Aim: Overall survival (OS) of mCRC pts has improved by the introduction of agents targeting VEGF and EGFR. In randomized clinical trials (RCTs), anti-EGFR MoAbs cetuximab and panitumumab achieved a significant improvement of overall response rate (ORR) and progression-free survival (PFS) in exon 2 KRAS WT pts, although the effect on OS was controversial. Recently, efficacy was further improved by validation of negative predictive biomarkers, i.e. mutations in exons 2-4 of KRAS and NRAS. In this trial-based meta-analysis, we sought to investigate the impact of anti-EGFR MoAbs on ORR, PFS and OS in pts with RAS WT CRC.

Methods: MEDLINE/PubMed, Cochrane Library, ASCO/ESMO abstracts were searched for phase II-III RCTs published from 2005 to present. The search was restricted to trials comparing anti-EGFR MoAbs plus chemotherapy with chemotherapy +/- bevacizumab or best supportive care in mCRC. Data extraction was conducted according to PRISMA statement. Statistical analyses were conducted to calculate the summary hazard ratio (HR) for PFS and OS, and the summary risk ratio (RR) for ORR with relative 95% Confidence Intervals (CIs) by using random-effects or fixed-effects models based on heterogeneity of included studies.

Results: After screening, 7 studies were included: 5 first-line [MRC-COIN, PRIME, FIRE-3, OPUS, PEAK] and 2 second/third line [AMG 2002048, AMG 20050181], accounting for 2235 RAS WT pts. The anti-EGFR MoAbs decreased the risk of progression in the overall population (HR = 0.63; 95%CI, 0.49–0.82; p = 0.0006) and in the first-line setting (HR = 0.74; 95%CI, 0.58–0.93; p = 0.01). Similarly, the risk of death was reduced in the overall population (HR = 0.86; 95%CI, 0.76–0.96; p = 0.008) and in first-line studies (HR = 0.84; 95%CI, 0.74–0.95; p = 0.006). No significant heterogeneity was found. The ORR was increased in the overall population (RR = 1.64; 95%CI, 1.09–2.48; p = 0.02) and in chemo-naive pts (HR = 1.16; 95%CI, 1.03–1.31; p = 0.01).

Conclusions: This is the first meta-analysis conducted to estimate the effect of anti-EGFR MoAbs in RAS WT mCRC. Besides the improvement of ORR and PFS, we report a significant effect on OS, which was also maintained in first-line studies.

Disclosure: All authors have declared no conflicts of interest.