Association between use of antibiotics (ATB) and clinical outcomes with tislelizumab (tisle) monotherapy

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Background

Immune checkpoint inhibitors (ICIs) have changed the therapeutic landscape of many cancers but ICI efficacy varies greatly. Retrospective analyses showed ATB may have a negative impact on ICI efficacy. However, heterogeneous results induced by ATB observed across studies may be due to population diversity, different definitions of ATB use, limited sample size, etc.

Methods

Data from 5 tisle monotherapy studies were analysed. Patients were dichotomized by timing of IV/oral ATB use; ±30 days of Day 1 tisle treatment was 'ATB+', otherwise 'ATB-'. Propensity score weighting was employed to correct for bias from unbalanced baseline characteristics. Survival probability was estimated by the Kaplan–Meier method and compared by log-rank test. Cox model of overall survival (OS) was used to compute hazard ratio (HR) and 95% confidence interval (CI). Landmark analysis was conducted to explore the association of ATB use and OS across time to mitigate guarantee-time bias.

Results

217/1183 (18%) patients received ATB. OS was significantly decreased in the ATB+ group vs the ATB- group (HR: 1.5; 95% CI: 1.3–1.9, p<0.0001). In the ATB+ group, OS was significantly decreased with prophylactic vs non-prophylactic ATB treatment (HR: 2.5; 95% CI: 1.5–4, p<0.0001). A significant association between ATB use and decreased OS was shown in patients with esophageal squamous cell carcinoma (ESCC) (HR: 3.0; 95% CI: 1.3–7.2, p<0.01), hepatocellular carcinoma (HCC) (HR: 1.8; 95% CI: 1.1–2.9, p<0.01) and urothelial carcinoma (UC) (HR: 2.3; 95% CI: 1.3–3.9, p<0.001). A worse trend in OS was observed for non-small cell lung cancer (NSCLC) (HR: 1.6; 95% CI: 0.74–3.6, p=0.26). Landmark analysis identified the time intervals, as related to Day 1 of tisle treatment, when ATB use had a significant negative impact on OS per tumor type: Day -15–45 for ESCC, Day 19–45 for HCC, and Day -5–133 for UC. No significant time interval emerged in NSCLC.

Conclusions

In this pooled analysis, a negative association was observed between ATB use during tisle treatment and OS in a pooled population and in ESCC, HCC and UC. Time intervals in which ATB use had a significant negative impact on OS were identified per indication. Prophylactic ATB use showed a poorer OS outcome vs non-prophylactic ATB use.

Clinical trial identification

Pooled analysis of the following trials:

BGB-A317-001: NCT02407990

BGB-A317-102: CTR20160872

BGB-A317-203: NCT03209973

BGB-A317-204: CTR20170071

BGB-A317-208: NCT03419897