Preoperative (neoadjuvant) therapy with tislelizumab for locally advanced colorectal cancer with high microsatellite instability or deficient mismatch repair: an open-label, single-arm, multicenter phase II study

Authors:

Kefeng Ding,[1*†] Gong Chen,[2] Yao Ye,[1] Yue Liu,[1] Yanlai Sun,[3] Yang Gao,[3] Jingdong Zhang,[4] Shaozhong Wei,[5] Cong Li,[2] Dandan Li,[2] Yanbing Zhou,[6] Mulin Liu,[7] Juan Zhang,[8] Lilin Zhang,[9] Dalu Kong[10]

Affiliations:

[1]*The Second Affiliated Hospital of Zhejiang University School of Medicine, Zhejiang, China;*

[2]*Sun Yat-sen University Cancer Center, Guangdong, China;*

[3]*Shandong Cancer Hospital, Shandong, China;*

[4]*Liaoning Cancer Hospital, Liaoning, China;*

[5]*Hubei Cancer Hospital, Hubei, China;*

[6]*The Affiliated Hospital of Qingdao University, Shandong, China;*

[7]*The First Affiliated Hospital of Bengbu Medical College, Anhui, China;*

[8]*BeiGene (Beijing) Co., Ltd., Beijing, China;*

[9]*BeiGene (Shanghai) Co., Ltd., Shanghai, China*;

[10]*Tianjin Cancer Hospital, Tianjin, China*

Background: Tislelizumab (TIS), an anti-programmed cell death protein 1 (PD-1) antibody, demonstrated improved anti-tumor response and tolerable safety in patients (pts) with previously treated, locally advanced unresectable or metastatic microsatellite instability high/deficient mismatch repair (MSI-H/dMMR) solid tumors, including colorectal cancer (CRC; NCT03736889). Recent studies of other anti-PD-1 antibodies indicate potential clinical benefit of neoadjuvant anti-PD-1 therapy in pts with resectable MSI-H/dMMR CRC. Here, we report efficacy and safety outcomes of neoadjuvant TIS from a multicenter phase II trial (NCT05116085) in this population.

Methods: Pts aged ≥18 years with stage II/III MSI-H/dMMR CRC, ECOG PS 0-1, evaluable disease per RECIST v1.1, and eligible for R0 (complete) resection were enrolled. Pts received TIS 200 mg IV every 3 weeks for 3 cycles followed by surgical resection within 10 weeks of first TIS dose. The primary endpoint was major pathological response (MPR) rate (proportion of pts with ≤10% residual viable tumor in the surgically resected primary tumor). Secondary endpoints included pathological complete response (pCR) rate (proportion of pts with absence of residual tumor in the surgically resected specimen), and safety. The R0 resection rate was an exploratory endpoint.

Results: Overall, 33 pts were enrolled across eight sites in China. The median age of enrolled pts was 52.0 years (range: 23-84), 14 (42.4%) pts were male. Ten (30.3%) pts had rectal cancer and 23 (69.7%) colon cancer. At study entry, clinical tumor (T) stage was reported as T2, T3, and T4 in 1 (3.0%), 7 (21.2%), and 25 (75.8%) pts, respectively, and node (N) stage as N0, N1, and N2 in 6 (18.2%), 14 (42.4%), and 13 (39.4%) pts, respectively. All pts had a metastasis (M) stage of M0. A total of 29 (87.9%) pts underwent surgery and were evaluable for efficacy endpoints. Surgery was not performed in 4 pts, 3 of whom were managed non-operatively (1 pt had progressive disease). MPR and pCR rates were 89.7% and 62.1%, respectively (**Table**). Any-grade and grade ⩾3 TIS-related adverse events (TRAEs) were reported in 20 (60.6%) and 1 (3.0%) pts, respectively. Two (6.1%) pts experienced serious TRAEs; no TRAEs led to death or surgery cancellation. One pt (3.0%) experienced a TRAE (grade 2 hypothyroidism) leading to surgery delay. No grade ⩾3 or serious TIS-related surgery-relevant adverse events were reported. Immune-mediated adverse events were reported in 10 (30.3%) pts (all grade 1-2).

Conclusions: Neoadjuvant TIS was associated with high MPR and pCR rates and an acceptable safety profile, and did not compromise surgery in pts with resectable MSI-H/dMMR CRC.

	Total (n=29)
MPR, n (%)	26 (89.7)
95% CI	72.6, 97.8
pCR, n (%)	18 (62.1)
95% CI	42.3, 79.3
R0 surgical resection, n (%)	29 (100)

CI, confidence interval