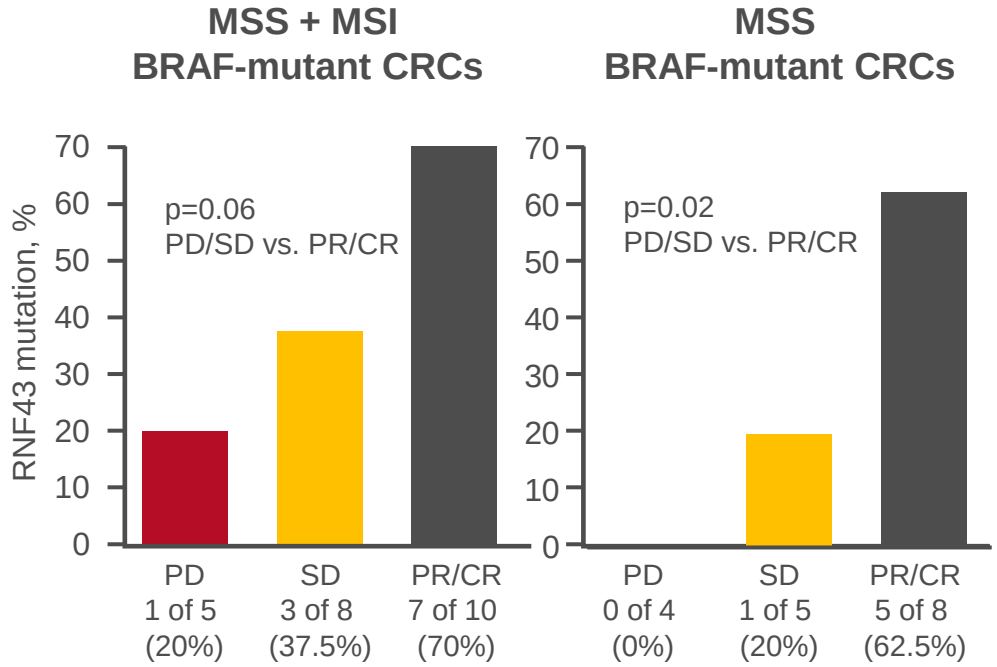

Elez E, et al. Ann Oncol 2021;32(suppl):abstr LBA-3

# LBA-3: Integrated analysis of cell free DNA (cfDNA) BRAF mutant allele fraction (MAF) and whole exome sequencing in BRAFV600E metastatic colorectal cancer (mCRC) treated with BRAF-antiEFGR +/- MEK inhibitors – Elez E, et al

## Key results (cont.)

### Overall survival




## Conclusions

- **In patients with BRAF V600E mCRC, cfDNA BRAF MAF could potentially be an independent prognostic biomarker for OS and RNF43 somatic mutations were enriched in those who responded to BRAF inhibitor combination therapies**

Elez E, et al. Ann Oncol 2021;32(suppl):abstr LBA-3

# LBA6: KRYSTAL-1: adagrasib (MRTX849) as monotherapy or combined with cetuximab (Cetux) in patients (pts) with colorectal cancer (CRC) harboring a KRASG12C mutation – Weiss J, et al

**Study objective**

- To evaluate the efficacy and safety of adagrasib alone or combined with cetuximab in the cohort of patients with CRC and harbouring a KRAS G12C mutation in the KRYSTAL-1 study

**Key patient inclusion criteria**

- Unresectable or mCRC
- KRAS G12C mutation
- No available treatment with curative intent or SoC

(n=565)

**Phase 1**
**Dose escalation**

Adagrasib
150, 300,
600, 1200 mg/day

**Phase 1b**
**Dose expansion + combination**

Adagrasib 600 mg/day
(n=2)

Adagrasib 600 mg/day + cetuximab
(n=32)

**Phase 2**

Adagrasib
600 mg/day
(n=44)

**PRIMARY ENDPOINT**

- Phase 1: RP2D, safety
- Phase 2: ORR (RECIST v1.1)

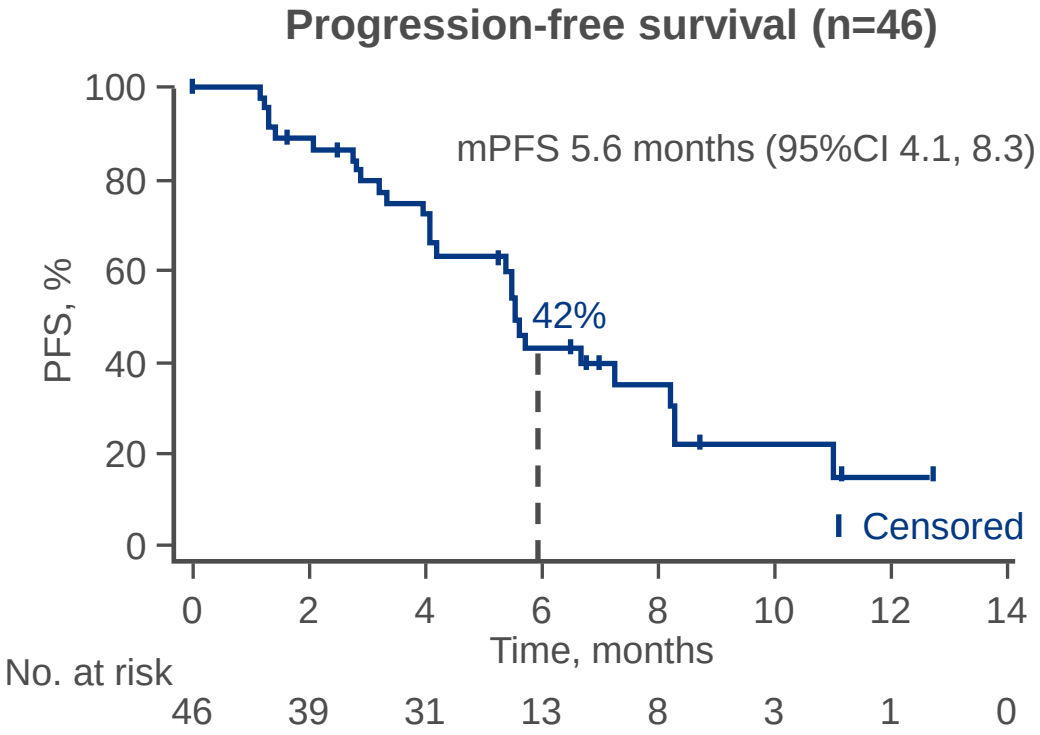
**SECONDARY ENDPOINTS**

- Phase 1: ORR, DoR, PFS, OS
- Phase 2: safety

Weiss J, et al. Ann Oncol 2021;32(suppl):abstr LBA6

# LBA6: KRYSTAL-1: adagrasib (MRTX849) as monotherapy or combined with cetuximab (Cetux) in patients (pts) with colorectal cancer (CRC) harboring a KRASG12C mutation – Weiss J, et al

## Key results




| | Adagrasib (n=45) | Adagrasib + cetuximab (n=28) |
|---|---|---|
| Response rate, n (%)<br>SD, n (%) | 10 (22)<br>29 (64) | 12 (43)<br>16 (57) |
| DCR, n (%) | 39 (87) | 28 (100) |
| DoR, mo | 4.2 | - |
| Median time to response, mo | 1.4 | 1.3 |

Weiss J, et al. Ann Oncol 2021;32(suppl):abstr LBA6

# LBA6: KRYSTAL-1: adagrasib (MRTX849) as monotherapy or combined with cetuximab (Cetux) in patients (pts) with colorectal cancer (CRC) harboring a KRASG12C mutation – Weiss J, et al

## Key results (cont.)

| Grade 3/4 TRAEs, % | Adagrasib (n=46) |
|---|---|
| Any | 30 |
| Diarrhoea | 7 |
| Fatigue | 4 |
| AST increased | 4 |
| ALT increased | 4 |
| QT prolongation | 2 |
| Anaemia | 2 |

| Grade 3/4 TRAEs, % | Adagrasib + cetuximab (n=32) |
|---|---|
| Any | 16 |
| Diarrhoea | 3 |
| Dermatitis acneiform | 3 |
| Infusion-related reaction | 3 |
| QT prolongation | 3 |
| Stomatitis | 3 |

## Conclusions

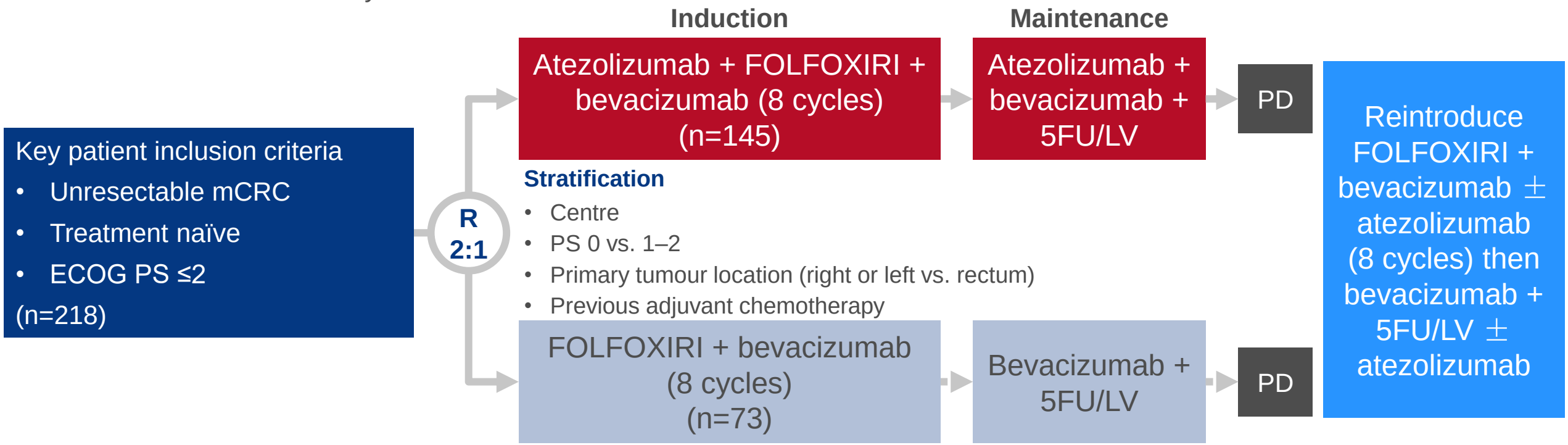
- **In previously treated patients with CRC harbouring a KRAS G12C mutation, adagrasib alone or combined with cetuximab demonstrated promising clinical activity and had a manageable safety profile**

Weiss J, et al. Ann Oncol 2021;32(suppl):abstr LBA6

# LBA20: FOLFOXIRI plus bevacizumab (bev) plus atezolizumab (atezo) versus FOLFOXIRI plus bev as first-line treatment of unresectable metastatic colorectal cancer (mCRC) patients: results of the phase II randomized AtezoTRIBE study by GONO – Cremolini C, et al

## Study objective

- To evaluate the efficacy and safety of 1L atezolizumab + FOLFOXIRI + bevacizumab in patients with unresectable mCRC in the AtezoTRIBE study




### PRIMARY ENDPOINT

- PFS

### SECONDARY ENDPOINTS

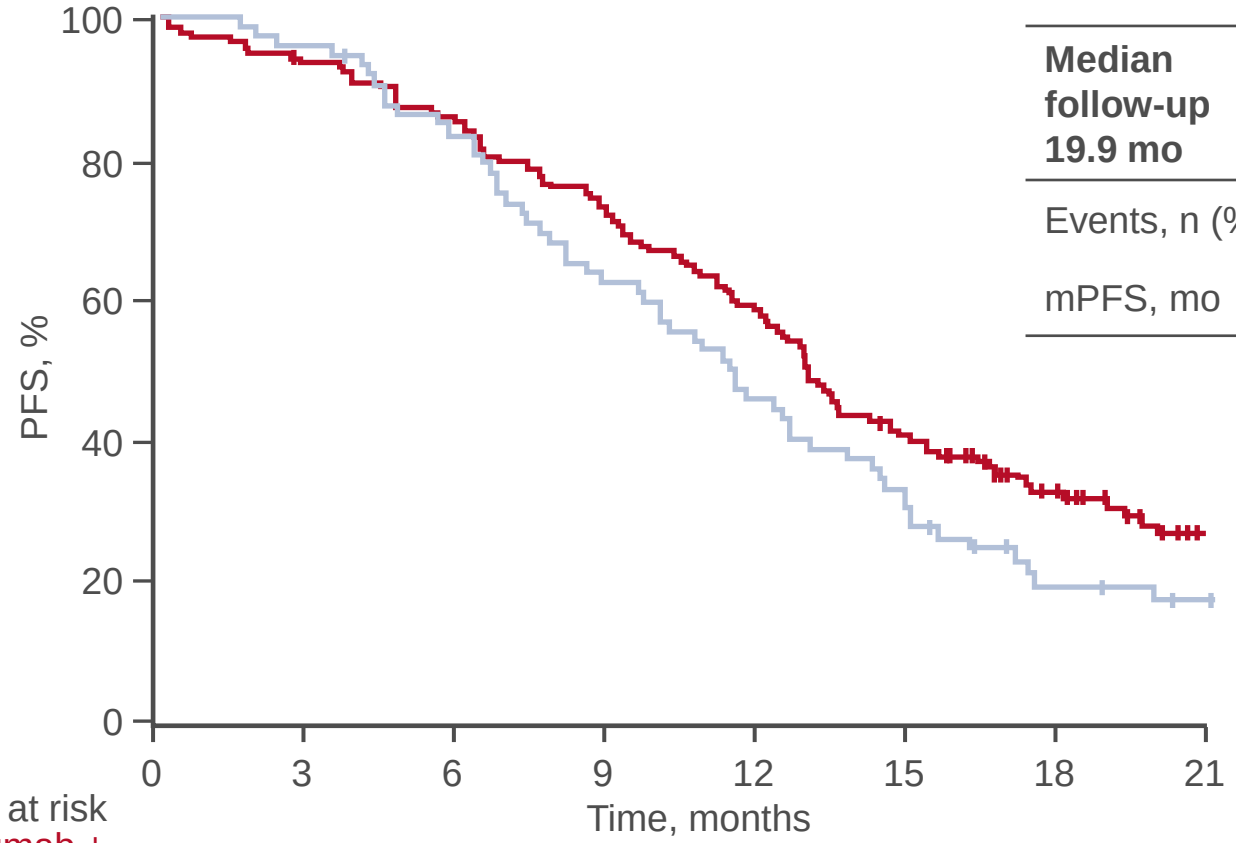
- Response, resection rate, safety

Cremolini C, et al. Ann Oncol 2021;32(suppl):abstr LBA20

# LBA20: FOLFOXIRI plus bevacizumab (bev) plus atezolizumab (atezo) versus FOLFOXIRI plus bev as first-line treatment of unresectable metastatic colorectal cancer (mCRC) patients: results of the phase II randomized AtezoTRIBE study by GONO – Cremolini C, et al

## Key results

### Progression-free survival




| Median follow-up 19.9 mo | Atezolizumab + FOLFOXIR + bev (n=145) | FOLFOXIRI + bev (n=73) |
|---|---|---|
| Events, n (%) | 99 (68) | 60 (82) |
| mPFS, mo | 13.1 | 11.5 |

HR 0.69 (80%CI 0.56, 0.85); p=0.012

Cremolini C, et al. Ann Oncol 2021;32(suppl):abstr LBA20

# LBA20: FOLFOXIRI plus bevacizumab (bev) plus atezolizumab (atezo) versus FOLFOXIRI plus bev as first-line treatment of unresectable metastatic colorectal cancer (mCRC) patients: results of the phase II randomized AtezoTRIBE study by GONO – Cremolini C, et al

## Key results (cont.)

| | Atezolizumab + FOLFOXIRI + bevacizumab (n=145) | FOLFOXIRI + bevacizumab (n=73) |
|---|---|---|
| Response rate, % | 59 | 64 |
| OR (80%CI); p-value | 0.78 (0.54, 1.15); 0.412 | |
| BOR, % | | |
| CR | 6 | 6 |
| PR | 53 | 59 |
| SD | 33 | 29 |
| PD | 3 | 4 |
| NA | 6 | 3 |
| R0 resection rate, % | 26 | 37 |
| p-value | 0.175 | |

| Grade 3/4 AEs occurring in ≥5%, % | Atezolizumab + FOLFOXIRI + bevacizumab (n=145) | FOLFOXIRI + bevacizumab (n=73) |
|---|---|---|
| Neutropenia | 41 | 36 |
| Diarrhoea | 15 | 12 |
| Febrile neutropenia | 10 | 10 |
| Asthenia | 5 | 6 |
| Stomatitis | 4 | 8 |
| Venous thromboembolism | 4 | 6 |

## Conclusions

- **In patients with unresectable mCRC, 1L atezolizumab + FOLFOXIRI + bevacizumab demonstrated a significant improvement in PFS over FOLFOXIRI + bevacizumab and was generally well-tolerated**

Cremolini C, et al. Ann Oncol 2021;32(suppl):abstr LBA20

# LBA21: Radioembolization with chemotherapy for colorectal liver metastases: a randomized, open-label, international, multicenter, phase 3 trial (EPOCH study) – Mulcahy MF, et al

## Study objective

- To evaluate the efficacy and safety of radioembolization + chemotherapy in patients with colorectal liver metastases in the EPOCH study

**Key patient inclusion criteria**

- Unresectable unilobar or bilobar colorectal liver metastases
- Eligible for 2L irinotecan- or oxaliplatin-based chemotherapy
- Bilirubin ≤1.2 ULN
- Albumin ≥3.0 g/dL
- ECOG PS 0–1

(n=428)

R 1:1

Y-90 Glass* + chemotherapy ± targeted therapy (n=215)

**Stratification**

- Unilobar/bilobar disease
- KRAS status
- 1L therapy (irinotecan- or oxaliplatin-based)

Chemotherapy ± targeted therapy (n=213)

Irinotecan- or oxaliplatin-based chemotherapy

PD/hepatic disease progression/ death

**PRIMARY ENDPOINTS**

- PFS, hepatic PFS (BICR)

**SECONDARY ENDPOINTS**

- OS, ORR, DCR, QoL, safety

*TARE with $Y^{90}$ glass microspheres – cycle 1, chemotherapy; cycle 2, Y-90 TARE; cycle 3, chemotherapy ± targeted therapy

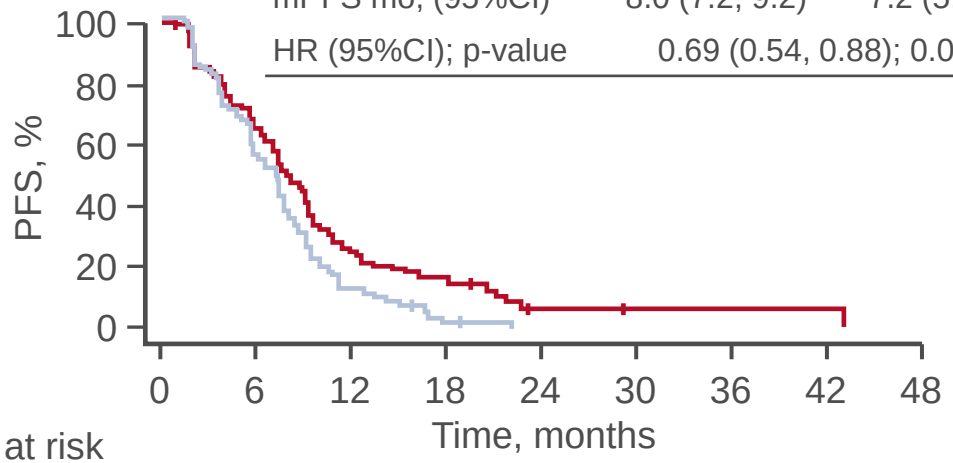
Mulcahy MF, et al. Ann Oncol 2021;32(suppl):abstr LBA21

# LBA21: Radioembolization with chemotherapy for colorectal liver metastases: a randomized, open-label, international, multicenter, phase 3 trial (EPOCH study) – Mulcahy MF, et al

## Key results

### Progression-free survival

| | Y-90 + chemo (n=215) | Chemo (n=213) |
|---|---|---|
| mPFS mo, (95%CI) | 8.0 (7.2, 9.2) | 7.2 (5.7, 7.6) |
| HR (95%CI); p-value | 0.69 (0.54, 0.88); 0.0013 | |



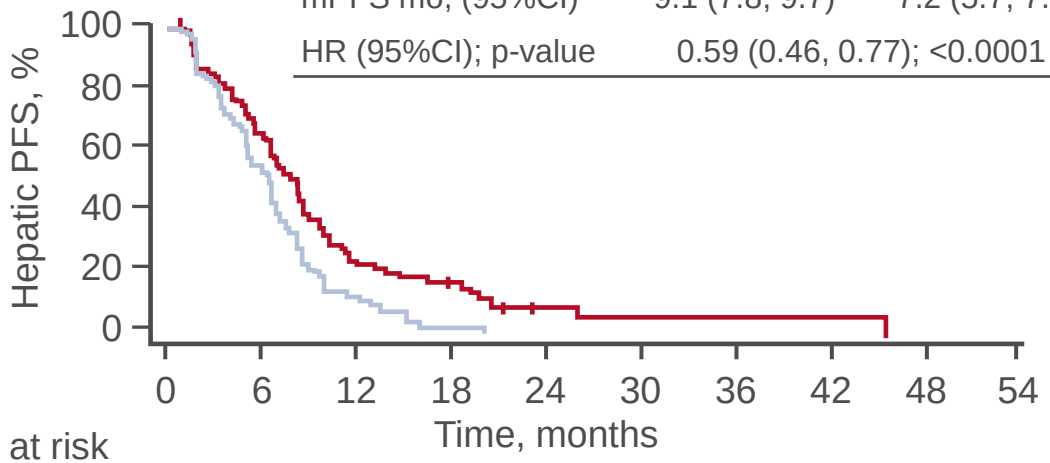

No. at risk

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Y-90 + CT | 215 | 111 | 29 | 13 | 2 | 1 | 1 | 1 | 0 |
| CT | 213 | 76 | 9 | 1 | 0 | 0 | 0 | 0 | 0 |

| PFS rate, % (95%CI) | 6 mo | 12 mo | 18 mo |
|---|---|---|---|
| Y-90 + chemo (n=215) | 65.2 (58.0, 71.5) | 25.8 (18.9, 33.1) | 16.7 (10.6, 23.9) |
| Chemo (n=213) | 55.4 (47.2, 62.8) | 13.2 (7.5, 20.5) | 1.8 (0.2, 8.1) |

### Hepatic progression-free survival

| | Y-90 + chemo (n=215) | Chemo (n=213) |
|---|---|---|
| mPFS mo, (95%CI) | 9.1 (7.8, 9.7) | 7.2 (5.7, 7.6) |
| HR (95%CI); p-value | 0.59 (0.46, 0.77); <0.0001 | |




No. at risk

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Y-90 + CT | 215 | 118 | 32 | 14 | 4 | 1 | 1 | 1 | 1 | 0 |
| CT | 213 | 76 | 9 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |

| Hepatic PFS rate, % (95%CI) | 6 mo | 12 mo | 18 mo |
|---|---|---|---|
| Y-90 + chemo (n=215) | 70.7 (63.6, 76.6) | 29.8 (22.4, 37.6) | 19.8 (13.0, 27.6) |
| Chemo (n=213) | 55.2 (47.1, 62.7) | 13.5 (7.7, 20.9) | 1.9 (0.2, 8.3) |

Mulcahy MF, et al. Ann Oncol 2021;32(suppl):abstr LBA21

# LBA21: Radioembolization with chemotherapy for colorectal liver metastases: a randomized, open-label, international, multicenter, phase 3 trial (EPOCH study) – Mulcahy MF, et al

## Key results (cont.)

| | Y-90 + chemotherapy (n=215) | Chemotherapy (n=213) |
|---|---|---|
| mOS, mo (95%CI) | 14.0 | 14.4 |
| HR (95%CI); p-value | 1.07 (0.86, 1.32); 0.7229 | |
| 12-mo OS, % (95%CI) | 56.3 (49.2, 62.8) | 62.4 (55.0, 68.9) |
| ORR, n (%) [95%CI] | 73 (34.0) [28.0, 40.5] | 45 (21.1) [16.2, 27.1] |
| BOR, % | | |
| CR | 2 (0.9) | 3 (1.4) |
| PR | 71 (33.0) | 42 (19.7) |
| SD | 98 (45.6) | 110 (51.6) |
| PD | 27 (12.6) | 27 (12.7) |

| TEAEs, n (%) | Y-90 + chemotherapy (n=187) | Chemotherapy (n=207) |
|---|---|---|
| Any | 181 (96.8) | 194 (93.7) |
| Chemotherapy-related | 172 (92.0) | 189 (91.3) |
| Device-related | 103 (55.1) | 0 |
| Angiographic procedure-related | 55 (29.4) | 2 (1.0) |
| Grade ≥3 | 128 (68.4) | 102 (49.3) |
| Serious | 70 (37.4) | 43 (20.8) |
| Serious device-related | 20 (10.7) | 0 |
| Led to discontinuation | 24 (12.8) | 25 (12.1) |
| Led to death | 8 (4.3) | 4 (1.9) |

## Conclusions

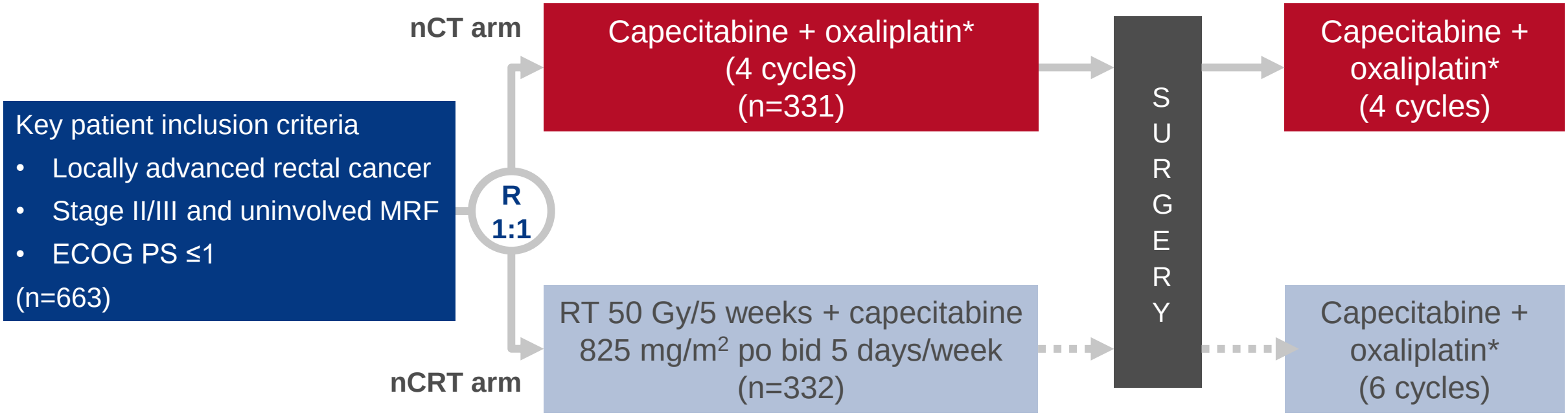
- **In patients with colorectal liver metastases, 2L Y-90 TARE + chemotherapy demonstrated significant improvement in PFS and hepatic PFS compared with chemotherapy alone, but did not provide any benefit in OS**

Mulcahy MF, et al. Ann Oncol 2021;32(suppl):abstr LBA21

# LBA22: Neoadjuvant chemotherapy with oxaliplatin and capecitabine versus chemoradiation with capecitabine for locally advanced rectal cancer with uninvolved mesorectal fascia (CONVERT): initial results of a multicenter randomised, open-label, phase III trial – Ding PR, et al

## Study objective

- To evaluate the efficacy and safety of neoadjuvant chemotherapy compared with chemoradiation in patients with locally advanced rectal cancer and uninvolved mesorectal fascia in the CONVERT study




### PRIMARY ENDPOINT

- 3-year local regional failure-free survival

### SECONDARY ENDPOINTS

- DFS, OS, pCR rate, TRG, R0 rate, safety

*Oxaliplatin 130 mg/m$^2$ iv over 2 h D1 + capecitabine 1000 mg/m$^2$ po bid D1–14 q3w

Ding PR, et al. Ann Oncol 2021;32(suppl):abstr LBA22

# LBA22: Neoadjuvant chemotherapy with oxaliplatin and capecitabine versus chemoradiation with capecitabine for locally advanced rectal cancer with uninvolved mesorectal fascia (CONVERT): initial results of a multicenter randomised, open-label, phase III trial – Ding PR, et al

## Key results

| All patients, n/N (%) | nCT | nCRT | p-value |
|---|---|---|---|
| pCR rate | 30/272 (11.0) | 36/261 (13.8) | 0.333 |
| cCR rate | 2/300 (0.7) | 5/289 (1.7) | 0.278 |
| ypstage 0–1 rate | 111/272 (40.8) | 119/261 (45.6) | 0.265 |
| Perioperative distant mets | 2/300 (0.7) | 9/289 (3.1) | 0.034 |

| Low LARC, n/N (%) | nCT | nCRT | p-value |
|---|---|---|---|
| pCR rate | 11/108 (10.2) | 15/105 (14.3) | 0.361 |
| cCR rate | 2/124 (1.6) | 3/118 (2.6) | 0.677 |
| ypstage 0–1 rate | 50/108 (46.3) | 50/105 (47.6) | 0.847 |
| Perioperative distant mets | 1/124 (0.8) | 3/118 (2.6) | 0.369 |

| All patients, n (%) | nCT (n=272) | nCRT (n=261) | p-value |
|---|---|---|---|
| pT4 | 41 (15.1) | 28 (10.7) | 0.135 |
| pN0 | 200 (73.5) | 214 (82.0) | 0.019 |
| TRG 0–1 | 63/263 (24.0) | 96/249 (38.6) | <0.001 |
| R0 resection | 271 (99.6) | 260 (99.6) | 0.999 |
| Spincter preservation | 258 (94.9) | 246 (94.3) | 0.760 |
| Preventive diverting ileostomy | 142 (52.2) | 166 (63.6) | 0.008 |
| Any postop complications | 48 (17.7) | 63 (24.1) | 0.065 |
| Anastomotic leak | 17 (6.3) | 16 (6.1) | 0.954 |
| Postop mortality (≤60 days) | 0 | 1 (0.4) | 0.490 |

| Within 5 cm from anal verge, n (%) | nCT (n=108) | nCRT (n=105) | p-value |
|---|---|---|---|
| pT4 | 4 (3.7) | 10 (9.5) | 0.103 |
| pN0 | 74 (68.5) | 88 (76.5) | 0.180 |
| TRG 0–1 | 25/105 (23.8) | 41/98 (41.8) | <0.001 |
| R0 resection | 107 (99.6) | 104 (99.6) | 0.999 |
| Spincter preservation | 95 (88.0) | 93 (86.6) | 0.890 |
| Preventive diverting ileostomy | 77 (71.3) | 76 (72.4) | 0.860 |
| Any postop complications | 26 (24.1) | 29 (27.6) | 0.555 |
| Anastomotic leak | 6 (5.6) | 6 (5.7) | 0.960 |
| Postop mortality (≤60 days) | 0 | 0 | - |

Ding PR, et al. Ann Oncol 2021;32(suppl):abstr LBA22

# LBA22: Neoadjuvant chemotherapy with oxaliplatin and capecitabine versus chemoradiation with capecitabine for locally advanced rectal cancer with uninvolved mesorectal fascia (CONVERT): initial results of a multicenter randomised, open-label, phase III trial – Ding PR, et al

## Key results (cont.)

| AEs, n (%) | Neoadjuvant phase | | Adjuvant phase | |
|---|---|---|---|---|
| | nCT (n=300) | nCRT (n=289) | nCT (n=235) | nCRT (n=222) |
| Any grade 3/4 | 37 (12.3) | 24 (8.3) | 12 (5.1) | 20 (9.0) |
| Grade 3/4 leukopenia | 9 (3.0) | 14 (4.8) | 2 (0.9) | 5 (2.3) |
| Grade 3/4 thrombocytopenia | 16 (5.3) | 3 (1.0) | 3 (1.3) | 14 (6.3) |
| Grade 3/4 diarrhoea | 4 (1.3) | 1 (0.3) | 0 | 1 (0.5) |
| Grade 3/4 genitourinary | 0 | 3 (1.0) | 0 | 0 |
| Mortality | 2 (0.7) | 0 | 0 | 0 |
| Received full dose of therapy | 259 (86.3) | 263 (91.0) | 124 (52.8) | 98 (44.1) |

## Conclusions

- **In patients with locally advanced rectal cancer with uninvolved mesorectal fascia, neoadjuvant chemotherapy demonstrated similar rates of pCR, cCR and downstaging as neoadjuvant chemoradiation and both arms had comparable overall safety**

Ding PR, et al. Ann Oncol 2021;32(suppl):abstr LBA22

# O-3: Characterization of KRAS mutation variants and prevalence of KRAS-G12C in gastrointestinal malignancies – Salem M, et al

**Study objective**

- To evaluate the prevalence of KRAS variants and identify potential biomarkers in patients with GI cancers

**Methods**

- Samples from 17,009 patients with GI cancers were assessed using Tempus xT or xF NGS
  - Of the samples, 9450 were KRAS wild-type and 7559 were KRAS mutant (325 G12C and 7234 non-G12C)
- Logistic regression analysis was used to determine the association between cancer subtypes and KRAS variants, the association between KRAS variants and immuno-oncology biomarkers and co-mutations between G12C and other oncogenes
- For multiple testing, a false discovery rate-adjusted (FDR) p-value was used with a cut-off of $p<0.05$ for significance

Salem M, et al. Ann Oncol 2021;32(suppl):abstr O-3

# O-3: Characterization of KRAS mutation variants and prevalence of KRAS-G12C in gastrointestinal malignancies – Salem M, et al

## Key results

| Frequency of KRAS G12C mutations, n (%) | Appendiceal (n=279) | CRC (n=6586) | SBA (n=630) | Pancreatic (n=5029) | Biliary tract (n=1481) | Gastric (n=1401) | Oesophageal (n=941) | HCC (n=467) | Anal (n=195) |
|---|---|---|---|---|---|---|---|---|---|
| KRAS G12C mutation | 11 (3.9) | 208 (3.1) | 9 (1.4) | 66 (1.3) | 18 (1.2) | 9 (0.6) | 3 (0.3) | 1 (0.2) | 0 |
| KRAS non-G12C mutation | 125 (44.8) | 2763 (42.0) | 142 (22.5) | 3627 (72.1) | 242 (16.3) | 168 (12.0) | 136 (14.5) | 23 (4.9) | 8 (4.1) |

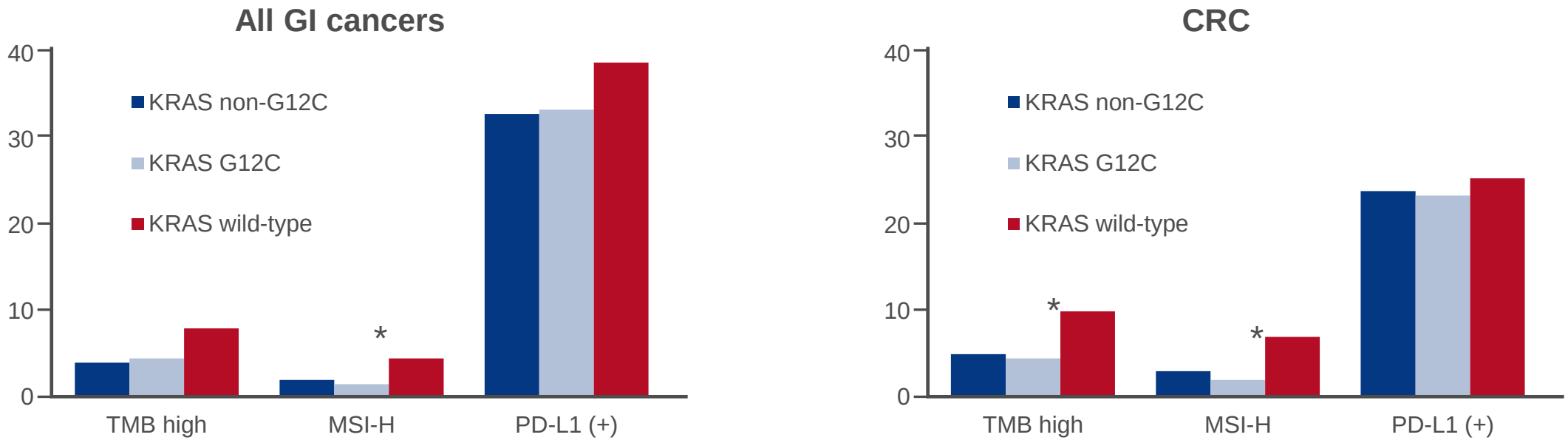
| KRAS variants, n (%) | G12D | G12V | G12C | G13D | G12R | Q61H | Others |
|---|---|---|---|---|---|---|---|
| All GI cancers | 2675 (35.4) | 1776 (23.5) | 325 (4.3) | 603 (8.0) | 656 (8.7) | 348 (4.6) | 177 (20.1) |
| CRC | 889 (29.9) | 595 (20.0) | 208 (7.0) | 469 (15.8) | 31 (1.0) | 125 (4.2) | 654 (22.0) |
| Appendiceal | 69 (50.7) | 35 (25.7) | 10 (7.4) | 10 (7.4) | 0 | 3 (2.2) | 9 (6.6) |
| Pancreatic | 1543 (41.8) | 1165 (31.6) | 66 (1.8) | 15 (0.4) | 595 (16.1) | 175 (4.7) | 134 (3.6) |

Salem M, et al. Ann Oncol 2021;32(suppl):abstr O-3

# O-3: Characterization of KRAS mutation variants and prevalence of KRAS-G12C in gastrointestinal malignancies – Salem M, et al

## Key results (cont.)

### Immune biomarkers according to KRAS status




## Conclusions

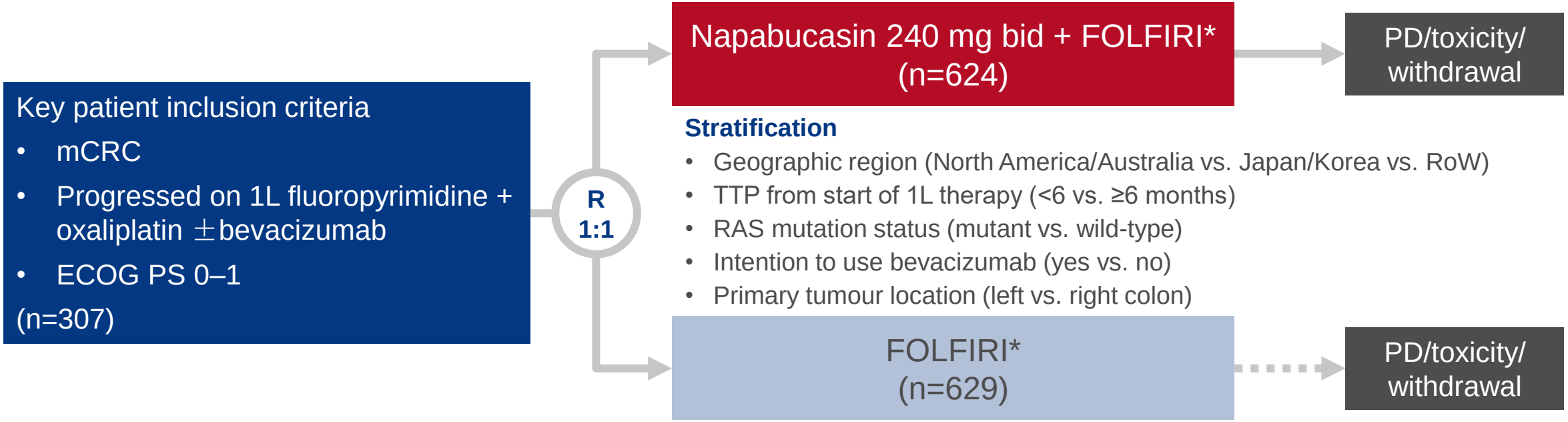
- **In patients with GI malignancies, G12D and G12V were the most common KRAS variants, although there were significant differences in the distribution of variants across cancer types**

Salem M, et al. Ann Oncol 2021;32(suppl):abstr O-3

# O-7: FOLFIRI ± napabucasin in patients with previously treated metastatic colorectal cancer (mCRC): overall survival results from the phase 3 CanStem303C study – Shah M, et al

## Study objective

- To evaluate the efficacy and safety of napabucasin + FOLFIRI in previously treated patients with mCRC in the CanStem303C study




### PRIMARY ENDPOINTS

- OS in overall population and in biomarker-positive subgroup

### SECONDARY ENDPOINTS

- PFS, DCR, ORR, safety

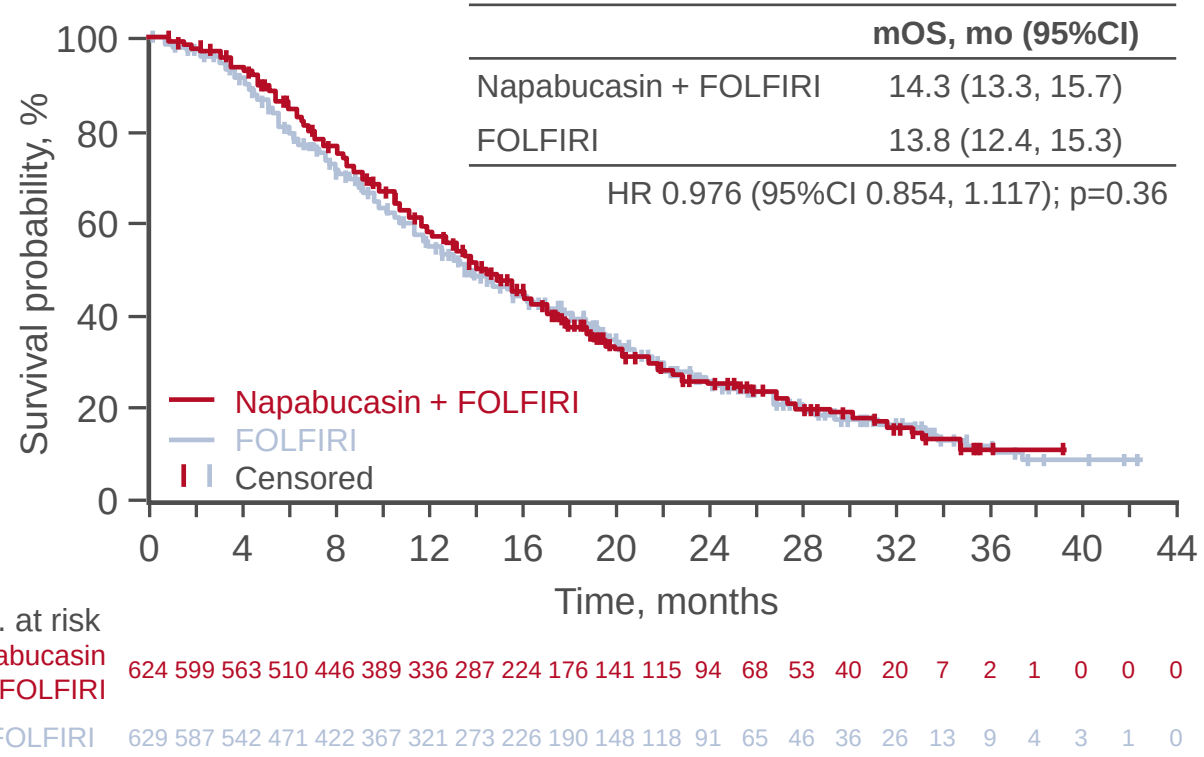
*FOLFIRI iv D1 q2w, ≥2 hours after first daily dose of napabucasin and bevacizumab could be added at investigator discretion

Shah M, et al. Ann Oncol 2021;32(suppl):abstr O-7

# O-7: FOLFIRI ± napabucasin in patients with previously treated metastatic colorectal cancer (mCRC): overall survival results from the phase 3 CanStem303C study – Shah M, et al

## Key results

### Overall survival in overall population

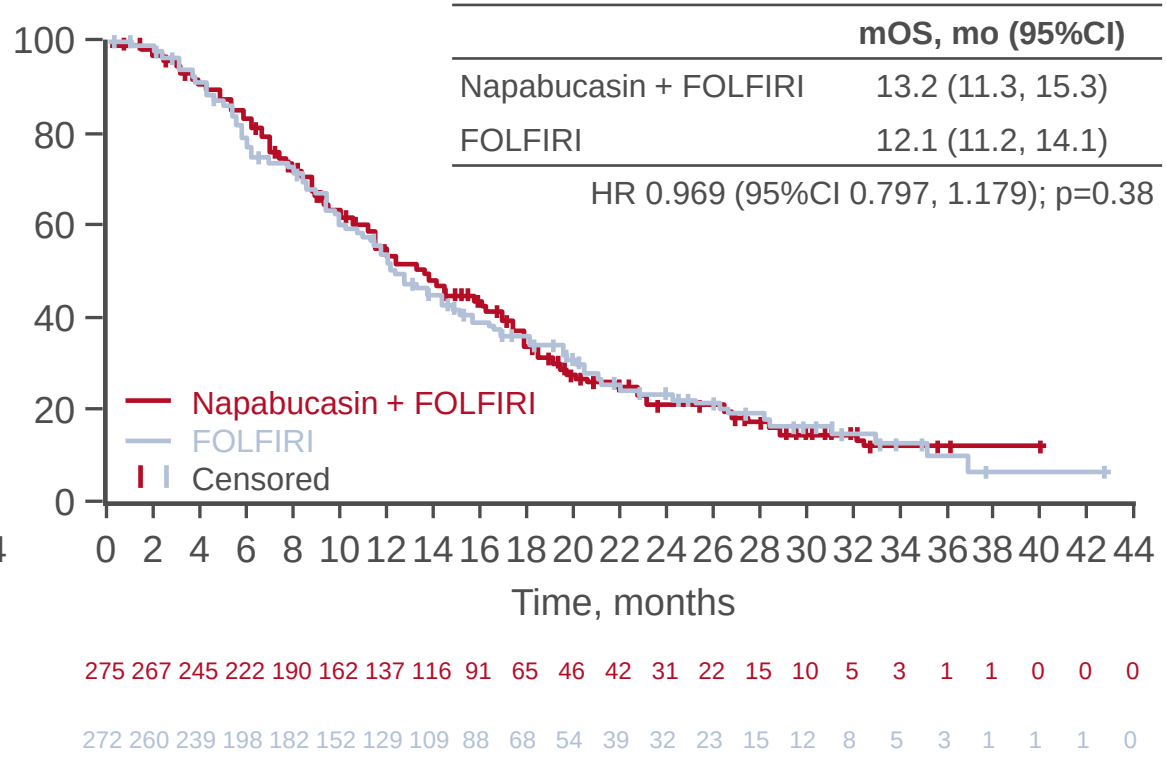



| | mOS, mo (95%CI) |
|---|---|
| Napabucasin + FOLFIRI | 14.3 (13.3, 15.7) |
| FOLFIRI | 13.8 (12.4, 15.3) |

HR 0.976 (95%CI 0.854, 1.117); p=0.36

| No. at risk | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Napabucasin + FOLFIRI | 624 | 599 | 563 | 510 | 446 | 389 | 336 | 287 | 224 | 176 | 141 | 115 | 94 | 68 | 53 | 40 | 20 | 7 | 2 | 1 | 0 | 0 | 0 |
| FOLFIRI | 629 | 587 | 542 | 471 | 422 | 367 | 321 | 273 | 226 | 190 | 148 | 118 | 91 | 65 | 46 | 36 | 26 | 13 | 9 | 4 | 3 | 1 | 0 |

### Overall survival in biomarker-positive subgroup




| | mOS, mo (95%CI) |
|---|---|
| Napabucasin + FOLFIRI | 13.2 (11.3, 15.3) |
| FOLFIRI | 12.1 (11.2, 14.1) |

HR 0.969 (95%CI 0.797, 1.179); p=0.38

| | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Napabucasin + FOLFIRI | 275 | 267 | 245 | 222 | 190 | 162 | 137 | 116 | 91 | 65 | 46 | 42 | 31 | 22 | 15 | 10 | 5 | 3 | 1 | 1 | 0 | 0 | 0 |
| FOLFIRI | 272 | 260 | 239 | 198 | 182 | 152 | 129 | 109 | 88 | 68 | 54 | 39 | 32 | 23 | 15 | 12 | 8 | 5 | 3 | 1 | 1 | 1 | 0 |

Shah M, et al. Ann Oncol 2021;32(suppl):abstr O-7

# O-7: FOLFIRI ± napabucasin in patients with previously treated metastatic colorectal cancer (mCRC): overall survival results from the phase 3 CanStem303C study – Shah M, et al

## Key results (cont.)

| | Overall population | | Biomarker-positive | |
|---|---|---|---|---|
| | Napabucasin + FOLFIRI (n=624) | FOLFIRI (n=629) | Napabucasin + FOLFIRI (n=275) | FOLFIRI (n=272) |
| mPFS, mo (95%CI) | 5.6 (5.4, 5.8) | 5.6 (5.5, 6.3) | 5.4 (4.1, 5.6) | 5.6 (4.4, 5.9) |
| HR (95%CI); p-value | 1.040 (0.917, 1.180); 0.73 | | 1.064 (0.883, 1.282); 0.74 | |
| | n=593 | n=609 | n=268 | n=266 |
| DCR, n (%) | 413 (69.6) | 421 (69.1) | 180 (67.2) | 187 (70.3) |
| Difference, % (95%CI); p-value | 0.1 (-4.9, 5.2); 0.48 | | -3.1 (-11.0, 4.7); 0.78 | |
| ORR, n (%) | 82 (13.8) | 89 (14.6) | 32 (11.9) | 37 (13.9) |
| Difference, % (95%CI); p-value | -0.9 (-4.8, 3.0); 0.68 | | -2.0 (-7.7, 3.7); 0.75 | |

| TEAEs, n (%) | Overall population | | Biomarker-positive | |
|---|---|---|---|---|
| | Napabucasin + FOLFIRI (n=622) | FOLFIRI (n=610) | Napabucasin + FOLFIRI (n=275) | FOLFIRI (n=269) |
| Grade ≥3 | 459 (73.8) | 407 (66.7) | 203 (73.8) | 191 (71.0) |
| Diarrhoea | 132 (21.2) | 43 (7.0) | 57 (20.7) | 18 (6.7) |
| Neutrophil count ↓ | 85 (13.7) | 117 (19.2) | 32 (11.6) | 56 (20.8) |
| Neutropenia | 83 (13.3) | 93 (15.2) | 33 (12.0) | 40 (14.9) |
| Serious | 231 (37.1) | 200 (32.8) | 106 (38.5) | 89 (33.1) |
| Led to modification | 526 (84.6) | 478 (78.4) | 225 (81.8) | 213 (79.2) |
| Led to discontinuation | 87 (14.0) | 41 (6.7) | 40 (14.5) | 15 (5.6) |
| Led to death | 19 (3.1) | 32 (5.2) | 11 (4.0) | 15 (5.6) |

## Conclusions

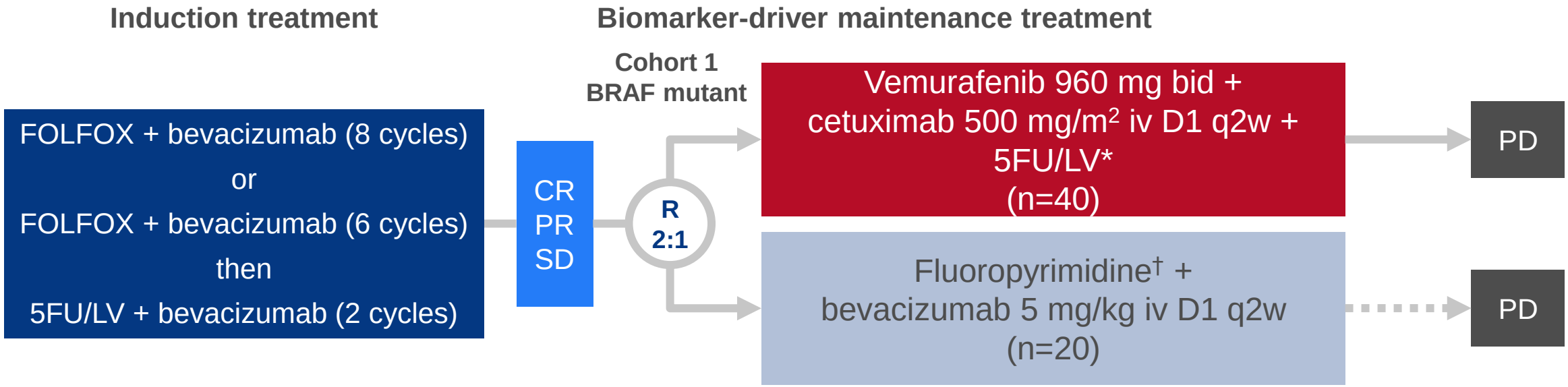
- **In patients with previously treated mCRC, napabucasin combined with FOLFIRI ± bevacizumab did not provide additional efficacy benefit, but demonstrated a manageable safety profile**

Shah M, et al. Ann Oncol 2021;32(suppl):abstr O-7

# O-9: 5-FU/LV + cetuximab + vemurafenib as maintenance therapy for BRAF-mutant (BRAFmut) metastatic colorectal cancer (mCRC): Efficacy, safety, and exploratory biomarker findings from Cohort 1 of the MODUL trial – Ducreux MP, et al

## Study objective

- To evaluate the efficacy and safety of vemurafenib + cetuximab + 5FU/LV as a 1L maintenance treatment in patients with MSS mCRC in Cohort 1 of the MODUL study (Cohort 2, BRAF wild-type; Cohort 3, HER2-positive; and Cohort 4, HER2-negative, BRAF WT)




### PRIMARY ENDPOINT

- PFS (RECIST v1.1)

### SECONDARY ENDPOINTS

- OS, ORR, DCR, TTR, DoR, change in ECOG, safety

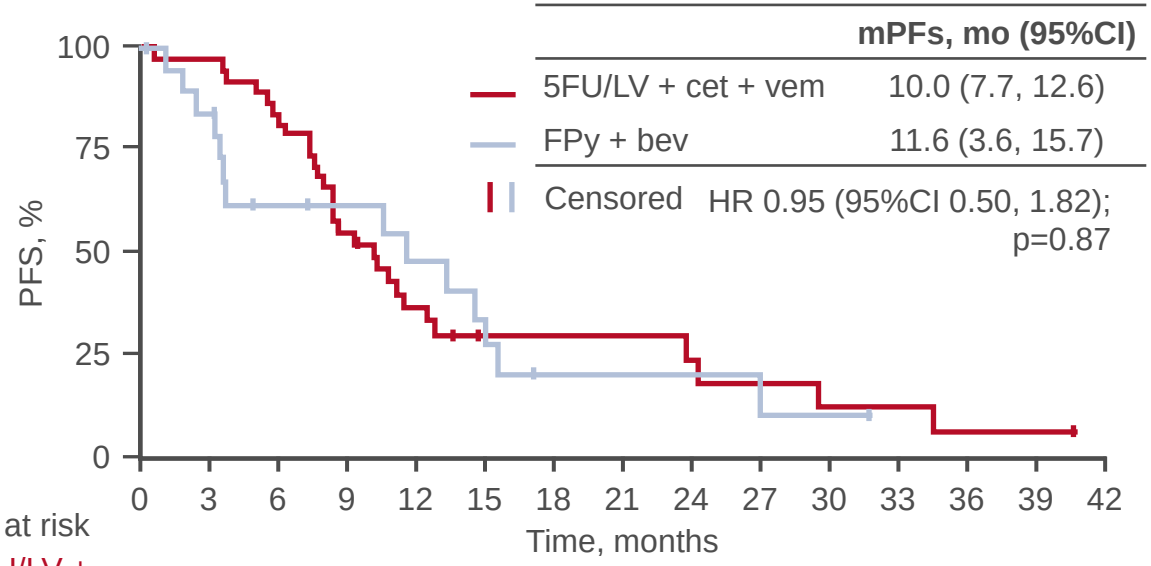
*5FU 1600–2400 mg/m$^2$ iv 46-hour infusion D1 q2w + LV 400 mg/m$^2$ 2-hour infusion D1 q2w;
†5FU 1600–2400 mg/m$^2$ iv 46-hour infusion D1 q2w + LV 400 mg/m$^2$ 2-hour infusion D1 q2w or capecitabine 1000 mg/m$^2$ bid D1–14 q3w

Ducreux MP, et al. Ann Oncol 2021;32(suppl):abstr O-9

# O-9: 5-FU/LV + cetuximab + vemurafenib as maintenance therapy for BRAF-mutant (BRAFmut) metastatic colorectal cancer (mCRC): Efficacy, safety, and exploratory biomarker findings from Cohort 1 of the MODUL trial – Ducreux MP, et al

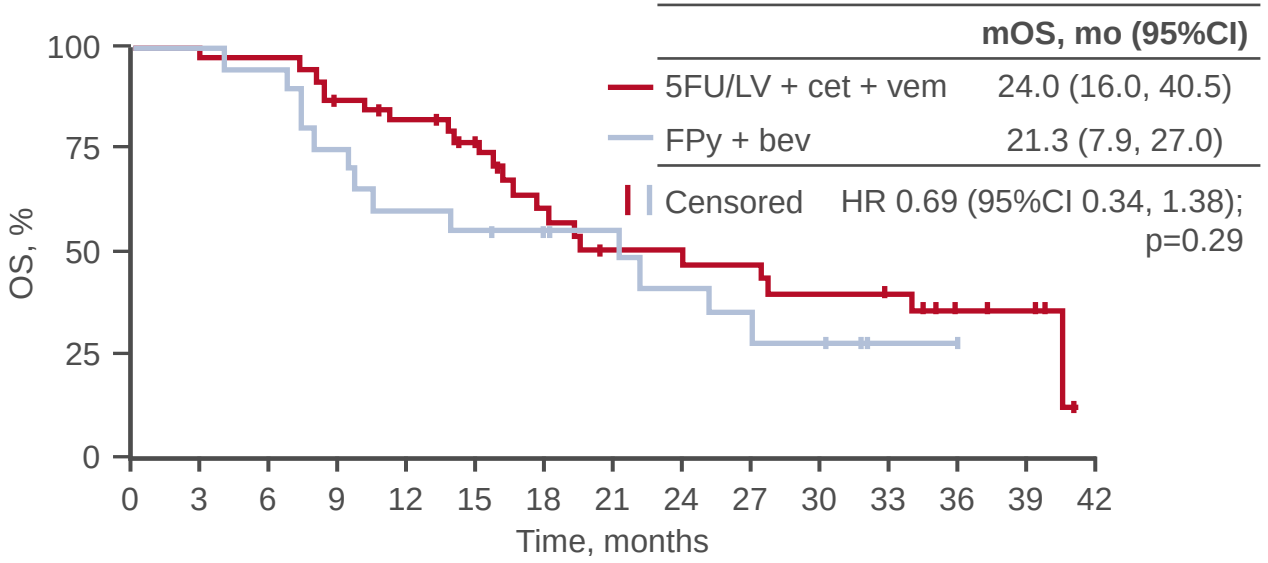
## Key results

### Progression-free survival




| No. at risk | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 5FU/LV + cet + vem | 40 | 37 | 31 | 19 | 11 | 5 | 5 | 5 | 4 | 3 | 2 | 2 | 1 | 1 | 0 |
| FPy + bev | 20 | 16 | 10 | 9 | 7 | 5 | 2 | 2 | 2 | 2 | 1 | 0 | 0 | 0 | 0 |

### Overall survival




| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 5FU/LV + cet + vem | 40 | 39 | 39 | 34 | 31 | 26 | 18 | 14 | 14 | 13 | 11 | 10 | 6 | 5 | 0 |
| FPy + bev | 20 | 20 | 19 | 15 | 12 | 11 | 9 | 8 | 6 | 4 | 4 | 1 | 0 | 0 | 0 |

Ducreux MP, et al. Ann Oncol 2021;32(suppl):abstr O-9

# O-9: 5-FU/LV + cetuximab + vemurafenib as maintenance therapy for BRAF-mutant (BRAFmut) metastatic colorectal cancer (mCRC): Efficacy, safety, and exploratory biomarker findings from Cohort 1 of the MODUL trial – Ducreux MP, et al

## Key results (cont.)

- ORR was 50% in the vemurafenib + cetuximab + 5FU/LV arm and 25% in the fluoropyrimidine + bevacizumab arm (p=0.06)

| TRAEs occurring in ≥20%, n (%) | Vemurafenib + cetuximab + 5FU/LV (n=40) | Fluoropyrimidine + bevacizumab (n=18) |
|---|---|---|
| Any | 40 (100) | 15 (83.3) |
| Arthralgia | 13 (32.5) | 0 |
| Rash | 12 (30.0) | 0 |
| Diarrhoea | 11 (27.5) | 5 (27.8) |
| Nausea | 11 (27.5) | 0 |
| Dermatitis acneiform | 11 (27.5) | 0 |
| Dry skin | 10 (25.0) | 3 (16.7) |
| Photosensitivity reaction | 8 (20.0) | 0 |

## Conclusions

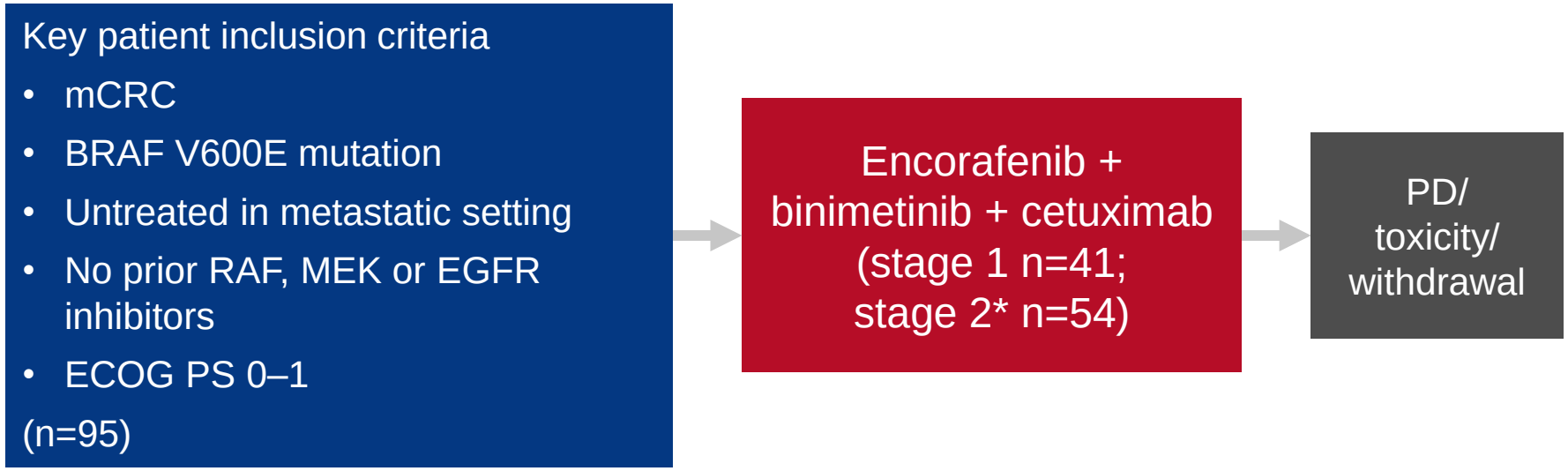
- **In patients with mCRC, maintenance therapy with vemurafenib + cetuximab + 5FU/LV in the 1L setting showed numerically longer mOS and ORR, but not PFS, compared with fluoropyrimidine + bevacizumab; there were no new safety findings**

Ducreux MP, et al. Ann Oncol 2021;32(suppl):abstr O-9

# O-10: ANCHOR CRC: results from a single-arm, phase 2 study of encorafenib, binimetinib plus cetuximab in previously untreated BRAF V600E–mutant metastatic colorectal cancer – Van Cutsem E, et al

## Study objective

- To evaluate the efficacy and safety of encorafenib + binimetinib + cetuximab as a 1L treatment for patients with BRAF V600E-mutant mCRC




### PRIMARY ENDPOINT

- ORR (investigator assessed)

### SECONDARY ENDPOINTS

- PFS, OS, PK, QoL, safety

*Enrolment after ≥12 responses occurred in stage 1

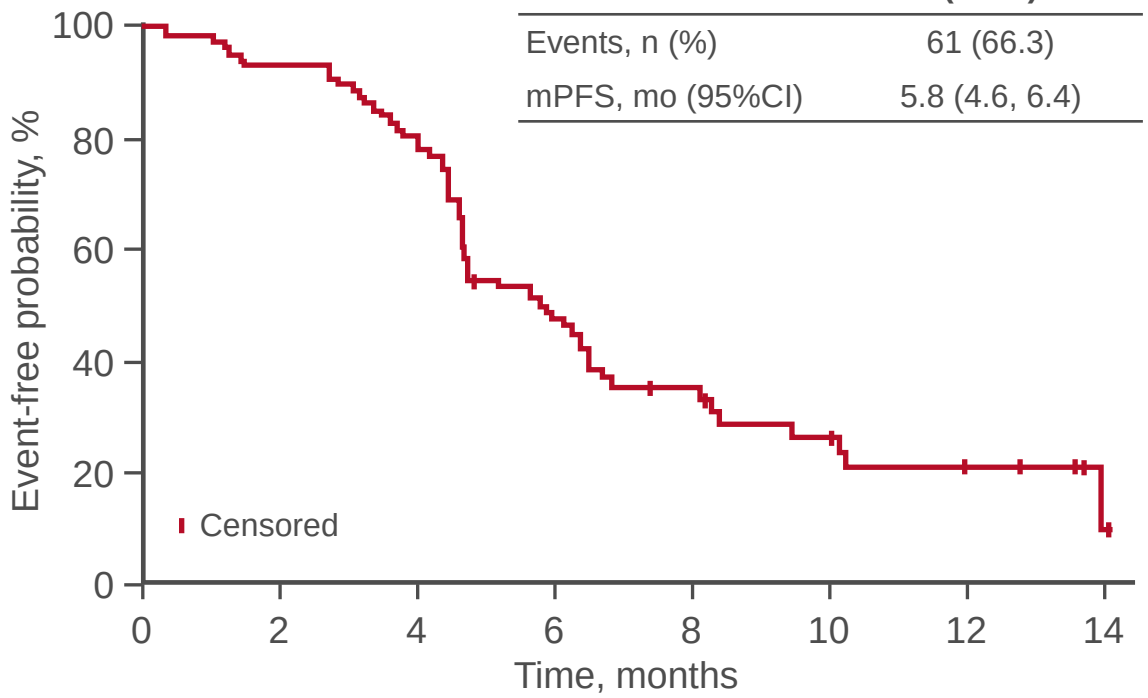
Van Cutsem E, et al. Ann Oncol 2021;32(suppl):abstr O-10

# O-10: ANCHOR CRC: results from a single-arm, phase 2 study of encorafenib, binimetinib plus cetuximab in previously untreated BRAF V600E–mutant metastatic colorectal cancer – Van Cutsem E, et al

## Key results

### Progression-free survival

| | Enco + bini + cet (n=92) |
|---|---|
| Events, n (%) | 61 (66.3) |
| mPFS, mo (95%CI) | 5.8 (4.6, 6.4) |

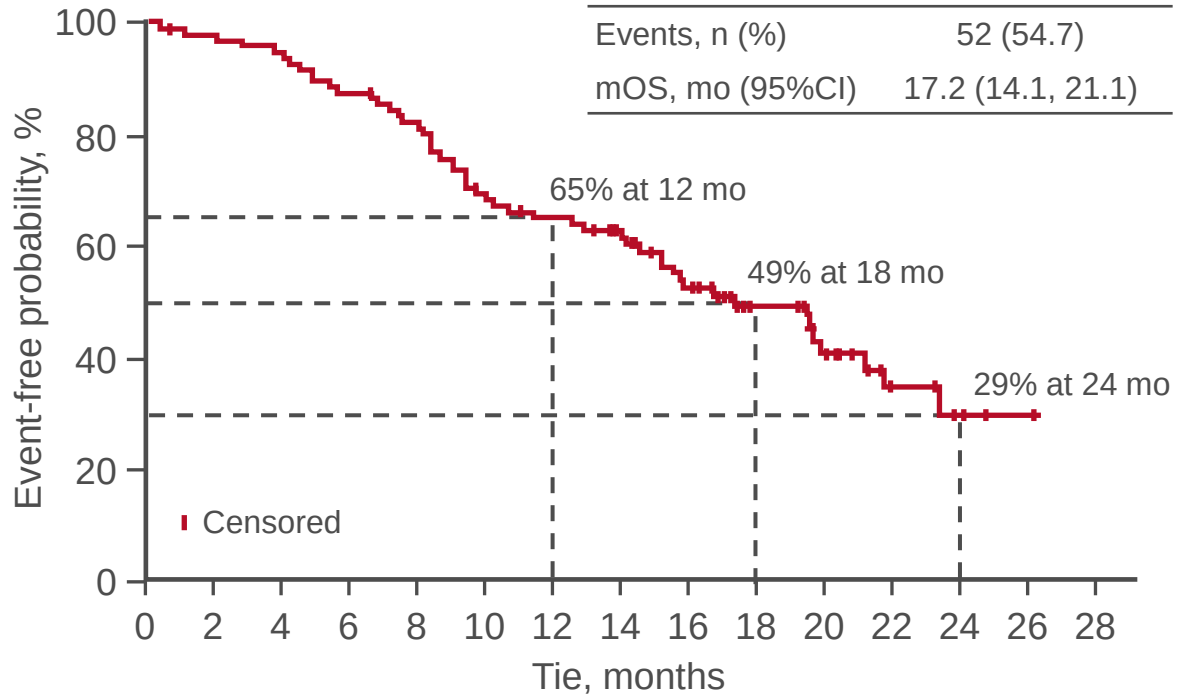



No. at risk

| 92 | 83 | 69 | 40 | 18 | 11 | 5 | 0 |
|---|---|---|---|---|---|---|---|

### Overall survival

| | Enco + bini + cet (n=95) |
|---|---|
| Events, n (%) | 52 (54.7) |
| mOS, mo (95%CI) | 17.2 (14.1, 21.1) |




No. at risk

| 95 | 91 | 88 | 82 | 75 | 62 | 58 | 51 | 41 | 26 | 17 | 8 | 2 | 1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

Van Cutsem E, et al. Ann Oncol 2021;32(suppl):abstr O-10

# O-10: ANCHOR CRC: results from a single-arm, phase 2 study of encorafenib, binimetinib plus cetuximab in previously untreated BRAF V600E–mutant metastatic colorectal cancer – Van Cutsem E, et al

## Key results (cont.)

| | Encorafenib + binimetinib + cetuximab (n=92) |
|---|---|
| ORR, n (%) [95%CI] | 44 (47.8) [37.3, 58.5] |
| BOR, n (%) | |
| CR | 0 |
| PR | 44 (47.8) |
| SD | 37 (40.2) |
| PD | 5 (5.4) |
| NE | 6 (6.5) |
| DCR, % | 88 |

| Grade ≥3 AEs occurring in ≥2%, n (%) | Encorafenib + binimetinib + cetuximab (n=92) |
|---|---|
| Anaemia | 10 (10.5) |
| Lipase increased | 10 (10.5) |
| Diarrhoea | 9 (9.5) |
| Nausea | 8 (8.4) |
| Amylase increased | 4 (4.2) |
| Abdominal pain | 4 (4.2) |
| Dermatits acneiform | 3 (3.2) |
| Vomiting | 3 (3.2) |
| Decreased appetite | 3 (3.2) |
| Asthenia | 2 (2.1) |

## Conclusions

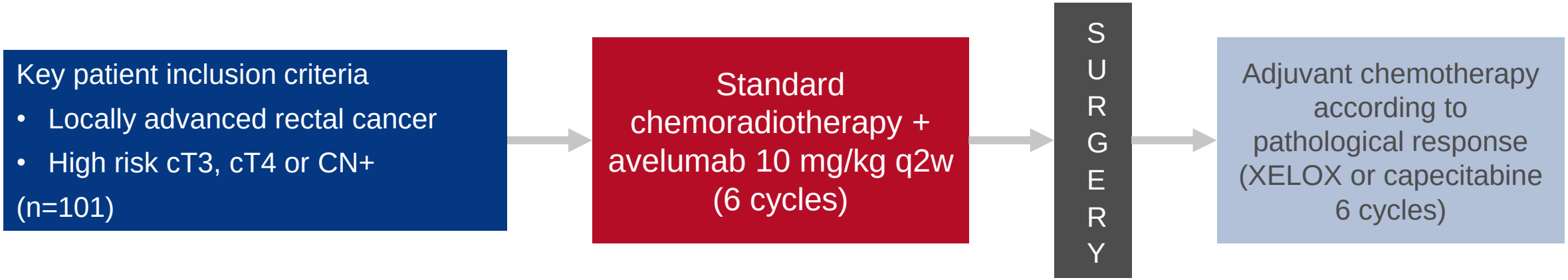
- **In patients with BRAF V600E-mutant mCRC, 1L encorafenib + binimetinib + cetuximab demonstrated encouraging clinical activity and was generally well-tolerated**

Van Cutsem E, et al. Ann Oncol 2021;32(suppl):abstr O-10

# O-12: Phase II study of preoperative (preop) chemoradiotherapy (CTTRT) plus avelumab (AVE) in patients (pts) with locally advanced rectal cancer (LARC): the AVANA study – Salvatore L, et al

**Study objective**

- To evaluate the efficacy and safety of preoperative chemoradiotherapy + avelumab in patients with locally advanced rectal cancer in the phase 2 AVANA study




**PRIMARY ENDPOINT**

- pCR

**SECONDARY ENDPOINTS**

- R0 resection rate, downstaging, local recurrence, sphincter preservation rate, PFS, OS, safety

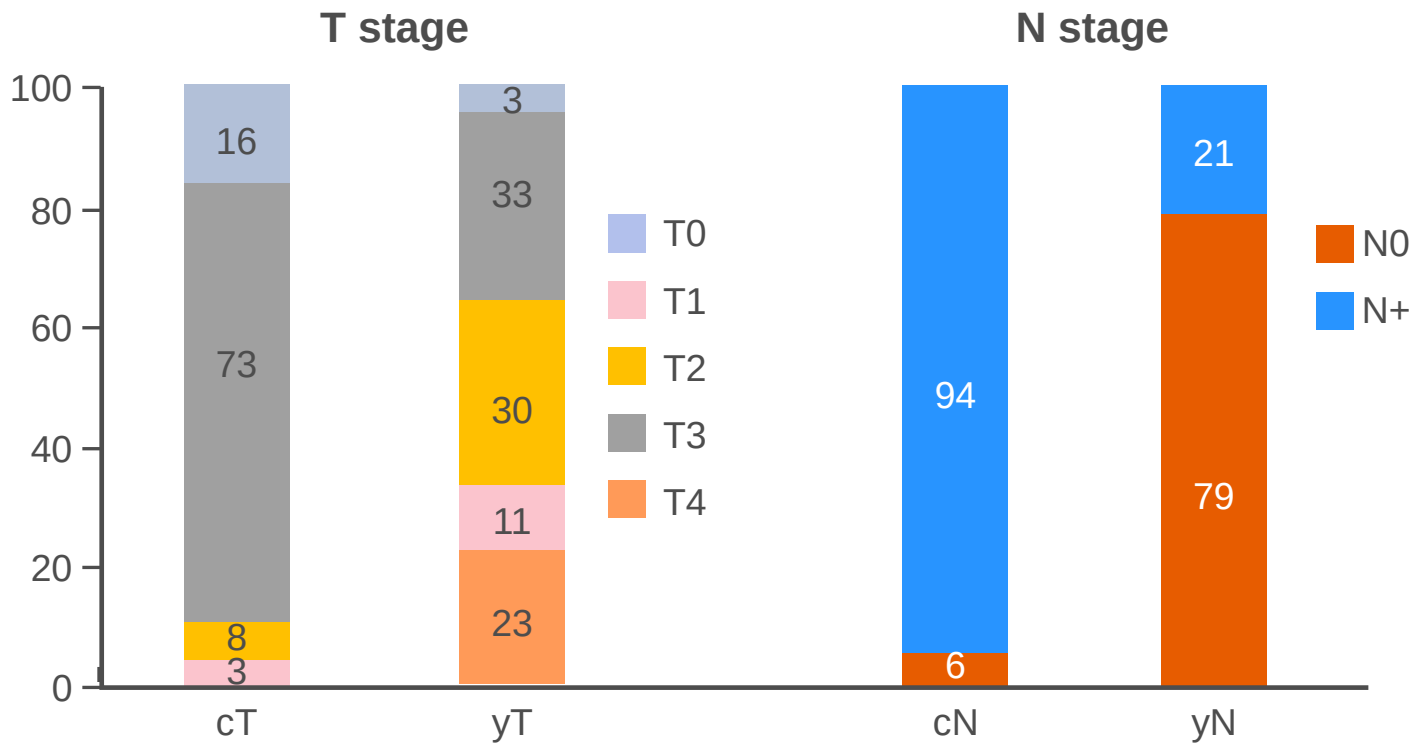
Salvatore L, et al. Ann Oncol 2021;32(suppl):abstr O-12

# O-12: Phase II study of preoperative (preop) chemoradiotherapy (CTTRT) plus avelumab (AVE) in patients (pts) with locally advanced rectal cancer (LARC): the AVANA study – Salvatore L, et al

## Key results

| | n=100* |
|---|---|
| yT stage, % | |
| yT0 | 23 |
| yT1 | 11 |
| yT2 | 30 |
| yT3 | 33 |
| yT4 | 3 |
| yN stage, % | |
| yN0 | 79 |
| yN+ | 21 |
| Pathological response, % | |
| Pathological complete response | 23 |
| Major pathological response | 60 |
| No response | 17 |

| | n=100 |
|---|---|
| Pathological complete response, n (%) [95%CI] | 23 (23) [16, 32] |
| Major pathological response, n (%) [95%CI] | 60 (6) [50, 69] |




*One patient was not evaluable, he refused surgery (bx: negative for cancer cells; CT scan; PR rectum, PD right adrenal gland)

Salvatore L, et al. Ann Oncol 2021;32(suppl):abstr O-12

# O-12: Phase II study of preoperative (preop) chemoradiotherapy (CTTRT) plus avelumab (AVE) in patients (pts) with locally advanced rectal cancer (LARC): the AVANA study – Salvatore L, et al

## Key results (cont.)

| Grade ≥3 AEs, % | n=101 |
|---|---|
| Diarrhoea | 3 |
| Nausea | 2 |
| Neutropenia | 1 |
| Vomiting | 1 |
| Asthenia | 1 |

| Grade ≥3 irAEs, % | n=101 |
|---|---|
| Any | 4 |
| Infusion reaction | 2 |
| Heart failure | 1 |
| Alanine aminotransferase increased | 1 |

## Conclusions

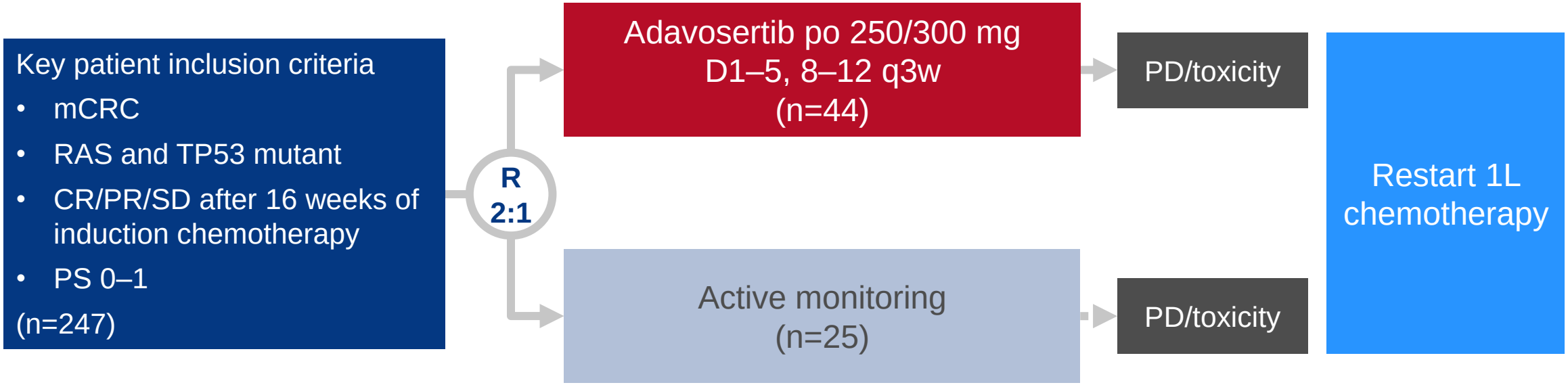
- **In patients with locally advanced rectal cancer, preoperative chemoradiotherapy + avelumab demonstrated encouraging activity and a manageable safety profile**

Salvatore L, et al. Ann Oncol 2021;32(suppl):abstr O-12

# 382O: Inhibition of WEE1 is effective in TP53 and RAS mutant metastatic colorectal cancer (mCRC): a randomised phase II trial (FOCUS4-C) comparing adavosertib (AZD1775) with active monitoring – Seligmann J, et al

**Study objective**

- To evaluate the efficacy and safety of adavosertib in patients with RAS and TP53 mutant mCRC in the FOCUS4-C study




**PRIMARY ENDPOINT**

- PFS

**SECONDARY ENDPOINTS**

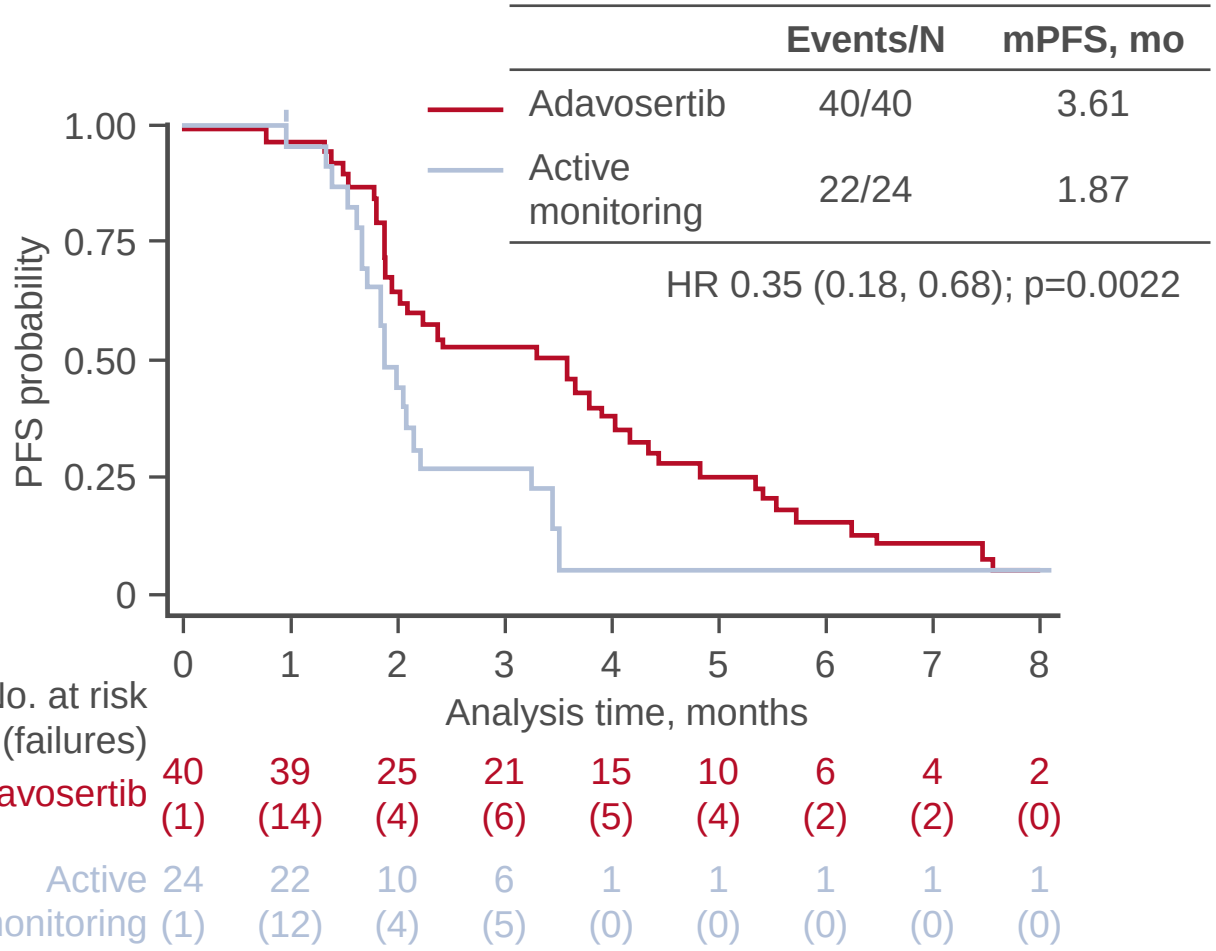
- OS, response, safety

Seligmann J, et al. Ann Oncol 2021;32(suppl):abstr 382O

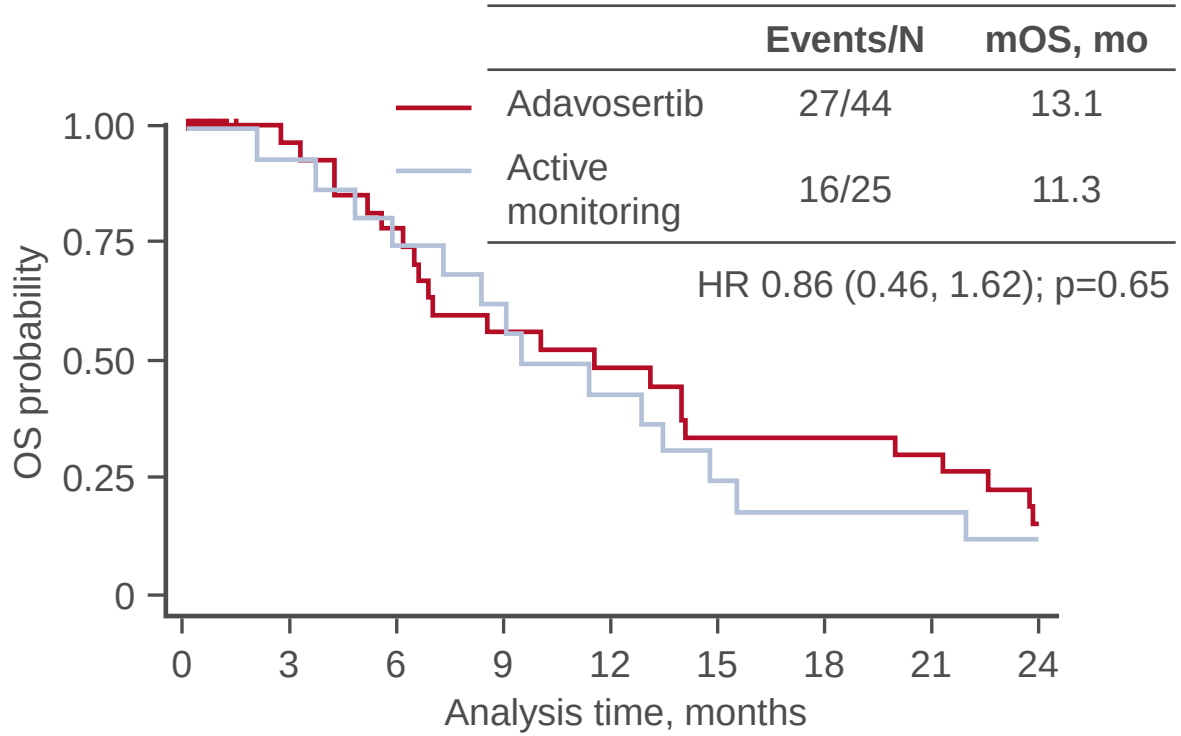
# 382O: Inhibition of WEE1 is effective in TP53 and RAS mutant metastatic colorectal cancer (mCRC): a randomised phase II trial (FOCUS4-C) comparing adavosertib (AZD1775) with active monitoring – Seligmann J, et al

## Key results

### Progression-free survival




### Overall survival




Seligmann J, et al. Ann Oncol 2021;32(suppl):abstr 382O

# 382O: Inhibition of WEE1 is effective in TP53 and RAS mutant metastatic colorectal cancer (mCRC): a randomised phase II trial (FOCUS4-C) comparing adavosertib (AZD1775) with active monitoring – Seligmann J, et al

## Key results (cont.)

| | Left-sided (n=47) | Right-sided (n=22) | Interaction p-value |
|---|---|---|---|
| PFS, HR (95%CI) | 0.24 (0.11, 0.51) | 1.02 (0.41, 2.56) | 0.043 |

| | n | mOS, mo | HR (95%CI); p-value |
|---|---|---|---|
| RAS WT/TP53 WT (REF) | 17 | 21.63 | |
| MSI-H | 20 | 7.82 | 9.05 (4.17, 19.60) |
| BRAF | 60 | 10.85 | 2.72 (1.39, 5.32); <0.001 |
| RAS WT/TP53 Mut | 118 | 20.88 | 1.21 (0.63, 2.33); 0.004 |
| RAS Mut/TP53 WT | 79 | 16.44 | 1.52 (0.78, 2.96); 0.2 |
| RAS Mut/TP53 Mut | 144 | 14.86 | 2.06 (1.08, 3.93); 0.028 |

| Most common grade ≥3 AEs for adavosertib, % | Adavosertib 250 mg | Adavosertib 300 mg |
|---|---|---|
| Fatigue | 9 | 14 |
| Diarrhoea | | 14 |
| Nausea | | 5 |

## Conclusions

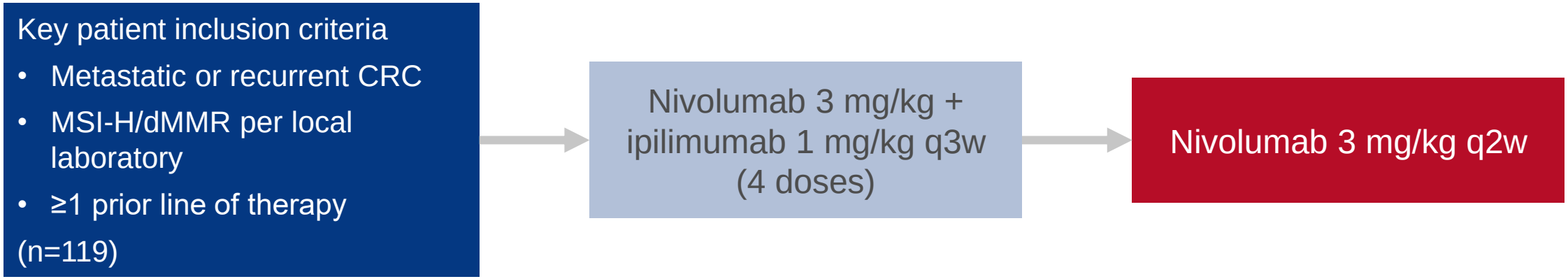
- **In patients with TP53 and RAS mutant mCRC after induction chemotherapy, adavosertib demonstrated a significant improvement in PFS and was generally well-tolerated**

Seligmann J, et al. Ann Oncol 2021;32(suppl):abstr 382O

# SO-27: Nivolumab plus low-dose ipilimumab in previously treated patients with microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC): 4-year follow-up from CheckMate 142 – André T, et al

## Study objective

- To evaluate the long-term efficacy and safety of nivolumab + low-dose ipilimumab in previously treated patients with MSI-H/dMMR mCRC in the CheckMate 142 study




### PRIMARY ENDPOINT

- ORR (RECIST v1.1, investigator assessed)

### SECONDARY ENDPOINTS

- ORR (BICR), DCR*, DoR, PFS, OS, safety

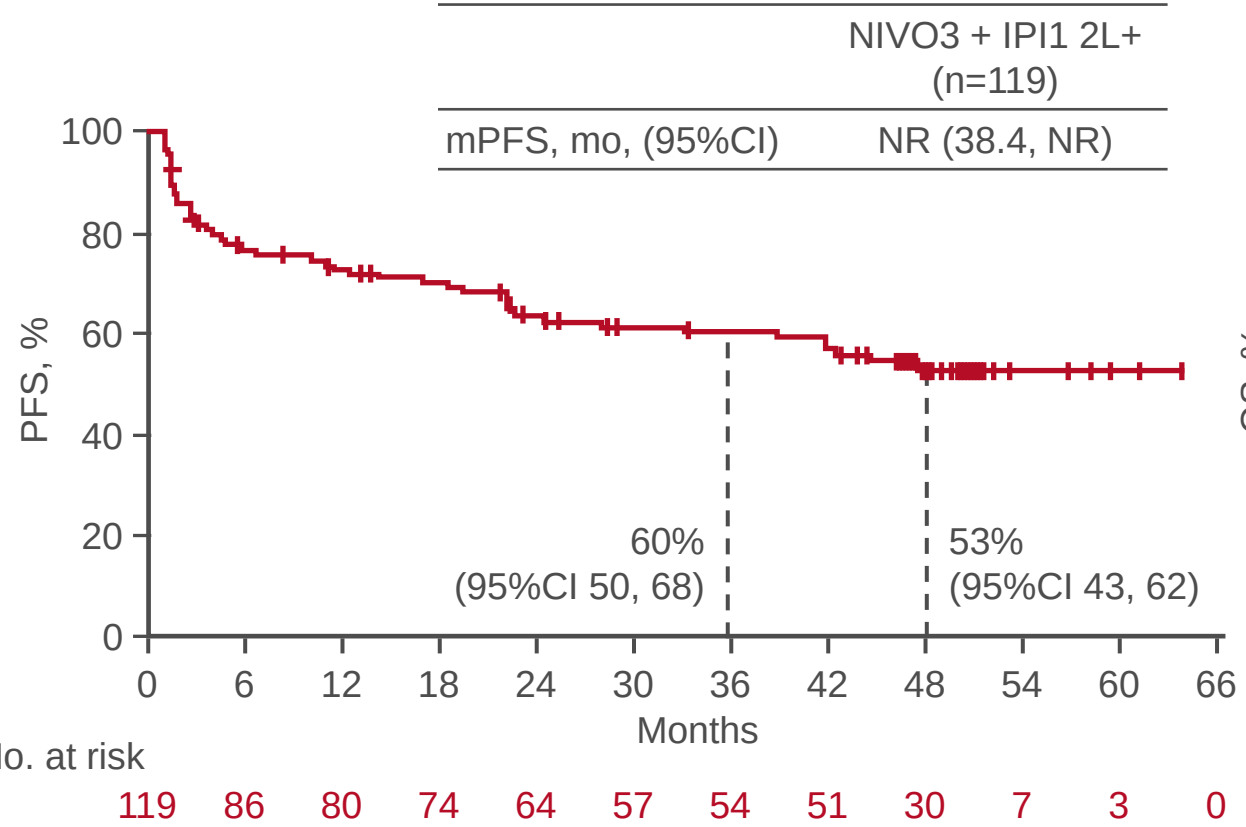
*Patients with a CR, PR or SD for ≥12 weeks divided by the number of treated patients

André T, et al. Ann Oncol 2021;32(suppl):abstr SO-27

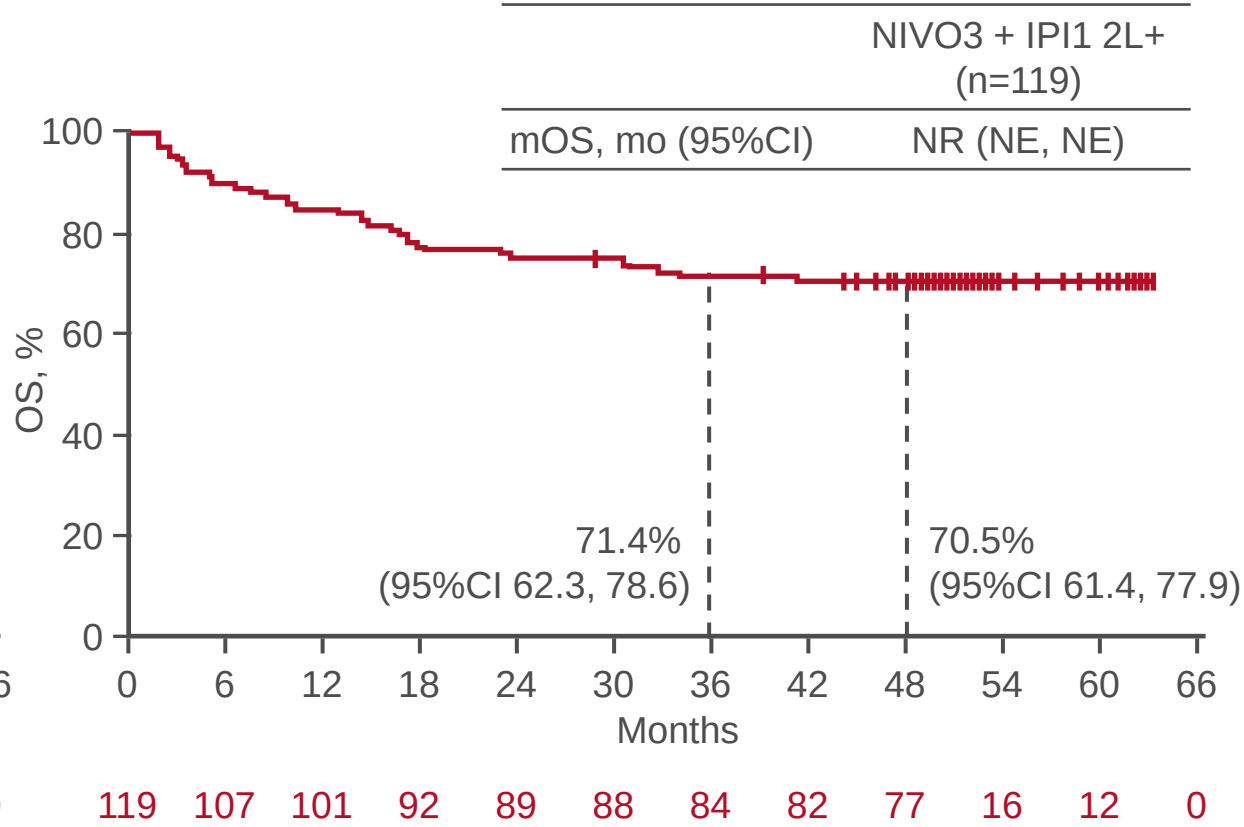
# SO-27: Nivolumab plus low-dose ipilimumab in previously treated patients with microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC): 4-year follow-up from CheckMate 142 – André T, et al

## Key results

### Progression-free survival




### Overall survival




André T, et al. Ann Oncol 2021;32(suppl):abstr SO-27

# SO-27: Nivolumab plus low-dose ipilimumab in previously treated patients with microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC): 4-year follow-up from CheckMate 142 – André T, et al

## Key results

| Follow-up of 50.9 months | NIVO3 + IPI1 ≥2L (n=119) |
|---|---|
| ORR, n (%) [95%CI] | 77 (65) [55, 73] |
| BOR, n (%) | |
| CR | 15 (13) |
| PR | 62 (52) |
| SD | 25 (21) |
| PD | 14 (12) |
| NE | 3 (3) |
| DCR, n (%) [95%CI] | 96 (81) [72, 87] |
| Median TTR, months (range) | 2.8 (1.1 to 37.1) |
| Median DoR, months (range) | NR (1.4+ to 58.0+) |

| Grade 3/4 TRAEs, n (%) | NIVO3 + IPI1 ≥2L (n=119) |
|---|---|
| Any | 38 (32) |
| Serious | 24 (20) |
| Led to discontinuation | 12 (10) |
| Select | |
| Hepatic | 14 (12) |
| Endocrine | 7 (6) |
| Skin | 5 (4) |
| Gastrointestinal | 4 (3) |
| Renal | 2 (2) |
| Pulmonary | 1 (<1) |

## Conclusions

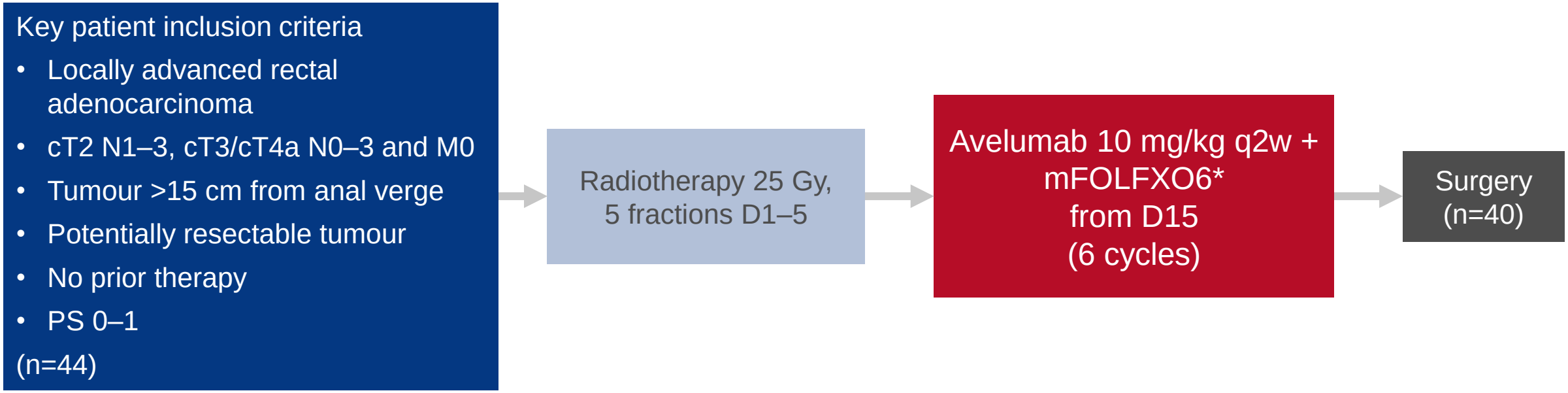
- **In previously treated patients with MSI-H/dMMR mCRC, nivolumab + ipilimumab demonstrated durable clinical and survival benefit with a manageable safety profile**

André T, et al. Ann Oncol 2021;32(suppl):abstr SO-27

# SO-30: Efficacy and safety of neoadjuvant short-course radiation followed by mFOLFOX-6 plus avelumab for locally-advanced rectal adenocarcinoma: Averectal study – Shamseddine AI, et al

## Study objective

- To evaluate the efficacy and safety of neoadjuvant short-course radiation followed by mFOLFOX6 + avelumab in patients with locally advanced rectal adenocarcinoma in the Averectal study




### PRIMARY ENDPOINT

- pCR†

### SECONDARY ENDPOINTS

- PFS, TRG, biomarkers, QoL, safety

*Oxaliplatin 85 mg/m$^2$ 2-hour infusion + leucovorin 400 mg/m$^2$ over 2 hours followed by a 48-hour infusion of 5FU 200 mg/m$^2$; †no viable tumour cells on the resected specimen

Shamseddine AL, et al. Ann Oncol 2021;32(suppl):abstr SO-30

# SO-30: Efficacy and safety of neoadjuvant short-course radiation followed by mFOLFOX-6 plus avelumab for locally-advanced rectal adenocarcinoma: Averectal study – Shamseddine AI, et al

## Key results

| TRG, n (%) | n=40 |
|---|---|
| 0 (pCR, no viable tumour cells) | 15 (37.5) |
| 1 (<10% viable tumour cells) | 12 (30.0) |
| 2 (10–50% viable tumour cells) | 9 (22.5) |
| 3 (>50% viable tumour cells) | 4 (10.0) |

| TRG | n (%) | Median immunoscore | Median immunoscore |
|---|---|---|---|
| 0 | 11 (34) | 70 | 63.91 |
| 1 | 11 (34) | 63.5 | |
| 2 | 7 (22) | 38.2 | 40.69 |
| 3 | 3 (10) | 61.4 | |
| Total | 32 (100) | 70 | 62.45 |

| Downstaging, n ( %) | n | T1–2N0 | T0N0 |
|---|---|---|---|
| T3/T4 N+ | 35 | 6 (17) | 13 (37) |

Major pathological response rate (TRG 0 + 1) was 67.5%

| Grade 3/4 AEs, n (%) | n=291 |
|---|---|
| Avelumab related | 0 |
| Surgery related | |
| Electrolyte imbalance | 12 (5.0) |
| Pelvic abscess | 4 (1.3) |
| Perforation and anastomosis leak | 2 (<1) |
| Small bowel obstruction | 2 (<1) |

## Conclusions

- **In patients with locally advanced rectal adenocarcinoma, neoadjuvant short-course radiation + avelumab demonstrated a significant improvement in pCR and had an acceptable safety profile**

Shamseddine AL, et al. Ann Oncol 2021;32(suppl):abstr SO-30