Letters

RESEARCH LETTER

Long-term Immunogenicity of BNT162b2 Vaccine in Patients With Solid Tumors

In previous cohort studies, administration of the BNT162b2 vaccine in patients with solid tumors demonstrated a favorable safety and efficacy profile following the second vaccination, although gradual immunogenicity was observed compared with the general population.\(^1\) We had previously demonstrated at 6 months postvaccination a steady decline in antibody titers and seropositivity rates among patients with solid tumors treated at a center in Haifa, Israel, that were comparable with the general population.\(^2\) Because of declined immunity, a booster dose had been recommended by medical authorities.

Although humoral response was extensively studied in patients with cancer, to our knowledge, there are few data regarding cellular immunity and the association with vaccine efficacy. In this study, we prospectively explored cellular and humoral pathways at 6 months postvaccination in patients with cancer who were receiving active antineoplastic treatment, as well as a subset of patients following receipt of a booster dose.

Methods | This analysis is a follow-up report of our prospective study evaluating BNT162b2 vaccination outcomes in patients with solid tumors who had been receiving active treatment at first vaccination at a center in Haifa, Israel, and throughout the 12-month study follow-up period and were vaccinated with at least 2 doses as described.\(^2\) The study protocol was approved by the institutional ethics committee of Rambam Health Care Campus and followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline, and participants provided written informed consent. Serum samples and peripheral blood mononuclear cells were collected at 6 months postvaccination for the entire cohort (N = 169) and additionally after administration of a booster dose in a subset of patients (37 [22%]). The S1/S2 immunoglobulin G assay was performed as described,\(^2\) and an enzyme-linked immune absorbent spot assay (Mabtech) to quantify interferon-\(\gamma\)-producing T cells was used to assess T-cell response. Patients' electronic medical records were reviewed for documentation of COVID-19 infection until January 8, 2022.

The difference in spot-forming units (SFUs) was assessed using the \(t\) test and 1-way analysis of variance. The association between SFU and neutralizing antibody titers at 6 months was examined by Pearson correlation. Statistical significance was set a priori at \(P < .05\). The data were analyzed using R, version 4.0.5 (R Foundation).

Results | Of the 169 patients, 97 (57%) were men; the mean (SD) age was 66 (11) years. Most patients (137 [81%]) had metastatic disease. Common cancers were gastrointestinal (55 [33%]), lung (38 [23%]), breast (28 [17%]), and genitourinary (21 [12%]). Treatments consisted of chemotherapy (97 [57%]), biological agents (61 [36%]), immunotherapy (63 [37%]), or combined modalities. A total of 134 patients (79%) were evaluated for T-cell response because of a low viable cell count. Age, sex, and cancer type were not associated with cellular response. Although treatment with chemotherapy was associated with humoral response, SFU was not associated with treatment type (Figure 1). We found a significant correlation between serological and cellular response (Figure 2), while 5 (22%) of the seronegative patients had SFU levels equal to or higher than the mean SFU of the seropositive patients.

Following receipt of a booster dose, 113 (67%) demonstrated a significant increase in cellular immune response (9.2 vs 31.3 SFU/10⁶ peripheral blood mononuclear cells; \(P = .02\)), and 100% had an increase in antibody levels (117 vs 732 AU/10⁴).

Figure 1. Association of Treatment Type With T-Cell Response

Violin plots comparing spot-forming unit (SFU)/10⁶ cells at 6 months postvaccination between treatment types (\(F\) value, \(-0.8\)). The violin plots represent the data distribution and are based on the density of data points. The big black dot represents the mean, the black dots represent each individual sample, and the black line represents 2 standard deviations. PBMCs indicate peripheral blood mononuclear cells.

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mL; \( P < .001 \)). At 12 months postvaccination, there were no documented COVID-19 cases.

**Discussion** | In this cohort study, we found a durable cellular and humoral response in patients with cancer with solid tumors who were receiving active treatment. Humoral and cellular response were associated, although B-cell response was negatively associated with chemotherapy,\(^2\) whereas T-cell response seemed to be unaffected, which may have been associated with a differential association of chemotherapy with B-cell counts.\(^3\) Novel variants, such as Omicron, have the ability to evade a B-cell response but are associated with a T-cell response, emphasizing its importance.\(^4\) Thus, T-cell response might confer immunity to SARS-CoV-2 in seronegative patients. None of the patients developed COVID-19 infection after 12 months, which supports this hypothesis, although undocumented cases could not be excluded. The fact that study analysis occurred before the Omicron climax in Israel may be a limitation. Taken together, these results suggest that in patients with solid tumors, the BNT162b2 vaccine exerts a cellular and humoral sustainable response that is manifested by a low infectivity rate.

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