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Neoadjuvant short-course radiotherapy followed by camrelizumab and chemotherapy in locally advanced rectal cancer (LARC): The phase 3 UNION trial

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Background

Despite the use of neoadjuvant chemoradiotherapy, recurrence and distant metastasis remain common in LARC. Effective immunotherapy-based strategies for the predominantly proficient mismatch repair/microsatellite-stable population remain limited. UNION is the first phase 3 trial to evaluate a neoadjuvant strategy incorporating radiotherapy, immunotherapy, and chemotherapy in LARC. Here we present the prespecified event-free survival (EFS) analysis.

Methods

Patients with cT3-4 or N+ rectal adenocarcinoma (tumor located ≤10 cm from the anal verge) were randomly assigned (1:1) to receive short-course radiotherapy (SCRT; 25 Gy/5f; experimental group) or long-course chemoradiotherapy (50.4 Gy/28f with concurrent capecitabine 825 mg/m² twice daily; standard of care group) followed by 2 neoadjuvant cycles and 6 adjuvant cycles of capecitabine and oxaliplatin (CAPOX). The experimental group additionally received neoadjuvant and adjuvant camrelizumab (200 mg, day 1) since CAPOX treatment for up to 17 cycles. The primary endpoint was blinded independent review committee (BIRC)-assessed pathological complete response rate. Key secondary endpoints with prespecified α allocation were investigator-assessed EFS and overall survival.

Results

Between July 2021 and March 2023, 231 patients were randomized to the experimental group (n=113) and standard of care group (n=118). As of October 1, 2025, the median follow-up duration was 36.8 months (95% CI, 34.8-37.8) and 35.6 months (95% CI, 34.3-36.9), respectively. The 3-year EFS rate was significantly higher in the experimental group compared with standard of care (91.3% [95% CI, 83.9-95.4] vs 77.4% [95% CI, 67.9-84.4], hazard ratio=0.33 [95% CI, 0.15-0.71], P=0.0029). BIRC-assessed EFS consistently favored the experimental group. During the whole treatment period, the incidence of grade ≥3 treatment-related adverse events was 51.3% (59/115) and 48.2% (54/112), respectively.

Conclusions

UNION is the first phase 3 trial to demonstrate a significant improvement in EFS with an immunotherapy-based regimen in LARC. This neoadjuvant strategy represents a new standard of care.

Clinical trial identification

NCT04928807.

Legal entity responsible for the study

The authors.

Funding

Jiangsu Hengrui Pharmaceuticals Co., Ltd.

Disclosure

Z. Hou: Financial Interests, Personal, Full or part-time Employment: Jiangsu Hengrui Pharmaceuticals Co., Ltd.. All other authors have declared no conflicts of interest.

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