oral abstracts

CALGB/SWOG 80405: PHASE III TRIAL OF IRINOTECAN/5-FU/LEUCOVORIN (FOLFIRI) OR OXALIPLATIN/5-FU/LEUCOVORIN (mFOLFOX6) WITH BEVACIZUMAB (BV) OR CETUXIMAB (CET) FOR PATIENTS (PTS) WITH KRAS WILD-TYPE (WT) UNTREATED METASTATIC ADENOCARCINOMA OF THE COLON


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Introduction: FOLFIRI or mFOLFOX6, combined with BV or CET, are 1st-line treatments for MCRC. The optimal antibody combination is unknown.

Methods: Pts with KRAS wt (codons 12 and 13) MCRC and performance status 0-1 received FOLFIRI or mFOLFOX6 (MD/pt choice at enrollment) and randomized to either CET 400 mg/m2 X 1, then 250 mg/m2 qw or BV 5 mg/kg q2w. The original study included unselected MCRC pts receiving FOLFIRI or mFOLFOX6 and randomized to CET, BV or both. In June, 2009, it was amended to include only pts w/ KRAS wt tumors (codon 12 and 13) and to delete the combination CET + BV arm. Rx continued until progression, death, unacceptable toxicity, curative surgery; treatment holidays of 4 wks permitted. Accrual goal was 1142 pts. 1° endpoint was overall survival (OS). Subsequent therapies up to MD.

Results: Between 11/2005 and 3/2012, 3058 unselected pts enrolled, 2334 KRAS wt pts randomized; final N =1137, median f/u = 24 mos; Median age – 59 y; 61% male. Chemo/BV – 559; chemo/CET – 578. FOLFIRI = 27%, mFOLFOX6 = 73%. OS analysis planned at 849 events; futility boundary for efficacy crossed at 10th interim analysis. OS - chemo/BV v. chemo/CET = 29.04 (25.66 - 31.21) v. 29.93 (27.56 - 31.21) mos; HR = 0.92 (0.78, 1.09) (p value = 0.34). PFS (by investigator): chemo/BV v. chemo/CET: 10.84 (9.86 - 11.4) v. 10.45 (9.66 - 11.33) mos. 94 pts attained NED status following surgery, median f/u 40 mos (range 8.0 - 86.0). There was no difference in outcomes or serious toxicity based on gender or treatment. A QOL sub-study has been presented. Analyses underway include expanded RAS; chemotherapy – biologic interactions, subsequent therapies, impact of prior adjuvant therapy (9%), pharmacoeconomics.

Conclusion: Chemo/CET and chemo/BV equivalent in OS in pts KRAS wt (codons 12 + 13) MCRC; either is appropriate in 1st line. Overall OS of 29 + mos in all pts represents a new standard for KRAS wt CRC and confirms progress in MCRC. The preference for FOLFOX limits chemotherapy comparison although analysis underway. Expanded RAS and other molecular and clinical information may identify subsets of pts who get more or less benefit from specific regimens.