

Comparative efficacy and safety of tislelizumab (TIS) vs other anti-PD-1 treatments in first-line (1L) gastric or gastroesophageal junction cancer (GC/GEJC): A network meta-analysis (NMA)

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Background: Anti-PD-1 treatments such as nivolumab (NIV) or pembrolizumab (PEM) given 1L in combination with chemotherapy (CT) have been found to extend overall survival (OS) and improve response in unresectable, locally advanced, or metastatic GC/GEJC. NMAs were conducted to determine the relative efficacy and safety of TIS+CT (from RATIONALE-305) compared to NIV+CT and PEM+CT in 1L GC/GEJC.

Methods: A systematic literature review identified the ATTRACTION-4 part 2 and CheckMate 649 trials as relevant for NIV+CT, and KEYNOTE-062 and KEYNOTE-859 for PEM+CT. Bayesian fixed-effect NMAs were conducted using identified trial data. Efficacy outcomes were progression-free survival (PFS) and OS, and safety was assessed through grade ≥ 3 treatment-related adverse events (TRAEs). Markov chain Monte Carlo methods modeled hazard ratios (HRs) or odds ratios and 95% credible intervals (CrIs). Subgroup analyses were conducted by PD-L1 status for efficacy outcomes.

Results: The five trials were able to form a network with placebo+CT as a common comparator and were similar in terms of baseline characteristics, trial design, and eligibility requirements. TIS+CT showed comparable efficacy to NIV+CT and PEM+CT. The HR for OS was 0.98 (95% CrI: 0.83-1.16) for TIS+CT vs NIV+CT and 1.00 (95% CrI: 0.85-1.19) for TIS+CT vs PEM+CT. In PD-L1 $\geq 5\%$ and $\geq 1\%$ subgroups, TIS+CT demonstrated similar efficacy compared to NIV+CT and PEM+CT for OS. PFS was 1.02 (95% CrI: 0.85-1.22) for TIS+CT vs NIV+CT and 1.00 (95% CrI: 0.83-1.19) for TIS+CT vs PEM+CT. Grade ≥ 3 TRAEs statistically favored TIS+CT compared to NIV+CT and numerically favored TIS+CT compared to PEM+CT.

Conclusion: Compared to the currently recommended anti-PD-1 therapies, TIS+CT is similarly efficacious while maintaining a similar or more favorable safety profile in the 1L treatment of GC/GEJC.

Disclosure Statement: The authors declare that there are conflicts of interest.