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Article

Immunogenicity and Safety of the BNT162b2 mRNA COVID-19 Vaccine Among Actively Treated Cancer Patients

Hagai Ligumsky, MD, PhD [1,2,*] Esraa Safadi, BSc,[2] Tal Etan, MD,[1,2] Noam Vaknin, BSc [2] Manuel Waller, MA,[1] Assaf Croll, BSc,[2] Alla Nikolaevski-Berlin, PhD,[1] Inbal Greenberg, MSc [1,2] Tami Halperin, PhD,[3] Asaf Wasserman, MD,[1,4] Lior Galazan, BSc,[5] Nadir Arber, MD,[5] Ido Wolf, MD,[1,2]

[1]Oncology Division, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel; [2]Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel; [3]Human Immunodeficiency Virus Lab, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel; [4]Infectious Diseases Unit, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel; and [5]The Integrated Cancer Prevention Center, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

*Correspondence to: Hagai Ligumsky, MD, PhD, Division of Oncology, Tel Aviv Medical Center, 6 Weizmann St, Tel Aviv, 6423906 Israel (e-mail: hagail@tlvmc.gov.il).

Abstract

Background: Activity and safety of the SARS-CoV-2 BNT162b2 vaccine in actively treated patients with solid tumors is currently unknown. **Methods:** We conducted a retrospective study of 326 patients with solid tumors treated with anticancer medications to determine the proportion of cancer patients with immunogenicity against SARS-CoV-2 following 2 doses of the BNT162b2 vaccine. The control group comprised 164 vaccinated healthy adults. Anti-SARS-CoV-2 S immunoglobulin G antibodies were measured using a level greater than 50 AU/mL as a cutoff for seropositivity. Information on adverse effects was collected using a questionnaire. All statistical tests were 2-sided. **Results:** Most patients (205, 62.9%) were treated with chemotherapy either alone or with additional therapy; 55 (16.9%) were treated with immune checkpoint inhibitors and 38 (11.7%) with targeted therapy alone; 28 (8.6%) received other combinations. The vaccine was well tolerated, and no severe side effects were reported. Among patients with cancer, 39 (11.9%) were seronegative compared with 5 (3.0%) of the control group ($P = .001$). Median immunoglobulin G titers were statistically significantly lower among patients with cancer compared with control (931 AU/mL vs 2817 AU/mL, $P = .003$). Seronegativity proportions were higher in the chemotherapy-treated group (n = 19; 18.8%) compared with the immune checkpoint inhibitor–treated patients (n = 5; 9.1%) and with those treated with targeted therapy (n = 1; 2.6%) ($P = .02$). Titers were also statistically significantly different among treatment types ($P = .002$). **Conclusions:** The BNT162b2 vaccine is safe and effective in actively treated patients with cancer. The relatively lower antibody titers and lower proportion of seropositive patients, especially among chemotherapy-treated patients, call for continuing the use of personal protective measures in these patients, even following vaccination.

ARTICLE

Patients with cancer are at increased risk for morbidity and mortality from COVID-19 (1), and active treatment may further increase these risks (2). Yet, patients with cancer were excluded from the pivotal trials of the COVID-19 vaccines (3-5), and the safety and efficacy of the vaccine in this large and vulnerable population are currently unknown. Despite a lack of data, current guidelines of both the American Society for Clinical Oncology and the European Society for Medical Oncology strongly support vaccination of patients with cancer treated with systemic anticancer therapy (6,7).

On December 19, 2020, the Israeli Ministry of Health launched a national mass vaccination campaign, aiming at rapid vaccination of the entire adult Israeli population. All Israeli citizens aged 16 years or older who were not previously infected with SARS-CoV-2 were eligible for the mRNA BNT162b2 vaccine. Vaccines were readily available, free of charge, and administered as recommended by the manufacturer at a 21-day interval. The second dose was omitted if the patient contracted SARS-CoV-2 infection following the first dose. By April 30, 2021, 5 048 333 Israelis (55.8% of the Israeli population) were already fully vaccinated. Although data were lacking, the Israeli Ministry of Health not only recommended vaccination of all patients with cancer but also prioritized them to be vaccinated at the early stages of the campaign, regardless of disease stage, performance status, or life expectancy.

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Accumulating data indicate that the BNT162b2 vaccine is indeed safe in actively treated cancer patients. We have recently reported on the short-term safety of 2 doses of the BNT162b2 vaccine in 134 patients with a variety of solid cancers treated with immune checkpoint inhibitors (ICI) (8), and Monin et al. (9) reported on the safety of the vaccine in a cohort of 151 patients, of whom 95 had solid cancers and 25 received 2 doses. No unexpected or severe side effects were noted in both studies. Similarly, the vaccine was also found to be safe among patients with chronic lymphocytic leukemia (CLL) (10). Although data regarding safety are accumulating and reassuring, data regarding activity of the BNT162b2 vaccine are lacking. Direct assessment of the ability of the BNT162b2 vaccine to reduce morbidity and mortality among patients with cancer is limited because of the small number of cancer patients relative to the general population and because of the presence of major confounding factors, including social distancing and the low prevalence of SARS-CoV-2 infection in the general population following mass vaccination. Indeed, a cohort of nearly 600 000 individuals was required to determine the efficacy of the BNT162b2 vaccine at the national level (11). To overcome this obstacle, several surrogate markers for the activity of the vaccine are being used; the most common is a direct measurement of anti-SARS-Cov-2 spike (S) antibody titers in the serum. Recent studies used this test and reported on antigenicity and seroconversion in patients with malignant diseases. A recent study from our institution noted an antibody response in only 40% of 167 patients with CLL receiving 2 doses of the BNT162b2 vaccine (10), and low responses were also noted in a cohort of 29 multiple myeloma patients (12). Response to this vaccine in patients with solid cancers was evaluated in 2 small cohorts (9,13). Although both studies reported on approximately 95% immunogenicity following the second vaccine dose, no association with either tumor or treatment type could be determined in either of these studies because of the small number of patients. We describe here safety and antibody response following administration of the second dose of the BNT162b2 vaccine in a cohort of 326 actively treated patients with solid tumors.

ARTICLE

Methods

Study Design

This retrospective cohort study was designed to evaluate the safety and efficacy of the BNT162b2 vaccine in actively treated patients with solid cancers. The study was conducted at the Oncology Division of Tel Aviv Sourasky Medical Center (TASMC), a tertiary referral center with more than 4000 new cancer patients a year. The study was approved by the institutional review board.

Patient Population

The national vaccination campaign was initiated on December 20, 2020, and administration of the second dose started on January 10, 2021. The antibody response to the BNT162b and mRNA-1273 vaccine shows a steep rise up to approximately 40 days following full vaccination, followed by a steady state afterwards (14,15). To avoid a bias associated with this period of antibody response upregulation, we aimed to evaluate the efficacy of the vaccine 2 months following the second dose. Thus, blood collection was initiated on March 15, 2021, and the last patient was recruited by April 30, 2021. During this period, all patients with solid tumors actively treated at the day-care center of the oncology division at this time were approached and offered to participate in the study. Active treatment was defined as any IV anticancer medication administered during a period starting at 2 weeks before the first vaccine dose and ending 2 weeks after the second vaccine dose.

The control group consisted of fully vaccinated healthy adults with no personal history of cancer or active immune suppressive medications who were either health-care workers at the oncology division of TASMC offered to be tested for anti-SARS-CoV-2 S immunoglobulin G (IgG) antibodies or individuals opted to test immunogenicity at the Integrated Cancer Prevention Center at TASMC. The control group was recruited at the same period for the purpose of this study.

Following signing an informed consent form, participants filled a detailed questionnaire regarding side effects of the vaccines, and blood was captured for immunogenicity analysis. Clinical data were retrieved from the hospital electronic medical records.

Immunogenicity Analysis

Humoral response was evaluated by testing anti-SARS-CoV-2 S Receptor Binding Domain IgG antibody (Ab) titer. The presence of anti-SARS-CoV-2 S IgG antibodies was evaluated by using SARS-CoV-2 IgG assay chemiluminescent microparticle immunoassay intended for the quantitative detection of Receptor Binding Domain IgG antibody levels to SARS-CoV-2 (SARS-CoV-2 IgG II Quant, Abbott, Ireland). Results were provided in arbitrary units (AU/mL) ranging from 0 to 40 000 for anti-S antibodies [level > 50 AU/mL considered positive according to the manufacturer's instructions (16)].

Outcomes

The primary endpoint was proportion of cancer patients with immunogenicity against SARS-CoV-2, defined as antibody titer level > 50 AU/mL, following 2 doses of the BNT162b2 vaccine compared with the healthy individuals. The secondary endpoints were antibody titer levels in cancer patients compared with the control group, association between seropositivity and cancer treatment, and safety.

Statistical Analysis

All variables were characterized by appropriate descriptive measures. Clinical characteristics, anti-SARS-CoV-2 S IgG antibodies, and proportion of immunogenicity (seronegativity/positivity) comparisons were done using the Mann-Whitney *U* test (numerical variables) and the χ^2 test (categorical variables). The Kruskal-Wallis test was used to evaluate differences in numerical variables (eg, age and SARS-CoV-2 S AU IgG titer) among different cancer types and treatment types (eg, chemotherapy vs immunotherapy vs targeted therapy). Multiple comparisons of numerical variables were performed using the Mann-Whitney test with Bonferroni correction.

A multivariable logistic regression model was used to evaluate the association between being a cancer patient and anti-SARS-CoV-2 S IgG antibodies adjusted for age and sex, and to evaluate the effect of age, metastatic disease, time from second vaccination to IgG test, treatment type (chemotherapy vs no chemotherapy), and cancer type on seronegativity or positivity. All statistical tests were 2-sided, and a *P* value less than .05 was

considered statistically significant. Statistical analysis was conducted using SPSS software. Transforming data to logs and plots formation were performed using GraphPad Prism version 9.0.1 for Windows.

Results

Patient Characteristics

Between March 15 and April 30, 2021, 326 out of 1383 (23.6%) actively treated patients with cancer agreed to participate in the study. Their characteristics are presented in Table 1. The median age was 66 years, most (n = 203, 62.3%) were women, and the most common tumor types were gastrointestinal (n = 84, 25.8%) followed by breast (n = 82, 25.2%) and lung (n = 45, 13.8%) cancer. Most patients (n = 205, 62.9%) were treated with chemotherapy either alone (n = 101 patients) or in combination with additional therapy (ICI, targeted therapy, radiation, and hormonal therapy; 104 patients): 55 (16.9%) were treated with ICI, 38 (11.6%) with targeted therapy alone, and 28 (8.6%) received other treatments (eg, radiation alone or in combination with ICI or targeted therapy). Most patients (n = 230, 70.6%) had metastatic disease. As expected from the study design, the median time from second vaccine dose to antibody testing was 78 days (range = 21-115 days).

The control group included 164 individuals. Their median age was statistically significantly younger than the cancer patients' cohort (54 vs 64 years, respectively, $P < .001$; Table 1). Time from second vaccine dose to antibody testing in the control group was 72 days (range = 21-115 years, $P = .08$ compared with the cancer patients).

Adverse Events

Information on adverse effects was collected using a detailed questionnaire. The vaccine was well tolerated, with local pain (n = 64, 19.6%), weakness (n = 57, 17.5%), myalgia (n = 41, 12.6%), and headache (n = 21, 6.4%) the most prevalent (Figure 1). Importantly, no severe side effects, either life threatening or requiring hospitalization, were reported.

Immunogenicity Following Vaccination

Immunogenicity was assessed by measuring anti-SARS-CoV-2 S IgG antibodies titer. According to the manufacturer's instructions (16) and based on previous reports, a titer greater than 50 AU/mL was considered as seropositive (17,18). Using this cut-point, 39 (11.9%) cancer patients compared with 5 (3.0%) of the control group were found to be seronegative (Table 2, $P = .001$). Moreover, median IgG titers were statistically significant lower in the patient group compared with the healthy controls (931 AU/mL vs 2817 AU/mL, $P = .003$; Table 2), with an odds ratio of 4.33 (95% CI = 1.66 to 11.23). The distribution of antibody titers is presented in Figure 2. A multivariable logistic regression model indicated no statistically significant interaction between either age ($P = .15$) or sex ($P = .11$) and antibody titer levels.

To identify additional factors contributing for reduced response to the BNT162b2 vaccine, we also compared characteristics of the 39 patients with negative antibody titer (<50 AU/mL) with the 287 patients with positive antibody titers (Table 3). Although no statistically significant differences were found between the 2 groups in age, sex, metastatic disease status, time to IgG test, or treatment type (chemotherapy-based vs no-chemotherapy-based treatment), the analysis is considered exploratory because of the relatively small number of patients who remained seronegative. Moreover, there was no statistically significant association between cancer type and immunogenicity status ($P = .21$; Table 3). However, statistically significant differences were found in the distribution of antibody titers among the different cancer types ($P = .02$). Multicomparisons analysis between specific cancer types revealed a statistically significant difference between gynecological cancers and gastrointestinal cancers ($P = .02$), because the distribution of the number of antibodies in gynecological cancer tends to be higher than in gastrointestinal cancer. All other comparisons were not statistically significant (Figure 3).

Similarly, multivariable logistic regression models (generated separately for men and women because they differ by distinct cancer diagnosis) did not show any statistically significant association between seropositivity in patients with cancer and age, sex, or cancer type variables (data not shown).

Finally, we analyzed the association between either antibody titers or immunogenicity and treatment administered (Table 4). Because of the heterogeneity of chemotherapy-based combinations, the analysis was restricted to patients receiving only a single type of systemic therapy: chemotherapy alone (n = 101), ICI alone (n = 55), or targeted therapy alone (n = 38). Seronegativity proportions were higher in the chemotherapy-treated group (18.8%) compared with 9.1% in the ICI-treated patients and 2.6% in those treated with targeted therapy ($P = .02$ for the comparison between the groups; Table 4). Antibody titers differ statistically significantly between treatments ($P = .002$), and further examination of the differences between each pair of treatments revealed a statistically significant difference between chemotherapy and targeted therapy ($P = .001$; Figure 4).

As expected from routine clinical practice, the distribution of tumor types, and therefore also sex and age, were different according to treatment type. For example, no women with breast cancer were treated with ICI, and 20 (36.4%) of the ICI-treated group had non-small cell lung cancer (Table 4). None of the study participants, either patients with cancer or the healthy individuals, reported contracting COVID-19 following the second vaccine dose.

Discussion

We report here on the safety and efficacy of the COVID-19 vaccine BNT162b2 in a large, unselected population of patients with solid tumors at the time of active anticancer treatment. Importantly, all patients received 2 doses of the vaccine at the recommended schedule of days 1 and 21. Moreover, immunogenicity was examined 6 weeks following the second dose, a time expected to represent the steady state of protective antibodies levels.

Our data indicate the vaccine to be highly effective in this population, with 88% having protective levels of anti-SARS-CoV-2 S antibodies compared with 97% in healthy controls. However, chemotherapy-treated patients had a lower proportion of patients (81%) with protective antibody levels. Similarly, lower response rates were also noted in cancer patients following influenza vaccination (19).

Two small studies reported on 95% seropositivity in 18 (9) and 40 (13) patients with solid tumors receiving 2 doses of the BNT162b2 vaccine. In addition to sample size, major advantages of this study were the inclusion of only actively treated patients on one hand, without any selection and regardless of clinical

Table 1. Clinical characteristics of study participants

Characteristics	Cancer patients (N = 326)	Healthy controls (N = 164)	P
Median age, y (range)	66 (29-89)	54 (24-90)	<.001[a]
Female, No. (%)	203 (62.3)	100 (60.9)	.78[b]
Days from 2nd dose to COVID-19 Ab test, median (range)	78 (21-115)	72 (21-115)	.08[a]
Cancer type, No. (%)			
Gastrointestinal	84 (25.8)	NA	
Breast	82 (25.2)	NA	
NSCLC	45 (13.8)	NA	
Gynecological	41 (12.6)	NA	
Genitourinary	29 (8.9)	NA	
Skin cancers including melanoma	13 (4.0)	NA	
CNS	12 (3.7)	NA	
Sarcoma	10 (3.1)	NA	
Head and neck	7 (2.1)	NA	
Other	3 (0.9)	NA	
Cancer stage, No. (%)			
Local	96 (29.4)	NA	
Metastatic	230 (70.6)	NA	

[a]P values derived from the nonparametric Mann-Whitney *U* test, 2-sided. Ab = antibody; CNS = central nervous system; NA = not applicable; NSCLC = non-small cell lung cancer.
[b]P values derived from the parametric χ^2, 2-sided.

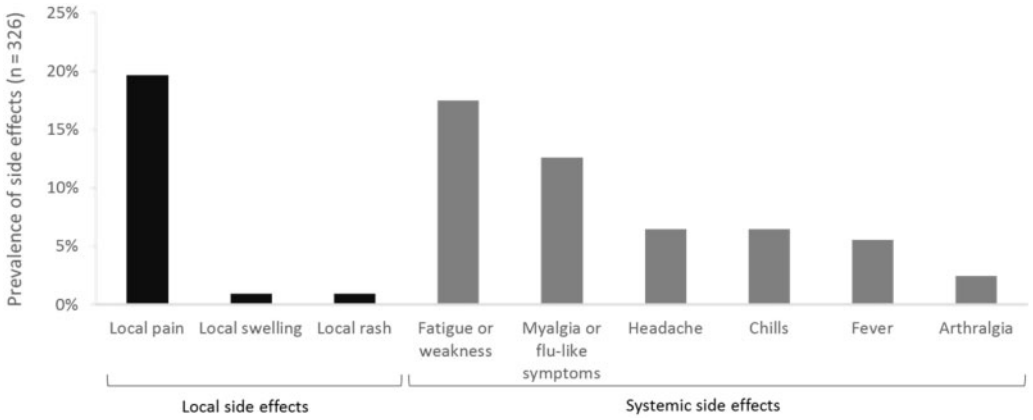

Figure 1. Local and systemic side effects following BNT162b2 mRNA vaccination among actively treated cancer patients. **Bars** show the proportion of participants reporting on each side effect. Only side effects reported by more than 1% of the patients are presented.

Table 2. Immunogenicity in patients with cancer compared with healthy controls

Variables	Cancer patients (N = 326)	Healthy controls (N = 164)	P
Median IgG Ab titer (range), AU/mL	931 (0-40 000)	2817 (0-40 000)	.003[a]
Seronegative (<50 AU/mL), No. (%)	39 (11.9)	5 (3.0)	.001[b]
IgG titer (AU/mL) by range, No. (%)			
50-100	21 (6.4)	0 (0.0)	.001[b]
101-1000	114 (35.0)	31 (18.9)	
1001-5000	106 (32.5)	74 (45.1)	
5001-10 000	24 (7.4)	33 (20.1)	
<10 001	22 (6.7)	21 (12.9)	

[a]P values derived from the nonparametric Mann-Whitney *U* test, 2-sided. Comparison of median IgG Ab between cancer patients and control group was adjusted for age and sex using a logistic regression model including these variables. Ab = antibody; IgG = immunoglobulin G.
[b]P values derived from the parametric χ^2, 2-sided.

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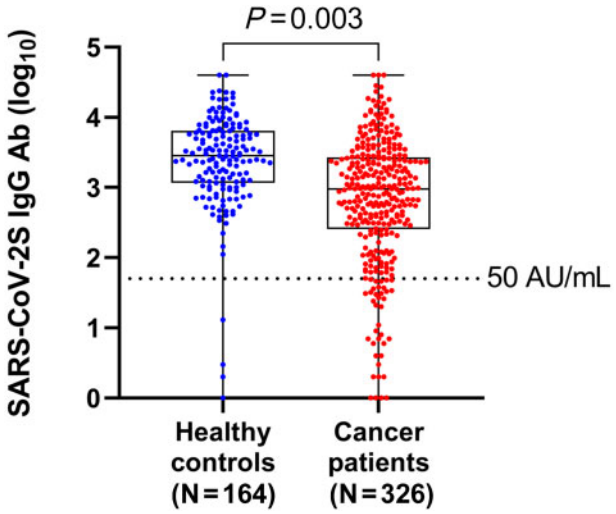

Figure 2. Lower SARS-CoV-2 S immunoglobulin G (IgG) antibody (Ab) among patients with solid cancers. SARS-CoV-2 S IgG Ab values in serum samples of actively treated patients with cancer (N = 326 patients) and healthy controls (N = 164). **Box plots** represent serum SARS-CoV-2 S IgG Ab values. Ends of the boxes are the upper and lower quartiles, and medians are marked by **horizontal lines** inside the boxes. Every **dot** represents 1 participant's level of antibodies. **Error bars** represent the range between minimal and maximal points. The y-axis (log_{10} scale) represents SARS-CoV-2 S IgG Ab values transformed to log_{10} scale. The statistical significance of the differences was determined using the 2-sided Mann-Whitney test adjusted for age and sex. **Dashed line** represents cutoff level of seropositivity (50 AU/mL). Cancer patients had lower plasma levels of SARS-CoV-2 S IgG Ab compared with healthy controls ($P = .003$).

characteristics on the other hand. Thus, our findings may better represent the general population of actively treated patients with cancer.

Development of anti-S antibodies is indicative of an immune response to the vaccine but is not synonymous to protection from clinical infection (20). The cutoff for a positive response in the assay that we used is defined as 50 AU/mL in accordance to validation studies for this specific test (16). However, although seropositivity is generally considered to be protective (20), antibody levels above this cutoff may also be important (21) because the correlation between titer levels following vaccination and vaccination efficacy is not well characterized in COVID-19.

Indeed, differences in antibody titers between patients with cancer and healthy controls were highly statistically significant, with a median titer of nearly threefold higher in the control group (Table 2). It remains to be elucidated whether these differences will translate to higher chances of SARS-CoV-2 infection.

The immune response may also be evaluated by testing T-cell response following vaccination. However, T-cell response might be affected in patients with cancer because of the effect of systemic therapy or disease itself. Nevertheless, it was also demonstrated that T-cell response correlates with antibody titers in healthy individuals and cancer patients, with 88% of cancer patients showing T-cell response and 95% showing seropositivity following the second dose of vaccine (9,14). Because antibody titers strongly correlate with T-cell response but are much easier to evaluate, this is possibly the preferred method for screening large number of patients.

The relatively high rates of seropositivity observed in patients with solid cancer are in stark contrast to recent reports in patients with CLL (10) or other immunodeficiency states, including hemodialysis (17) and solid organ transplant recipients (22). This may reflect the relatively smaller immunosuppressive effects of solid tumors and their treatments compared with hematologic malignancies.

Because only 39 (11.9%) of the patients did not show response to the vaccine, no clear association between clinical characteristics and response could be identified. The differences in distribution of antibody titers across tumor types and treatment types may signal an association between these factors and lower response, but because of the small number of patients, this study should be considered primarily hypothesis generating, and larger studies are required to substantiate these observations.

There are several limitations to this study: the patient population was compared with healthy controls consisting substantially of younger health-care workers, yet SARS-CoV-2 S Ab levels were statistically significantly lower in the patient population after adjusting for age and sex. Although anti-SARS-CoV-2 S testing was offered to all patients, a low (24%) participation rate of active patients in this study was noted. This may be due

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Table 3. Comparison between cancer patients with either seropositive or seronegative response to the BNT162b2 vaccine

Variables	SARS-CoV-2 S IgG seropositive (n = 287)	SARS-CoV-2 S IgG seronegative (n = 39)	P
Median age (range), y	66 (22-91)	67 (35-89)	.25[a]
Female, No. (%)	174 (60.6)	29 (74.4)	.10[b]
Metastatic disease, No. (%)	205 (71.4)	25 (64.1)	.74[b]
Median days from 2nd vaccination to COVID-19 Ab test	76 (23-115)	76 (2-99)	.47[a]
Chemotherapy-based treatment, No. (%)	176 (61.3)	29 (74.4)	.12[b]
Cancer type, No. (%)			.21[c]
Gastrointestinal	78 (27.2)	6 (15.4)	
Breast cancer	68 (23.7)	14 (35.9)	
NSCLC	40 (13.9)	5 (12.8)	
Gynecological	39 (13.6)	2 (5.1)	
Genitourinary	24 (8.4)	5 (12.8)	
Other	38 (13.2)	7 (17.9)	
COVID-19 infection, No.	0	0	>.99

[a]P values derived from the nonparametric Mann-Whitney *U* test, 2-sided. Ab = antibody; IgG = immunoglobulin G; NSCLC = non-small cell lung cancer.
[b]P values derived from the parametric χ^2 test, 2-sided.
[c]P value derived from χ^2 test, 2-sided.

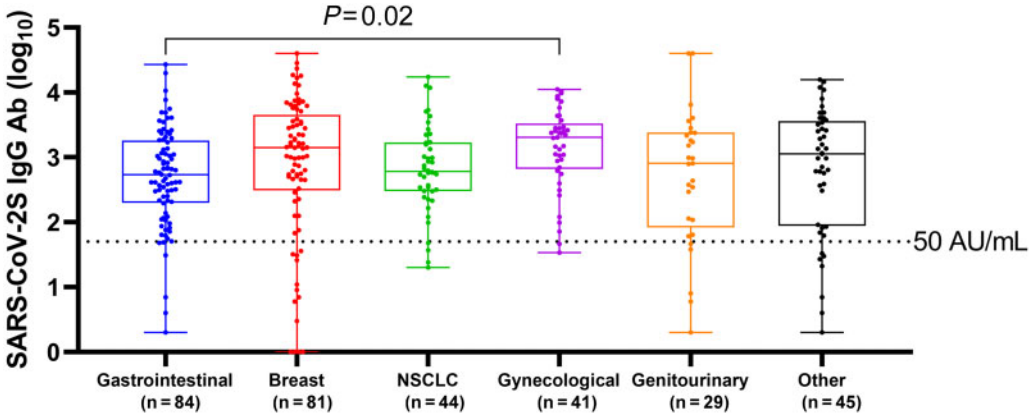

Figure 3. Differences in the distribution of SARS-CoV-2 S immunoglobulin G (IgG) antibody (Ab) across different cancer types. SARS-CoV-2 S IgG Ab values in serum samples of actively treated patients with cancer (N = 326 patients) are shown by cancer type. **Box plots** represent serum SARS-CoV-2 S IgG Ab values. Ends of the boxes are the upper and lower quartiles, and medians are marked by **horizontal lines** inside the boxes. Every **dot** represents 1 participant's level of Ab. **Error bars** represent the range between minimal and maximal points. The y-axis (log_{10} scale) represents SARS-CoV-2 S IgG Ab values transformed to log_{10} scale. The **dashed line** represents cutoff level of seropositivity (50 AU/mL). Statistical analyses were determined using the Kruskal-Wallis test and the Mann-Whitney test with Bonferroni correction for multiple comparisons. Patients with gynecological cancers had higher SARS-CoV-2 S IgG Ab values compared with patients with gastrointestinal cancers ($P = .02$, 2-tailed). All other comparisons did not reach statistical significance. NSCLC = non-small cell lung cancer.

Table 4. Immunogenicity of BNT162b2 vaccine by treatment type

Variables	Chemotherapy (n = 101)	ICI (n = 55)	Targeted therapy (n = 38)	P
Median age (range), y	67 (22-84)	69 (27-91)	63 (33-85)	.01[a]
Female, No. (%)	67 (66.3)	21 (38.2)	29 (76.3)	<.001[b]
Metastatic disease, No. (%)	63 (62.4)	39 (70.9)	26 (68.4)	.52[b]
Cancer diagnosis, No. (%)				.002[b]
Gastrointestinal	36 (35.6)	7 (12.7)	3 (7.9)	
Breast cancer	27 (26.7)	0 (0.0)	13 (34.2)	
NSCLC	5 (5.0)	20 (36.4)	2 (5.3)	
Other	33 (32.7)	28 (50.9)	20 (52.6)	
Median IgG titer (range), AU/mL	578 (0-28 229)	793 (2-12 658)	1895 (46-40 000)	.002[a]
Seronegative <50 IU, No. (%)	19 (18.8)	5 (9.1)	1 (2.6)	.02[b]

[a]P values derived from the nonparametric Kruskal-Wallis test, 2-sided. Ab = antibody; ICI = immune checkpoint inhibitors; IgG = immunoglobulin G; NSCLC = non-small cell lung cancer.
[b]P values derived from the parametric χ^2 test, 2-sided.

ARTICLE

to lack of clinical relevance of this test for patients with cancer at the time of the study because the Israeli authorities stated that the antibody levels have no clear clinical value. Analysis of SARS-CoV-2 S Ab levels was based on a 1-time blood collection. Because it was reported that Ab levels achieve a steady state at approximately 40 days following full vaccination, however, 1-time sampling may not reflect steady Ab levels; a serial testing over time is needed to define the optimal time point for Ab testing in this population and the course of serum Ab levels over time.

We aimed to evaluate SARS-CoV-2 S Ab levels of patients with cancer receiving different types of systemic therapy. However, because of the small number of patients, they were grouped into 3 major treatment types so an analysis of the specific effects of each drug and combinations could not be performed. There is a need to further dissect the effect of systemic chemotherapy by individual drugs or drug classes to better characterize which patients are at greater risk.

None of the patients with cancer participating in this study contracted symptomatic SARS-CoV-2 infection. This may be attributed not only to the vaccine but also to the low prevalence of SARS-CoV-2 infection in Israel during the study period and possibly to strict adherence of cancer patients to personal safety and social distancing. Longer follow-up time and more SARS-CoV-2 S Ab testing may help clarify these points.

As expected from previous reports (9,10,13), no severe side effects were noted. Importantly, despite the relatively longer period from the second vaccine dose, no new safety signals were observed, regardless of treatment type. This finding strengthens the current recommendations to vaccinate all patients with cancer regardless of treatment type.

In conclusion, our study indicates the BNT162b2 mRNA vaccine as safe and effective in actively treated patients with cancer. However, the relatively lower antibody titers and lower proportion of patients with seropositive response, especially among chemotherapy-treated patients, call for continuing the use of personal protective measures in these patients, even following vaccination.

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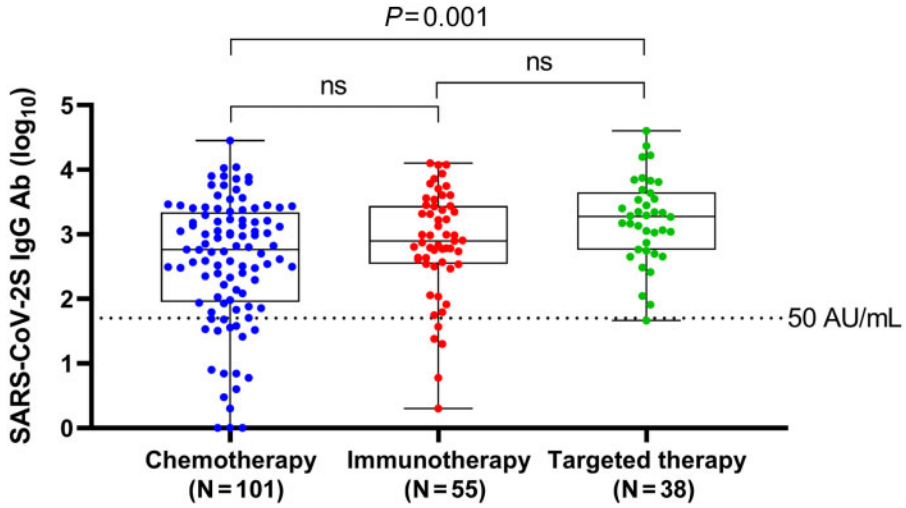

Figure 4. Differences in the distribution of SARS-CoV-2 S immunoglobulin G (IgG) antibody (Ab) in patients receiving different anticancer treatments. SARS-CoV-2 S IgG Ab values in serum samples of cancer patients treated with chemotherapy (n = 101), immunotherapy (n = 55), and targeted therapy (n = 38, **green dots**). **Box plots** represent serum SARS-CoV-2 S IgG Ab values. Ends of the boxes are the upper and lower quartiles, and medians are marked by **horizontal lines** inside the boxes. Every **dot** represents 1 participant's level of antibodies. **Error bars** represent the range between minimal and maximal points. The y-axis (log_{10} scale) represents SARS-CoV-2 S IgG Ab values transformed to log_{10} scale. The **dashed line** represents the cutoff level of seropositivity (50 AU/mL). Statistically analyses were determined using the Kruskal-Wallis test and the Mann-Whitney test with Bonferroni correction for multiple comparisons. Patients treated with targeted therapy had higher SARS-CoV-2 S IgG Ab values compared with patients treated with chemotherapy (P = .001, 2-tailed). All other comparisons did not reach statistical significance. ns = nonstatistically significant.

Notes

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Author contributions: Conceptualization, H.L, I.W.; Methodology, H.L, I.W.; Investigation, All authors.; Formal Analysis, H.L, A.N, I.G, I.W.; Writing, original draft, H.L, T.E, A.NB, I.W.; Writing, editing and revisions, H.L., T.E., I.W.

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Data Availability

The data underlying this article cannot be shared publicly due to ethical guidelines, aiming to protect the privacy of individuals that participated in the study. The data may be shared on reasonable request to the corresponding author, after permission from the institutional review board.

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