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THE EFFECT OF ANTIBIOTIC THERAPY ON IMMUNOTHERAPY OUTCOMES IN THE TREATMENT OF ACQUIRED BACTERIAL INFECTIONS DURING STAGE IV CANCER TREATMENT

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Background The gut microbiome can modulate therapeutic responses to immune checkpoint inhibitor (ICI) treatment in cancer.¹ Antibiotics play a detrimental role on outcomes in patients on ICIs.² Despite this association, there's limited evaluation on antibiotic subclasses and outcomes. The goal of our study is to determine what effect the spectrum of bacterial coverage or duration of therapy may have on ICI treatment.

Methods Our study is a retrospective cohort analysis using EMR data at Ochsner Medical Center from 2018–2020. IRB approval was obtained on 511 patients receiving immunotherapy. The primary endpoints for the study were time to treatment failure (TTF) and overall survival (OS). Anaerobic and aerobic antibiotics were defined by CLSI 2020 guidelines. TTF was defined as disease progression or death, which results in cessation of immunotherapy.

Results Of the 511 patients studied 42 were excluded. There were 203 patients in the anaerobic therapy group, 157 in the aerobic therapy group, and 123 in the no-antibiotic group. The median time for antibiotic therapy based on class was 19 days for aerobic and anaerobic therapy was 37 days.

TTF between antibiotic (anaerobic and aerobic) groups and untreated patients was significantly shorter (HR 1.28 and $p=0.0435$). There was a trend to decreased TTF with anaerobic antibiotics vs no therapy or aerobic therapy, but not statistically significant (HR 1.42 and 1.17 respectively; $p=0.0762$). Median TTF was 189 days (anaerobic) vs 337 days (aerobic) in the shorter antibiotic duration groups ($p .074$). No significant difference was noted when assessing for OS but adjusted for race, there was a difference noted in OS for any antibiotic use vs no antibiotic therapy in African Americans (N=70; HR 1.98; $p=0.03$).

Conclusions Our data supports the conclusion that antimicrobials significantly decrease the TTF of immune checkpoint inhibitors. There was no statistically significant difference in TTF or OS between antimicrobial subclasses, though a numerical trend for shorter TTF with anaerobic antibiotics. Cytokine modulation due to an altered microbiome from bacterial infection or antimicrobial administration plays a significant role in the cancer outcomes of ICI treatments.³ Possible limitations of this study include our limited population size, heterogeneity in specific antibiotics with differences in degree of anaerobic coverage, and the lack of analysis on interactions between specific ICI and antimicrobial agents. Future studies analyzing mechanisms of interaction between the microbiome, antimicrobials, and immune checkpoint inhibitors.

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