236 PREDICTORS OF ICI RENAL TOXICITY: A PATHOLOGICAL APPROACH

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Background Inflammatory response in unintended tissues and organs associated with the use of immune checkpoint inhibitors also known as immune related adverse events (irAEs) is a management challenge, and renal irAEs are associated with increased patient morbidity and mortality. The most common renal toxicity is acute interstitial nephritis (AIN), characterized by infiltration of renal tissue with immune cells, and may be analogous to kidney transplant rejection. Using both clinical variables and tissue findings we evaluated a large cohort of ICI cases to determine predictors of renal response and overall survival.

Methods We retrospectively reviewed all patients treated with ICI (August 2007 to August 2020) at MD Anderson Cancer Center. A total of 38 patients with biopsy confirmed AIN and available tissue were identified. All slides were reviewed by two board certified renal pathologists and the severity of inflammation and chronicity was graded using transplant rejection BANFF criteria. Patients were categorized as renal responders if creatinine improved or returned to baseline after treatment and non-responders if it did not. Fisher's exact tests for categorical variables and t-test/ANOVA or the counterparts of the non-parametric approaches (Wilcoxon rank-sum or Kruskal-Wallis) for continuous variables were used to compare patient's characteristics between groups. The distribution of overall survival (OS) was estimated by the Kaplan-Meier method. Log-rank test was performed to test the difference in survival between groups.

Results Based on the detailed pathological findings, patients with increased interstitial fibrosis were less likely to have renal response with treatment compared to patients with less fibrosis, ($p < 0.05$). Inflammation, tubulitis, number of eosinophils and neutrophils had no impact on renal response. Patients with response within 3 months of AKI treatment had a superior OS in comparison to patients who responded late (12-month OS rate: 77% vs 27%, $p < 0.05$). Notably, patients who received concurrent ICI and achieved renal response within 3 months had the best OS while those who did not receive concurrent ICI nor achieved renal response had worst OS (12-month OS rate: 100% (renal response and concurrent ICI) vs 72% (renal response with no concurrent ICI), vs 27% (no renal response and nonconcurrent ICI) ($p < 0.05$).

Conclusions This is the first analysis of ICI induced nephritis where a detailed pathological and clinical evaluation was performed to predict renal response. Our findings highlight the importance of early diagnosis and treatment of ICI-AIN while continuing concurrent ICI therapy.

Ethics Approval This retrospective study was approved by the institutional review board at The University of Texas MD Anderson Cancer Center, and the procedures followed were in accordance with the principles of the Declaration of Helsinki.

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