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Efficacy and safety of the BNT162b2 mRNA COVID-19 vaccine in participants with a history of cancer: subgroup analysis of a global phase 3 randomized clinical trial



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ABSTRACT

Introduction: Individuals with an underlying malignancy have high risk of poor COVID-19 outcomes. In clinical trials, COVID-19 vaccines were safe and efficacious against infection, hospitalization, and death, but most trials excluded participants with cancer. We report results from participants with a history of past or active neoplasm (malignant or benign/unknown) and up to 6 months' follow-up post-dose 2 from the placebo-controlled, observer-blinded trial of the 2-dose BNT162b2 mRNA COVID-19 vaccine.

Patients and methods: Between July 2020–January 2021, 46,429 participants aged ≥ 12 years were randomized at 152 sites in 6 countries. Healthy participants with pre-existing stable neoplasm could participate; those receiving immunosuppressive therapy were excluded. Data are reported for participants, aged ≥ 16 years for safety and ≥ 12 years for efficacy, who had any history of neoplasm at baseline (data cut-off: March 13, 2021). Adverse-event (AE) data are controlled for follow-up time before unblinding and reported as incidence rates (IRs) per 100 person-years follow-up.

Results: At baseline, 3813 participants had a history of neoplasm; most common malignancies were breast ($n = 460$), prostate ($n = 362$), and melanoma ($n = 223$). Four BNT162b2 and 71 placebo recipients developed COVID-19 from 7 days post-dose 2; vaccine efficacy was 94.4% (95% CI: 85.2, 98.5) after up to 6 months' follow-up post-dose 2. This compares favorably with vaccine efficacy of 91.1% in the overall trial population after the same follow-up. AEs were reported at IRs of 95.4 (BNT162b2) and 48.3 (placebo) per 100 person-years. Most common AEs were reactogenicity events (injection-site pain, fatigue, pyrexia). Three BNT162b2 and 1 placebo recipients withdrew because of vaccine-related AEs. No vaccine-related deaths were reported.

Conclusion: In participants with past or active neoplasms, BNT162b2 vaccine has a similar efficacy and safety profile as in the overall trial population. These results can inform BNT162b2 use during the COVID-19 pandemic and future trials in participants with cancer.

Clinical trial number: NCT04368728.

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Abbreviations: AE, adverse event; APC, antigen presenting cell; CI, confidence interval; COVID-19, coronavirus disease 2019; FDA, Food and Drug Administration; HIV, human immunodeficiency virus; IR, incidence rate; LNP, lipid nanoparticles; MedDRA, Medical Dictionary for Regulatory Activities; mRNA, messenger ribonucleic acid; modRNA, modified ribonucleic acid; NAAT, nucleic acid amplification test; US, United States; UTR, untranslated region; VE, vaccine efficacy.

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1. Introduction

Compared with the general population, people with cancer are at increased risk for adverse outcomes due to coronavirus disease 2019 (COVID-19), including hospitalization, intensive care unit admission, intubation or mechanical ventilation, and death [1–10]. People with cancer often also have a number of additional risk factors, including lung inflammation, immunosenescence, and comorbidities that may predispose them to adverse COVID-19 outcomes [7]. Active cancer and recent or current cancer-specific therapy, including treatment with immune checkpoint inhibitors, appear to confer higher risk of severe COVID-19 and mortality [1–9,11]. Advanced age, male sex, and underlying hematologic malignancy also confer a particularly high risk for adverse COVID-19 outcomes [1–6,9,11].

Recommendations for cancer management during the COVID-19 pandemic have emphasized balancing the risk of exposure to the SARS-CoV-2 virus, while avoiding unnecessary delays in cancer treatment [12–14]. Organizations including the American Society of Clinical Oncology and the United States (US) Centers for Disease Control and Prevention released recommendations early in the pandemic that people with cancer should be vaccinated against COVID-19, once vaccines were available [10,15,16]. In addition, in August 2021, the US Food and Drug Administration (FDA) also recommended a third vaccine dose for individuals who have undergone solid organ transplantation or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise [17].

Patients with a history of malignant tumors may have compromised immunity due to immunosenescence, prior treatments, and comorbidities, which may hinder the efficacy of COVID-19 vaccines. However, many vaccine trials excluded participants with active cancer or who were receiving immunosuppressive treatments. The randomized, placebo-controlled, observer-blinded phase 1/2/3 trial of the BNT162b2 mRNA COVID-19 vaccine (COMIRNATY[®], tozinameran; Fig. 1) included a significant number

of participants with a history of neoplasm (malignancy or benign/unknown tumor) at baseline, either past or active (those receiving immunosuppressive treatment were excluded). In response to the need for direct evidence of vaccine efficacy and safety in people with cancer, we report a post hoc subgroup analysis of clinical efficacy and safety in participants with a history of neoplasm from this study. In the overall trial population, BNT162b2 was 95% effective in preventing COVID-19 from 7 days post-dose 2 in participants ≥ 16 years of age after a median follow-up of 2 months [18]. Subsequent analyses in adolescents (aged 12–15 years) demonstrated non-inferior immunogenicity relative to young adults (aged 16–25 years), and 100% efficacy was observed [19]. Updated vaccine efficacy after up to 6 months of follow-up in the overall trial population remained high after dose 2 (91%) [20]. On the basis of these results, in December 2020, the BNT162b2 COVID-19 vaccine was granted Emergency Use Authorization by the US FDA and conditional marketing authorization in the European Union for immunization of individuals ≥ 12 years of age [21–23]. The BNT162b2 COVID-19 vaccine was subsequently granted issuance of a license from the FDA following a Biologics License Application on August 23, 2021, for use in individuals ≥ 16 years of age [24]. The current post hoc subgroup analysis included trial participants who at baseline had a prior diagnosis of any malignancy or other neoplasm (ie, including benign tumors and those with unknown etiology), but who were not receiving immunosuppressive therapy.

2. Methods

2.1. Trial design

The randomized, placebo-controlled, observer-blinded global phase 3 clinical trial of the vaccine was conducted as part of a phase 1/2/3 trial (NCT04368728) to evaluate BNT162b2 safety, immunogenicity, and efficacy. The study design and population

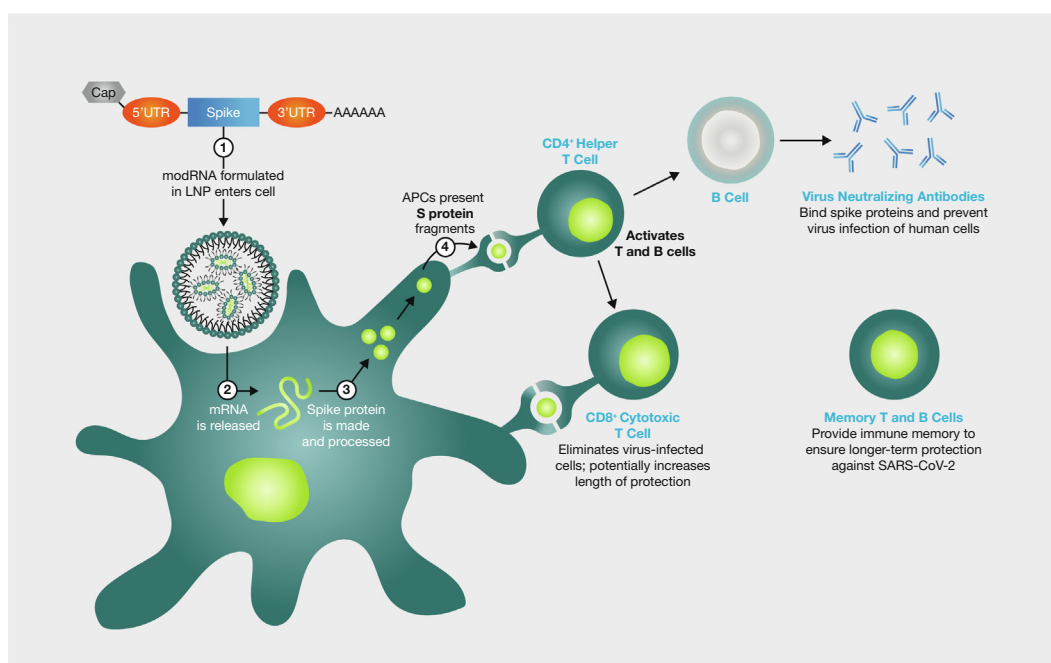


Fig. 1. Mode of action of the BNT162b2 vaccine. APC = antigen presenting cell; LNP = lipid nanoparticles; mRNA = messenger ribonucleic acid; modRNA = modified ribonucleic acid; UTR = untranslated region.

have been described in detail elsewhere [18,19]; aspects relevant to the present subgroup analysis are summarized below.

Healthy male and female participants aged ≥ 12 years were randomized 1:1 to receive 2 doses of the BNT162b2 vaccine (30 μg) or saline placebo, administered 21 days apart, delivered in the deltoid muscle. The primary objectives were to evaluate BNT162b2 efficacy against laboratory-confirmed COVID-19 occurring from 7 days after the second vaccine dose and to define the safety profile. After external data monitoring committee review and Emergency Use Authorization by the FDA on December 10, 2020, participants were allowed to unblind and those in the placebo arm could crossover and receive the vaccine. Blinded, placebo-controlled data prior to unblinding for crossover up to March 13, 2021, are reported herein. Participants had up to 6 months of follow-up post-dose 2 prior to unblinding.

2.2. Participants

A total of 46,429 participants aged ≥ 12 years were randomized at 152 sites in 6 countries between July 2020 and January 2021.

A full list of inclusion and exclusion criteria is available in the study protocol as reported elsewhere [18]. Healthy participants with pre-existing stable neoplasm, ie, not requiring a significant change in their cancer therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were eligible to participate in the study. Exclusion criteria included clinical or virologic COVID-19 diagnosis or SARS-CoV-2 infection prior to vaccination, previous coronavirus vaccination, or diagnosis of an immunocompromising or immunodeficiency disorder. Individuals receiving immunosuppressive therapy including cytotoxic agents or systemic corticosteroids, e.g., for cancer or an autoimmune disease, were excluded. Participants who received short-term (<14 days) corticosteroids for treatment of an acute illness could enroll in the study ≥ 28 days after corticosteroid therapy discontinuation. Prohibited medications (resulting in exclusion from per protocol analyses) within 60 days before enrollment through study conclusion included chronic systemic treatment with known immunosuppressant medications, radiotherapy, and treatment with blood/plasma products or immunoglobulins.

2.3. Subgroup analysis

Medical history was collected at baseline and categorized according to Medical Dictionary for Regulatory Activities (MedDRA) system organ class and preferred term; the numbers and proportions of participants with comorbidities that increase the risk for severe COVID-19 illness were determined by vaccine group, according to the pre-specified trial statistical analysis plan. We report post hoc analyses of efficacy and safety data from subgroups of participants with any cancer-related medical history at baseline. Because immunosuppressive therapy was an exclusion criterion for the study, patients with cancer who were actively receiving cytotoxic immunosuppressive agents or immune checkpoint inhibitors were not included in the study. For the purposes of the present analysis, the subgroup of participants with a history of cancer was defined as participants who had a history of past or active malignancy or other neoplasm (including benign neoplasms and those of unknown etiology). Medical history data were reviewed and participants were further classified according to history of malignant tumor, benign tumor, or other non-specific neoplasm (including those with unknown etiologies). Additional supportive post hoc analyses were performed for the subset of participants with malignancies only (ie, excluding those with benign neoplasms or those with unknown etiologies); separate analyses were also performed for subsets of participants with solid and hematologic malignancies.

2.4. Endpoints and analysis methods

Participants were monitored for potential COVID-19 throughout the trial and tested for SARS-CoV-2 if they developed symptoms potentially indicative of COVID-19. Vaccine efficacy was evaluated in all randomized participants aged ≥ 12 years who received both doses within acceptable time frames and had no major protocol deviations (evaluable efficacy population). BNT162b2 efficacy against confirmed COVID-19 with an onset of 7 or more days after the second vaccine dose was summarized in participants without serologic or virologic evidence of SARS-CoV-2 infection up to 7 days after the second dose and in all vaccinated participants regardless of evidence of prior infection [18,19].

Participants reported all adverse events (AEs) and serious AEs from receipt of the first vaccine dose through 1 month and 6 months, respectively, after the second vaccine dose. For the present analysis, the safety population included all participants ≥ 16 years of age who received at least 1 dose of the study intervention. AEs were summarized for each vaccine group by relationship to study vaccine as judged by the investigator, severity, and MedDRA (v23.1) system organ class and preferred term. AE data are controlled for follow-up time before unblinding and reported as incidence rate (IR) per 100 person-years of blinded follow-up, calculated as the number of participants reporting an event over the total exposure time, from dose 1 to end of blinded follow-up, across all participants in the group. Corresponding exact 2-sided 95% confidence intervals (CIs) were determined on the basis of the link between the Poisson and Chi-square distributions.

3. Results

3.1. Participants

CONSORT diagrams of study flow and baseline characteristics of the overall trial population have been previously published [18,19]. Among 44,047 participants aged ≥ 16 years in the overall trial population, 3813 participants had a history of any neoplasm (malignant or benign/unknown) at baseline (past or active; however, those on active immunosuppressive treatment were excluded from the trial). Overall, the majority of these participants were female (63.3%), white (88.7%), and from the US (91.2%) (Table 1). Participants in this subgroup tended to be older than in the overall trial population (median age of 64.0 years and 51.0 years, respectively; Table 1).

Among the 3813 participants included in the current analysis, 2335 participants had a past or active malignant tumor, including 149 with an active malignancy at baseline, while 1478 had a benign or unknown tumor (Table 2). Most malignancies were solid tumors ($n = 2259$), most commonly breast cancer ($n = 460$), prostate cancer ($n = 362$), and melanoma ($n = 223$). Relatively few participants ($n = 97$) had a history of hematologic malignancy, which included lymphomas and leukemias.

3.2. Efficacy

Among 3538 evaluable participants aged ≥ 12 years with a history of any past or active neoplasm (malignant or benign) and without evidence of prior SARS-CoV-2 infection, there were 4 COVID-19 cases with onset from 7 days through 6 months post-dose 2 in BNT162b2 vaccine recipients versus 71 cases in placebo recipients, representing vaccine efficacy of 94.4% (95% CI: 85.1, 98.5) (Table 3). Similarly, when all evaluable participants in the subgroup were included in the analysis, regardless of evidence of prior SARS-CoV-2 infection ($n = 3636$), vaccine efficacy remained at 94.4% (95% CI: 85.2, 98.5), with 4 COVID-19 cases among

Table 1

Demographic and baseline disease characteristics of the subgroup of participants with any history of past or active neoplasm (malignancy or benign/unknown tumor) at baseline and the overall trial population, by vaccine group (safety population).

Characteristic	Participants with any history of neoplasm (malignant or benign/unknown)		Overall trial population
	BNT162b2 (n = 1902)	Placebo (n = 1911)	Total (N = 44,047)
Female sex, n (%)	1215 (63.9)	1198 (62.7)	21,627 (49.1)
Age at vaccination			
Mean (SD)	62.0 (11.8)	61.6 (12.2)	49.7 (16.0)
Median (range)	64.0 (16–86)	64.0 (16–91)	51.0 (16–91)
Race, n (%)			
White	1689 (88.8)	1692 (88.5)	36,120 (82.0)
Black or African American	127 (6.7)	133 (7.0)	4216 (9.6)
American Indian or Alaska Native	8 (0.4)	10 (0.5)	438 (1.0)
Asian	44 (2.3)	46 (2.4)	1894 (4.3)
Native Hawaiian or other Pacific Islander	5 (0.3)	2 (0.1)	90 (0.2)
Multiracial	25 (1.3)	18 (0.9)	1083 (2.5)
Not reported	4 (0.2)	10 (0.5)	206 (0.5)
Ethnicity, n (%)			
Hispanic or Latinx	271 (14.2)	280 (14.7)	11,399 (25.9)
Non-Hispanic or non-Latinx	1617 (85.0)	1615 (84.5)	32,423 (73.6)
Not reported	14 (0.7)	16 (0.8)	225 (0.5)
Baseline SARS-CoV-2 status, n (%)			
Positive ^a	27 (1.4)	34 (1.8)	1405 (3.2)
Negative ^b	1857 (97.6)	1868 (97.7)	42,365 (96.2)
Missing	18 (0.9)	9 (0.5)	277 (0.6)

COVID-19 = coronavirus disease 2019; NAAT = nucleic acid amplification test.

^aPositive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.

^bNegative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.

BNT162b2 recipients and 71 COVID-19 cases among placebo recipients (Table 3 and Fig. 2). When only the subset of participants with a history of malignant neoplasms were included in the analysis (n = 2222), vaccine efficacy was similarly high (92.9%), with 3 COVID-19 cases among BNT162b2 recipients and 40 COVID-19 cases among placebo recipients, regardless of prior SARS-CoV-2 infection status. The efficacy observed in participants with a history of any neoplasm compares favorably with that observed in the overall trial population during the same time period (91.1%).

The COVID-19 cases observed among participants with a history of malignancy in the BNT162b2 group included a 56-year-old female with a past history of uterine carcinoma in situ (in 2010) who developed COVID-19 approximately 3 months after dose 2; a 65-year-old female with a past history of lymphoma (1998) and skin neoplasms (pre-cancerous skin lesion in 2008 and basal

Table 2

Cancer-related medical history in the subgroup of participants with any history of past or active neoplasm (malignancy or benign/unknown tumor) at baseline, by vaccine group (safety population).

Characteristic	Participants with any history of neoplasm (malignant or benign/unknown)	
	BNT162b2 (n = 1902)	Placebo (n = 1911)
Cancer-related medical history, n (%) ^a		
Malignancy (past or active)	1186 (62.4)	1149 (60.1)
Active malignancy	68 (3.6)	81 (4.2)
Solid tumor	1148 (60.4)	1111 (58.1)
Breast cancer	237 (12.5)	223 (11.7)
Prostate cancer	178 (9.4)	184 (9.6)
Melanoma	118 (6.2)	105 (5.5)
Other tumors ^b	676 (35.5)	663 (34.7)
Hematologic malignancy	46 (2.4)	51 (2.7)
Benign or unknown neoplasm	716 (37.6)	762 (39.9)

^a Participants with multiple occurrences of the same preferred term are counted only once. Participants with multiple neoplasms (based on preferred term) are counted in each relevant category.

^b The cases counted in the 'Other tumors' category were comprised of confirmed malignancies with <100 cases per tumor type.

cell carcinoma in 2020) who developed confirmed COVID-19 approximately 2 months after dose 2; and a 69-year-old male with a past history of prostate cancer (2018) who developed COVID-19 approximately 2.5 months after dose 2. A 62-year-old female with a history of uterine leiomyoma, hypertension, diabetes, and hypercholesterolemia was also diagnosed with COVID-19 approximately 3.5 months after BNT162b2 dose 2. None of these participants were hospitalized due to COVID-19.

3.3. Safety

AEs were reported over a total exposure time (ie, dose 1 to end of blinded follow-up) of 700 person-years for both the BNT162b2 vaccine and placebo recipient groups with a history of any neoplasm (malignant or benign/unknown). AEs and vaccine-related AEs were reported more frequently among BNT162b2 (IR: 95.4 and 69.4 per 100 person-years exposure, respectively) than placebo recipients (IR: 48.3 and 16.7, respectively) (Table 4). AEs were generally reported at slightly higher IRs in this subgroup than in the overall clinical trial population. Few participants with a history of neoplasm reported severe AEs (IR: 5.6, BNT162b2; 3.6, placebo; per 100 person-years) or serious AEs (IR: 6.7, BNT162b2; 3.6, placebo). Two BNT162b2 vaccine recipients reported serious AEs that were considered vaccine-related: 1 participant experienced ventricular arrhythmia on the day of dose 2 and 1 experienced lymphadenopathy on day 13 post-dose 1 (this participant also experienced non-serious vaccine-related AEs of chills, injection-site erythema, injection-site pain, and injection-site warmth, and withdrew from the study because of AEs). Both serious vaccine-related AEs resolved. Six BNT162b2 vaccine recipients and 4 placebo recipients withdrew from the study because of AEs; among them, 3 and 1 participants, respectively, withdrew because of AEs that were considered vaccine-related (all reactogenicity events; BNT162b2: 1 participant with lymphadenopathy as described above, 1 participant with injection-site swelling on the day of dose 1, and 1 participant with abdominal discomfort, diarrhea, eye pain, fatigue, headache, and

Table 3

Vaccine efficacy against COVID-19 at least 7 days after the second vaccine dose among participants with any history of past or active neoplasm (malignancy or benign/unknown tumor) at baseline and the overall trial population (evaluable efficacy population).

	BNT162b2 Participants with event (n)	Surveillance time ^a (N at risk)	Placebo Participants with event (n)	Surveillance time ^a (N at risk)	Vaccine efficacy % (95% CI) ^b
COVID-19 occurrence ≥ 7 days after dose 2 in participants without evidence of previous infection					
Any neoplasm (malignant or benign/unknown)	4	0.516 (1750)	71	0.510 (1788)	94.4 (85.1, 98.5)
Malignant neoplasm ^c	3	0.323 (1091)	40	0.309 (1084)	92.8 (77.4, 98.6)
Solid tumor	3	0.312 (1054)	39	0.299 (1046)	92.6 (76.8, 98.5)
Hematologic malignancy	1	0.013 (45)	1	0.014 (50)	−5.9 (−8214.6, 98.7)
Overall study population	77	6.247 (20,712)	850	6.003 (20,713)	91.3 (89.0, 93.2)
COVID-19 occurrence ≥ 7 days after dose 2 in participants with or without evidence of previous infection					
Any neoplasm (malignant or benign/unknown)	4	0.530 (1802)	71	0.523 (1834)	94.4 (85.2, 98.5)
Malignant neoplasm ^c	3	0.330 (1119)	40	0.314 (1103)	92.9 (77.6, 98.6)
Solid tumor	3	0.319 (1082)	39	0.304 (1065)	92.7 (77.0, 98.6)
Hematologic malignancy	1	0.013 (45)	1	0.014 (50)	−5.9 (−8214.6, 98.7)
Overall study population	81	6.509 (21,642)	873	6.274 (21,689)	91.1 (88.8, 93.0)

CI = confidence interval; COVID-19 = coronavirus disease 2019.

^aTotal surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after dose 2 to the end of the surveillance period.

^bCI for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

^cExcluding participants with benign or unknown neoplasms.

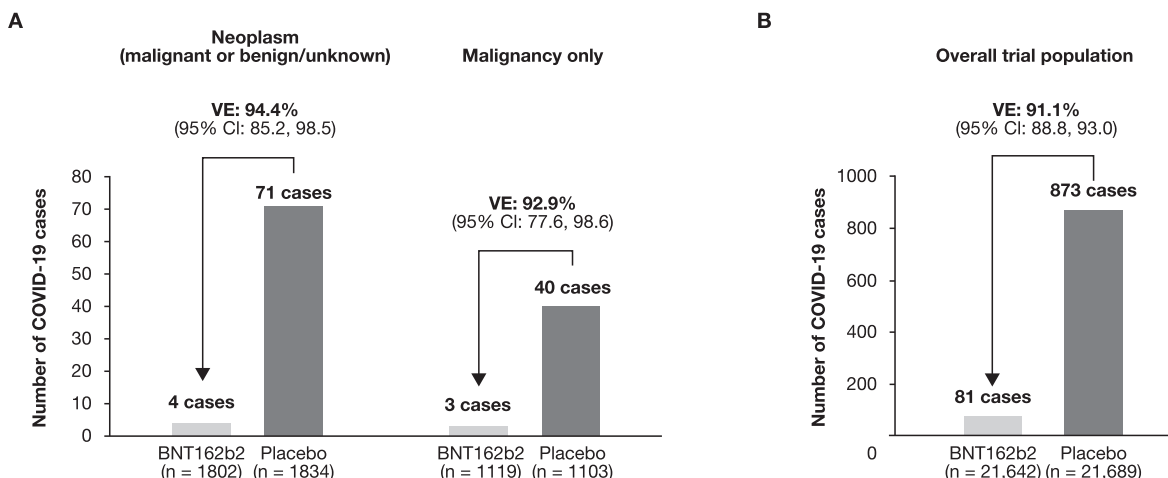


Fig. 2. Confirmed COVID-19 occurrence at least 7 days after the second vaccine dose among participants with A) any history of past or active neoplasm (malignancy or benign/unknown tumor) at baseline, and B) the overall trial population (evaluable efficacy population; participants with or without evidence of previous infection). CI = confidence interval; COVID-19 = coronavirus disease 2019; VE = vaccine efficacy.

muscle weakness on the day after dose 1; placebo: 1 participant with cheilitis, dry mouth, dysgeusia, eczema, parosmia, pruritus, and maculo-papular rash on day 16 after placebo dose 1). Three participants died during the study (1 in the BNT162b2 group and 2 in the placebo group); none of the deaths were considered vaccine related.

Consistent with the previously reported safety profile for the full clinical trial population [18,19], the most common AEs (any causality) were reactogenicity events, including injection-site pain, fatigue, and pyrexia (Table 4). These events were reported at similar IRs in the subgroup of participants with a history of neoplasm as in the overall trial population during the same follow-up period.

The frequency and pattern of AEs were similar among the subset of participants who had past or active malignant neoplasms only as for the overall subgroup of participants with a history of any neoplasm (malignant or benign/unknown) (Table 5).

4. Discussion

Approximately 8% of participants (>3800) from the phase 3 trial of the BNT162b2 mRNA COVID-19 vaccine had at baseline a history

of past or active neoplasm (malignancy or benign/non-specific tumor). Patients with a history of malignant tumors may have compromised immunity due to immunosenescence, prior treatments, and comorbidities, which may hinder the efficacy of vaccines against COVID-19. In the current analysis of the subgroup of participants with a history of past or active neoplasm, the BNT162b2 vaccine had similarly high efficacy and an acceptable safety profile compared with the overall clinical trial population with up to 6 months of follow-up post-dose 2. BNT162b2 demonstrated similarly high efficacy and acceptable safety in the subset of participants with a history of malignant tumors only. Our results obtained in a randomized, controlled clinical trial setting, together with emerging results from real-world cohort studies of COVID-19 vaccines in individuals with cancer, provide scientific evidence to support priority vaccination of patients with cancer, as recommended early in the pandemic by prominent oncology and public health organizations [10,15,16]. However, it should be noted that this trial enrolled only people with stable disease at baseline who were not receiving immunosuppressive therapy. As such, it included relatively few participants with an active malignancy (n = 149), and most participants included in the present analysis

Table 4
Summary of AEs by vaccination group among participants with any history of past or active neoplasm (malignancy or benign/unknown tumor) at baseline and the overall trial population (safety population^a).

	Participants with any history of neoplasm (malignant or benign/unknown)						Overall trial population					
	BNT162b2 (N = 1898)			Placebo (N = 1908)			BNT162b2 (N = 21,926)			Placebo (N = 21,921)		
	n	IR/100 person-yrs ^b	(95% CI)	n	IR/100 person-yrs ^b	(95% CI)	n	IR/100 person-yrs ^c	(95% CI)	n	IR/100 person-yrs ^c	(95% CI)
Any AE	669	95.4	(88.3, 102.9)	336	48.3	(43.3, 53.7)	6947	83.2	(81.3, 85.2)	3568	43.4	(42.0, 44.9)
Related ^d	487	69.4	(63.4, 75.9)	116	16.7	(13.8, 20.0)	5246	62.9	(61.2, 64.6)	1313	16.0	(15.1, 16.9)
Severe	39	5.6	(4.0, 7.6)	25	3.6	(2.3, 5.3)	356	4.3	(3.8, 4.7)	256	3.1	(2.7, 3.5)
Life-threatening	3	0.4	(0.1, 1.3)	6	0.9	(0.3, 1.9)	48	0.6	(0.4, 0.8)	54	0.7	(0.5, 0.9)
Serious AE	47	6.7	(4.9, 8.9)	25	3.6	(2.3, 5.3)	268	3.2	(2.8, 3.6)	268	3.3	(2.9, 3.7)
Related ^d	2	0.3	(0.0, 1.0)	0	0.0	(0.0, 0.5)	4	0.0	(0.0, 0.1)	1	0.0	(0.0, 0.1)
Severe	25	3.6	(2.3, 5.3)	14	2.0	(1.1, 3.4)	148	1.8	(1.5, 2.1)	156	1.9	(1.6, 2.2)
Life-threatening	3	0.4	(0.1, 1.3)	6	0.9	(0.3, 1.9)	48	0.6	(0.4, 0.8)	54	0.7	(0.5, 0.9)
AE leading to withdrawal	6	0.9	(0.3, 1.9)	4	0.6	(0.2, 1.5)	45	0.5	(0.4, 0.7)	51	0.6	(0.5, 0.8)
Related ^d	3	0.4	(0.1, 1.3)	1	0.1	(0.0, 0.8)	13	0.2	(0.1, 0.3)	12	0.1	(0.1, 0.3)
Severe	1	0.1	(0.0, 0.8)	0	0.0	(0.0, 0.5)	10	0.1	(0.1, 0.2)	12	0.1	(0.1, 0.3)
Life-threatening	1	0.1	(0.0, 0.8)	3	0.4	(0.1, 1.3)	15	0.2	(0.1, 0.3)	16	0.2	(0.1, 0.3)
Death	1	0.1	(0.0, 0.8)	2	0.3	(0.0, 1.0)	15	0.2	(0.1, 0.3)	14	0.2	(0.1, 0.3)
Most common AEs^e												
Injection-site pain	266	37.9	(33.5, 42.8)	26	3.7	(2.4, 5.5)	2917	35.0	(33.7, 36.2)	399	4.9	(4.4, 5.4)
Fatigue	129	18.4	(15.4, 21.9)	41	5.9	(4.2, 8.0)	1466	17.6	(16.7, 18.5)	379	4.6	(4.2, 5.1)
Pyrexia	129	18.4	(15.4, 21.9)	3	0.4	(0.1, 1.3)	1520	18.2	(17.3, 19.2)	78	0.9	(0.8, 1.2)
Chills	119	17.0	(14.1, 20.3)	12	1.7	(0.9, 3.0)	1368	16.4	(15.5, 17.3)	121	1.5	(1.2, 1.8)
Headache	116	16.5	(13.7, 19.8)	34	4.9	(3.4, 6.8)	1348	16.2	(15.3, 17.0)	429	5.2	(4.7, 5.7)
Myalgia	111	15.8	(13.0, 19.1)	12	1.7	(0.9, 3.0)	1245	14.9	(14.1, 15.8)	170	2.1	(1.8, 2.4)
Pain	69	9.8	(7.7, 12.5)	10	1.4	(0.7, 2.6)	628	7.5	(6.9, 8.1)	62	0.8	(0.6, 1.0)
Arthralgia	33	4.7	(3.2, 6.6)	12	1.7	(0.9, 3.0)	281	3.4	(3.0, 3.8)	122	1.5	(1.2, 1.8)
Nausea	30	4.3	(2.9, 6.1)	5	0.7	(0.2, 1.7)	277	3.3	(2.9, 3.7)	88	1.1	(0.9, 1.3)
Injection-site erythema	28	4.0	(2.7, 5.8)	2	0.3	(0.0, 1.0)	185	2.2	(1.9, 2.6)	29	0.4	(0.2, 0.5)
Pain in extremity	25	3.6	(2.3, 5.3)	9	1.3	(0.6, 2.5)	189	2.3	(2.0, 2.6)	52	0.6	(0.5, 0.8)
Diarrhea	23	3.3	(2.1, 4.9)	16	2.3	(1.3, 3.7)	255	3.1	(2.7, 3.5)	189	2.3	(2.0, 2.7)
Injection-site swelling	21	3.0	(1.9, 4.6)	1	0.1	(0.0, 0.8)	140	1.7	(1.4, 2.0)	23	0.3	(0.2, 0.4)

AE = adverse event; CI = confidence interval; COVID-19 = coronavirus disease 2019; HIV = human immunodeficiency virus; IR = incidence rate; MedDRA = Medical Dictionary for Regulatory Activities; yrs = years.

^aHIV-positive participants were excluded from the safety analyses.

^bTotal exposure (dose 1 to end of blinded follow-up) across participants in the group (BNT162b2: 700 person-years; placebo: 700 person-years). IR calculated as number of participants reporting the event/total exposure time in 100 person-years across all participants in the specified group, with exact 2-sided CI based on the link between the Poisson and Chi-square distributions.

^cTotal exposure (dose 1 to end of blinded follow-up) across participants in the group (BNT162b2: 8340 person-years; placebo: 8220 person-years).

^dAssessed by the investigator as related to investigational vaccine.

^eBased on MedDRA preferred term; AEs (any causality) with IR \geq 3.0 per 100 person-years in either vaccine group for the subgroup of participants with a history of cancer are summarized here.

Table 5
Summary of AEs by vaccination group among participants with a malignancy at baseline (past or ongoing) (safety population^a).

	BNT162b2 (N = 1182)			Placebo (N = 1146)		
	n	IR/100 person-yrs ^b	(95% CI)	n	IR/100 person-yrs ^b	(95% CI)
Any AE	412	94.3	(85.4, 103.8)	201	48.3	(41.9, 55.5)
Related ^c	307	70.2	(62.6, 78.5)	63	15.1	(11.6, 19.4)
Severe	24	5.5	(3.5, 8.2)	16	3.8	(2.2, 6.2)
Life-threatening	3	0.7	(0.1, 2.0)	6	1.4	(0.5, 3.1)
Serious AE	28	6.4	(4.3, 9.3)	19	4.6	(2.7, 7.1)
Related ^c	1	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Severe	15	3.4	(1.9, 5.7)	10	2.4	(1.2, 4.4)
Life-threatening	3	0.7	(0.1, 2.0)	6	1.4	(0.5, 3.1)
AE leading to withdrawal	4	0.9	(0.2, 2.3)	3	0.7	(0.1, 2.1)
Related ^c	1	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Severe	0	0.0	(0.0, 0.8)	0	0.0	(0.0, 0.9)
Life-threatening	1	0.2	(0.0, 1.3)	3	0.7	(0.1, 2.1)
Death	1	0.2	(0.0, 1.3)	2	0.5	(0.1, 1.7)
Most common AEs^d						
Injection-site pain	173	39.6	(33.9, 45.9)	14	3.4	(1.8, 5.6)
Fatigue	85	19.4	(15.5, 24.0)	27	6.5	(4.3, 9.4)
Pyrexia	81	18.5	(14.7, 23.0)	2	0.5	(0.1, 1.7)
Chills	79	18.1	(14.3, 22.5)	5	1.2	(0.4, 2.8)
Headache	75	17.2	(13.5, 21.5)	16	3.8	(2.2, 6.2)
Myalgia	67	15.3	(11.9, 19.5)	6	1.4	(0.5, 3.1)
Pain	44	10.1	(7.3, 13.5)	7	1.7	(0.7, 3.5)
Nausea	20	4.6	(2.8, 7.1)	3	0.7	(0.1, 2.1)
Arthralgia	18	4.1	(2.4, 6.5)	6	1.4	(0.5, 3.1)
Pain in extremity	17	3.9	(2.3, 6.2)	5	1.2	(0.4, 2.8)
Injection-site erythema	16	3.7	(2.1, 5.9)	2	0.5	(0.1, 1.7)
Diarrhea	14	3.2	(1.8, 5.4)	10	2.4	(1.2, 4.4)

AE = adverse event; CI = confidence interval; HIV = human immunodeficiency virus; IR = incidence rate; MedDRA = Medical Dictionary for Regulatory Activities; yrs = years.

^aHIV-positive participants were excluded from the safety analyses.

^bTotal exposure (dose 1 to end of blinded follow-up) across participants in the group (BNT162b2: 440 person-years; placebo: 420 person-years). IR calculated as number of participants reporting the event/total exposure time in 100 person-years across all participants in the specified group, with exact 2-sided CI based on the link between the Poisson and Chi-square distributions.

^cAssessed by the investigator as related to investigational vaccine.

^dBased on MedDRA preferred term; AEs (any causality) with IR \geq 3.0 per 100 person-years in either group are summarized here.

were cancer survivors. This is understandable, given the rapid initiation and enrollment of this trial in 2020 during the global COVID-19 pandemic. In addition, the vast majority of malignancies (past or ongoing) were solid tumors (97%; n = 2259). While evidence from real-world studies indicates that some patients with hematologic malignancies do not mount adequate immune responses to COVID-19 vaccination [25–30], the low number of participants with hematologic malignancies in our study limits the ability to make conclusions about efficacy in this population.

In the primary analysis of BNT162b2 vaccine efficacy, the vaccine demonstrated high efficacy against COVID-19 infection, with 95% vaccine efficacy observed at least 7 days after the second vaccination in the overall clinical trial population [18], and similarly high efficacy (91%) observed in the overall population of participants aged \geq 12 years at a subsequent analysis after up to 6 months of follow-up post-dose 2 [20]. The high efficacy observed in the current analysis of participants with a history of any past or active neoplasm (malignant or benign/unknown; 94%) and those with malignant neoplasms only (93%) compares favorably with these results. The BNT162b2 vaccine had a favorable safety profile in the subgroup of participants with a history of any neoplasm, with an AE profile generally consistent with that observed in the overall study population [18]. The most common AEs were reactogenicity events, including injection-site pain, fatigue, and pyrexia, and very few AEs were severe in intensity. The favorable safety and tolerability profile of BNT162b2 in our analysis is in agreement with results recently reported from real-world COVID-19 vaccine studies that included individuals with active cancer and those receiving anticancer treatment [30–33].

Patients with cancer may receive systemic immunosuppressive therapies as part of their anticancer treatment, which has broadly resulted in exclusion of these patients from the randomized, phase 3 COVID-19 vaccine trials [18,34–37]. Indeed, the present subgroup analysis is based on participants with a history of cancer who were not receiving active immunosuppressant therapy, because this was an exclusion criterion for the BNT162b2 vaccine clinical trial [18]. The phase 3 study of the Ad26.COV2.S vaccine (Johnson & Johnson) included a small number of participants with cancer at baseline (0.5%) but excluded participants receiving anti-neoplastic and immunomodulating agents or radiotherapy within 6 months before enrollment [34]. Similarly, the phase 3 trial of the mRNA-1273 COVID-19 vaccine (Moderna) excluded participants receiving systemic immunosuppressants or immune-modifying drugs [36]. Although subgroup analyses of participants with certain pre-existing conditions associated with severe COVID-19 (e.g., chronic lung disease and significant cardiac disease) have been reported from that study, results from participants with cancer were not reported [36].

Since the efficacy of COVID-19 vaccines in patients with cancer receiving active antitumor systemic treatment has not been evaluated in the randomized, controlled trial setting, real-world effectiveness data will be essential to better understand the clinical profile of COVID-19 vaccines in these patients. Indeed, initial real-world data are beginning to be reported from cohort studies of patients with cancer who have received COVID-19 vaccines, including the BNT162b2 mRNA COVID-19 vaccine [30–33,38–40]. The results have provided encouraging safety data and suggested a similar AE profile for the BNT162b2 vaccine among patients with cancer (including those treated with checkpoint inhibitors)

[30–33,41–43] as that observed in the overall randomized clinical trial population [18–20].

In recent real-world studies, lower serological responses to COVID-19 vaccination regimens have generally been reported in cohorts of patients with hematologic malignancies compared with patients with solid tumors and healthy controls, with the lowest responses among patients on active treatment [25–29,44,45]. Particularly low antibody responses to the first BNT162b2 vaccine dose have been reported in patients with cancer, highlighting the potential importance of additional doses [27,32,39,40,43,46]. Even with two vaccine doses, many patients with hematologic malignancies remain at risk for not producing adequate antibody responses [25–30]. In a recent cohort study of patients with solid and hematologic cancer ($n = 88$), a third COVID-19 vaccine dose potentiated immune responses in most patients, although a few patients (particularly those who received anti-CD20 therapy) did not have a serological response even after a third dose [26]. The ability to draw conclusions about the safety and efficacy of the BNT162b2 vaccine in patients with hematologic malignancies in our subgroup analysis is limited by the very low number of participants with a history of these types of malignancies (<3%; $n = 97$). In this small subset of participants with a history of hematologic malignancies, one case of COVID-19 was reported in a BNT162b2 vaccine recipient with a history of lymphoma > 20 years prior to study vaccination, and one case was reported in a placebo recipient.

Data from cohort studies of patients with solid tumors receiving anticancer treatment indicate that most patients mount an acceptable antibody response after 2 doses of BNT162b2, but antibody titers are generally lower than in people without cancer [27,38,47,48]. For example, among 102 patients with solid tumors receiving anticancer treatment at a single Israeli center, 92 (90%) patients and all (78/78) healthy controls were seropositive for SARS-CoV-2 anti-spike IgG 13–54 days after receiving a second BNT162b2 dose, with durable seropositivity (87%) observed among the patients with cancer after 4 months of follow-up [38,49]. However, despite this high seroconversion rate, significantly lower IgG titers were observed among the patients with cancer versus controls in that study [38,49].

Emerging real-world effectiveness results following mass BNT162b2 vaccination campaigns, which included people with cancer and other underlying health conditions, have been generally consistent with the high efficacy observed in the phase 3 clinical trial [18,19], but specific data on BNT162b2 antibody responses and efficacy in subsets of people with cancer have not been reported [50,51]. One recent descriptive report of > 6000 individuals with cancer vaccinated with BNT162b2 from a single US institution showed low rates of breakthrough infection (1 case) with no unexpected safety signals; however, this study did not include a placebo/unvaccinated control group or a comparator group of vaccine recipients without cancer [33]. Similarly, low rates of COVID-19 were reported in patients with cancer who received 2-dose COVID-19 vaccine regimens at a single center in France [52]. It remains unclear whether the lower antibody responses observed in some cohort studies translate into a difference in COVID-19 vaccine efficacy in people with cancer; therefore, efficacy/effectiveness data in these populations are needed to understand the level of protection.

As described above, limitations of this analysis include the exclusion of participants receiving concurrent immunosuppressive therapy (e.g., chemotherapy) from the trial and the low number of participants with active cancer and hematologic malignancies. This selected clinical trial population may not reflect the heterogeneous group of patients with cancer. In addition, these observations came largely from white participants, and results may not be generalizable to people of other racial identification. Participants in the

subgroup tended to be older than those in the overall study population. Since this was a post-hoc subgroup analysis, the study was not powered for formal statistical analysis of vaccine efficacy in participants with a history of cancer. While the descriptive summary of vaccine efficacy presented provides strong evidence of high vaccine efficacy in this subgroup, immunogenicity data are not reported.

Given the low number of participants with hematologic malignancies and exclusion of participants on immunosuppressive treatment, further prospective studies will be needed to inform on vaccine efficacy in these patients. Poor immune responses to mRNA COVID-19 vaccines have been demonstrated in people who are immunocompromised, including solid organ transplant recipients [53–55]. The US FDA authorized a third dose of the BNT162b2 vaccine in individuals ≥ 12 years of age who have undergone solid-organ transplantation or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise [17]. With the recent spread of COVID-19 variants of concern such as the Delta and Omicron variants, it is also unclear if the current 2-dose vaccine regimen will be sufficient in patients with hematologic malignancies and those undergoing immunosuppressive treatment. Hence, a prospective trial of BNT162b2 in patients with cancer and patients on immunosuppressive therapies was initiated in October 2021 (NCT04895982). This study is expected to provide comprehensive immunogenicity and T-cell response data in patients with cancer (non-small cell lung cancer or chronic lymphocytic leukemia) who are on anticancer treatment, including after a third BNT162b2 vaccine dose. An additional trial evaluating safety and efficacy of a booster dose of BNT162b2 in participants who previously received 2 doses has recently completed recruitment (NCT04955626), and results are awaited.

5. Conclusions

The BNT162b2 mRNA COVID-19 vaccine demonstrated robust efficacy and acceptable safety in clinical trial participants with a history of past or active neoplasms, who were not receiving immunosuppressive treatment, and who had up to 6 months of follow-up post-dose 2. The efficacy and safety in these participants were similar to the overall clinical trial population. These results support the current recommendations to consider immunizing people living with cancer against COVID-19 using the BNT162b2 mRNA COVID-19 vaccine and provide the foundation to plan future trials in these populations.

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Data sharing statement

Upon request, and subject to review, Pfizer will provide the data that support the findings of this study. Subject to certain criteria, conditions and exceptions, Pfizer may also provide access to the related individual de-identified participant data. See <https://www.pfizer.com/science/clinical-trials/trial-data-and-results> for more information.

Author contributions

Pfizer was responsible for the design and conduct of the trial, data collection, and the data analysis. BioNTech was the sponsor

of the trial and manufactured the BNT162b2 clinical trial material. All authors were involved in data interpretation as well as the writing, reviewing, and approving of the manuscript. All trial data were available to all the authors, who vouch for its accuracy and completeness. An independent data and safety monitoring board reviewed efficacy and unblinded safety data.

Declaration of Competing Interest

SJT: investigator on Pfizer COVID-19 vaccine trials, single consulting engagement and ad hoc advisory board member for Pfizer; JLP, SPL, SH, NK, RB, KL, XX, KK, SSD, CL, WCG: employees of Pfizer and hold Pfizer stock/stock options; EL, OT, US: employees of BioNTech; TG: nothing to disclose.

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References

- [1] Kuderer NM, Choueiri TK, Shah DP, Shyr Yu, Rubinstein SM, Rivera DR, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet* 2020;395(10241):1907–18.
- [2] Martín-Moro F, Marquet J, Piris M, Michael BM, Sáez AJ, Corona M, et al. Survival study of hospitalised patients with concurrent COVID-19 and haematological malignancies. *Br J Haematol*. 2020;190(1):e16–20. <https://doi.org/10.1111/bjh.16801>.
- [3] Rührich MM, Giessen-Jung C, Borgmann S, Classen AY, Dolf S, Grüner B, et al. COVID-19 in cancer patients: clinical characteristics and outcome-an analysis of the LEOSS registry. *Ann Hematol*. 2021;100(2):383–93.
- [4] Venkatesulu BP, Chandrasekar VT, Girdhar P, Advani P, Sharma A, Elumalai T, et al. A systematic review and meta-analysis of cancer patients affected by a novel coronavirus. *JNCI Cancer Spectr*. 2021;5(2):pkaa102.
- [5] Lee LYW, Cazier JB, Starkey T, Briggs SEW, Arnold R, Bisht V, et al. COVID-19 prevalence and mortality in patients with cancer and the effect of primary tumour subtype and patient demographics: a prospective cohort study. *Lancet Oncol*. 2020;21(10):1309–16.
- [6] Grivas P, Khaki AR, Wise-Draper TM, French B, Hennessy C, Hsu C-Y, et al. Association of clinical factors and recent anti-cancer therapy with COVID-19 severity among patients with cancer: a report from the COVID-19 and Cancer Consortium. *Ann Oncol* 2021;32(6):787–800.
- [7] Derosa L, Melenotte C, Griscelli F, Gachot B, Marabelle A, Kroemer G, et al. The immuno-oncological challenge of COVID-19. *Nat Cancer* 2020;1(10):946–64.
- [8] Luo J, Rizvi H, Egger JV, Preeshagur IR, Wolchok JD, Hellmann MD. Impact of PD-1 blockade on severity of COVID-19 in patients with lung cancers. *Cancer Discov* 2020;10(8):1121–8.
- [9] Robilotti EV, Babady NE, Mead PA, Rolling T, Perez-Johnston R, Bernardes M, et al. Determinants of COVID-19 disease severity in patients with cancer. *Nat Med* 2020;26(8):1218–23.
- [10] US Centers for Disease Control and Prevention (CDC). Underlying Medical Conditions Associated With High Risk for Severe COVID-19: *Information for Healthcare Providers*, May 13, 2021. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html>. [accessed August 23, 2021]
- [11] Sharafeldin N, Bates B, Song Q, Madhira V, Yan Y, Dong S, et al. Outcomes of COVID-19 in patients with cancer: report from the National COVID Cohort Collaborative (N3C). *J Clin Oncol* 2021;39(20):2232–46.
- [12] American Society of Clinical Oncology (ASCO). ASCO Special Report: A Guide to Cancer Care Delivery During the COVID-19 Pandemic. July 29, 2021. Available from: <https://www.asco.org/sites/new-www.asco.org/files/content-files/2020-ASCO-Guide-Cancer-COVID19.pdf>. [accessed August 23, 2021]
- [13] Curigliano G, Banerjee S, Cervantes A, Garassino MC, Garrido P, Girard N, et al. Managing cancer patients during the COVID-19 pandemic: an ESMO multidisciplinary expert consensus. *Ann Oncol* 2020;31(10):1320–35.
- [14] Poon D-C, Chan C-K, Chan T-W, Cheung F-Y, Ho L-Y, Kwong P-K, et al. Prostate cancer management in the era of COVID-19: Recommendations from the Hong Kong Urological Association and Hong Kong Society of Uro-oncology. *Asia Pac J Clin Oncol* 2021;17(S3):48–54.
- [15] National Comprehensive Cancer Network (NCCN). Recommendations of the NCCN COVID-19 Vaccination Advisory Committee. June 9, 2021. Available from: <https://www.nccn.org/covid-19/>. [accessed August 23, 2021]
- [16] American Society of Clinical Oncology (ASCO). COVID-19 Vaccines & Patients With Cancer 2021. Available from: <https://www.asco.org/covid-resources/vaccines-patients-cancer>. [accessed August 23, 2021]
- [17] US Food and Drug Administration (FDA). Fact sheet for healthcare providers administering vaccine. August 23, 2021. Available from: <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine>. [accessed September 6, 2021]
- [18] Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020;383(27):2603–15.
- [19] Frenck RW, Klein NP, Kitchin N, Gurtman A, Absalon J, Lockhart S, et al. Safety, immunogenicity, and efficacy of the BNT162b2 Covid-19 vaccine in adolescents. *N Engl J Med* 2021;385(3):239–50.
- [20] Thomas SJ, Moreira ED, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine through 6 months. *N Engl J Med*. 2021;385(19):1761–73.
- [21] Pfizer-BioNTech. Pfizer-BioNTech COVID-19 vaccine emergency use authorization combined full prescribing information and fact sheet. June 25, 2021. Available from: <https://www.pfizer.com/products/product-detail/pfizer-biontech-covid-19-vaccine>. [accessed August 23, 2021]
- [22] Pfizer-BioNTech. Pfizer and BioNTech receive authorization in the European Union for COVID-19 vaccine. December 21, 2020. Available from: <https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-receive-authorization-european-union>. [accessed August 23, 2021]
- [23] Pfizer-BioNTech. Pfizer and BioNTech receive first authorization in European Union for COVID-19 vaccine in adolescents. May 28, 2021. Available from: <https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-receive-first-authorization-european>. [accessed August 23, 2021]
- [24] US Food and Drug Administration (FDA). FDA Approves First COVID-19 Vaccine, 2021. Available from: <https://www.fda.gov/news-events/press-announcements/fda-approves-first-covid-19-vaccine>. [accessed August 23, 2021]
- [25] Greenberger LM, Saltzman LA, Senefeld JW, Johnson PW, DeGennaro LJ, Nichols GL. Antibody response to SARS-CoV-2 vaccines in patients with hematologic malignancies. *Cancer Cell* 2021;39(8):1031–3.
- [26] Shapiro LC, Thakkar A, Campbell ST, Forest SK, Pradhan K, Gonzalez-Lugo JD, et al. Efficacy of booster doses in augmenting waning immune responses to COVID-19 vaccine in patients with cancer. *Cancer Cell* 2021. <https://doi.org/10.1016/j.ccell.2021.11.006>.
- [27] Addeo A, Shah PK, Bordry N, Hudson RD, Albracht B, Di Marco M, et al. Immunogenicity of SARS-CoV-2 messenger RNA vaccines in patients with cancer. *Cancer Cell* 2021;39(8):1091–1098.e2.
- [28] Benjamini O, Rokach L, Itchaki G, Braester A, Shvidel L, Goldschmidt N, et al. Safety and efficacy of BNT162b mRNA Covid19 Vaccine in patients with chronic lymphocytic leukemia. *Haematologica* 2021. <https://doi.org/10.3324/haematol.2021.279196>.
- [29] Lim SH, Campbell N, Johnson M, Joseph-Pietras D, Collins GP, O'Callaghan A, et al. Antibody responses after SARS-CoV-2 vaccination in patients with lymphoma. *Lancet Haematol* 2021;8(8):e542–4.
- [30] Herishanu Y, Avivi I, Aharon A, Shefer G, Levi S, Bronstein Y, et al. Efficacy of the BNT162b2 mRNA COVID-19 vaccine in patients with chronic lymphocytic leukemia. *Blood* 2021;137(23):3165–73.
- [31] Waissengrin B, Agbarya A, Safadi E, Padova H, Wolf I. Short-term safety of the BNT162b2 mRNA COVID-19 vaccine in patients with cancer treated with immune checkpoint inhibitors. *Lancet Oncol* 2021;22(5):581–3.
- [32] Monin L, Laing AG, Muñoz-Ruiz M, McKenzie DR, del Molino del Barrio I, Alaguthurai T, et al. Safety and immunogenicity of one versus two doses of the COVID-19 vaccine BNT162b2 for patients with cancer: interim analysis of a prospective observational study. *Lancet Oncol* 2021;22(6):765–78.
- [33] Subbiah IM, Williams LA, Peek A, Shete S, Granwehr BP, D'Aichiardi D, et al. Real-world patient-reported and clinical outcomes of BNT162b2 mRNA COVID-19 vaccine in patients with cancer. *J Clin Oncol*. 2021;39(15 suppl): abstr 6510.
- [34] Sadoff J, Gray G, Vandebosch An, Cárdenas V, Shukarev G, Grinsztejn B, et al. Safety and efficacy of single-dose Ad26.COV2.S vaccine against Covid-19. *N Engl J Med* 2021;384(23):2187–201.
- [35] Logunov DY, Dolzhikova IV, Shcheblyakov DV, Tukhvatulin AI, Zubkova OV, Dzharullaeva AS, et al. Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. *Lancet* 2021;397(10275):671–81.
- [36] Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med*. 2021;384(5):403–16.
- [37] Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet* 2021;397(10269):99–111.
- [38] Massarweh A, Eliakim-Raz N, Stemmer A, Levy-Barda A, Yust-Katz S, Zer A, et al. Evaluation of seropositivity following BNT162b2 messenger RNA vaccination for SARS-CoV-2 in patients undergoing treatment for cancer. *JAMA Oncol* 2021;7(8):1133–40. <https://doi.org/10.1001/jamaoncol.2021.2155>.
- [39] Bird S, Panopoulou A, Shea RL, Tsui M, Saso R, Sud A, et al. Response to first vaccination against SARS-CoV-2 in patients with multiple myeloma. *Lancet Haematol* 2021;8(6):e389–92.
- [40] Barrière J, Chamorey E, Adjoutah Z, Castelnau O, Mahamat A, Marco S, et al. Impaired immunogenicity of BNT162b2 anti-SARS-CoV-2 vaccine in patients treated for solid tumors. *Ann Oncol* 2021;32(8):1053–5.

- [41] Chen Y-W, Tucker MD, Beckermann KE, Iams WT, Rini BI, Johnson DB. COVID-19 mRNA vaccines and immune-related adverse events in cancer patients treated with immune checkpoint inhibitors. *Eur J Cancer* 2021;155:291–3. <https://doi.org/10.1016/j.ejca.2021.07.017>.
- [42] So ACP, McGrath H, Ting J, Srikandarajah K, Germanou S, Moss C, et al. COVID-19 Vaccine Safety in Cancer Patients: A Single Centre Experience. *Cancers (Basel)* 2021;13(14):3573. <https://doi.org/10.3390/cancers13143573>.
- [43] Terpos E, Zagouri F, Lontos M, Skirou AD, Koutsoukos K, Markellos C, et al. Low titers of SARS-CoV-2 neutralizing antibodies after first vaccination dose in cancer patients receiving checkpoint inhibitors. *J Hematol Oncol* 2021;14(1):86. <https://doi.org/10.1186/s13045-021-01099-x>.
- [44] Terpos E, Trougakos IP, Gavriatopoulou M, Papassotiriou I, Skirou AD, Ntanasis-Stathopoulos I, et al. Low neutralizing antibody responses against SARS-CoV-2 in older patients with myeloma after the first BNT162b2 vaccine dose. *Blood* 2021;137(26):3674–6.
- [45] Thakkar A, Gonzalez-Lugo JD, Goradia N, Gali R, Shapiro LC, Pradhan K, et al. Seroconversion rates following COVID-19 vaccination among patients with cancer. *Cancer Cell* 2021;39(8):1081–1090.e2.
- [46] Palich R, Veyri M, Marot S, Vozy A, Gligorov J, Maingon P, et al. Weak immunogenicity after a single dose of SARS-CoV-2 mRNA vaccine in treated cancer patients. *Ann Oncol* 2021;32(8):1051–3.
- [47] Palich R, Veyri M, Vozy A, Marot S, Gligorov J, Benderra M-A, et al. High seroconversion rate but low antibody titers after two injections of BNT162b2 (Pfizer-BioNTech) vaccine in patients treated with chemotherapy for solid cancers. *Ann Oncol* 2021;32(10):1294–5. <https://doi.org/10.1016/j.annonc.2021.06.018>.
- [48] Goshen-Lago T, Waldhorn I, Holland R, Szwarcwort-Cohen M, Reiner-Benaim A, Shachor-Meyouhas Y, et al. Serologic Status and Toxic Effects of the SARS-CoV-2 BNT162b2 Vaccine in Patients Undergoing Treatment for Cancer. *JAMA Oncol* 2021;7(10):1507–13. <https://doi.org/10.1001/jamaoncol.2021.2675>.
- [49] Eliakim-Raz N, Massarweh A, Stemmer A, Stemmer SM. Durability of Response to SARS-CoV-2 BNT162b2 Vaccination in Patients on Active Anticancer Treatment. *JAMA Oncol* 2021;7(11):1716–8. <https://doi.org/10.1001/jamaoncol.2021.4390>.
- [50] Dagan N, Barda N, Kepten E, Miron O, Perchik S, Katz MA, et al. BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting. *N Engl J Med* 2021;384(15):1412–23.
- [51] Abu-Raddad LJ, Chemaitelly H, Butt AA. National Study Group for COVID-19 Vaccination. Effectiveness of the BNT162b2 Covid-19 vaccine against the B.1.1.7 and B.1.351 variants. *N Engl J Med* 2021;385(2):187–9.
- [52] Heudel P, Favier B, Assaad S, Zrouba P, Blay J-Y. Reduced SARS-COV-2 infection and death after two doses of COVID-19 vaccines in a series of 1503 cancer patients. *Ann Oncol* 2021;32(11):1443–4. <https://doi.org/10.1016/j.annonc.2021.07.012>.
- [53] Boyarsky BJ, Werbel WA, Avery RK, Tobian AAR, Massie AB, Segev DL, et al. Antibody Response to 2-Dose SARS-CoV-2 mRNA Vaccine Series in Solid Organ Transplant Recipients. *JAMA* 2021;325(21):2204–6. <https://doi.org/10.1001/jama.2021.7489>.
- [54] Kamar N, Abravanel F, Marion O, Couat C, Izopet J, Del Bello A. Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients. *N Engl J Med* 2021;385(7):661–2.
- [55] Marion O, Del Bello A, Abravanel F, Couat C, Faguer S, Esposito L, et al. Safety and Immunogenicity of Anti-SARS-CoV-2 Messenger RNA Vaccines in Recipients of Solid Organ Transplants. *Ann Intern Med* 2021;174(9):1336–8.