Cetuximab (Cmab) plus irinotecan (I) versus panitumumab (Pmab) in patients with refractory metastatic colorectal cancer (mCRC) in Ontario

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Background: In the BOND trial (Cunningham et al, NEJM 2004) for refractory mCRC, the addition of I to an EGFR antibody improved tumor response rate and time to progression but not overall survival (OS). We assessed the ‘real world’ efficacy and toxicity of combination versus monotherapy in i) all-comers and ii) older patients (pts) who are under-represented in randomized trials.

Methods: In Ontario, universal public funding is available for either Cmab + I combination or Pmab monotherapy only in pts with refractory non-mutated Kras mCRC. All pts diagnosed before Dec 2012 and treated with an EGFR antibody for mCRC were identified from the Ontario drug database and linked to the Ontario Cancer Registry and other administrative databases to ascertain baseline characteristics, health services utilization and outcomes. Multivariable Cox and logistic models were constructed to compare the time to treatment discontinuation, overall survival (OS), ED or hospital visits between Cmab + I and Pmab, adjusting for observable confounders (including age, gender, year of diagnosis, stage at presentation, duration of prior treatment in 1st and 2nd line, previous liver resection, rural residence and income quintile) using propensity score methods.

Results: 1081 pts were identified (Cmab + I: 278, Pmab: 803); median age: 60 (21.1% >age 70), 36.4% female, 36.2% rectal cancer and 60.1% stage IV at presentation. After adjusting for confounders, the use of Cmab + I as compared to Pmab alone was associated with a prolonged time to treatment discontinuation [median: 3.5 mos vs. 2.8 mos, HR 0.63, 95%CI 0.53-0.75, p < 0.001] and an improved OS compared to Pmab alone [median: 8.8 mos vs. 5.9 mos, HR 0.62, 95% CI 0.53-0.73, p < 0.001]. Both had similar 14-day mortality and incidence of ED or hospital visits. Interaction tests of treatment effect and age were >0.05.

Conclusions: ‘Real world’ data suggest a possible OS benefit with Cmab + I compared to Pmab alone, without an associated increase in toxicity. Pts age ≥70 appear to experience similar benefit and toxicity from combination therapy. These results suggest a need for adequately powered randomized trials to compare Cmab + I and Pmab like the ongoing ICECREAM study.

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