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MEETING SUMMARY
ESMO 2018, Munich, Germany

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HIGHLIGHTS ON COLORECTAL CANCER

DISCLAIMER

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The views expressed within this presentation are the personal opinion of the author. They do not necessarily represent the views of the author's academic institution or the rest of the GI CONNECT group

TRIBE 2: A PHASE III, RANDOMIZED STRATEGY STUDY BY GONO IN THE 1ST- AND 2ND-LINE TREATMENT OF UNRESECTABLE mCRC PATIENTS

C Cremolini et al. Abst #LBA20

TRIBE 2 DESIGN

- Comparison of:
  - upfront exposure to FOLFOXIRI (Arm B)
  - with pre-planned sequential treatment (FOLFOX-FOLFIRI; Arm A)

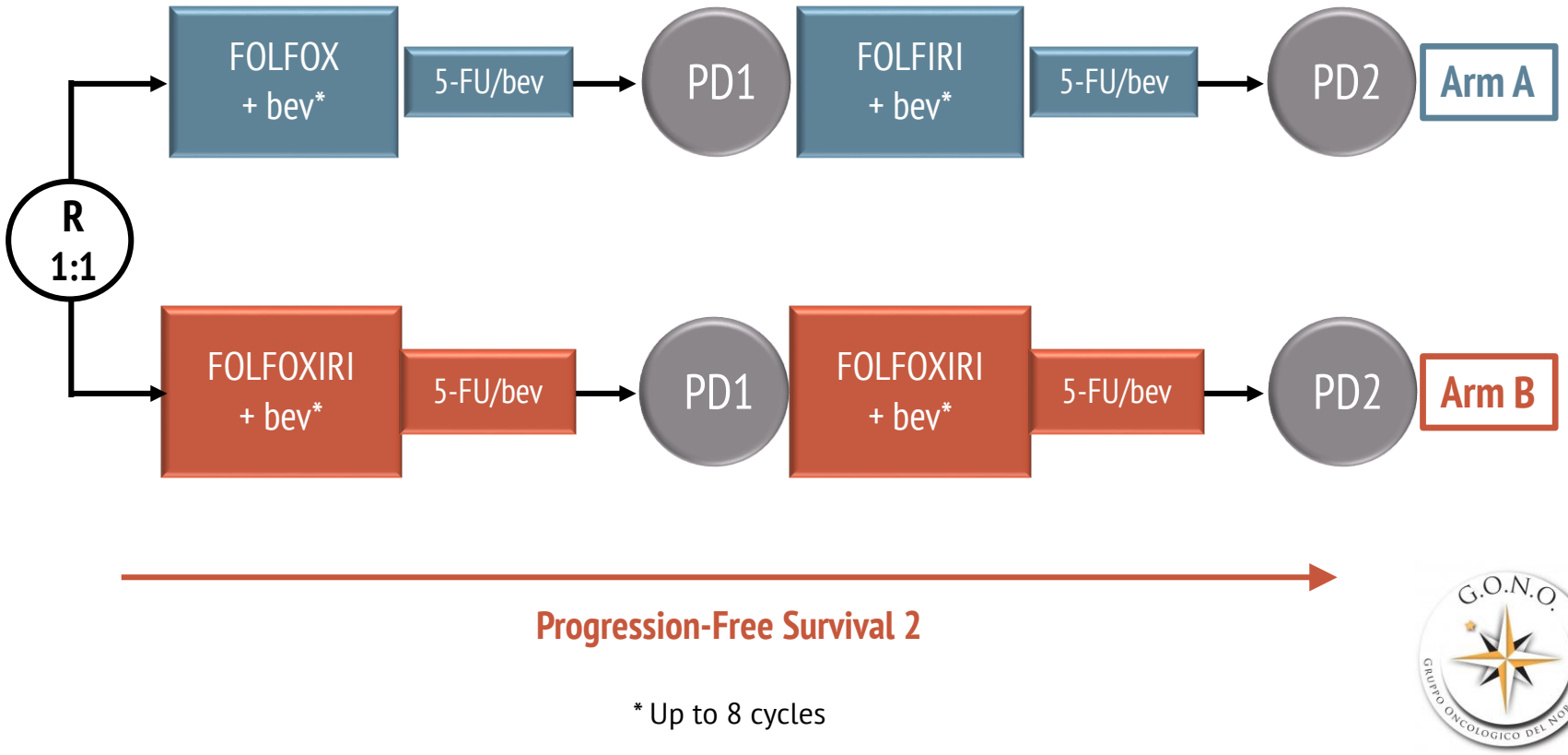
  both in combination with sustained bevacizumab

- **Primary endpoint:** PFS2

- **Eligibility:**
  - unresectable mCRC
  - no previous systemic treatment for mCRC
  - ECOG PS ⩽2 (ECOG PS 0 if aged 71–75 years)
  - no previous adjuvant oxaliplatin

ECOG PS, Eastern Cooperative Oncology Group performance status; FOLFIRI, folinic acid, fluorouracil and irinotecan; FOLFOX, folinic acid, fluorouracil and oxaliplatin; FOLFOXIRI, folinic acid, fluorouracil, oxaliplatin and irinotecan; mCRC, metastatic colorectal cancer; PFS2, second-line progression-free survival
Cremolini C et al. Presented at: ESMO 2018 (abstr LBA20)

TRIBE 2: STUDY DESIGN



* Up to 8 cycles

5-FU, fluorouracil; bev, bevacizumab; FOLFIRI, folinic acid, fluorouracil and irinotecan; FOLFOX, folinic acid, fluorouracil and oxaliplatin; FOLFOXIRI, folinic acid, fluorouracil, oxaliplatin and irinotecan; PD, progressive disease; R, randomization

Cremolini C et al. Presented at: ESMO 2018 (abstr LBA20)

TRIBE 2 RESULTS (ARM A vs ARM B)

- N=679, well-balanced patient characteristics
- Met **primary endpoint** of improvement in PFS2 with triplet plus bev and improved ORR
  - Sequential doublet (A) vs triplet (B):
    - **PFS2:** 16.2 vs 18.9 months (HR=0.69 [95%CI, 0.57-0.83], p<0.001)
    - **ORR:** 50% vs 61% (OR=1.55 [95%CI, 1.14-2.10], p=0.005)
- **Safety:** More diarrhoea (17%), neutropenia (50%) and febrile neutropenia (7%) in Arm B
- OS results immature

bev, bevacizumab; CI, confidence interval; HR, hazard ratio; OR, odds ratio; ORR, objective response rate; OS, overall survival; PFS2, second-line progression-free survival

Cremolini C et al. Presented at: ESMO 2018 (abstr LBA20)

KEY MESSAGES

- Supports the use of upfront triplet chemotherapy in fit mCRC patients
- Useful design, with maintenance 5-FU/ bevacizumab following up to 8 cycles of induction
- OS results immature and will be presented next year
- Role of the contribution of bevacizumab to 5-FU unclear

5-FU, fluorouracil; bev, bevacizumab; OS, overall survival

INTERAACT: A MULTICENTRE OPEN LABEL RANDOMISED PHASE II ADVANCED ANAL CANCER TRIAL OF CDDP PLUS 5-FU VS CARBOPLATIN PLUS WEEKLY PACLITAXEL IN PATIENTS WITH INOPERABLE LOCALLY RECURRENT OR METASTATIC TREATMENT NAÏVE DISEASE - AN INTERNATIONAL RARE CANCERS INITIATIVE TRIAL

S. Rao et al. Abst #LBA21

INTERAACT TRIAL

- First randomised trial to examine chemotherapy strategy in locally advanced or metastatic anal cancer
- Carboplatin/paclitaxel vs cisplatin/5-FU
- International collaboration
- **Primary endpoint:** ORR
- Phase II selection trial 'Pick the winner' design to inform chemotherapy backbone for phase III

5-FU, fluorouracil; ORR, overall response rate
Rao S et al. Presented at: ESMO 2018 (abstr LBA21)

INTERAACT STUDY RESULTS

- N=91
- No difference in **ORR** between arms
- Non-statistically significant improvement in **PFS** with carboplatin/paclitaxel vs cisplatin/5-FU (5.7 vs 8.1, p=0.375)
- However significant **OS** benefit with carboplatin/paclitaxel vs cisplatin/5-FU (20 vs 12.3 months, p=0.014)
- More toxicity with cisplatin/5-FU
- **Interpretation:** carboplatin/paclitaxel should be new standard of care for advanced anal cancer

5-FU, fluorouracil; ORR, overall response rate; OS, overall survival; PFS, progression-free survival
Rao S et al. Presented at: ESMO 2018 (abstr LBA21)

DURABLE CLINICAL BENEFIT WITH NIVOLUMAB PLUS LOW-DOSE IPILIMUMAB AS 1ST-LINE THERAPY IN MSI-H/DMMR mCRC

HJ Lenz et al. Abst #LBA18-PR

CHECKMATE-142

- 3rd arm of this trial presented at ESMO 2018
- First-line nivolumab plus low-dose ipilimumab in first-line treatment
  - Less toxic schedule than previous arms
  - Nivolumab (3mg/kg Q2W) + low-dose ipilimumab (Q6W)
- Non-randomised study
- **Primary endpoint:** ORR
- **Secondary endpoints:** of DCR, PFS, OS, safety

DCR, disease control rate; ESMO, European Society for Medical Oncology; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q2W, once every 2 weeks; Q6W, once every 6 weeks

Lenz HJ et al. Presented at: ESMO 2018 (abstr LBA18-PR)

CHECKMATE-142 RESULTS

- N=45 patients, ECOG PS 0–1
- Median follow-up 13.8 months
- **ORR** = 60%; **CR** = 7%; **DCR** = 84%
- Benefit seen in poor prognostic groups, including *RAS* and *RAF*-mutant patients
- Durable responses seen
  - 74% benefit for >6 months
- 1-year **PFS** is 77%
- Less toxicity seen with this regimen than Q3W ipilimumab:
  - grade 3-4 adverse events = 16%
  - low rate of discontinuation due to AEs (7%)

AE, adverse event; CR, complete response; DCR, disease control rate; ECOG PS, Eastern Cooperative Oncology Group performance status; ORR, objective response rate; PFS, progression-free survival; Q3W, once every 3 weeks; RAF, rapidly accelerated fibrosarcoma; RAS, rat sarcoma

Lenz HJ et al. Presented at: ESMO 2018 (abstr LBA18-PR)

COMMENTS

- Exciting data in this small sub-population of patients
- Efficacy similar to previous Checkmate-142 arms but with more tolerable regimen
- RR similar to triplet chemotherapy, but less toxic
- Need longer follow-up as durability of response will be key
- Non-randomised; will this data be sufficient to move to routine practice?
- Scheduling will be key, in terms of tolerability and cost-effectiveness

RR, response rate

FLUOROPYRIMIDINE + BEVACIZUMAB + ATEZOLIZUMAB VS FP/BEV IN BRAF WT mCRC: FINDINGS FROM COHORT 2 OF MODUL - A MULTICENTRE, RANDOMIZED TRIAL OF BIOMARKER-DRIVEN MAINTENANCE TREATMENT FOLLOWING 1ST-LINE INDUCTION THERAPY

A. Grothey et al. Abst #LBA19

MODUL

- Biomarker-stratified platform phase II trial testing novel strategies in mCRC
- Maintenance setting of mCRC following 16 weeks induction FOLFOX + bev
- This abstract reports FP/bev + atezolizumab vs FP/bev in BRAFwt patients
- **Primary endpoint:** PFS

BRAF, rapidly accelerated fibrosarcoma isoform B; bev, bevacizumab; FOLFOX, folinic acid, fluorouracil and oxaliplatin; FP, fluoropyrimidine; mCRC, metastatic colorectal cancer; PFS, progression-free survival; VEGF, vascular endothelial growth factor; wt, wild type

Grothey A et al. Presented at: ESMO 2018 (abstr LBA19)

MODUL RESULTS

- 445 patients randomised in this comparison
- No difference in **PFS** (HR=0.96, p=0.73)
- No **OS** benefit (but immature)
- No significant benefit in examined sub-groups
- Consistent with IMBLAZE 147
- VEGF inhibition in combination with PD-1/PD-L1 inhibition not a strategy to make 'a cold tumour hot'

HR, hazard ratio; OS, overall survival; PD-1, programmed cell death-1; PD-L1, programmed death-ligand 1; PFS, progression-free survival; VEGF, vascular endothelial growth factor

Grothey A et al. Presented at: ESMO 2018 (abstr LBA19)

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