



Impact of COVID-19 vaccination on cancer patients: safety, efficacy, and long-term effects

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Abstract

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), led to a worldwide pandemic in 2020. Cancer patients represent a highly vulnerable group for COVID-19 infection and are associated with poor outcomes due to their immunosuppressive status, owing to malignancy itself or anticancer therapies. Several approved COVID-19 vaccines were assessed for their effectiveness in the general population. However, initially, cancer patients were excluded from large landmark trials, leading to a paucity of data. This article presents a narrative review that synthesizes findings from peer-reviewed clinical trials, real-world cohort studies, and expert guidelines to assess the current evidence. This review assesses the safety, efficacy, and long-term effectiveness of COVID-19 vaccination in patients with cancer. Accumulated evidence from multiple clinical trials and real-world data suggests that COVID-19 vaccines are generally well-tolerated, safe, and efficacious in patients with both solid and hematologic types of cancer, eliciting moderate adverse reactions and rare severe reactions, including immune-related adverse events, thrombotic events, and anaphylaxis. Vaccine-induced humoral response and cellular response are often weakened in cancer patients, especially those with hematologic malignancies, compared to those of non-cancerous individuals. However, the immunogenicity in cancer patients improves significantly with booster doses. Further, seroresponse against SARS-CoV-2 variants increases with additional booster doses, signifying the importance of personalized booster approaches. Despite this, vaccinated cancer patients develop breakthrough infections, which are associated with hospitalization and higher mortality compared to the general population. Moreover, long-term follow-up of vaccinated cancer patients suggests that they demonstrate durable immune responses, with rare reports of cancer recurrence or remission that require further evaluation. Collectively, COVID-19 vaccination is a practical and valuable approach for alleviating risk and improving outcomes in patients with cancer.

Keywords COVID-19 vaccination · Cancer patients · Booster doses · Long-term effectiveness · Immunogenicity · Breakthrough infections

Abbreviations

COVID-19 Coronavirus disease 2019
SARS-CoV-2 Severe acute respiratory syndrome coronavirus 2

WHO World Health Organization
ICI Immune checkpoint inhibitor
HSCT Hematopoietic stem cell transplantation
CAR-T Chimeric antigen receptor T cell therapy
irAE Immune-related adverse event
VIIT Vaccine-induced immune thrombotic thrombocytopenia
TTS Thrombosis with thrombocytopenia syndrome
PEG Polyethylene glycol
CMI Cell-mediated immunity
ISR Immune status ratio
Nab Neutralizing antibody
MM Multiple myeloma
CTCL Cutaneous T cell lymphoma
MF Mycosis fungoides

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LyP	Lymphomatoid papulosis
pcALCL	Primary cutaneous anaplastic large-cell lymphoma
SLR	Systematic literature review
ASCO	American Society of Clinical Oncology
ESMO	European Society for Medical Oncology
NCCN	National Comprehensive Cancer Network
CDC	Centers for Disease Control and Prevention
FDA	Food and Drug Administration
MHRA	Medicines and Healthcare Products Regulatory Agency
VAERS	Vaccine Adverse Event Reporting System
BNT162b2	Pfizer-BioNTech COVID-19 mRNA Vaccine
mRNA-1273	Moderna COVID-19 mRNA Vaccine
Ad26.COV2.S	Johnson & Johnson COVID-19 Vaccine
ChAdOx1	Oxford/AstraZeneca COVID-19 Vaccine

Introduction

The coronavirus disease 2019 (COVID-19) is caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which has led to widespread morbidity and mortality [1]. Since the declaration of the COVID-19 outbreak as a pandemic on 11 March 2020 by the World Health Organization (WHO), this disease has affected more than 778 million individuals worldwide, resulting in over 7 million deaths [2]. The SARS-CoV-2 virus infects the general population, but individuals of older age or with cardiovascular disease, diabetes mellitus, kidney disease, or cancer are at a higher risk of severe SARS-CoV-2 infection and COVID-19 outcomes. Individuals with cancer, particularly those who are undergoing active anticancer treatment or are under immunosuppressants, are a susceptible population with a heightened risk of severe COVID-19 symptoms [4, 5]. Cancer patients with either hematologic malignancies or solid tumors are more likely to develop severe respiratory complications, experience prolonged hospital stays, and face higher mortality rates compared to individuals without cancer [6, 7].

In light of these backgrounds, the accelerated development and distribution of COVID-19 vaccines emerged as an indispensable treatment strategy to control viral dissemination and protect vulnerable individuals [8]. However, although these vaccines have shown strong safety and efficacy in the general population, their impact on cancer patients remains inadequately characterized. Most pivotal clinical trials excluded individuals with active malignancies or those receiving immunosuppressive therapies, resulting in a significant knowledge gap regarding vaccine performance in this subgroup. There is a lack of comprehensive data on

how cancer type, treatment modality, degree of immunosuppression, and timing of vaccination affect immunogenicity, safety, and durability of protection in cancer patients. Furthermore, the potential impact of booster doses and emerging viral variants on long-term outcomes in cancer patients remains poorly understood or underexplored [9].

Individuals suffering from malignancies undergo various therapies, including radiotherapy, hormonal therapy, chemotherapy, immunotherapy, and targeted therapy, all of which can compromise the body's immune system and impair its ability to fight infections, such as SARS-CoV-2 infection [10]. These underlying immunosuppressive conditions result in weaker antibody responses after vaccination and a higher risk of breakthrough infections [11]. Moreover, patients with underlying hematologic malignancies demonstrate lower seroconversion rates post-vaccination compared to those with solid cancers [12]. Thus, the clinical utility of COVID-19 vaccination in cancer patients remains under investigation, especially concerning its protective efficacy and risk–benefit profile amid complex treatment regimens [13].

To date, more than 10 major COVID-19 vaccines, including vaccines developed by Pfizer (BNT162b2) and Moderna (mRNA-1273), have been administered across the globe while keeping susceptible populations and frontline workers in the world at the highest priority for vaccination [14]. According to WHO data, over 200 additional vaccines are in various pre-clinical and clinical stages of development to meet the needs of the global population [15]. Several clinical trials have assessed the effects of COVID-19 vaccines in healthy populations, reporting high efficacy and tolerability with minimal side effects or breakthrough [4, 5, 13, 16–19]. The lack of targeted data on cancer patients introduces uncertainty into clinical decision-making. Real-world evidence is beginning to emerge, but significant questions remain about the durability of immunity, optimal vaccination schedules, and the incidence of adverse events among different cancer subpopulations. Furthermore, as new SARS-CoV-2 variants continue to evolve, assessing the need and timing for booster doses in immunocompromised cancer patients becomes increasingly vital.

Patients with cancer, particularly those undergoing active treatment or receiving immunosuppressants, were excluded from clinical trials; consequently, data on the clinical efficacy of COVID-19 vaccination in this group remain limited. Thus, while evidence suggests that COVID-19 vaccination is effective in eliciting immune responses, the extent of this response and its implications for individuals who have cancer remain a matter of ongoing exploration. Furthermore, although initial studies suggest that COVID-19 vaccines are generally safe for cancer patients, ongoing research is examining potential short- and long-term side effects that may affect cancer therapies and overall patient well-being

[18, 19]. While booster doses are recommended and enhance immune responses in cancer patients, emerging studies indicate that repeated administration may contribute to T cell exhaustion. Earlier researchers, including Benitez Fuentes et al. (2022) [19], reported that the third vaccine dose was associated with signs of lymphocyte exhaustion, including increased expression of immune checkpoint markers such as PD-1 and TIM-3, which raises concerns about potential long-term immunological impairment in some patients. Furthermore, the SARS-CoV-2 virus continues to mutate and emerge as new variants, which can impact ongoing vaccination programs. Hence, there is a requirement for additional or booster doses to immunize patients with cancer against new variants. Hence, there is a requirement for additional or booster doses to immunize patients with cancer against new variants.

This review aims to provide an in-depth analysis of the impact of COVID-19 vaccination on patients with different malignancy types, focusing on efficacy, tolerability, and long-term effectiveness by evaluating the available literature. This review aims to explore the several risk factors and features of cancer associated with increased susceptibility of cancer patients to COVID-19 infections. The efficacy of vaccination, measured in terms of seroconversion rates and antibody responses, as well as any adverse effects related to vaccinations, and the potential long-term impact of COVID-19 vaccines in cancer patients, is also discussed. By examining the available literature, the review explores cancer-related risk factors contributing to the increased susceptibility of cancer patients to COVID-19. This review incorporates the most recent real-world data on third and fourth booster doses, including their impact on breakthrough infections, immunogenicity, and adverse outcomes across various cancer subtypes. It also examines growing evidence of immune exhaustion from repeated boosters and explores innovative strategies, such as personalized booster schedules and heterologous vaccine combinations. Additionally, the review addresses vaccination challenges and presents recommended guidelines for vaccinating cancer patients.

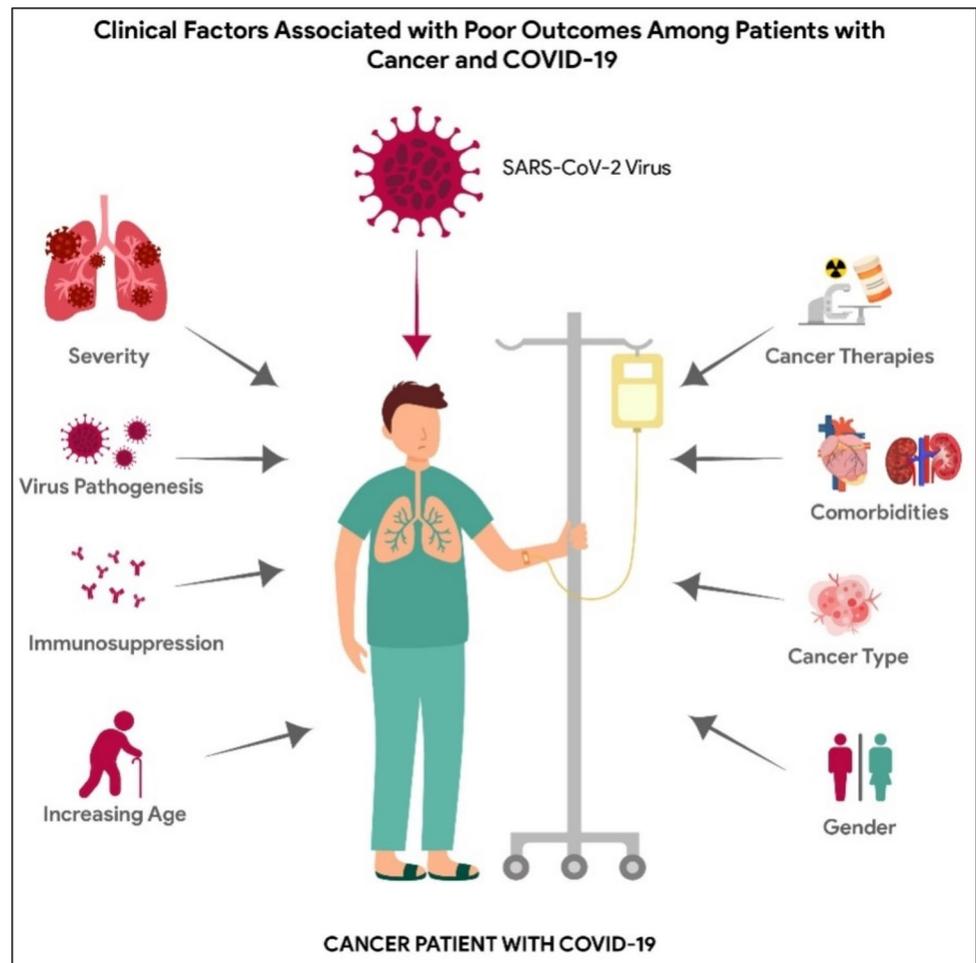
COVID-19 and cancer: a multifaceted interaction

Cancer patients infected with SARS-CoV-2 have significantly different demographics and clinical signatures in contrast to the general population. This is due to the variable degree of complexity involved in tumor biology, differences in individual patient responses, and diverse anti-tumor therapies [20]. Individuals suffering from various types of malignancies are a susceptible population with the risk of developing severe COVID-19 conditions [12, 18]. Various groups of bodies have investigated the performance of patients with

cancer and COVID-19 and suggested various risk factors and predictors associated with poor or severe outcomes of COVID-19 infections. For instance, the COVID-19 and Cancer Consortium (CCC19) gathered data from almost 5000 patients with cancer infected with the SARS-CoV-2 virus. They reported that older age, male gender, comorbidities such as cardiovascular disease, lung disease, nephrological disease, ethnicity, poor Eastern Cooperative Oncology Group performance status, antitumor therapy including cytotoxic drugs, and hematologic cancers (leukemia and lymphoma) were related to the severity of SARS-CoV-2 infections [3]. Abnormal hematological levels and elevated levels of creatinine, troponin, and C-reactive protein were associated with severe COVID-19 symptoms, as detailed in Fig. 1. Cancer patients who were found COVID-19-positive early in the pandemic had worse outcomes than those found later during the pandemic. Specific anti-neoplastic therapies (e.g., etoposide along with platinum, and DNA methyltransferase inhibitors) were linked with a high mortality rate [3]. UK Coronavirus Cancer Monitoring Project (UKCCMP), a clinical registry that monitors the COVID-19 positive patients in real-time, investigated 800 cancer patients co-infected with the SARS-CoV-2 virus and reported that the mortality of the cancer patients with COVID-19 was majorly due to the increasing age, male gender, and diseases such as cardiovascular disease and hypertension. Additionally, the authors reported that they were not able to identify the negative association of anticancer therapies that were given 4 weeks before the COVID-19 infection with increased risk of mortality [21]. Furthermore, the Thoracic Cancers International COVID-19 Collaboration (TERAVOLT) registry observed that patients with thoracic cancer display severity of COVID-19 disease owing to increasing age, smoking habits, and co-occurrence of other morbid diseases, with a mortality rate as high as 33% among those patients [22]. Additionally, other studies including large cohorts of cancer patients with COVID-19 suggest that approximately 20% to > 70% of patients receiving different anticancer therapies demonstrate severe COVID-19 illness, and these patients showed mortality rates ranging between 13 and 33% [20, 23–29].

Taken together, these studies suggest that COVID-19 severity is more likely due to the increasing male gender, pre-existing comorbidities, and less likely due to the active anticancer treatment; however, other features such as the type of malignancies and type of anticancer drugs administered to patients should not be overlooked. For instance, two separate teams of investigators established that the administration of immune checkpoint inhibitors (ICI) in cancer patients is related to an increased rate of hospitalization and COVID-19 severity [30, 31]. Figure 1 shows the clinical factors associated with poor outcomes among cancer patients with cancer and COVID-19.

Fig. 1 Clinical factors associated with poor outcomes among cancer patients with cancer and COVID-19



Overview of COVID-19 vaccines

According to WHO data, as of 22 July 2020, a total of 13.64 billion COVID-19 vaccine doses have been administered [32]. Sixty-seven percent of the total population is vaccinated with a complete primary series of a COVID-19 vaccine, and 32% of the total population is immunized with at least one booster dose of a COVID-19 vaccine [32], as depicted in Fig. 2. The WHO reports that over 288 vaccines against the SARS-CoV-2 virus are under various stages of development, with 184 in the pre-clinical phase and 104 in the clinical phase [15].

More than twelve of these vaccines have already been approved for use in various countries [14]. Among them, IncoVacc (Bharat Biotech), Sputnik Light and Sputnik V (Gamaleya), Jcovden (Johnson & Johnson), Vaxzevria (Oxford/AstraZeneca), Covishield (Serum Institute of India with (Oxford/ AstraZeneca formulation), and Convidecia (Cansino) utilize recombinant non-replicating

viral vector to elicit the natural immunogenicity of the COVID-19 virus. Spikevax (Moderna) and Comirnaty (BioNTech/Pfizer) utilize messenger RNA (mRNA) that encodes proteins. Nuvaxovid (Novavax), Covovax (Serum Institute of India), and SKYCovione (SK Bioscience Co. Ltd.) utilize protein subunit vaccines. Covaxin (Bharat Biotech), Covilo (Sinopharm), and CoronaVac (Sinovac) utilize inactivated whole-virion vaccines (Fig. 2).

All these vaccines utilize these different types of viral platforms to elicit antibody responses and T cell responses in the body, particularly against the receptor-binding domain (RBD) of the SARS-CoV-2 spike (S) protein, which is responsible for entry of the virus into the respiratory epithelial cells of the human host via its contact with the epithelial angiotensin-converting enzyme 2 (ACE-2) receptor [9]. Overall, the cellular response and humoral response against the SARS-CoV-2 virus are required for immunity against the COVID-19 infection; therefore, the efficacy of COVID-19 vaccines should be judged based on both responses [9] (Fig. 3).

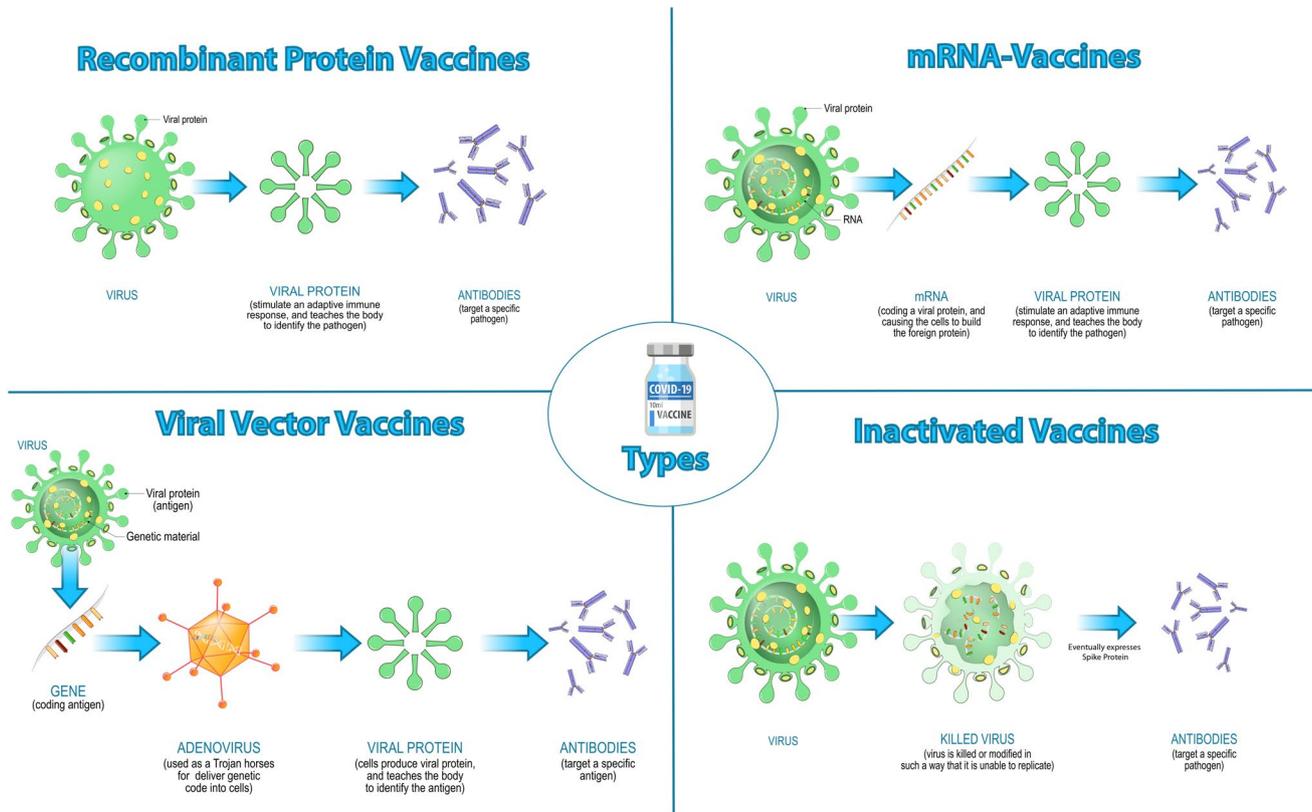


Fig. 2 Overview of different COVID-19 vaccine types. Vaccines, such as recombinant protein vaccines, mRNA vaccines, viral vector vaccines, and inactivated vaccines, eventually express the spike protein to elicit an immune response

Safety of COVID-19 vaccination in cancer patients

The approved COVID-19 vaccines have been studied extensively in various phases of clinical development, and their safety profiles have been reported, along with cautioning against the occurrence of general adverse events, immune-related adverse events, and serious adverse events.

A. General adverse events

Accumulated evidence suggests that the approved vaccines, such as those developed by Moderna, Pfizer, Bharat Biotech, Johnson & Johnson, AstraZeneca, and Sinopharm, are safe and well-tolerated. In a study conducted by Cai et al., a comprehensive analysis was performed by collecting real-world data from the Vaccine Adverse Event Reporting System (VAERS) [16]. The authors reported that the m-RNA-based vaccines such as those from Moderna and Pfizer-BioNTech showed no toxicities in patients with cancer with mild local reactions such as sore arm, injection site pain, nausea, swelling, headache, and myalgia; however, incidence of chills, pyrexia, injection site erythema, etc. was higher in patients vaccinated with Moderna compared to those with

Pfizer-BioNTech vaccine. On the contrary, frequent events of systemic reactions such as fatigue, dizziness, and dyspnea occurred in patients vaccinated with the Pfizer-BioNTech vaccine [16]. These symptoms occur more frequently in females and young patients, typically within 1 week of vaccination. Polack et al. and Monin et al. also conducted an extensive cohort study reporting that the Pfizer-BioNTech vaccine is safe and well tolerated, with only mild to moderate adverse events limited to mild-to-moderate pain at the injection site, fatigue, and headache [33, 34].

B. Specific safety concerns in cancer subgroups

In a study, Thakkar et al. investigated the effect of three vaccines: BNT162b2 (Pfizer), mRNA-1273 (Moderna), and Ad26.COV2 (Johnson & Johnson) in 134 patients with solid tumors (including breast, thoracic, gastrointestinal, and gynecologic) and 66 patients with hematologic malignancies (including lymphoid, myeloid, and plasma cell). The authors found that grade 1–2 adverse events (mild to moderate) occurred in 37% of the population vaccinated with the BNT162b2 vaccine, 34% of the population vaccinated with the mRNA1273 vaccine, and 26% of the population immunized with Ad26.COV-2 vaccine [35]. Herishanu et al.

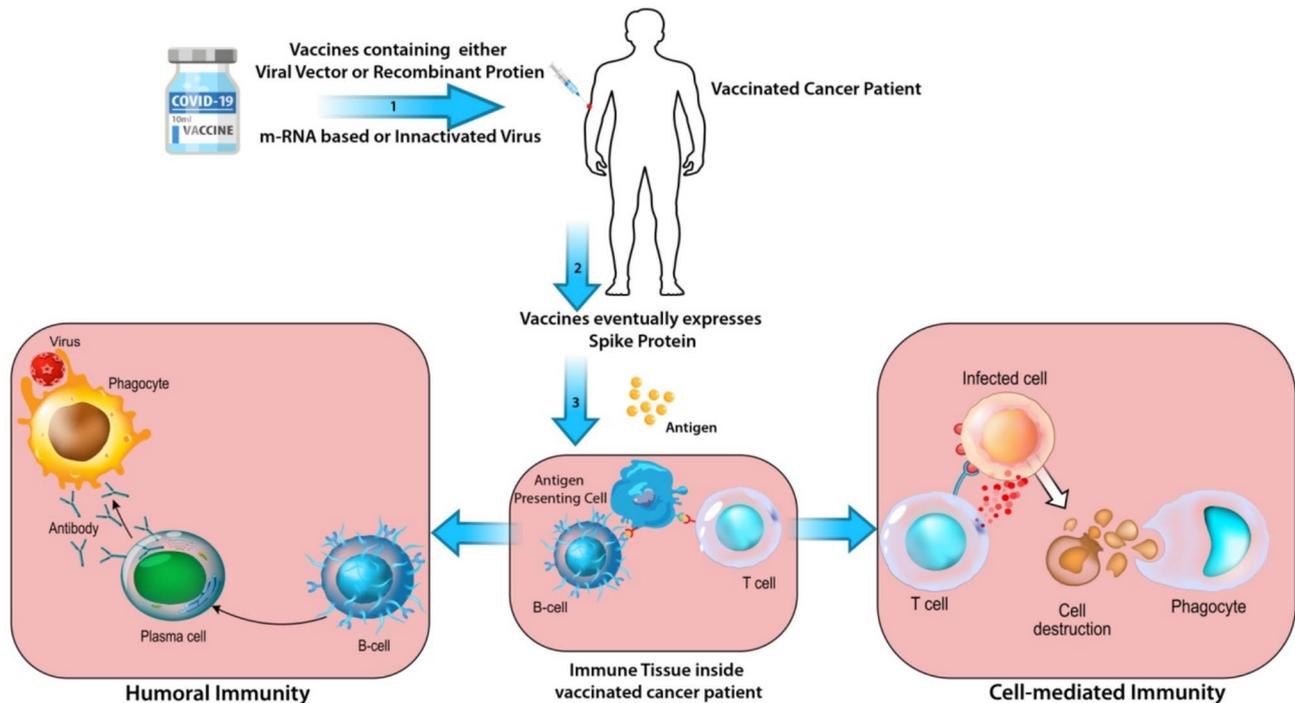


Fig. 3 Mechanisms of immunity triggered by various types of COVID-19 vaccines in cancer patients. All COVID-19 vaccines (viral vector, recombinant protein, mRNA, and inactivated virus) ultimately express the viral spike protein, which is presented by antigen-present-

ing cells to either B cells or T cells to elicit both humoral immunity and cell-mediated immunity in vaccinated individuals, including those with cancer

[36] assessed the safety profile of the BNT162b2 vaccine in patients with chronic lymphocytic leukemia. They reported that 31% and 33.5% of patients exhibited mild local reactions, characterized by pain at the injection site and redness. In comparison, 12.5% and 23.4% of participants demonstrated systemic adverse events, such as weakness, fever, chills, and headache, after receiving the first and second vaccine doses, respectively. Pimpinelli et al. [37] investigated the safety of COVID-19 vaccines in patients with multiple myeloma and those undergoing active anticancer therapy. They observed that only two patients vaccinated with BNT162b2 experienced mild adverse reactions. Masarweh et al. also found no adverse effects of BNT162b2 on patients with cancer undergoing active antitumor therapy, including chemotherapy, radiotherapy, and immunotherapy [39]. In a meta-analysis study conducted by Ge et al., patients who undergo HSCT or CART therapy showed mild to moderate adverse events limited to common local reactions such as pain and swelling, and systemic reactions including fever, myalgia, and fatigue [38]. Overall, these studies suggest that COVID-19 vaccines are well tolerated by patients with cancer, irrespective of the fact that they have solid or hematological cancer, multiple myeloma, or are undergoing active antitumor treatment, HSCT, or CART therapy, and are comparable to the general population.

C. Immune-related adverse events (irAEs)

Several studies have found an elicitation of immune-related adverse events (irAEs) in cancer patients treated with ICIs following COVID-19 vaccination [39]. Seven clinical studies, including both retrospective and prospective studies, reported immune-related adverse events (irAEs) in patients treated with ICI vaccines, including BNT162b2, mRNA-1273, CoronoVac, BBIBP-CorV, ChAdOx1 nCoV-19, and Ad26.COVS [4, 30, 40–44]. These studies reported an incidence of lower-grade irAEs in cancer patients ranging from 0% to 23.6%. However, there were three case reports of patients treated with ICI vaccinated with BNT162b2, one patient demonstrated cytokine release syndrome, another case demonstrated grade-4 necrotizing myopathy, and the third case displayed aggravation of psoriasis [45–47]. Studies suggest that irAEs due to the COVID-19 vaccine in ICI-treated patients can be managed by close monitoring of the ICI-treated patients.

D. Thrombotic events

Several studies reported that a rare syndrome of thrombosis, frequently known as vaccine-induced immune thrombotic thrombocytopenia (VIIT), occurred in patients receiving

vaccines such as ChAdOx1 nCoV-19, Ad.26. COV2.S, BNT162b2, and mRNA-1273 [48–50]. The Medicines and Healthcare Products Regulatory Agency (MHRA) was prompted by 309 reports, mostly females with VIIT, including 116 cases of cerebral venous sinus thrombosis with thrombocytopenia (TTS), with a mortality rate of 18% [51]. An extensive cohort study of 281,264 individuals from Denmark and Norway who received the ChAdOx1 nCoV-19 vaccine also reported 59 cases of TTS events [52]. Hence, MHRA advised caution while administering the ChAdOx1 nCoV-19 vaccine to people who might be at risk of coagulation owing to pre-existing medical conditions, including cancer, which itself is allied with an increased risk of TTS [53]. TTS following the use of Ad.26.COV2.S as well as mRNA-based BNT162b2 and mRNA-1273 has also been reported; however, the patient population was between 15 and 20 only [54, 55]. Since the occurrence of these reports, some countries restricted the usage of these vaccines for vulnerable populations; however, the FDA and MHRA advised the usage of vaccines with caution, weighing in their benefits rather than the risks for the majority of people [56].

E. Allergic reactions

Anaphylaxis is a severe allergic reaction that can occur in people, including cancer patients, after any vaccination and can be life-threatening if not treated immediately. Several reports of allergic reactions in patients who received BNT162b2 and mRNA-1273 have been submitted to the CDC by VAERS for evaluation. CDC identified 66 cases (47 post-administration of the BNT162b2 vaccine, at a reporting rate of 4.7 cases/million doses, and 19 post-administration of the mRNA-1273 vaccine, at a reporting rate of 2.5 cases/million doses) [57]. Additionally, in a meta-analysis study, Sobczak and Pawliczak pooled data from six published articles [57–62] and 4 databases [51, 63–65] and compared the number of anaphylaxis reactions post-administration of BNT162b2, m-RNA-1273, ChAdOx1 nCoV-19, and Ad26.COV2.S vaccines compared to mRNA-based BNT162b2 and mRNA-1273 vaccines. Recent studies conducted in Korea, Ontario, Germany, and Singapore also reported anaphylaxis reactions post-administration of authorized COVID-19 vaccines and postulated that polyethylene glycol (PEG2000) might be responsible for the elicitation of such allergic reactions [67–70]. However, due to the small sample size, the exact mechanism could not be concluded. In all these studies, anaphylaxis reactions were more prevalent in females and occurred more frequently in young to middle-aged individuals. Since these reports, the CDC and

WHO have recommended that epinephrine be administered in all such cases, facilities should have the necessary supplies, and caregivers should be trained to manage anaphylaxis. Additionally, the CDC and WHO recommend the use of COVID-19 vaccines with caution by asking the patient, including cancer patients, for their allergies before vaccine administration [71, 72].

Efficacy of COVID-19 vaccination in cancer patients

A. Immunogenicity studies

Humoral response

Studies have suggested that seropositivity rates in cancer patients' post-vaccination are lower than those observed in noncancerous patients but higher than those present in patients with hematologic malignancies [73, 74]. Further, the seroconversion rate is also affected by antitumor therapies. However, endocrine treatment and immunotherapy might not affect the seroconversion rate in cancer patients [73, 75]. Several studies evaluated the seroresponse rate following two doses of m-RNA-based vaccines, m-RNA 1273 and BNT162b2, and reported the seroconversion rate to range from 75 to 100% [19, 41, 73, 74, 76–87]. Further, with the increase from two doses to 3 and 4, the seroconversion rate ranges from 85 to 100% [76, 80–84]. The rate of seroconversion in patients with hematologic malignancies was reduced compared to that in patients with solid tumors. These studies confirmed that humoral immunity was increased after the administration of additional vaccine doses in patients with both types of cancer, solid and hematologic, who had responded partially after receiving two doses of vaccine. Meta-analysis as per Martins-Branco et al. [80] pooled estimates calculated using random-effects models with heterogeneity reporting (e.g., I^2 and τ^2). Moreover, neutralization antibody (nAb) titers also augmented post 3 and 4 doses of vaccines in patients with both cancer types, as per earlier researchers [80–82] as detailed in Table 1 and recent studies [75, 79, 85, 87, 88] as mentioned in Table 2.

Cellular response

The immune response to a COVID-19 vaccination is generally assessed in terms of humoral immunity by measuring the antibody titers developed in cancer patients; however, the cellular response to a COVID-19 vaccination can also specify the protection against SARS-CoV-2 infection in patients with cancer. T cell responses have been assessed rarely, but it has been observed that patients who

Table 1 Vaccine response in patients with solid tumors

Study	No. of doses	Study cohort	Vaccine(s)	Seropositivity rate (%)*	nAb response (%)	T cell response (%)	Key findings
Becerril-Gaïtan et al. [74]	1 / 2	Meta-analysis (35 studies; 6 cancer-focused)	mRNA-1273, BNT162b2, ChAdOx1, Ad26, COV2.S, CoronaVac	45 / 95	Not reported	78 (n = 84), 60 (n = 634)	Higher response after 2 doses; improved T cell activation
Lee et al. [55]	1 / 2	SLR (11 studies, 827 cancer pts)	Same as above	55 / 90	Not reported	Not reported	Marked increase in seropositivity with second dose
Corti et al. [73]	2	SLR (36 studies)	Same as above	85 (range 48–100)	Not reported	Not reported	Wide variation across studies; overall high response
Martins-Branco et al. [80]	2	SLR/meta-analysis (89 studies, 30,183 pts)	Same as above	94 (range 64–99)	Not reported	68	Strong seropositivity and T cell response
Oosting et al. [41]	1 / 2	503 solid tumor pts by therapy	mRNA-1273	1st dose: Immuno 37%, Chemo 32%, Chemo-immuno 33% 2nd dose: Immuno 93%, Chemo 84%, Chemo-immuno 89%	Not reported	Immuno 67%, Chemo 66%, Chemo-immuno 53%	Therapy type affects immune response
Debie et al.	2 / 3	141 cancer pts (solid/hematologic)	BNT162b2	2nd dose: targeted/hormonal 97%, Chemo 100%, Immuno 100%, Chemo-immuno 100% 3rd dose: All groups 100%	Not reported	3rd dose: Immuno 88%, others 100%	Strong booster effect
Debie et al. [76]	2 / 3	51 solid tumor pts	mRNA-1273, BNT162b2	2nd dose 53%, 3rd dose 96%	2nd dose 59%, 3rd dose 97%	Not reported	Marked booster effect on humoral response
Fendler et al.	3	353 pts (solid/hematologic)	BNT162b2	Not reported	nAb (Delta) 67	73	Reasonable variant-specific response
Su et al. [80]	2 / 3	131 solid tumor pts (heterologous vs. homologous 3rd dose)	CoronaVac, ChAdOx1, mRNA vaccines	2nd dose: CoronaVac/ChAdOx1 16%, ChAdOx1/ChAdOx1 10% 3rd dose: CoronaVac/ChAdOx1 91%, ChAdOx1/ChAdOx1 90%	Omicron BA.2: CoronaVac/ChAdOx1 86%, ChAdOx1/ChAdOx1 78%	Not reported	Heterologous boosting improves response
Fendler et al. [81]	3 / 4	157 cancer patients	BNT162b2	D3: targeted/hormonal 98%, Chemo 100%, Immuno 100% D4: All 100%	Not reported	Not reported	Strong 4th dose response across therapies
Luangdilok et al. [82]	3 / 4	395 solid/hematologic cancer pts	mRNA-1273, BNT162b2	3rd dose 99%, 4th dose 100%	Not reported	Not reported	Excellent seroconversion post-booster

a, Range of seropositivity identified in all the studies.

Table 2 Vaccine response in patients with hematologic malignancies

Study	No. of doses	Study cohort	Vaccine(s)	Seropositivity rate (%) ^a	nAb response (%)	T cell response (%)	Key findings
Gagelmann et al. [79]	1 / 2	SLR/meta-analysis (49 studies, 11,086 pts)	mRNA-1273, BNT162b2, ChAdOx1, Ad26, COV2.S	1st: 37%, 2nd: 64% (range 29–87)	Not reported	52	Limited serologic response; T cell immunity detected
Teh et al. [87]	1 / 2	SLR/meta-analysis (44 studies, 7064 pts)	Same as above	Range 37–51	Range 62–66	T cell 33–86 (varied by dose); total 45–75	High inter-study variability
Corti et al. [73]	2	SLR (36 studies)	Same as above	54	Not reported	Not reported	Moderate seropositivity overall
Martins-Branco et al. [78]	2	SLR/meta-analysis (89 studies, 30,183 pts)	Same as above	60 (range 42–78)	Not reported	59	Better T cell responses than serology
Debie et al. [76]	2 / 3	141 solid/hematologic pts	BNT162b2	Rituximab-treated 21%	Rituximab 14	Not reported	B cell depletion impairs vaccine efficacy
Uparapat et al. [75]	2 / 3	Meta-analysis (12 studies, 1479 pts)	Same as above	Overall 68%; treated 59%, untreated 80%	41 (range 3–83)	67	Treatment status greatly impacts response
Greenberger et al. [86]	3	49 B cell malignancy pts	mRNA-1273, BNT162b2	65	Not reported	Not reported	Moderate response post-3rd dose
Haggenburg et al. [85]	3	684 hematologic malignancy pts	mRNA-1273	79	WT 100%, Delta 98%, Omicron BA.1 92	Not reported	Strong variant-specific nAb response
Sherman et al. [89]	3	94 lymphoid malignancy pts	mRNA-1273, BNT162b2	68	Not reported	Not reported	Moderate boost post-third dose
Debie et al. [83]	3 / 4	157 cancer pts	BNT162b2	3rd 96%, 4th 100%	Not reported	Not reported	Booster doses enhance response
Ehmsen et al. [84]	3 / 4	395 pts	mRNA-1273, BNT162b2	3rd 80%, 4th 87%	Not reported	Not reported	Stepwise increase with each dose
Fendler et al. [88]	3 / 4	80 blood cancer pts	BNT162b2	WT 87%, Delta 72%, Omicron BA.1 62	WT 98%, Delta 78%, Omicron BA.1 79	WT CD4 + 59%, CD8 + 56%; Omicron CD4 + 31–59%, CD8 + 34–44	Robust nAb and T cell responses against variants

^a b, Range of seropositivity identified in all the studies.

demonstrate lower humoral responses often show higher T cell responses.

Several studies have been conducted to measure T cell responses to authorized vaccines in cancer patients, reporting higher variability in the data. For instance, in patients with solid malignancies, including those undergoing active anti-tumor therapies, the T cell responses ranged from 53 to 78% of the patients (Table 1). In patients with hematologic malignancies, the cellular response ranged from 31 to 86% of the patients (Table 2). Interestingly, Fendler et al. reported the T cell response to BNT162b2 vaccines in patients with hematologic malignancies and found that the vaccine showed T cell responses against: 31% of patients for Omicron CD4+ and 34% of patients for Omicron CD8+, after dose 3, which increased to 59% of patients for Omicron CD4+ and 44% of patients for Omicron CD8+ [88]. All these studies confirm the efficacy of the approved vaccines and that cancer patients require more than two doses of vaccines for a greater level of protection against SARS-CoV-2 infection.

B. Real-world effectiveness data

Cancer patients are at risk of developing COVID-19 post-vaccination, also termed as breakthrough infections. Several researchers have examined patients who developed COVID-19 disease after receiving more than one dose of the vaccine. Gong et al. [3] evaluated the relationship between COVID-19 vaccinations and breakthrough infections in a large cohort of 289,400 patients with solid or hematological malignancies and 1,157,600 non-cancer patients [90]. This study reported that vaccinated cancer patients had a significantly greater risk of breakthrough infections and severe COVID-19 disease, including hospitalization and death, irrespective of the cancer type and active chemotherapy. Along similar lines, Song et al. assessed 1460 patients who encountered breakthrough infections post-vaccination. Patients with cancer, especially those with hematologic cancers, showed higher risks of breakthrough infection and disease severity compared to healthy individuals, and there was a decrease after the second dose of the COVID-19 vaccine, especially in MM patients [69]. Other studies conducted by Schmidt et al. and Sgherza et al. also ascertained that patients with malignancies who experience breakthrough infections, despite receiving a series of primary vaccines, remain at higher risk of developing severe COVID-19 disease [91, 92].

C. Efficacy against variants of concern

Multiple new variants of the SARS-CoV-2 virus have emerged since the onset of the pandemic. These variants are Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617.2), and Omicron (B.1.1.529) [93]. These variants are of the most

significant concern, as the current vaccines remain ineffective against them. Many researchers have evaluated the effect of booster doses of COVID-19 vaccines on variants such as Omicron in patients with cancer and COVID-19 and reported their limited effectiveness [82, 85, 88].

Recent subvariants of Omicron, including BA.2 and BA.5, have demonstrated enhanced transmissibility and immune evasion properties, posing significant challenges for immunocompromised populations, particularly those with cancer. BA.5, in particular, has demonstrated an enhanced ability to evade neutralizing antibodies induced by prior infection or vaccination. In cancer cohorts, especially those undergoing chemotherapy or immunotherapy, the immune response to these subvariants is notably diminished.

Emerging data suggest a stark disparity in vaccine-induced immunity between cancer patients and healthy individuals. A prospective study by Lee et al. (2023) found that following a third dose of an mRNA vaccine, only 56% of patients with solid tumors developed detectable neutralizing antibodies against BA.5, compared to 87% in non-cancer controls. Hematological malignancy patients fared worse, with response rates below 30%, indicating profound immunosuppression. Moreover, T cell-mediated immunity—crucial for long-term protection—was significantly impaired against BA.2-specific epitopes, highlighting the limited breadth of cellular immune protection in these groups.

The recurrence of SARS-CoV-2 infections in cancer patients is increasingly reported, often associated with re-exposure to subvariants like BA.5. Retrospective analyses of hospital records in Europe and North America have shown reinfection rates of up to 22% among cancer patients within 6 months of initial infection during the Omicron wave, with BA.5 responsible for over 60% of documented reinfections. These reinfections, though sometimes mild, are associated with increased hospitalization rates and delays in cancer treatment protocols.

Given this evolving landscape, variant-adapted vaccines are being explored. Preliminary trials involving bivalent boosters targeting BA.4/BA.5 spike proteins have shown improved immunogenicity in cancer patients, though the durability of protection remains uncertain. Additionally, monoclonal antibody therapies previously used for prophylaxis have demonstrated reduced efficacy against these newer subvariants, necessitating the urgent development of next-generation therapeutics tailored to immunocompromised populations.

Long-term effects of COVID-19 vaccination in cancer patients

A. Durability of immune response

The long-term effects of COVID-19 vaccination in cancer patients remain insufficiently defined due to the limited

and fragmented nature of the available data. However, recent studies suggest that although antibody titers tend to decline over time, booster doses significantly enhance and sustain immunogenicity, as detailed in Table 3. Mancuso et al. assessed 88 multiple myeloma (MM) patients over 12 months post-mRNA vaccination. Seropositivity was 88.2% at baseline but dropped after 6 months. However, titers increased to 99% post-booster, although cell-mediated immunity (CMI) remained low (36.2%) [94]. Similarly, Schmidt et al. followed 71 pediatric cancer patients for 12 months after receiving the BNT162b2 vaccine. The study found that 66% of children developed durable immunity, particularly those who had completed treatment [95].

Heudel et al. [96] tracked 2391 cancer patients for 142 days. Of these, only 1.6% contracted COVID-19, with six deaths attributed to single-dose vaccination, advanced age, or recent anti-CD20 therapy. The study emphasized that patients receiving two or more doses were significantly protected. In genitourinary cancer patients, Meza et al. found [97] that the immune status ratio (ISR) increased after 2 months post-vaccination, declined at 6 months, but improved again following booster doses, particularly in patients not receiving active treatment. Giuseppe et al. [98] observed that 23.1% of MM patients failed to respond to two BNT162b2 doses. Lack of seroconversion was associated with severe plasmacytosis and low hemoglobin levels. These findings consistently support that although immune responses decline over time, booster doses can restore and sustain both humoral and cellular immunity in cancer patients. Longer follow-up studies are needed to monitor immunogenicity beyond 12 months and explore mechanistic pathways, such as chronic inflammation or immune activation, that may impact recurrence or remission.

B. Impact of booster doses

Booster doses play a critical role in strengthening and prolonging vaccine-induced immunity in cancer patients, as detailed in Table 4. Multiple studies underscore their efficacy, particularly among those who were initially non-responsive. Rottenberg et al. [99] reported significantly increased antibody levels after a third dose of BNT162b2

in patients with solid tumors undergoing active treatment. Thakkar et al. [100] showed that 57% of seronegative patients seroconverted after a third dose and 67% after a fourth dose. These responses lasted up to 6 months [100]. Tan et al. [101] analyzed over 73,000 cancer patients and found that third and fourth mRNA doses significantly reduced COVID-19 severity. Earlier studies showed that 88% of 72 treated cancer patients were seropositive post-booster. Mondaca et al. [81] examined homologous and heterologous booster strategies. Both reported that while seropositivity was high across regimens, neutralizing antibody levels were higher in homologous groups and notably lower in patients with hematologic malignancies [81].

Emerging real-world studies further support these findings, indicating that booster doses not only enhance antibody titers but also reduce hospitalization and mortality rates among actively treated oncology patients, especially during waves of Omicron and its subvariants [102].

Recent data also emphasize the importance of individualized booster strategies, as patients with hematological malignancies continue to exhibit lower neutralizing responses even after repeated dosing, necessitating alternative approaches such as pre-exposure prophylaxis or heterologous boosting. Importantly, new evidence, such as the study by Mondaca et al. [113], raises concern about T cell exhaustion following multiple booster doses, highlighting the potential for diminished cellular immunity over time and reinforcing the need for longitudinal immunomonitoring in this vulnerable population. Additionally, global mitigation strategies and their influence on cancer care disruptions have been widely reviewed, further contextualizing the evolving landscape of cancer vaccination amidst COVID-19 [113].

C. Impact on cancer recurrence or progression

Emerging reports have raised questions about the relationship between COVID-19 vaccination and tumor dynamics. While rare, both recurrence and remission of cancers have been reported post-vaccination. Panou et al. reported [106] two relapses of cutaneous T cell lymphoma shortly after vaccination; conversely, Gambichler et al. [107] and Sousa et al. [108] documented spontaneous remission of primary

Table 3 Long-term effect of COVID-19 vaccines on patients with cancer

Cancer type	Vaccination doses	Immunogenicity	T cell response	Reference
Multiple myeloma	2+ booster	94% seroconversion post-booster; IgG titer up to 2500 U/mL	47% positive at 12 months	Mancuso et al. [94]
Pediatric cancers	2+ booster	66% long-term immunity	80–100% in off-treatment patients	Heudel et al. [96]
Mixed cancers	1–3 doses	1.6% COVID-19 incidence; 6 deaths	Low in immunosuppressed	Giuseppe et al. [98]
Genitourinary cancers	2+ booster	ISR increased post-boost	100% in off-treatment	Meza et al. [97]
Multiple myeloma	2 doses	76.9% seroconversion	No CMI data; linked to plasmacytosis	Schmidt et al. [95]

Table 4 Effect of booster doses of COVID-19 vaccine in patients with cancer

Authors	Population	Vaccine type (booster dose)	Outcomes
Rottenberg et al. [99]	Patients with solid tumors on active treatment	BNT162b2 booster	Significant increase in antibody levels post third dose; safe and well-tolerated
Thakkar et al. [100]	Patients with solid and hematologic malignancies	mRNA-based (3rd and 4th doses)	57% seroconversion after 3rd dose in initial non-responders; 67% response with 4th dose
Tan et al. [101]	73,608 cancer patients and 621,475 matched controls	mRNA (3rd and 4th doses)	Significant reduction in severe COVID-19 outcomes; sustained protection for 5 + months
Ligumsky et al. [102]	72 cancer patients on active treatment	BNT162b2	High seropositivity (88%) though lower antibody titers than healthy controls
Mai et al. [104]	849 hematologic, 82 solid cancer patients	Various (systematic review)	Seroconversion: 44% (hematologic), 80% (solid); booster improves immune response
Lee et al. [105]	361,098 individuals with cancer	Third mRNA dose	Effectiveness: 94.5% against death, 80.5% hospitalization; lymphoma patients had lowest response
Fendler et al. [81]	353 cancer patients with 82 hematologic vs. 271 solid cancer patients	BNT162b2 booster after either BNT162b2 or ChAdOx1	Lower immune responses in hematologic malignancy patients
Mondaca et al. [103]	109 patients previously vaccinated with CoronaVac (84) or BNT162b2 (25)	BNT162b2 booster after either CoronaVac or BNT162b2	High seropositivity in both heterologous and homologous schedules; higher neutralizing antibody (Nab) in homologous group

cutaneous anaplastic large-cell lymphoma and metastatic salivary gland carcinoma, respectively, after vaccination. While causality remains unconfirmed, these findings suggest a potential link between immune activation and tumor response. Mechanistically, vaccine-induced cytokine storms or T cell priming may influence the tumor microenvironment. However, robust cohort-based and mechanistic studies are essential to validate these observations.

Despite these reports, current evidence remains anecdotal and insufficient to establish causality or generalizability. Most available data are limited to isolated case reports and lack longitudinal follow-up or appropriate controls. Potential biological mechanisms—such as vaccine-induced immune modulation, systemic inflammation, or altered cytokine profiles—may play a role in either promoting tumor surveillance or triggering relapse in immunologically active malignancies. These effects could be more pronounced in cancers with known immune involvement, such as lymphomas or melanoma. To bridge these knowledge gaps, future research should prioritize well-designed prospective cohort studies that track cancer recurrence or progression post-vaccination, stratified by tumor type, treatment status, and immune response profiles. Integration of biomarkers and immunological correlates could offer mechanistic insights and inform personalized vaccination strategies in oncology settings.

Challenges and mitigation strategies in vaccinating cancer patients

Vaccinating cancer patients against COVID-19 presents several complex challenges due to their unique immunological profiles and treatment regimens. One of the most significant barriers is the immunosuppression caused by cancer itself and the therapies used to treat it, such as chemotherapy, immune checkpoint inhibitors (ICI), and anti-CD20 monoclonal antibodies. These treatments often suppress both humoral and cellular immunity, resulting in diminished responses to vaccination. As a consequence, many cancer patients, particularly those with hematologic malignancies, exhibit reduced seroconversion rates and weakened long-term immunity. This leaves them more vulnerable to breakthrough infections, even after receiving full vaccination schedules. Studies have consistently shown that patients with blood cancers tend to mount the weakest responses to COVID-19 vaccines, further emphasizing the critical need for tailored vaccination strategies in this population.

Beyond immunological barriers, several novel logistical and systemic challenges complicate vaccination efforts in cancer patients. Coordinating vaccine administration with ongoing cancer treatments is often difficult, as the optimal timing for vaccination—especially around chemotherapy or B cell-depleting therapies—remains uncertain. Many patients reside in rural or resource-limited areas, where

access to healthcare is limited and vaccination logistics are more challenging to manage. Additionally, vaccine hesitancy among cancer patients poses another major obstacle. Concerns about potential side effects, compounded by misinformation or inadequate communication from healthcare providers, contribute to reluctance or refusal to get vaccinated. Disparities in access to booster doses or newer vaccine formulations further exacerbate the issue, with inequitable distribution across healthcare systems disproportionately affecting vulnerable populations.

To address these challenges, several mitigation strategies have been proposed and are beginning to be implemented in clinical practice. Personalized vaccine scheduling is one promising approach, in which immunization is timed strategically around treatment cycles—for instance, administered prior to chemotherapy—to maximize immune response. Educational campaigns, particularly those led by oncologists and trusted healthcare professionals, can help reduce vaccine hesitancy by providing clear, evidence-based information. These efforts must be accompanied by mobile vaccination clinics and remote outreach programs to ensure vaccine access in underserved or geographically isolated areas. Another important strategy is serological monitoring, involving routine testing of antibody and T cell levels after vaccination. This enables clinicians to identify non-responders early and prioritize them for booster doses. For patients who do not respond adequately to mRNA vaccines, alternate vaccine platforms—such as protein-based or intranasal vaccines—may offer a viable alternative. Together, these multifaceted strategies aim to improve both the effectiveness and equity of COVID-19 vaccination efforts in cancer patients, ensuring they receive the protection they need amid ongoing pandemic threats.

A. Psychosocial and quality-of-life impact of COVID-19 vaccination

Beyond immunological and logistical challenges, the psychosocial implications of COVID-19 vaccination among cancer patients are increasingly recognized as a vital aspect of supportive care. Vaccination not only reduces the clinical risk of infection but also alleviates psychological burdens, such as fear of contracting the virus during hospital visits or treatment sessions. Studies have shown that vaccinated cancer patients report improved emotional stability, reduced anxiety levels, and greater confidence in engaging with social and healthcare environments, ultimately enhancing their overall quality of life. Conversely, uncertainties regarding vaccine efficacy—particularly in immunocompromised individuals—and concerns about side effects may trigger

stress or emotional distress. For example, temporary adverse effects such as fatigue or fever may negatively influence a patient's perceived well-being, especially when compounded by ongoing cancer treatment side effects. Patients undergoing therapies like anti-CD20 monoclonal antibodies or CAR-T cells often remain concerned about insufficient protection despite full vaccination schedules, leading to persistent health-related anxiety. To address these issues, oncology care teams should integrate psychological counseling, tailored education on vaccine safety and efficacy, and proactive communication strategies into routine care. These efforts help reassure patients, manage expectations, and reinforce vaccine confidence—contributing to more holistic, patient-centered vaccination strategies in cancer care.

Clinical guidelines and recommendations

Several global health organizations, expert oncology groups, and advisory committees—including the American Society of Clinical Oncology (ASCO), the European Society of Medical Oncology (ESMO), and the National Comprehensive Cancer Network® (NCCN®)—have issued guidelines to prioritize COVID-19 vaccination for patients [109] with cancer, recognizing them as a vulnerable population due to heightened risks of infection severity and poor outcomes [110]. These guidelines emphasize timely and effective vaccination across cancer treatment contexts [111]. To streamline clinical decision-making and enhance visual accessibility, Table 5 summarizes and compares core guidance from ASCO, NCCN, and ESMO, with added input from other major oncologic societies.

Furthermore, recent evidence suggests substantial variability in vaccine-induced immune responses among different cancer subgroups. Severely immunocompromised patients, such as those receiving anti-CD20 monoclonal antibodies (e.g., rituximab) or chimeric antigen receptor T cell (CAR-T) therapies, exhibit markedly lower seroconversion and neutralizing antibody levels following COVID-19 vaccination. Studies have reported that up to 85% of patients treated with anti-CD20 therapies may fail to mount a detectable humoral response, even after booster doses. Similarly, CAR-T cell recipients often exhibit impaired B cell reconstitution, resulting in reduced or absent vaccine responsiveness. These findings have prompted recommendations for tailored vaccination schedules, including additional booster doses, passive immunization with monoclonal antibodies, and enhanced monitoring of immune responses in these high-risk cohorts. Integrating this subgroup-specific data into clinical guidelines is essential to optimizing protection strategies for the most vulnerable oncology patients.

Table 5 Comparative summary of COVID-19 vaccination guidelines in cancer patients

Organization	HSCT/CAR-T vaccination timing	Booster dose guidance	Preferred vaccine type	During active therapy	During neutropenia	Additional recommendations
ASCO	Revaccination post-HSCT or CAR-T regardless of prior vaccination	Additional doses for immunocompromised patients encouraged	mRNA vaccines preferred	Continue during therapy unless contraindicated	No specific guideline	Maintain protective behaviors (masking, distancing)
NCCN	Wait ≥ 3 months post-HSCT/CAR-T	Recommends booster and 3rd dose for active treatment or recent HSCT/CAR-T	mRNA vaccines preferred (Pfizer/Moderna)	Vaccinate during therapy when feasible	Delay if ANC $< 500/\mu\text{L}$, unless no expected recovery	Schedule vaccination separately from surgery; support CDC guidance
ESMO	No specific delay; prioritize regardless of treatment phase	Booster dose 3–6 months after full vaccination	mRNA vaccines or approved alternatives	Vaccination encouraged during treatment	No specific delay recommendation	Patients are high-priority group; early vaccination emphasized
CDC (U.S.)	Same as NCCN; follow ≥ 3 months delay post-HSCT/CAR-T	Recommends boosters for immunocompromised individuals	mRNA vaccines preferred	Continue vaccination if medically stable	Assess case-by-case	Additional doses depending on immunosuppression status
American Society of Hematology	Aligns with ASCO and NCCN; ≥ 3 months post-HSCT/CAR-T	Encourages boosters for hematologic malignancies	mRNA vaccines preferred	Supports timely vaccination	Individualized decision-making	Emphasizes close coordination with oncology care team
German Society of Hematology (DGHO)	Minimum 3 months post-HSCT/CAR-T	Recommends 3rd/booster dose in immune-compromised	mRNA or vector vaccines accepted	Supports vaccination during stable phases	Avoid during severe cytopenia	Advises serologic monitoring in select cases

Future perspectives, ongoing research, and limitations

Researchers are continuously working on the development of newer vaccine types that can be effective against the various variants of the constantly evolving SARS-CoV-2 virus. Next-generation vaccines, such as peptide-based vaccines, would depend on the silico predictions for identifying peptides specifying highly conserved immunecell epitopes to generate long-term immunogenicity in vulnerable populations, such as cancer [112]. Researchers have also found that hybrid immunity, which comes from the combination of both vaccination and infection, is much more promising than immunity provided by either vaccine or natural infection alone [113]. Furthermore, the role of monoclonal antibodies is being explored to provide added protection against COVID-19 to vulnerable populations, including cancer patients [114]. Thus, researchers are increasingly focused on developing vaccines that offer protection against the various emerging variants of the SARS-CoV-2 virus to provide more comprehensive immunity.

However, several limitations in the current body of research must be acknowledged. Most available data are derived from observational studies, which are subject to confounding variables and selection bias. Moreover, follow-up durations in many vaccine studies involving cancer patients remain relatively short, limiting insight into long-term immunity and safety. The evolving nature of SARS-CoV-2 variants also complicates interpretation, as vaccine efficacy may vary over time. There is also heterogeneity across patient populations, cancer types, and treatment regimens, making it difficult to generalize findings. As a result, ongoing and future studies must incorporate longer follow-ups, variant-specific immunity tracking, and stratified analyses by cancer subtype and immunosuppressive treatment.

Conclusion

COVID-19 vaccines are highly effective and safe for cancer patients; there are significant challenges in ensuring optimal efficacy. A single dose of COVID-19 vaccines yields a weaker immune response in cancer patients compared to healthy individuals. Moreover, seroconversion in patients with hematological malignancies is significantly lower than that in patients with solid tumors. Booster doses elicit a higher immune response and are highly recommended for cancer patients. Continuous monitoring and personalized vaccination approaches are crucial for enhancing the effectiveness of vaccines in this high-risk population. Future research should focus on refining vaccination protocols, investigating next-generation vaccines, and assessing the

efficacy of effective antiviral therapies, such as monoclonal antibodies, in providing long-term protection against COVID-19 in cancer patients.

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Data Availability The manuscript includes all necessary data, and related data may be provided upon request from the corresponding author/s.

Declarations

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References

- Hu B, Guo H, Zhou P, Shi ZL (2021) Characteristics of SARS-CoV-2 and COVID-19. *Nat Rev Microbiol* 19(3):141–154. <https://doi.org/10.1038/s41579-020-00459-7>
- COVID-19 cases | WHO COVID-19 dashboard. <https://data.who.int/dashboards/covid19/cases> Accessed on 06 Apr 2025
- Grivas P, Khaki AR, Wise-Draper TM et al (2021) Association of clinical factors and recent anticancer therapy with COVID-19 severity among patients with cancer: a report from the COVID-19 and Cancer Consortium. *Ann Oncol* 32(6):787–800. <https://doi.org/10.1016/j.annonc.2021.02.024>
- Mandal A, Singh P, Samaddar A et al (2021) Vaccination of cancer patients against COVID-19: towards the end of a dilemma. *Med Oncol* 38(8):92. <https://doi.org/10.1007/s12032-021-01540-8>
- Seneviratne SL, Yasawardene P, Wijerathne W, Somawardana B (2022) COVID-19 vaccination in cancer patients: a narrative review. *J Int Med Res* 50(3):03000605221086155. <https://doi.org/10.1177/03000605221086155>
- Belsky JA, Tullius BP, Lamb MG, Sayegh R, Stanek JR, Auletta JJ (2021) COVID-19 in immunocompromised patients: a systematic review of cancer, hematopoietic cell and solid organ transplant patients. *J Infect* 82(3):329–338. <https://doi.org/10.1016/j.jinf.2021.01.022>
- Rüthrich MM, Borgmann S, Classen AY et al (2021) COVID-19 in cancer patients: clinical characteristics and outcome—an analysis of the LEOSS registry. *Ann Hematol* 100(2):383–393. <https://doi.org/10.1007/s00277-020-04328-4>
- Wu JTY, La J, Branch-Elliman W et al (2022) Association of COVID-19 vaccination with SARS-CoV-2 infection in patients with cancer: a US nationwide veterans affairs study. *JAMA Oncol* 8(2):281. <https://doi.org/10.1001/jamaoncol.2021.5771>
- Kwok M, Fritsch EF, Wu CJ (2021) Cancer and COVID-19: on the quest for effective vaccines. *Blood Cancer Discov* 2(1):13–18. <https://doi.org/10.1158/2643-3230.BCD-20-0205>
- Parkman CA (2001) Therapies for cancer. *Case Manag* 12(2):30–32. <https://doi.org/10.1067/mcm.2001.114441>

11. Wang W, Kaelber DC, Xu R, Berger NA (2022) Breakthrough SARS-CoV-2 infections, hospitalizations, and mortality in vaccinated patients with cancer in the US between December 2020 and November 2021. *JAMA Oncol* 8(7):1027. <https://doi.org/10.1001/jamaoncol.2022.1096>
12. Ollila TA, Lu S, Masel R et al (2021) Antibody response to COVID-19 vaccination in adults with hematologic malignant disease. *JAMA Oncol* 7(11):1714. <https://doi.org/10.1001/jamaoncol.2021.4381>
13. Khawaja F, Angelidakis G, Feldman A et al (2023) COVID-19 in cancer patients: the impact of vaccination on outcomes early in the pandemic. *Cancer Med* 12(24):22006–22022. <https://doi.org/10.1002/cam4.6781>
14. WHO – COVID-19 vaccine tracker. <https://covid19.trackvaccines.org/agency/who/Accessed> on 06 Apr 2025
15. Ahmed S, Khan S, Imran I et al (2021) Vaccine development against COVID-19: study from pre-clinical phases to clinical trials and global use. *Vaccines* 9(8):836. <https://doi.org/10.3390/vaccines9080836>
16. Cai C, Peng Y, Shen E et al (2021) A comprehensive analysis of the efficacy and safety of COVID-19 vaccines. *Mol Ther* 29(9):2794–2805. <https://doi.org/10.1016/j.ymthe.2021.08.001>
17. Kotecha RS (2022) COVID-19 vaccination for children with cancer. *Pediatr Blood Cancer* 69(2):e29340. <https://doi.org/10.1002/pbc.29340>
18. Shear SL, Shams K, Weisberg J, Hamidi N, Scott SC (2023) COVID-19 vaccination safety profiles in patients with solid tumour cancers: a systematic review. *Clin Oncol* 35(7):e421–e433. <https://doi.org/10.1016/j.clon.2023.03.006>
19. Benitez Fuentes JD, Mohamed Mohamed K, de Luna Aguilar A, Jiménez García C, Guevara-Hoyer K, Fernandez-Arquero M, de la Rodríguez Peña M Antonia, García Bravo Laura, Jiménez Ortega Alejandro Francisco, Flores Navarro Paloma, Bartolome Arcilla Jorge, Alonso Arenilla Bárbara, Baos Muñoz Elvira, Delgado-Iribarren García-Campero Alberto, Montealegre Sanz María, Sanchez-Ramon Silvia, Perez Segura P (2022) Evidence of exhausted lymphocytes after the third anti-SARS-CoV-2 vaccine dose in cancer patients. *Front Oncol* 12:975980
20. Codacci-Pisanelli G, Giuliani J, Bonetti A (2021) The effect of COVID-19 pandemic on daily oncology clinical practice. *Crit Rev Oncol Hematol* 167:103272. <https://doi.org/10.1016/j.critrevonc.2021.103272>
21. Lee LY, Cazier JB, Angelis V et al (2020) COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. *Lancet* 395(10241):1919–1926. [https://doi.org/10.1016/S0140-6736\(20\)31173-9](https://doi.org/10.1016/S0140-6736(20)31173-9)
22. Garassino MC, Whisenant JG, Huang LC et al (2020) COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study. *Lancet Oncol* 21(7):914–922. [https://doi.org/10.1016/S1470-2045\(20\)30314-4](https://doi.org/10.1016/S1470-2045(20)30314-4)
23. Ma J, Yin J, Qian Y, Wu Y (2020) Clinical characteristics and prognosis in cancer patients with COVID-19: a single center's retrospective study. *J Infect* 81(2):318–356. <https://doi.org/10.1016/j.jinf.2020.04.006>
24. Goudsmit A, Cubilier E, Meert AP et al (2021) Factors associated with SARS-CoV-2 infection and outcome in patients with solid tumors or hematological malignancies: a single-center study. *Support Care Cancer* 29(11):6271–6278. <https://doi.org/10.1007/s00520-021-06175-z>
25. Assaad S, Avrillon V, Fournier ML et al (2020) High mortality rate in cancer patients with symptoms of COVID-19 with or without detectable SARS-CoV-2 on RT-PCR. *Eur J Cancer* 135:251–259. <https://doi.org/10.1016/j.ejca.2020.05.028>
26. Avdeev S, Moiseev S, Brovko M et al (2020) Low prevalence of bronchial asthma and chronic obstructive lung disease among intensive care unit patients with COVID-19. *Allergy* 75(10):2703–2704. <https://doi.org/10.1111/all.14420>
27. Dai M, Liu D, Liu M et al (2020) Patients with cancer appear more vulnerable to SARS-CoV-2: a multicenter study during the COVID-19 outbreak. *Cancer Discov* 10(6):783–791. <https://doi.org/10.1158/2159-8290.CD-20-0422>
28. Vijenthira A, Gong IY, Fox TA et al (2020) Outcomes of patients with hematologic malignancies and COVID-19: a systematic review and meta-analysis of 3377 patients. *Blood* 136(25):2881–2892. <https://doi.org/10.1182/blood.2020008824>
29. Zambelli A, Chiudinelli L, Fotia V et al (2021) Prevalence and clinical impact of SARS-CoV-2 silent carriers among actively treated patients with cancer during the COVID-19 pandemic. *Oncologist* 26(4):341–347. <https://doi.org/10.1002/onco.13654>
30. Guo M, Liu J, Miao R et al (2022) A single center retrospective study of the impact of COVID-19 infection on immune-related adverse events in cancer patients receiving immune checkpoint inhibitors. *J Immunother* 45(9):389–395. <https://doi.org/10.1097/CJI.0000000000000440>
31. Ma Y, Liu N, Wang Y et al (2021) Immune checkpoint blocking impact and nomogram prediction of COVID-19 inactivated vaccine seroconversion in patients with cancer: a propensity-score matched analysis. *J Immunother Cancer* 9(11):e003712. <https://doi.org/10.1136/jitc-2021-003712>
32. COVID-19 vaccines | WHO COVID-19 dashboard. <https://data.who.int/dashboards/covid19/vaccines> Accessed on 06 Apr 2025
33. Monin L, Laing AG, Muñoz-Ruiz M et al (2021) 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* 22(6):765–778. [https://doi.org/10.1016/S1470-2045\(21\)00213-8](https://doi.org/10.1016/S1470-2045(21)00213-8)
34. Polack FP, Thomas SJ, Kitchin N et al (2020) Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. *N Engl J Med* 383(27):2603–2615. <https://doi.org/10.1056/NEJMoa2034577>
35. Thakkar A, Gonzalez-Lugo JD, Goradia N et al (2021) Seroconversion rates following COVID-19 vaccination among patients with cancer. *Cancer Cell* 39(8):1081–1090.e2. <https://doi.org/10.1016/j.ccell.2021.06.002>
36. Herishanu Y, Avivi I, Aharon A et al (2021) Efficacy of the BNT162b2 mRNA COVID-19 vaccine in patients with chronic lymphocytic leukemia. *Blood* 137(23):3165–3173. <https://doi.org/10.1182/blood.2021011568>
37. Pimpinelli F, Marchesi F, Piaggio G et al (2021) Fifth-week immunogenicity and safety of anti-SARS-CoV-2 BNT162b2 vaccine in patients with multiple myeloma and myeloproliferative malignancies on active treatment: preliminary data from a single institution. *J Hematol Oncol* 14(1):81. <https://doi.org/10.1186/s13045-021-01090-6>
38. Ge C, Du K, Luo M et al (2022) Serologic response and safety of COVID-19 vaccination in HSCT or CAR T-cell recipients: a systematic review and meta-analysis. *Exp Hematol Oncol* 11(1):46. <https://doi.org/10.1186/s40164-022-00299-6>
39. Ruiz JI, Lopez-Olivo MA, Geng Y, Suarez-Almazor ME (2023) COVID-19 vaccination in patients with cancer receiving immune checkpoint inhibitors: a systematic review and meta-analysis. *J Immunother Cancer* 11(2):e006246. <https://doi.org/10.1136/jitc-2022-006246>
40. Chen YW, Tucker MD, Beckermann KE, Iams WT, Rini BI, Johnson DB (2021) COVID-19 mRNA vaccines and immune-related adverse events in cancer patients treated with immune checkpoint inhibitors. *Eur J Cancer* 155:291–293. <https://doi.org/10.1016/j.ejca.2021.07.017>
41. Oosting SF, Van Der Veldt AAM, GeurtsvanKessel CH et al (2021) mRNA-1273 COVID-19 vaccination in patients receiving chemotherapy, immunotherapy, or chemoimmunotherapy for solid tumours: a prospective, multicentre, non-inferiority

- trial. *Lancet Oncol* 22(12):1681–1691. [https://doi.org/10.1016/S1470-2045\(21\)00574-X](https://doi.org/10.1016/S1470-2045(21)00574-X)
42. Lasagna A, Agustoni F, Percivalle E et al (2021) A snapshot of the immunogenicity, efficacy and safety of a full course of BNT162b2 anti-SARS-CoV-2 vaccine in cancer patients treated with PD-1/PD-L1 inhibitors: a longitudinal cohort study. *ESMO Open* 6(5):100272. <https://doi.org/10.1016/j.esmoop.2021.100272>
 43. Waissengrin B, Agbarya A, Safadi E, Padova H, Wolf I (2021) Short-term safety of the BNT162b2 mRNA COVID-19 vaccine in patients with cancer treated with immune checkpoint inhibitors. *Lancet Oncol* 22(5):581–583. [https://doi.org/10.1016/S1470-2045\(21\)00155-8](https://doi.org/10.1016/S1470-2045(21)00155-8)
 44. Strobel SB, Machiraju D, Kälber KA, Hassel JC (2022) Immune-related adverse events of COVID-19 vaccination in skin cancer patients receiving immune-checkpoint inhibitor treatment. *Cancer Immunol Immunother* 71(8):2051–2056. <https://doi.org/10.1007/s00262-021-03133-w>
 45. Mieczkowska K, Kaubisch A, McLellan BN (2021) Exacerbation of psoriasis following COVID-19 vaccination in a patient previously treated with PD-1 inhibitor. *DermatolTher* 34(5). <https://doi.org/10.1111/dth.15055>
 46. Blaise M, Rocher F, Spittler H, et al (2022) Severe necrotizing myopathy after COVID-19 vaccine with BNT162b2 and regimen with ipilimumab plus nivolumab in a patient with advanced melanoma. *J EurAcadDermatolVenereol* 36(2). <https://doi.org/10.1111/jdv.17760>
 47. Au L, Fendler A, Shepherd STC et al (2021) Cytokine release syndrome in a patient with colorectal cancer after vaccination with BNT162b2. *Nat Med* 27(8):1362–1366. <https://doi.org/10.1038/s41591-021-01387-6>
 48. Cines DB, Bussel JB (2021) SARS-CoV-2 vaccine-induced immune thrombotic thrombocytopenia. *N Engl J Med* 384(23):2254–2256. <https://doi.org/10.1056/NEJMe2106315>
 49. See I, Su JR, Lale A et al (2021) US case reports of cerebral venous sinus thrombosis with thrombocytopenia after Ad26.COV2.S vaccination, march 2 to april 21, 2021. *JAMA* 325(24):2448. <https://doi.org/10.1001/jama.2021.7517>
 50. Hafeez MU, Ikram M, Shafiq Z et al (2021) COVID-19 vaccine-associated thrombosis with thrombocytopenia syndrome (TTS): a systematic review and post hoc analysis. *Clinical and Applied Thrombosis/Hemostasis* 27:10760296211048816. <https://doi.org/10.1177/10760296211048816>
 51. Coronavirus vaccine—weekly summary of Yellow Card reporting. GOV.UK. 2021. <https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting>. Accessed 06 Apr 2025
 52. Pottgård A, Lund LC, Karlstad Ø, et al (2021) Arterial events, venous thromboembolism, thrombocytopenia, and bleeding after vaccination with Oxford-AstraZeneca ChAdOx1-S in Denmark and Norway: population based cohort study. *BMJ*. Published online May 5 n1114. <https://doi.org/10.1136/bmj.n1114>
 53. MHRA issues new advice, concluding a possible link between COVID-19 vaccine AstraZeneca and extremely rare, unlikely to occur blood clots - GOV.UK
 54. Østergaard SD, Schmidt M, Horváth-Puhó E, Thomsen RW, Sørensen HT (2021) Thromboembolism and the Oxford–AstraZeneca COVID-19 vaccine: side-effect or coincidence? *Lancet* 397(10283):1441–1443. [https://doi.org/10.1016/S0140-6736\(21\)00762-5](https://doi.org/10.1016/S0140-6736(21)00762-5)
 55. Lee E, Cines DB, Gernsheimer T et al (2021) Thrombocytopenia following Pfizer and Moderna SARS-CoV-2 vaccination. *Am J Hematol* 96(5):534–537. <https://doi.org/10.1002/ajh.26132>
 56. FDA and CDC lift recommended pause on Johnson & Johnson (Janssen) COVID-19 vaccine use following thorough safety review _ FDA
 57. Shimabukuro TT, Cole M, Su JR (2021) Reports of anaphylaxis after receipt of mRNA COVID-19 vaccines in the US—december 14, 2020–january 18, 2021. *JAMA* 325(11):1101. <https://doi.org/10.1001/jama.2021.1967>
 58. Shimabukuro T, Nair N (2021) Allergic reactions including anaphylaxis after receipt of the first dose of Pfizer-BioNTech COVID-19 vaccine. *JAMA* 325(8):780. <https://doi.org/10.1001/jama.2021.0600>
 59. Klein NP, Lewis N, Goddard K et al (2021) Surveillance for adverse events after COVID-19 mRNA vaccination. *JAMA* 326(14):1390. <https://doi.org/10.1001/jama.2021.15072>
 60. Blumenthal KG, Robinson LB, Camargo CA et al (2021) Acute allergic reactions to mRNA COVID-19 vaccines. *JAMA* 325(15):1562. <https://doi.org/10.1001/jama.2021.3976>
 61. Hashimoto T, Ozaki A, Bhandari D, Sawano T, Sah R, Tanimoto T (2021) High anaphylaxis rates following vaccination with the Pfizer BNT162b2 mRNA vaccine against COVID-19 in Japanese healthcare workers: a secondary analysis of initial post-approval safety data. *J Travel Med* 28(7):taab090. <https://doi.org/10.1093/jtm/taab090>
 62. CDC COVID-19 Response Team, (2021) Food and Drug Administration. Allergic reactions including anaphylaxis after receipt of the first dose of Moderna COVID-19 vaccine — United States, December 21, 2020–January 10, 2021. *MMWR Morb Mortal Wkly Rep*. 70(4):125–129. <https://doi.org/10.15585/mmwr.mm7004e1>
 63. CDC. CDC Works 24/7. Centers for disease control and prevention. 2021. <https://www.cdc.gov/index.htm>. Accessed 06 Apr 2025
 64. Canada PHA of. COVID-19 vaccine safety: weekly report on side effects following immunization. aem. 2021. <https://healthinfobase.canada.ca/covid-19/vaccine-safety/Accessed> 06 Apr 2025
 65. European database of suspected adverse drug reaction reports. 2021. <https://www.adrreports.eu/>. Accessed 20 Oct 2021. Accessed 06 Apr 2025
 66. Sobczak M, Pawliczak R (2022) The risk of anaphylaxis behind authorized COVID-19 vaccines: a meta-analysis. *ClinMol Allergy* 20(1):1. <https://doi.org/10.1186/s12948-022-00167-y>
 67. Lim XR, Leung BP, Ng CYL et al (2021) Pseudo-anaphylactic reactions to Pfizer BNT162b2 vaccine: report of 3 cases of anaphylaxis post Pfizer BNT162b2 vaccination. *Vaccines* 9(9):974. <https://doi.org/10.3390/vaccines9090974>
 68. Barth I, Weißer K, Gaston-Tischberger D, Mahler V, Keller-Stanislawski B (2023) Anaphylactic reactions after COVID-19 vaccination in Germany. *Allergol Sel* 7(1):90–100. <https://doi.org/10.5414/ALX02374E>
 69. Song JE, Oh GB, Park HK, Lee SS, Kwak YG (2021) Survey of adverse events after the first dose of the ChAdOx1 nCoV-19 vaccine: a single-center experience in Korea. *Infect Chemother* 53(3):557. <https://doi.org/10.3947/ic.2021.0044>
 70. (ARCHIVED) Reports of events managed as anaphylaxis following COVID-19 vaccines in Ontario_ December 13, 2020 to March 6, 2021 - covid-19-anaphylaxis-epi-summary.
 71. Management of anaphylaxis at COVID-19 vaccination sites | CDC. <https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html> Accessed on 06 Apr 2025
 72. Clarification on the COVID-19 vaccine allergies | WHO | Regional Office for Africa. <https://www.afro.who.int/news/clarification-covid-19-vaccine-allergies> Accessed on 06 Apr 2025
 73. Corti C, Antonarelli G, Scotté F et al (2022) Seroconversion rate after vaccination against COVID-19 in patients with cancer—a

- systematic review. *Ann Oncol* 33(2):158–168. <https://doi.org/10.1016/j.annonc.2021.10.014>
74. Becerril-Gaitan A, Vaca-Cartagena BF, Ferrigno AS et al (2022) Immunogenicity and risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection after coronavirus disease 2019 (COVID-19) vaccination in patients with cancer: a systematic review and meta-analysis. *Eur J Cancer* 160:243–260. <https://doi.org/10.1016/j.ejca.2021.10.014>
 75. Uaprasert N, Pitakkitnukun P, Tangcheewinsirikul N, Chiasakul T, Rojnuckarin P (2022) Immunogenicity and risks associated with impaired immune responses following SARS-CoV-2 vaccination and booster in hematologic malignancy patients: an updated meta-analysis. *Blood Cancer J* 12(12):173. <https://doi.org/10.1038/s41408-022-00776-5>
 76. Debie Y, Vandamme T, Goossens ME, Van Dam PA, Peeters M (2022) Antibody titres before and after a third dose of the SARS-CoV-2 BNT162b2 vaccine in patients with cancer. *Eur J Cancer* 163:177–179. <https://doi.org/10.1016/j.ejca.2021.12.025>
 77. Lee ARYB, Wong SY, Chai LYA, et al (2022) Efficacy of COVID-19 vaccines in immunocompromised patients: systematic review and meta-analysis. *BMJ*. Published online March 2 e068632. <https://doi.org/10.1136/bmj-2021-068632>
 78. Martins-Branco D, Nader-Marta G, Tecic Vuger A et al (2023) Immune response to anti-SARS-CoV-2 prime-vaccination in patients with cancer: a systematic review and meta-analysis. *J Cancer Res Clin Oncol* 149(7):3075–3080. <https://doi.org/10.1007/s00432-022-04185-w>
 79. Gagelmann N, Passamonti F, Wolschke C et al (2021) Antibody response after vaccination against SARS-CoV-2 in adults with hematological malignancies: a systematic review and meta-analysis. *Haematologica* 107(8):1840–1849. <https://doi.org/10.3324/haematol.2021.280163>
 80. Martins-Branco D, Nader-Marta G, Tecic Vuger A, Debie Y, Ameye L, Brandão M, Punie Kevin, Loizidou Angela, Willard-Gallo Karen, Spilleboudt Chloe, Awada Ahmad, Piccart Martine, De Azambuja E (2023) Immune response to anti-SARS-CoV-2 prime-vaccination in patients with cancer: a systematic review and meta-analysis. *J Cancer Res Clin Oncol* 149(7):3075–3080
 81. Fendler A, Shepherd STC, Au L et al (2022) Immune responses following third COVID-19 vaccination are reduced in patients with hematological malignancies compared to patients with solid cancer. *Cancer Cell* 40(2):114–116. <https://doi.org/10.1016/j.ccell.2021.12.013>
 82. Luangdilok S, Wanchajiraboon P, Pakvisal N et al (2022) Immunogenicity after a third COVID-19 mRNA booster in solid cancer patients who previously received the primary heterologous CoronaVac/ChAdOx1 vaccine. *Vaccines* 10(10):1613. <https://doi.org/10.3390/vaccines10101613>
 83. Debie Y, Van Dam PA, Goossens ME, Peeters M, Vandamme T (2023) Boosting capacity of a fourth dose BNT162b2 in cancer patients. *Eur J Cancer* 179:121–123. <https://doi.org/10.1016/j.ejca.2022.11.016>
 84. Ehmsen S, Asmussen A, Jeppesen SS et al (2022) Increased antibody titers and reduced seronegativity following fourth mRNA COVID-19 vaccination in patients with cancer. *Cancer Cell* 40(8):800–801. <https://doi.org/10.1016/j.ccell.2022.06.012>
 85. Haggensburg S, Hofsink Q, Lissenberg-Witte BI et al (2022) Antibody response in immunocompromised patients with hematologic cancers who received a 3-dose mRNA-1273 vaccination schedule for COVID-19. *JAMA Oncol* 8(10):1477. <https://doi.org/10.1001/jamaoncol.2022.3227>
 86. Greenberger LM, Saltzman LA, Senefeld JW, Johnson PW, DeGennaro LJ, Nichols GL (2021) Antibody response to SARS-CoV-2 vaccines in patients with hematologic malignancies. *Cancer Cell* 39(8):1031–1033. <https://doi.org/10.1016/j.ccell.2021.07.012>
 87. Teh JSK, Coussement J, Neoh ZCF et al (2022) Immunogenicity of COVID-19 vaccines in patients with hematologic malignancies: a systematic review and meta-analysis. *Blood Adv* 6(7):2014–2034. <https://doi.org/10.1182/bloodadvances.202106333>
 88. Fendler A, Shepherd STC, Au L et al (2022) Functional immune responses against SARS-CoV-2 variants of concern after fourth COVID-19 vaccine dose or infection in patients with blood cancer. *Cell Rep Med* 3(10):100781. <https://doi.org/10.1016/j.xcrm.2022.100781>
 89. Sherman AC, Desjardins M, Cheng CA et al (2022) Severe acute respiratory syndrome coronavirus 2 messenger RNA vaccines in allogeneic hematopoietic stem cell transplant recipients: immunogenicity and reactivity. *Clin Infect Dis* 75(1):e920–e923. <https://doi.org/10.1093/cid/ciab930>
 90. Gong IY, Vijenthira A, Powis M et al (2023) Association of COVID-19 vaccination with breakthrough infections and complications in patients with cancer. *JAMA Oncol* 9(3):386. <https://doi.org/10.1001/jamaoncol.2022.6815>
 91. Schmidt AL, Labaki C, Hsu CY et al (2022) COVID-19 vaccination and breakthrough infections in patients with cancer. *Ann Oncol* 33(3):340–346. <https://doi.org/10.1016/j.annonc.2021.12.006>
 92. Sgherza N, Mestice A, Larocca AMV, Musto P (2024) Antibody response to breakthrough SARS-CoV-2 infection in “booster” vaccinated patients with multiple myeloma according to B/T/NK lymphocyte absolute counts and anti-CD38 treatments. *Mediterr J Hematol Infect Dis* 16(1):e2024022. <https://doi.org/10.4084/MJHID.2024.022>
 93. Saini KS, Martins-Branco D, Tagliamento M et al (2021) Emerging issues related to COVID-19 vaccination in patients with cancer. *Oncol Ther* 9(2):255–265. <https://doi.org/10.1007/s40487-021-00157-1>
 94. Mancuso K, Zamagni E, Solli V et al (2023) Long term follow-up of humoral and cellular response to mRNA-based vaccines for SARS-CoV-2 in patients with active multiple myeloma. *Front Oncol* 13:1208741. <https://doi.org/10.3389/fonc.2023.1208741>
 95. Schmidt KLJ, Severeijns NR, Dautzenberg NMM et al (2024) Long-term immunity after BNT162b2 mRNA COVID-19 vaccination in pediatric patients with cancer. *EJC Paediatric Oncology* 4:100172. <https://doi.org/10.1016/j.ejcped.2024.100172>
 96. Heudel P, Favier B, Solodky ML et al (2022) Survival and risk of COVID-19 after SARS-COV-2 vaccination in a series of 2391 cancer patients. *Eur J Cancer* 165:174–183. <https://doi.org/10.1016/j.ejca.2022.01.035>
 97. Meza L, Zengin Z, Salgia S et al (2023) Twelve-month follow-up of the immune response after COVID-19 vaccination in patients with genitourinary cancers: a prospective cohort analysis. *Oncologist* 28(9):e748–e755. <https://doi.org/10.1093/oncolo/oyad067>
 98. Giuseppe M, Claudia R, Antonella M, Angelo S, Domenico P (2022) Long follow-up of symptomatic multiple myeloma patients after COVID-19 vaccination (BNT162b2): a single-institution retrospective experience. *Leuk Res Rep* 18:100342. <https://doi.org/10.1016/j.lrr.2022.100342>
 99. Rottenberg Y, Grinshpun A, Ben-Dov IZ, Oiknine-Djian E, Wolf DG, Kadouri L (2022) Assessment of response to a third dose of the SARS-CoV-2 BNT162b2 mRNA vaccine in patients with solid tumors undergoing active treatment. *JAMA Oncol* 8(2):300. <https://doi.org/10.1001/jamaoncol.2021.6764>
 100. Thakkar A, Pradhan K, Duva B et al (2023) Study of efficacy and longevity of immune response to third and fourth doses of COVID-19 vaccines in patients with cancer: a single arm clinical trial. *Elife* 12:e83694. <https://doi.org/10.7554/eLife.83694>

101. Tan WC, Tan JYJ, Lim JSJ et al (2023) COVID-19 severity and waning immunity after up to 4 mRNA vaccine doses in 73 608 patients with cancer and 621 475 matched controls in Singapore: a nationwide cohort study. *JAMA Oncol* 9(9):1221. <https://doi.org/10.1001/jamaoncol.2023.2271>
102. Shah R, Hanna NM, Loo CE, David M, Mafra A, Fink H, McFerran Ethna, Garcia Montse, Ghodssighassemabadi Robabeh, Acharya Suryakanta, Niyibaga Jean, Langselius Oliver, Frick Clara, Lasebikan Nwamaka, Vignat Jerome, Steinberg Julia, Hughes Suzanne, Kircher Colleen Elizabeth, Goldie Catherine Lindsay, Egger Sam, Sullivan Richard, Ginsburg Ophira, Bray Freddie, Caruana Michael, Hui Harriet, Ilbawi André Michel, Canfell Karen, Soerjomataram I (2025) The global impact of the COVID-19 pandemic on delays and disruptions in cancer care services: a systematic review and meta-analysis. *Nat Cancer* (1). <https://doi.org/10.1038/s43018-024-00880-4>
103. Mondaca S, Walbaum B, Le Corre N et al (2023) Influence of SARS-CoV-2 mRNA vaccine booster among cancer patients on active treatment previously immunized with inactivated versus mRNA vaccines: a prospective cohort study. *Vaccines* 11(7):1193. <https://doi.org/10.3390/vaccines11071193>
104. Mai AS, Lee ARYB, Tay RYK et al (2022) Booster doses of COVID-19 vaccines for patients with haematological and solid cancer: a systematic review and individual patient data meta-analysis. *Eur J Cancer* 172:65–75. <https://doi.org/10.1016/j.ejca.2022.05.029>
105. Lee LYW, Ionescu MC, Starkey T et al (2022) COVID-19: third dose booster vaccine effectiveness against breakthrough coronavirus infection, hospitalisations and death in patients with cancer: a population-based study. *Eur J Cancer* 175:1–10. <https://doi.org/10.1016/j.ejca.2022.06.038>
106. Panou E, Nikolaou V, Marinos L et al (2022) Recurrence of cutaneous T-cell lymphoma post viral vector COVID-19 vaccination. *J Eur Acad Dermatol Venereol* 36(2). <https://doi.org/10.1111/jdv.17736>
107. Gambichler T, Boms S, Hessam S et al (2021) Primary cutaneous anaplastic large-cell lymphoma with marked spontaneous regression of organ manifestation after SARS-CoV-2 vaccination. *Br J Dermatol* 185(6):1259–1262. <https://doi.org/10.1111/bjd.20630>
108. Sousa LGD, McGrail DJ, Li K et al (2022) Spontaneous tumor regression following COVID-19 vaccination. *J Immunother Cancer* 10(3):e004371. <https://doi.org/10.1136/jitc-2021-004371>
109. Kamboj M, Bohlke K, Baptiste DM et al (2024) Vaccination of adults with cancer: ASCO guideline. *J Clin Oncol* 42(14):1699–1721. <https://doi.org/10.1200/JCO.24.00032>
110. NCCN cancer and COVID-19 vaccination. <https://www.eviq.org.au/getmedia/6de8cf1f-54d5-4c5d-9045-f3b5ff384bbc/2021-covid-19-vaccination-guidance-v8-0.pdf.aspx> Accessed on 06 Apr 2025
111. Garassino MC, Vyas M, De Vries EGE, Kanesvaran R, Giuliani R, Peters S (2021) The ESMO call to action on COVID-19 vaccinations and patients with cancer: vaccinate. monitor educate. *Ann Oncol* 32(5):579–581. <https://doi.org/10.1016/j.annonc.2021.01.068>
112. Al-Fattah Yahaya AA, Khalid K, Lim HX, Poh CL (2023) Development of next generation vaccines against SARS-CoV-2 and variants of concern. *Viruses* 15(3):624. <https://doi.org/10.3390/v15030624>
113. Shah R, Loo CE, Hanna NM, Hughes S, Mafra A, Fink H, ... & Soerjomataram, I (2024) Global review of COVID-19 mitigation strategies and their impact on cancer service disruptions. *J Cancer Policy* 41, 100486.3
114. Campagna R, Dominelli F, Zingaropoli MA, Ciurluini F, Grilli G, Amoroso A, De Domenico Angelo, Amatore Donatella, Lia Maria Stella, Cortesi Enrico, Picone Vincenzo, Mastroianni Claudio Maria, Ciardi Maria Rosa, De Santis Riccardo, Lista Florigio, Antonelli Guido, Turriziani O (2024) COVID-19 vaccination in cancer patients: immune responses one year after the third dose. *Vaccine* 42(10):2687–2694

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