TPS3640 Poster Session

Neoadjuvant cetuximab plus tislelizumab combined with chemotherapy in pMMR RAS/BRAF wild-type (wt) locally advanced rectal cancer (LARC): A prospective, multicenter, phase II study.

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Background: For patients (pts) with locally advanced rectal cancer (LARC), chemoradiotherapy followed by total mesorectal excisionis is recommended as standard therapy according to the NCCN guidelines. However, there is no stratification strategy for neoadjuvant therapy based on molecular alterations, and radiotherapy is insufficient with pathologic complete response (pCR) rates at 11%-15%. There is an urgent need for new therapeutical options to improve the pCR rate in these pts. Adding anti-EGFR therapy to neoadjuvant chemotherapy may improve progression-free survival for RAS/BRAF WT LARC pts. Furthermore, previous studies demonstrated that combining anti-EGFR with immune checkpoint inhibitors could further improve pCR rate. Cetuximab, an anti-EGFR monoclonal antibody, has gained FDA approval for RAS WT metastatic colorectal cancer. Tislelizumab, an anti-PD-1 monoclonal antibody, is effective in blocking PD-1/PD-L1 interaction in preclinical experiments. This study introduces an innovative approach, combining Cetuximab, Tislelizumab and chemotherapy, as a total neoadjuvant therapy for pMMR RAS/BRAF wt LARC pts. **Methods:** This prospective, multi-center, phase II study investigated the efficacy and safety of neoadjuvant treatment with FOLFOX chemotherapy plus Cetuximab and Tislelizumab for MSS-RAS/BRAF WT LARC. Eligible participants were 18 years or older, with an ECOG PS of 0–2, primary, and a biopsy-proven tumors meeting all the following criteria: clinical tumour stage cT3-4 N0M0 or cT1-4N+M0, tumor distance from the anus≦10 cm, no distant metastasis. Pts initially received a cycle chemotherapy of FOLFOX pending genetic results. Eligible pts with MSS-RAS/BRAF WT LARC then underwent 5 preoperative neoadjuvant cycles of mFolfOx6 (oxaliplatin 85 mg/m^2, D1; leucovorin 200 mg/m^2,D1; 5-FU bolus 400 mg/m2 D1 then 2.4 g/m^2,D2-3) + Cetuximab (500mg/m2, D1, q2w) + Tislelizumab (200mg, D1, q2w). Subsequently, pts underwent TME about 4 weeks after the last cycle. Imaging evaluation will be conducted 6 weeks after the initiation of treatment, pts with regressed tumors will receive a standard chemoradiotherapy. The primary endpoint was pCR rate. Secondary endpoints included the Neoadjuvant Rectal Score, Objective Response Rate, R0 resection rate, Major Pathological Response rate, Anal Sparing rate, 3-year Disease-Free Survival, 3-year Local Recurrence Rate, 3-year Overall Survival. Based on a review of the literature, the estimated pCR rate for standard preoperative neoadjuvant chemoradiotherapy is approximately 15%. The expected pCR rate for the MSS-RASwt/BRAFwt group is around 30%, with a one-sided significance level (α) of 0.05 and a power (1-β) of 0.8, using the Simon two-stage method, the sample size is calculated to be 25 cases. The study started in middle 2022 and is recruiting. Clinical trial information: ChiCTR2200062002. Research Sponsor: None.