

A matching-adjusted indirect comparison of tislelizumab versus camrelizumab as second-line treatment for patients with advanced or metastatic esophageal squamous cell carcinoma

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Background: The efficacy and safety of programmed cell-death protein 1 (PD-1) inhibitors monotherapy in the second line therapy of advanced or metastatic esophageal squamous cell carcinoma (ESCC) have been demonstrated in multiple clinical trials. In the global phase 3 RATIONALE 302 (NCT03430843) and the phase 3 ESCORT trial conducted in Mainland China (NCT03099382), tislelizumab and camrelizumab both showed significant survival benefit versus chemotherapy for patients with advanced or metastatic ESCC. No head-to-head comparison has been made for any PD-1 inhibitors. This study aimed to indirectly compare the efficacy of tislelizumab versus camrelizumab as second-line treatment for patients with advanced or metastatic ESCC.

Methods: An anchored matching-adjusted indirect comparison (MAIC) was conducted using individual patient data (IPD) from RATIONALE 302 study (n=512) and published aggregate data from ESCORT study (n=448). To adjust for cross-trial differences, IPD from patients in RATIONALE 302 were reweighted by method of moment to match the data (including age, sex, Eastern Cooperative Oncology Group Performance Status, histologic grade, country, programmed cell death ligand 1 [PD-L1] expression, metastases sites on liver, lung, bone, brain, and lymph node, prior therapies in surgery, radiotherapy, and platinum-based chemotherapy) of patients from ESCORT. Efficacy outcomes included overall survival (OS), progression free survival (PFS) (tumor response was evaluated every 6 weeks in RATIONALE 302 and every 8 weeks in ESCORT), and objective response rate (ORR). A stratified Cox model was used to estimate the hazard ratio (HR) of the survival endpoints as the proportional hazard assumption was not violated. Sensitivity analysis was performed excluding patients with pre-randomized

investigator choice of paclitaxel therapy in RATIONALE 302.

Results: The baseline characteristics were different between RATIONALE 302 and ESCORT. Patients in RATIONALE 302 had lower rate of high PD-L1 expression, higher rate of liver metastases, etc. Therefore, MAIC was conducted to adjust all the baseline characteristics of RATIONALE 302 to match with those of ESCORT.

After matching, the effective sample size of RATIONALE 302 was 166. The HR for OS and PFS between tislelizumab versus chemotherapy was 0.67 (95% CI: 0.48-0.95) and 0.83 (95% CI: 0.57-1.21), respectively. The risk difference of ORR for tislelizumab versus chemotherapy was 12.7% (95% CI: 2.0%-24.3%). For tislelizumab versus camrelizumab, after matching, the HR in OS and PFS was 0.94 (95% CI: 0.60, 1.29) and 1.21 (95% CI: 0.83-1.58), respectively, and the risk difference of ORR was -1.1% (95% CI: -13.9%-11.7%).

After matching, the median OS of tislelizumab changed from 8.6 (95% CI: 7.5-10.4) to 9.9 (95% CI: 7.0-16.8) months. The median PFS of tislelizumab changed from 1.6 (95% CI: 1.4-2.7) to 1.5 (95% CI: 1.4-4.2) months. The risk difference of ORR for tislelizumab versus chemotherapy changed from 10.5% (95%CI: 4.4%-16.8%) to 12.7% (95% CI: 2.0%-24.3%). Sensitivity analysis showed consistent results.

Conclusions: After adjusting the patient population from RATIONALE 302 trial to match with those in ESCORT trial, tislelizumab showed similar efficacy with camrelizumab as second line treatment for ESCC, and an improved estimated efficacy with numerical increase in median OS and higher ORR when compared with the original efficacy results.