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Impact of antibiotic (ATB) exposure prior to immune checkpoint inhibitor (ICI) treatment on overall survival (OS): A population-based study

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Background

ICIs are a common therapeutic option for many solid tumors. While prior studies have shown that ATB exposure may negatively impact ICI outcomes through gut microbiome changes, many were small studies with heterogeneity in ATB classes and exposure windows. Here, we performed a population level retrospective cohort study to evaluate the impact of ATB exposure prior to ICI on OS.

Methods

We used administrative data to identify a cohort of cancer patients ≥ 65 years of age receiving ICIs from June 2012 to October 2018 in Ontario, Canada and deterministically linked with databases to obtain socio-demographic and clinical co-variates and ATB prescription claims. Multivariable cox-proportional hazard models evaluated the impact of ATB exposure both within 1 year and 60 days prior to starting ICI on OS, adjusted for age, gender, body mass index, comorbidities, autoimmune history, hospitalization in the past year and treatment facility level at start of ICI therapy.

Results

Among 2737 patients, median age 73; 43% received Nivolumab, 41% Pembrolizumab and 13% Ipilimumab; 53% were lung cancer, 34% melanoma. Median ATB treatment duration for patients receiving ATB within 1 year (59%) and 60 days (19%) prior to ICI were 14 days (SD=32) and 9 days (SD=13) respectively. Median OS estimate was 306 days. Any ATB exposure within 1 year prior to ICI was associated with worse OS (aHR=1.12 95% CI [1.12-1.23] p=0.03). A nonsignificant dose effect was seen based on weeks of ATB exposure 1 year prior to ICI (aHR=1.01 per week [1.00-1.02] p=0.10). ATB class analysis identified fluroquinolone exposure within 1 year (aHR=1.26 [1.13-1.40] p<0.001) and 60 days before ICI (aHR=1.20 [0.99-1.45] p=0.06) were associated with worse OS; with a dose effect based on total weeks of exposure over 1 year (aHR=1.07 per week [1.03-1.11] p<0.001) and 60 days (aHR=1.12 per week [1.03-1.23] p=0.01). Subgroup analysis showed similar results for patients receiving anti-PD1 ICIs and those with lung cancer and melanoma.

Conclusions

Exposure to ATBs and specifically fluroquinolones prior to ICI therapy is associated with worse OS. Interventions aimed at altering the gut microbiome may be required to help improve outcomes for patients on ICIs with prior ATB exposure.

Legal entity responsible for the study

The authors.

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