Updated Results of the MEK inhibitor trametinib (T), BRAF inhibitor dabrafenib (D), and anti-EGFR antibody panitumumab (P) in patients (pts) with BRAF V600E mutated (BRAFm) metastatic colorectal cancer (mCRC)


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Introduction: BRAF V600E mutations occur in 5-10% of CRC and confer a poor prognosis. Unlike BRAFm melanoma, BRAF or MEK inhibitor monotherapy is ineffective for BRAFm mCRC. Preclinical data suggest that combined inhibition of the EGFR and MAPK pathways is required to maximally inhibit BRAFm CRC. Here we provide an update of this ongoing study.

Methods: Eligible pts with BRAFm mCRC received doublet, D + P or T + P, or triplet, D + T + P therapy.

Results: D + P: 20 pts received the full doublet dose (D 150 mg twice daily [BID] + P 6 mg/kg every 2 weeks [Q2W]). T + P 13 pts received the full doublet dose (T 2 mg once daily [QD] + P 6 mg/kg Q2W). Triplet: 35 pts received D + T + P including 24 pts that received full dose triplet (D 150 mg BID + T 2 mg QD + P 6 mg/kg Q2W). One subject on T + P had dose limiting toxicity due to grade 3 acneiform rash. As of March 16, 2015, the most common adverse events (AEs) for D + P were dermatitis acniform (55%; all Grade [G] 1/2) and fatigue (45%; all G1/2). For T + P and D + T + P, respectively, diarrhea (G1/2 57%, G3 0%; G1/2 60%, G3 9%) and dermatitis acniform (G1/2 28%, G3 14%; G1/2 47%; G3 9%) were the most common AEs. Due to significant dermatologic toxicity with full dose T + P, lower dose cohorts are being explored. The confirmed response rate was 10% for D + P and 26% for D + T + P (Table). All regimens reduced levels of pERK in on-treatment biopsies taken at day 15 relative to pre-dose biopsies (D + P 23 ± 9%; T + P 50 ± 31%; D + T + P 55 ± 33%). Updated results for the T + P dose cohorts including safety and response rate will be presented.

Conclusion: Full dose T + P was associated with significant dermatologic toxicity. Encouraging clinical activity with acceptable tolerability was seen with D + T + P in BRAFm mCRC.

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