Immune Checkpoint Inhibitor Induced Hepatitis Injury: Risk Factors, Outcomes, and Impact on Survival

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Purpose: Immune checkpoint inhibitors (ICIs) are associated with a unique set of immune-related adverse events (irAEs). Few studies have evaluated risk factors and outcomes of patients who develop ICI-induced hepatitis (ICIH).

Methods: We utilized an institutional database of patients with advanced cancers treated with ICI to identify patients with ICIH. irAEs were graded using the Common Terminology Criteria for Adverse Events v4. Overall survival (OS) was calculated from the date of ICI to death from any cause or the date of the last follow-up. OS with 95% confidence intervals were estimated using the Kaplan–Meier method and stratified by occurrence of ICIH.

Results: We identified 1,096 patients treated with ICI . The most common ICIs were PD1/L1 (n=774) and CTLA-4 inhibitors (n=195). ICIH occurred among 64 (6%) patients: severity was < grade 3 in 30 and ≥ grade 3 in 24 patients (3.1% overall). Median time to ICIH was 63 days. ICIH was more frequent in women (p=0.038), in patients treated with combination ICIs (p<0.001), and when given as first line therapy (p=0.018). Occurrence of ICIH was associated with significantly longer OS, median 37.0 months (95% CI 21.4, NR) compared to 11.3 months (95% CI 10, 13, p<0.001); there was no difference in OS between patients with ≥ grade 3 ICIH vs grade 1-2.

Conclusion: Female sex, combination immunotherapy, and first line of immunotherapy were associated with ICIH. Patients with ICIH had improved clinical survival compared to those that did not develop ICIH.

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