470P Safety run-in evaluation of the phase I trial of trifluridine/tipiracil (FTD/TPI) in combination with oxaliplatin and a monoclonal antibody (bevacizumab or nivolumab) in patients (pts) with metastatic colorectal cancer (mCRC)

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Background: The addition of the monoclonal antibody bevacizumab to chemotherapy has shown survival benefits in pts with mCRC. Another potential strategy is to combine chemotherapy with immunotherapies to enhance antitumor effect of the immune system. In vivo studies have shown an increase in anti-tumor activity when combining FTD/TPI with oxaliplatin or bevacizumab; and an increase in tumor immunogenicity after treatment with FTD/TPI and oxaliplatin, leading to a better tumor response to anti-PD-1 exposure.

Methods: Further to the dose-escalation part (24 pts), the recommended dose (RD) was defined as FTD/TPI 35 mg/m^2 bid, days 1–5 q14, together with oxaliplatin 85 mg/m^2 (day 1). Safety data were collected during expansion part from 12 evaluable pts treated with the doublet at the RD with either nivolumab 3 mg/kg (n = 6) or bevacizumab 5 mg/kg (n = 6) administered at day 1. Pts were monitored for safety for the first 2 months of treatment before allowing further enrollment. Eligibility criteria included measurable disease, performance status (PS) 0-1, normal organ function, and progression after >1 prior anti-tumor therapy (excluding oxaliplatin).

Results: Baseline characteristics were median age of 67 years (range 52 to 75 years); PS 0/1 (3/9 pts), male/female (8/4 pts); and colon/rectum (5/7 pts). Drugrelated adverse events (AEs) reported in $\geq$ 2 pts were neutropenia, diarrhoea, asthenia, and nausea; mainly (93%) grade 1-2. The most common grade 3 or 4 drugrelated event was neutropenia. Grade 1 neurotoxicity attributed to oxaliplatin was observed in 2 pts. No immune-related AE due to nivolumab were reported. Best overall response included 2 partial responses after 2 months of treatment (1 pt in bevacizumab cohort, 1 MSI-H pt in nivolumab cohort). Pharmacokinetics parameters for FTD/TPI were aligned with historical data.

Conclusions: The safety data showed that the two triplets were well tolerated. Expansion enrollment is continuing in both cohorts to confirm preliminary evidence of activity in a larger number of patients.

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