Immune-related adverse events in patients with cancer receiving influenza vaccination and immune checkpoint inhibitors

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Immune-related Adverse Events in Patients With Cancer Receiving Influenza Vaccination and Immune Checkpoint Inhibitors

To the Editor—With interest, we read the study by Chong et al [1] who reported that 20% of patients with cancer who received influenza vaccination concurrently with immune checkpoint inhibitors (ICIs) experienced immune-related adverse events (IRAEs). Their findings were comparable to the rates reported in historical studies and are relatively similar to the rate that we determined in our retrospective analysis (26%) [2]. However, this rate of 20% was not obtained by directly comparing patients from the same prospectively included cohort as we did. The use of historical controls complicates the interpretation of their data, since historical controls receiving ICIs may have received influenza vaccine as well, considering the vaccination coverage of 45–56% among patients with cancer in the United States [3, 4].

In addition, we question the duration of the period of follow-up for IRAEs after influenza vaccination (median, 1.4 years) considering the relatively low immunogenicity of antigens included in the influenza vaccine. The active immune response following influenza vaccination has already waned after a few months and hemagglutination-inhibition titers do not reliably persist year-round in older adults but regress to prevaccination levels in 360 days [5].

Nevertheless, both studies confirm that influenza vaccination during administration of ICIs is safe and that the reported high overall rate of IRAEs (12 of 23, 52%) in the study by Läubli et al [6] with fewer subjects may have been a chance finding. Therefore, seasonal influenza vaccination can still be advocated in patients with cancer receiving ICIs.

Note

Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Reply to Groeneveld et al

To the Editor—We appreciate the response by Groeneveld et al [1] to our article [2]. The authors bring up methodological limitations that are fully acknowledged and addressed in our study. There are no reliable estimates of influenza vaccine coverage among patients on immune checkpoint inhibitors (ICIs); the association between vaccine- and immune-related adverse events (IRAEs) remains unexamined in randomized controlled trials. Although key ICI clinical trials permitted inactivated influenza vaccine among enrolled subjects, IRAE rates were not specifically examined by vaccination status. A few recently conducted retrospective studies [2–5], including ours, examined this important clinical question. Despite the variability in study design among these reports, the findings consistently support that flu vaccine is safe and effective in patients on ICI.

With regard to the duration of immunity after influenza vaccine, antibody responses can persist over several seasons [6]. Therefore, we believe the extended follow-up beyond a typical influenza season is a cautious approach. With a median follow-up of 1.4 years, IRAE rates in our cohort remain comparable to historical studies, suggesting that there is even less chance that any IRAEs observed in our cohort of vaccinated patients on anti–programmed cell death protein 1 therapy were related to vaccination. We do not think this impacts our study conclusions. We appreciate the opportunity to clarify these issues.

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