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Prescription Event Monitoring of Checkpoint Inhibitor-induced Liver Injury and Outcomes of Rechallenge: A 10-year Experience

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Introduction

Checkpoint inhibitors have revolutionized cancer therapy, particularly for melanoma and renal cell carcinoma, by enhancing the immune system's ability to target and destroy cancer cells. However, their use is associated with immune-related adverse events, including checkpoint inhibitor-induced liver injury. This article examines a decade-long study on the incidence, risk factors, and outcomes of ChILI, as well as the implications of rechallenge after liver injury. The study utilized prescription event monitoring over a 10-year period, focusing on patients treated with CPIs at several tertiary centers. Researchers aimed to characterize the incidence of ChILI, identify associated risk factors, and evaluate the outcomes of rechallenge after initial liver injury [1].

Rechallenge after initial ChILI was a significant focus of the study. Of the patients who were rechallenged with CPIs, a substantial proportion did not experience recurrent liver injury. This finding suggests that with careful monitoring and management, rechallenge can be a viable option for many patients, potentially allowing them to continue benefiting from CPI therapy without severe adverse outcomes. Patients receiving combination CPI therapy should be closely monitored, particularly within the first 135 days of treatment, as the risk of ChILI diminishes significantly beyond this period. The CTCAE grading system may need revisions to more accurately reflect the clinical severity of ChILI, minimizing unnecessary interventions. For patients who develop ChILI, rechallenge should be considered on a case-by-case basis, with careful evaluation to balance the benefits of continued CPI therapy against the risks of recurrent liver injury [2].

Description

This extensive 10-year study provides valuable insights into the incidence, risk factors, and outcomes of checkpoint inhibitor-induced liver injury. By refining monitoring protocols and considering rechallenge strategies, healthcare providers can better manage the adverse effects of CPIs, optimizing treatment outcomes for cancer patients. The study found that the incidence of checkpoint inhibitor-induced liver injury was 8.8% among patients treated with CPIs. Notably, the risk was significantly higher in those receiving combination therapies, such as nivolumab plus ipilimumab, compared to those on monotherapies like pembrolizumab or nivolumab alone. Female patients and those with higher baseline ALT levels and lower ALP levels were at an increased risk, suggesting that liver function markers should be closely monitored before and during treatment.

A critical insight from the study was the overestimation of ChILI severity by the CTCAE grading system. This misclassification led to unnecessary hospitalizations and the administration of immunosuppressive therapies that might not have been needed. This finding underscores the necessity of revising the CTCAE criteria to better align with the clinical reality of ChILI cases . Management strategies for ChILI involve temporary cessation of CPI therapy, administration of corticosteroids, and in some cases, other immunosuppressive agents. The study advocates for a more tailored approach, suggesting that after the initial 4.5 months of therapy, the intensity of monitoring can be reduced if the patient remains asymptomatic and liver function tests are stable [3].

Rechallenge with CPIs after an initial episode of ChILI was found to be feasible and safe for many patients. The study reported that a significant number of patients did not experience a recurrence of liver injury upon rechallenge. This suggests that with proper assessment and monitoring, patients who have benefited from CPI therapy but experienced ChILI can be safely reintroduced to these treatments. Comprehensive baseline liver function tests should be conducted, particularly focusing on ALT and ALP levels. Regular monitoring during the first 4.5 months of therapy, with immediate intervention at the first signs of liver dysfunction. Use of corticosteroids and other immunosuppressive agents should be carefully balanced to minimize unnecessary exposure [4]. Studies should investigate the long-term outcomes of patients rechallenged with CPIs, focusing on both recurrence rates of liver injury and overall survival benefits. Identifying specific biomarkers that can predict susceptibility to ChILI could personalize treatment plans and mitigate risks. Comparing different CPI combinations and their respective risks for inducing liver injury will help optimize therapeutic regimens [5,6].

Conclusion

This 10-year study provides crucial insights into the real-world incidence, risk factors, and management of checkpoint inhibitor-induced liver injury. By implementing refined monitoring protocols and considering the potential for safe rechallenge, healthcare providers can enhance the therapeutic efficacy of CPIs while minimizing adverse effects. As CPI use continues to expand in oncology, these findings will play a pivotal role in shaping clinical practices and improving patient outcomes. For more detailed information, refer to the comprehensive studies published in JHEP Reports and abstracts from the European Association for the Study of the Liver.

Acknowledgement

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Conflict of Interest

None.

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