Risk of endocrine complications and elevated liver transaminases in patients with solid tumors treated with immune checkpoint inhibitors; A meta-analysis

H. Elhalawani1, M. Fouad2, O.M. Abdel-Rahman1
1Clinical Oncology, Ain Shams University Hospital, Cairo, Egypt
2Medical Microbiology and Immunology Department, Ain Shams University Faculty of Medicine, Cairo, Egypt

Aim: The feasibility and efficacy of immune checkpoint inhibitors for patients with advanced malignancies have been tackled in numerous trials in the past few years. We performed a systematic review and meta-analysis of the risk of endocrine adverse events, along with the incidence of elevated liver transaminases, associated with immune checkpoint inhibitors.

Methods: Eligible studies included randomized phase II and III trials of patients with solid tumors on ipilimumab, nivolumab, pembrolizumab, tremelimumab and pidilizumab; describing events of hypothyroidism, hyperthyroidism, hypopituitarism/hypophysitis and adrenal insufficiency; in addition to events of elevated liver transaminases [alanine aminotransferase (ALT) and aspartate aminotransferase (AST)].

Results: Our search strategy yielded 210 potentially relevant citations on immune checkpoint inhibitors from Pubmed/Medline, CENTRAL Cochrane registry and ASCO meeting library. After exclusion of ineligible studies, a total of 10 clinical trials evaluating ipilimumab, nivolumab, tremelimumab and pembrolizumab were considered eligible for the meta-analysis. The RR of all-grade hypothyroidism, hyperthyroidism, hypophysitis and adrenal insufficiency were 8.26 (95% CI: 4.67-14.62; p < 0.00001), 5.48 (95% CI: 1.33-22.53; p = 0.02); 22.03 (95% CI: 8.52-56.94; p < 0.00001), 3.87 (95% CI: 1.12-13.41; p =0.03) respectively. Whereas, the RR of all grade elevated ALT and AST was 2.29 (95% CI 1.14-4.62; p < 0.0001) and 1.5 (95% CI: 0.69-3.29; p = 0.31) respectively. While for high grade elevated ALT and AST, it was 9.42 (95% CI: 4.31-20.6; p < 0.0001) and 10.65 (95% CI: 4.16-27.27; p < 0.0001) respectively.

Conclusions: Our meta-analysis has demonstrated that the use of immune checkpoint inhibitors is associated with an increased risk of hypothyroidism, hyperthyroidism, hypophysitis and adrenal insufficiency compared to control. Moreover, the use of immune checkpoint inhibitors has a causal relationship to an increased risk of high grade elevated ALT and AST. Clinicians should be aware of these risks and perform regular monitoring.

Disclosure: All authors have declared no conflicts of interest.