484P Retrospective RAS analysis of the EPIC trial: Cetuximab plus irinotecan vs irinotecan in patients (pts) with second-line metastatic colorectal cancer (mCRC)

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Background: The multicenter, open-label, randomized, phase 3 EPIC study (EMR 062202-025) investigated the addition of cetuximab to irinotecan vs irinotecan in pts with EGFR-expressing mCRC who had previously progressed on first-line fluoropyrimidine- and oxaliplatin-based chemotherapy. The primary endpoint was overall survival (OS). We present the extended RAS analysis (KRAS/NRAS exons 2, 3, and 4) for the EPIC study population.

Methods: 1298 RAS-unselected pts were enrolled from May 2003 to February 2006. Existing DNA samples were reanalyzed using BEAMing (beads, emulsion, amplification, magnetics) technology. RAS wild-type (wt) status was defined as having all alleles be analyzable and a sum of RAS mutations of $\leq$ 5%. Baseline characteristics, efficacy, safety, and post-study therapy were assessed. 10.3% had no RAS data available.

Results: Among the 452 (231 in the cetuximab + irinotecan arm and 221 in the irinotecan arm) pts with RAS wt mCRC, baseline characteristics were comparable to those of the unselected population. 67.5% had 1 prior line of therapy. In the cetuximab + irinotecan vs irinotecan arms, median progression-free survival (PFS) was 5.4 vs 2.6 months (HR, 0.57 [95% CI, 0.46-0.69]; P < .0001), median OS was 12.3 vs 12.0 months (HR, 0.91 [95% CI, 0.71-1.17; P = .4645]), and overall response rate (ORR) was 29.4% vs 5.0% (OR, 8.12 [95% CI, 4.04-17.40]; P < .0001), respectively. 76.4% and 61.8% of pts in the cetuximab + irinotecan vs irinotecan arms, respectively, experienced a grade $\geq$ 3 adverse event. 47.1% of pts in the irinotecan arm received cetuximab in a subsequent line of therapy vs 11.3% in the cetuximab + irinotecan arm.

Conclusions: This retrospective analysis confirms that cetuximab-based therapy is suitable as a standard, second-line treatment for pts with RAS wt mCRC. Specifically, the addition of cetuximab to irinotecan significantly improved PFS and ORR in this population. A large proportion of pts in the irinotecan arm crossed over to receive post-study cetuximab, potentially masking any OS benefit of the addition of cetuximab to irinotecan in this study. Benefits appear clinically relevantly higher than for pts with RAS-unselected or KRAS wt mCRC.

Clinical trial identification: EMR 062202-025.

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