TPS3641 Poster Session

Node-sparing modified short-course radiotherapy combined with CAPOX and tislelizumab versus conventional short-course preoperative chemoradiotherapy for proficient mismatch repair or microsatellite stable locally advanced rectal cancer (mRCAT-III): A multicenter, randomized, open-label, phase 3 trial.

Zhangfa Song, Bingjun Bai, Huogang Wang, Jiawei Wang, Cheng Cai, Xiaonan Sun, Min Chen, Xing ben Gu, Weifeng Lao; Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, China; Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, China; Zhejiang University, Hangzhou, China; Colorectal Surgery, Zhejiang University Jinhua Hospital, Hangzhou, China; Sir Run Run Shaw Hospital Zhejiang University School of Medicine, Hangzhou, China; Sir Run Run Shaw Hospital, College of Medicine, Hangzhou, China

Background: Total neoadjuvant chemoradiotherapy is the standard of care for locally advanced rectal cancer (LARC) to control local recurrence and achieve organ preservation. However, for proficient mismatch repair (pMMR) or microsatellite stable (MSS) LARC, which accounts for nearly 90% of rectal cancers, conventional chemoradiotherapy has limited efficacy and is associated with significant side effects. Recent studies have shown that combining radiotherapy with immunochemotherapy can improve pathological complete response (pCR) rates, but the inclusion of tumor-draining lymph nodes (TDLNs) in the conventional irradiation field may impair T-cell immunity and reduce response to immunotherapy. Our previous phase II trial demonstrated that node-sparing modified short-course radiotherapy combined with chemotherapy and PD-1 blockade could achieve a high pCR rate of 78.8% in pMMR LARC[1]. Building on these findings, we initiated this phase III trial to compare this novel treatment regime with conventional short-course chemoradiotherapy in improving pCR rates. **Methods:** This is a phase III, open-label, multicenter, randomized trial conducted across 17 hospitals in China. A total of 170 eligible MSS/pMMR middle or low rectal cancer patients (cT3-4N0/+M0) will be recruited and randomly assigned (5:5:1) to three groups: control group (conventional short-course chemoradiotherapy), experimental group (node-sparing modified short-course chemoradiotherapy plus PD-1 blockade), and exploratory group (conventional short-course chemoradiotherapy plus PD-1 blockade). The innovative node-sparing modified short-course radiotherapy targets only the primary tumor bed, excluding TDLNs. Following randomization, patients will receive short-course radiotherapy (conventional or node-sparing) followed by four cycles of CAPOX ± tislelizumab: tislelizumab 200 mg IV on day 1, oxaliplatin 130 mg/m^2 IV on day 1, and capecitabine 1000 mg/m^2 orally on days 1-14, and Total mesorectal excision (TME) will be performed at weeks 14-15. The primary endpoint is pCR rate, while secondary endpoints include organ preservation rate, disease-free survival, overall survival, adverse effects, and quality of life. As of January 2025, 46 of the planned 170 patients have been enrolled. The Data Monitoring Committee (DMC) reviewed the trial in December 2024 and recommended continuing as planned. Reference: Annals of Oncology (2024) 24 (suppl_1): 1-20. 10.1016/iotech/iotech100744. Clinical trial information: NCT06507371. Research Sponsor: Sir Run Run Shaw Hospital Clinical Research Cultivation Program.