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Association of Biliary Disorders with Immune Checkpoint Inhibitors: A pharmacovigilance study

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Abstract

Background: Immune checkpoint inhibitors (ICIs), including anti-PD-1/L1 therapy and anti-CTLA-4 therapy, are associated with a unique spectrum of immune-related adverse events (irAEs). The association and clinical features of ICIs-related biliary disorders are not well characterized. Methods: Data were extracted from the US Food and Drug Administration Adverse Event Reporting System (FAERS) database. Bile duct and gallbladder diseases were defined by the Medical Dictionary for Regulatory Activities (MedDRA). We performed disproportionality analysis using reporting odds ratios (ROR) and information component (IC). The result was defined as a signal if the lower limit of the 95% confidence interval for ROR is over 1 and the number of cases [?]5, or the lower limit of 95% confidence interval for the IC (IC025)>0. Results: 906 reports of ICI-related bile duct and gallbladder events were identified. The mean age was 64.8±12.1 years and the AEs occurred more in men (60.1% vs 39.9%). ICIs were associated with increased reporting of bile duct diseases (ROR 3.35, 95%CI 3.07-3.66; IC0251.41), especially cholangitis (ROR 5.52, 95% CI 4.94-6.17; IC0251.93); while we didn't identify signal of gallbladder disease (ROR 0.96, 95%CI 0.86-1.08; IC025 -0.22). PD-1/L1 inhibitors and combination regimen were associated with a spectrum of distinct classes of bile duct disease while anti-CTLA-4 therapy (ipilimumab) had no association with any bile duct and gallbladder diseases. Conclusions: PD-1/L1 inhibitors showed increased reporting of cholangiopathy, especially for cholangitis. Physicians should be aware of this potential adverse event.

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