FOLFOXIRI + BEVACIZUMAB (BEV) IN PATIENTS (PTS) WITH PREVIOUSLY UNTREATED METASTATIC COLORECTAL CANCER (mCRC): FINAL SURVIVAL AND PHARMACOGENOMIC PROFILING RESULTS FROM THE OPAL STUDY

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Aim: The addition of BEV to standard doublet chemotherapy (CT) improves outcomes vs CT alone in pts with mCRC. Use of more intensive triplet CT may prolong overall survival (OS), progression-free survival (PFS), increase response rates and improve resectability rates but at the expense of greater toxicity. The OPAL study examined the effect of BEV + FOLFOXIRI on PFS in pts with previously untreated unresectable mCRC. Here we report final survival and pharmacogenetic results.

Methods: Eligible pts had histologically confirmed mCRC, ECOG PS ≤1 and were 18–70 years old. Pts received ≤12 cycles of FOLFOXIRI (infusional 5-fluorouracil [FU] 3200 mg/m², folinic acid [FA] 200 mg/m², oxaliplatin 85 mg/m² and irinotecan 165 mg/m²) + BEV 5 mg/kg q2w (induction phase) followed by ≤40 cycles of 5-FU/FA + BEV q2w (maintenance phase). PFS was the primary endpoint; secondary endpoints included OS, proportion of pts achieving resectability, safety, and prognostic value of pharmacogenetic profiling (single nucleotide polymorphisms (SNP) for VEGF-A, VEGFR 1-3, PDGFR beta, HIF 1 alpha, Neuropilin).

Results: 96 pts were enrolled. Of these, 90 received study medication and formed the safety population: 64 male, 26 female; median age 58 (range 28–71) years; ECOG performance status 0/1 in 49/41 pts; liver only disease in 35 pts. During induction phase a median number of 9.5 cycles FOLFOXIRI and BEV was administered. Relative dose intensities were 81-86% for all 4 drugs. The incidence of adverse events (AEs) was as previously reported and there were no new safety signals during induction phase. In total, 61 serious AEs occurred in 35 pts (38%). AEs resulting in death occurred in 3 pts (3%); these were not considered treatment-related by the investigators. Median PFS was 11.1 months (95% CI 9.4-12.0) and OS was 32.2m (95% CI 22.6-36.9). 52 pts were pharmacogenetically profiled and VEGFR 2 SNP 305 was associated with OS (CC – 12.4m, CT – 18.7m, and TT – 30.1m; p = 0.038).

Conclusions: FOLFOXIRI + BEV was feasible in this mCRC pt population. Survival was relevantly increased compared to standard three drug combinations in a molecularly unstratified pt population. VEGFR 2 SNPs might be prognostic for treatment with FOLFOXIRI + BEV.

Disclosure: A. Stein: Roche: membership on an advisory board, corporate-sponsored research. C. Bokemeyer: Roche: corporate-sponsored research. All other authors have declared no conflicts of interest.