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Review

The Efficacy and Immunogenicity of COVID-19 Vaccine: Special Focus on Patients with Cancer

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Abstract: Research indicates that immunization is the most efficacious approach for stopping the transmission of COVID-19. This study aims to offer immunization recommendations for patients with autoimmune/ autoinflammatory rheumatological disorders, immunodeficiencies, cancer, diabetes, chronic respiratory, and cardiovascular diseases. The intended audience includes doctors, medical personnel, and patients. This review study involved conducting a search in scholarly electronic databases, including ISI, Google Scholar, Scopus, and PubMed. The issue of COVID-19 vaccinations and the vaccination of patients with certain disorders was informed by the latest and pertinent authoritative publications published between 1980 and 2024. When autoimmune illness patients effectively manage their disease activity and there is no concurrent infection, they should receive the COVID-19 vaccination. Low-intensity immunosuppression does not reduce the antibody response to vaccinations. Immunization using all forms of vaccination, excluding live attenuated vaccines, is efficacious for all individuals with cancer, except for those undergoing anti-B cell therapy. Additionally, it is recommended to administer vaccinations to individuals who have underlying conditions such as obesity, cardiovascular diseases, respiratory diseases, and diabetes, as these conditions heighten the chance of developing severe cases of COVID-19. To combat the COVID-19 virus, the most effective approach is to increase vaccination coverage in order to stimulate immune responses. This paper provides a thorough examination of the latest developments and existing challenges in the area of COVID-19 vaccines against cancer. Additionally, it explores the prospective future uses of vaccines in cancer immunotherapies.

Keywords: SARS-CoV-2 Virus; COVID-19; Vaccination; Vaccine Efficacy; mRNA Vaccine; Cancer

1. Introduction

To date, vaccination has proven to be the most effective means of disease control and prevention [1]. The effective creation and utilization of vaccines have spared countless lives. The sole means of protection against contagious diseases is vaccines. Instead, the emphasis is on using them to combat allergies and cancer. Molecular biology and immunology come together to create the innovative messenger RNA (mRNA) vaccination. Gene therapy intricately connects to this technology. Foreign mRNA containing genetic instructions for producing antigens penetrates so-

matic cells, stimulating antigen production and triggering an immune response via the cellular system [2]. The COVID-19 pandemic has brought significant attention to mRNA, the molecule responsible for conveying the cell's instructions for protein synthesis. Countless people worldwide have been administered mRNA vaccinations, which effectively protect against severe COVID-19 caused by the SARS-CoV-2 infection [3].

Cancer is the pathological proliferation of cells in the body caused by a disruption in their normal functioning. This can happen in any part of the body due to a malfunction in the cellular mechanisms that regulate cell division and reproduction. Consequently, old cells fail to die, and abnormal cells continue to grow and form. This leads to the formation of tumors and the manifestation of cancer symptoms [4]. Cancer vaccines are used either to treat established cancers (therapeutic vaccinations) or to prevent cancer (prophylactic vaccinations) [5]. Both forms of immunization have the ability to reduce the size of the cancer. Individuals with cancer receive therapeutic vaccinations designed to enhance their body's innate immune response against existing malignancies. These vaccinations aim to suppress the growth of current cancers, halt the recurrence of cured cancers, or eradicate cancer cells that previous treatments have failed to eliminate.Conversely, preventive vaccines are administered to those who are in good health and are specifically formulated to combat cancer-causing viruses and thwart viral infections.At present, the Food and Drug Administration has approved two vaccinations to prevent viral infections that can result in cancer [6].

The first vaccine available is the hepatitis B vaccine, which protects against the hepatitis B virus, an infectious pathogen linked to some forms of liver cancer. The Gardasil vaccine is another immunization that provides protection against two specific strains of human papillomavirus (HPV16 and HPV18). These strains are responsible for 70% of cervical cancer incidences globally [6]. Furthermore, Gardasil also provides protection against infections caused by HPV types 6 and 11 [7]. These two categories account for 90% of genital warts. At present, there are no officially authorized therapeutic vaccinations. Nevertheless, numerous therapeutic vaccines are undergoing rigorous testing on human subjects.

While the COVID-19 mRNA vaccines have proven remarkable, researchers have harbored a longstanding aspiration to employ mRNA vaccines for an entirely distinct objective: combating cancer. Researchers have been conducting small studies to test mRNA-based cancer therapy vaccines for nearly a decade, and their initial results have been encouraging [8]. Multiple clinical trials are underway to evaluate the efficacy of therapeutic mRNA vaccines in individuals diagnosed with different forms of cancer, such as pancreatic cancer, colorectal cancer, and melanoma [9]. Several vaccinations are currently undergoing evaluation in conjunction with immunomodulatory medicines to enhance the body's immune response against malignancies [10]. However, the US Food and Drug Administration has not yet licensed any mRNA cancer vaccine for standalone use or in conjunction with other cancer therapies. The future of mRNA vaccine technology faces the obstacle of not having a reliable mRNA delivery mechanism. This difficulty has persisted throughout many years of research and development, despite efforts to enhance the safety, efficacy, and scalability of mRNA vaccines. It has been elevated. mRNA-based vaccinations provide unique advantages, especially in the management of cancers and viral infections [11].

Phase I clinical trials have demonstrated the safety of mRNA vaccines in stimulating the production of antibodies. Nucleases swiftly break down the transcribed RNA [12]. While damaged mRNA components may cause excessive immune system activation, establishing an effective mRNA repair system can be beneficial. Enhance data and eliminate adverse consequences [13,14]. Researchers have extensively studied many delivery vectors and modified mRNAs to evaluate their therapeutic efficacy, particularly in the context of the COVID-19 pandemic [15–17]. Finally, significant mRNA vaccine manufacturing is moving towards industrialization.

2. Types of COVID-19 Vaccine Platforms

Since the onset of the COVID-19 pandemic, experts worldwide have been endeavoring to gain a more comprehensive understanding of the 2019 coronavirus. To develop effective vaccines and treatments against this virus, it is crucial to have a precise understanding of its structure and reproductive mechanisms. The spike protein is crucial for the virus to bind to cells in the body and cause disease [18]. Due to this factor, numerous coronavirus vaccines employ various mechanisms to target this specific region of the virus and activate the body's immune response. The primary platforms among them are the inactivated virus vaccine, the viral vector vaccine, the mRNA vaccine, and the recombinant protein vaccine [19]. The swift production and clinical advancement of efficient vaccines to mitigate the outbreak of SARS-CoV-2 is a demonstration of extensive research and progressive advancements in the fields of immunology, vaccinology, and adjuvant biology over the course of several decades. It has been sci-

entifically demonstrated to be more efficacious than anticipated in the battle against COVID-19, offering a fresh push for the field of vaccinology in relation to numerous other contagious illnesses. Several recent prominent and detailed review publications have already compared the specifics of vaccines, clinical trial data, parameters, and safety profiles. Therefore, it is unnecessary to reiterate those points here [20,21]. The time span between the identification of a novel pathogen sequence and the large-scale distribution of the vaccine was less than one year. Over a hundred vaccines have been created, with more than a hundred of them undergoing clinical testing. Currently, there are approximately 24 licensed vaccinations that are being utilized [22]. The success rates have been remarkably high, with a mere 10 sample vaccines being discarded during clinical testing due to inadequate effectiveness. Nevertheless, the field of vaccinology, which has achieved significant scientific advancements, has encountered an inequitable worldwide distribution [23]. Over 9 billion doses of the vaccine have been provided, which is sufficient to provide one dose to every eligible individual worldwide. However, there has been a significant transformation in the delivery of vaccines [24]. Currently, almost 50% of the global population remains unvaccinated, with just a mere 4% of individuals in low-income countries having received their initial vaccine dosage [25]. Comprehensive studies examining extensive research on vaccine efficacy consistently demonstrated an 80–90% success rate in preventing both symptomatic and asymptomatic diseases in individuals who completed the full vaccination regimen (**Table 1**). The majority of the studies included in the analysis showed a significant level of effectiveness. Three vaccines showed exceptional effectiveness (> 90%) in preventing COVID-19 infection during clinical trials: Pfizer-BioNTech (about 95%), Moderna (nearly 94%), and Sputnik V (roughly 92%). By comparison, the vaccines produced by Oxford-AstraZeneca demonstrated an efficacy rate of approximately 70%, while the Janssen vaccine exhibited an efficacy range of 54–72% against both mild and severe forms of COVID-19 infection. The mRNA vaccines have demonstrated notable efficacy in avoiding infection and provide a large level of protection against severe illness, hospitalization, and death. Moreover, the Moderna, Sputnik V, Janssen, and Oxford-AstraZeneca vaccines have demonstrated significant efficacy in reducing the likelihood of severe manifestations of COVID-19 infection and mortality. In contrast, the published studies for the Pfizer-BioNTech vaccine did not include this information. The Moderna vaccine surpasses the Pfizer vaccine in terms of temperature needs, as it permits higher storage and transit temperatures, therefore streamlining logistics. Several governments have issued Emergency Use Authorization (EUA) for multiple vaccines produced by various companies that have shown significant efficacy. Conducting a longitudinal assessment of vaccination recipients is crucial as it yields insights into whether immunization can confer long-lasting protection.

Table 1. Comparing the Effectiveness of Different COVID-19 Vaccines.

Study ID	Vaccine	Manufacturer	Platform	Target	Trial Phase	Effectiveness
Falsey et al., 2021 [26]	AZD1222 (ChA-dOx1nCoV19)	University of Oxford & AstraZeneca	chimpanzee adenoviral vector	spike protein; nCoV-19	III	74.0% (95% CI: 65.3 to 80.5; $P < 0.001$)
Halperin et al., 2022 [27]	Ad5-nCoV	CanSino Biologics	human adenovirus type 5	spike protein; nCoV-19	III	57·5% (95% CI: 39·7 to 70·0, $p = 0·0026$)
Sadoff et al., 2022 [28]	Ad26-SARS-CoV-2	Johnson & Johnson & Janssen	human adenovirus type 26	spike protein; nCoV-19	III	52.9% (95% CI: 47.1 to 58.1)
Logunov et al., 2021 [29]	Sputnik V	Gamaleya Research Institute of Epidemiology and Microbiology	Gam-COVID-Vac combined vector vaccine	spike protein; nCoV-19	III	91·6% (95% CI: 85.6 to 95.2)
Kimberly et al., 2022 [30]	INO-4800	Inovio Pharmaceuticals	plasmid DNA vaccine	spike protein; nCoV-19	II/III	———
Kow, Ramachandram and Hasan, 2022 [31]	BNT162b2	Pfizer–BioNTech	mRNA vaccine	NSP5 and Mpro	III	81% (95% CI: 69 to 88%)
Baden et al., 2021 [32]	mRNA-1273	Moderna and NIAID	mRNA vaccine	spike protein; nCoV-19	III	94.1% (95% CI: 89.3 to 96.8%; $P < 0.001$)

3. Immunogenicity of COVID-19 Vaccines

The global COVID-19 vaccination program has encountered notable obstacles in terms of vaccine safety and immunogenicity. However, it is worth noting that the program has maintained a commendable safety record, considering the administration of billions of vaccine doses across various age groups in over 180 countries. The vaccination rate in most countries exceeded initial projections. Reports emerged of severe or deadly negative occurrences, in-

cluding anaphylaxis, myocarditis, and occasionally fatal blood clotting events accompanied by a low platelet count. Events varied to some extent depending on the type of vaccination used. Adenovirus-based vaccinations specifically cause vaccine-induced thrombocytopenia and thrombosis (VITT) [33–35]. The adverse event reporting in the UK revealed a total of 260 cases of vaccine-induced thrombocytopenia (VITT) out of 31 million vaccine doses administered. These cases were more prevalent among younger individuals [36]. The mortality rate among the initial cases was 22%. There were a limited number of instances where individuals who received mRNA vaccinations experienced myocarditis and pericarditis. Reports from the United Kingdom indicate that there is an estimated excess of 1 to 2 cases of myocarditis per million for the first dose of AZ/ChadOx1 and Pfizer/BNT162b2 vaccines, and 6 cases per million for Moderna/mRNA-1273. In comparison, the incidence of myocarditis is much higher, at 40 cases per million during the month following the SARS-CoV-2 infection without vaccination [37].

4. Immunological Considerations of Current COVID-19 Vaccines

It was first thought that the interaction between the receptor-binding domain (RBD) of the spike protein and human angiotensin-converting enzyme 2 (ACE2) was the main way that the SARS-CoV-2 virus could be spread. Also producing high levels of neutralizing antibodies (nAbs) against specific areas of the virus, known as epitopes, would effectively prevent infection. This has resulted in a diverse range of strategies to achieve spike expression stability, whether or not it leads to immunity (**Table 2**). The mRNA vaccine platforms (Pfizer, Moderna) and adenovirus vaccine platforms (AstraZeneca, Gamaleya, Johnson & Johnson) that have been approved in clinical trials have been tested in different places and for different diseases. The majority of vaccination campaigns in Europe and North America began in late 2020 or early 2021, which delayed the gathering of sufficient data on vaccine durability and progressive infections until late 2021 [38]. The immune response to a live infection likely shows lower durability in comparison to the recurring vulnerability to human common cold viruses [39]. The levels of antibodies following vaccination with an mRNA vaccine are often higher compared to those following a viral infection. In contrast, the levels of antibodies following adenoviral vaccines are roughly similar to those seen after a viral infection. The levels of serum antibodies decline rapidly in the months following vaccination, although the strength and amount of the immune response greatly improve in people who have been infected and then vaccinated [40,41]. It took about 4 to 5 months for antibody levels to drop faster than expected in both infected and vaccinated groups, as shown by antibody binding assays or functional neutralization assays [42,43]. Based on the readiness of memory T and B cells, data on progression, hospitalizations, and deaths that happened at least 5 months after the second dose of the vaccine show that infection precursors have become much more common in order to lower the concentration of antibodies that fight infections [44]. Due to the significant impact of delta and omicron infections and reinfections, many nations have made it compulsory to administer a third booster dose of the vaccination [45]. The United States authorizes the administration of heterologous boosters 2 months after Johnson & Johnson immunizations and 6 months after mRNA vaccines. Knowing that an individual has received a vaccination reduces the likelihood of hospitalization and mortality. Furthermore, individuals who receive two or three doses of the vaccine can still contract the SARS-CoV-2 infection, potentially without showing symptoms, and transfer it to others [46]. The majority of countries currently prioritize mRNA vaccines for their booster programs. Given the expenses and logistical challenges associated with booster shots, this strategy restricts their broader availability. Stimulation of AZ/ChAdOx1 as a third dosage. Researchers have found that administering AZ/ChAdOx1 as a third dosage booster remains effective; people exposed to either adenovirus or mRNA amplification strongly link the presence of neutralizing antibodies to a high level of protection against illness from a circulating species of concern.

Table 2. Various Immune Responses Associated with Different COVID-19 Vaccines.

Vaccine Name	Types of Immune Responses		References
	Humoral	Cell-Mediated	
AZD1222 (ChAdOx1nCoV19)	Induced spike and receptor-binding domain (RBD) antibodies, especially IgG1 and IgG3 neutralizing antibody (nAb) titres	CD4+ and CD8+ T-cell responses IFNγ and IL-23 secretion	[47,48]
Ad5-nCoV	Induced spike and receptor-binding domain (RBD) antibodies neutralizing antibody (nAb) titres	Increasing T-cell IFNγ secretion	[49,50]

Table 2. *Cont.*

Vaccine Name	Types of Immune Responses		References
	Humoral	Cell-Mediated	
Ad26-SARS-CoV-2	Induced spike and receptor-binding domain (RBD) antibodies neutralizing antibody (nAb) titres	Spike-specific IFN-γ CD8+ and CD4+ T-cell responses	[51]
Sputnik V	Induced spike and receptor-binding domain (RBD) antibodies neutralizing antibody (nAb) titres	CD4+ and CD8+ T-cell responses IFNγ secretion	[52,53]
INO-4800	Induced spike and receptor-binding domain (RBD) antibodies neutralizing antibody (nAb) titres	CD4+ and CD8+ T-cell responses	[54,55]
BNT162b2	Induced spike and receptor-binding domain (RBD) antibodies neutralizing antibody (nAb) titres	CD4+ and CD8+ T-cell responses IFNγ and IL-23 secretion	[56,57]
mRNA-1273	Induced spike and receptor-binding domain (RBD) antibodies neutralizing antibody (nAb) titres	CD4+ and CD8+ T-cell responses IFNγ and TNF secretion	[58]

5. Safety of the COVID-19 Vaccine in Cancer

Breast cancer, also known as breast carcinoma, is a malignancy that originates in the breast tissue. Cancer initiation occurs when cellular proliferation becomes unregulated [59]. Breast cancer cells typically develop into a neoplasm, which is commonly detectable on X-rays or palpable as a mass. It is crucial to comprehend that the majority of breast lumps are benign, meaning they are not cancerous or malignant [60]. Benign breast tumors exhibit aberrant growth patterns, although they remain confined within the breast and do not metastasize. Although not life-threatening, certain benign breast tumors can increase the likelihood of developing breast cancer in women. Individuals diagnosed with cancer, especially metastatic cancer, blood cancers, and lung cancer, may undergo a more intense and serious disease progression. These individuals belong to a highly susceptible group and are at a significant risk of death due to infection [61]. COVID-19 vaccinations play a crucial role in mitigating the spread of diseases and minimizing the occurrence of severe cases. Nevertheless, individuals diagnosed with cancer are frequently not considered for vaccination at first due to the scarcity of data regarding the safety and effectiveness of standard vaccines in this specific group [62].**Table 3** provides a summary of the safety and types of vaccines used in breast cancer.

Table 3. Available Evidence About COVID-19 Vaccine in Breast Cancer.

Study ID	Vaccination Coverage	Frequency of Total AEs		Number of Patients	Type of Vaccine	Findings
		After 1st Dose	After 2nd Dose			
Zhang et al., 2023, China [63]	22.4%	13.3%	9.9%	15,455	BBIBP-CorV, CoronaVac, KCONVAC, and WIBP-CorV	Heightened favorable attitude and improved acceptance towards COVID-19 vaccinations
Forster et al., 2023, Germany [64]	94.7%	44.7%	———	114	BioNTech/Pfizer, AstraZeneca, and Moderna	The administration of COVID-19 vaccines is favorably correlated with an improvement in the HR-QoL in patients.
Xu et al., 2023, China [65]	50.2%	12.7%	14.7%	1,459	BBIBP-CorV, CoronaVac, KCONVAC, and WIBP-CorV	Promoting awareness and bolstering confidence in the safety of vaccines while undergoing cancer treatment.
Jiang et al., 2023, China [66]	58.1%	6.22%	———	479	Sinovac, Sinopharm, CanSinoBIO and Zifivax	Providing focused care and support to older survivors can enhance the rate of immunization.
De Placido et al., 2022, Italy [67]	74%	5%	———	50	BNT162b2	Immunization booster seems to be required
Joudi et al., 2022, Iran [68]	75%	———	———	160	BBIBP-CorV	Tolerable and effective method
Forster et al., 2021, Germany [69]	74.3%	22.5%	35.1%	218	BioNTech/Pfizer, Vaxzevria (AstraZeneca) and Moderna	Patients tolerate the vaccination
Zagouri et al., 2021, Greece [70]	84.4%	19.1%	———	161	BNT162b2, AZD1222 and mRNA-1273	Minimizing the ambiguity surrounding the level of SARS-CoV-2 immunity in cancer patients undergoing therapy

Note: HR-QoL: Health-Related Quality of Life.

Table 4 provides a summary of the seroconversion rates from several studies. We must emphasize that the

research followed the manufacturer's recommended vaccine schedule. However, we need more evidence to evaluate the immune response when we delay vaccinations. Researchers are studying COVID-19 vaccines for cancer patients. Only 38% of solid tumor patients and less than 20% of hematological malignancy patients developed detectable levels of anti-S IgG antibodies 21 days after receiving the initial vaccine dose, according to the SOAP-02 study. In contrast, 94% of healthy people had IgG antibodies. Researchers also examined the effects of a second vaccine dose. They found that 95% of solid cancer patients who received a booster shot 3 weeks after the original dosage produced anti-S IgG antibodies 2 weeks later. Only 30% of non-booster injection recipients had these antibodies. In another study, only 29% of solid cancer patients receiving systemic chemotherapy, immunotherapy, biological agents, or a combination of these treatments tested positive for antibodies after the first dosage. 84% of healthy people reported being positive. Around two weeks following a second dose, 86% of patients tested positive for antibodies. Several studies have evaluated the immunological response to the COVID-19 vaccination in solid or hematologic malignancies. After two doses of the COVID-19 vaccination, solid cancer patients had a 94% seroconversion rate, compared to 100% in healthy people. Chemotherapy patients have decreased anti-spike antibody levels. Two other studies found that 90% and 95% of solid cancer patients had a positive antibody response following their second vaccine dosage, compared to 100% of healthy controls. Patients with hematologic malignancies had lower seroconversion rates than healthy people. A study found 100% seroconversion in healthy people two weeks following the second vaccine dose. Multiple myeloma patients had a seroconversion rate of 78.6%, whereas CML and MPN patients had 88%. Additional research found that 39.5% of chronic lymphocytic leukemia (CLL) patients sustained seroconversion after two vaccination doses, compared to 100% of healthy controls. 84.2% of multiple myeloma patients and 100% of the control group showed a positive antibody response. In patients with hematologic malignancies, two vaccination doses lowered antibody levels compared to healthy individuals.

Table 4. Immunologic Response Rates in Patients with Cancer following Two Doses of COVID-19 Vaccine.

Study ID, Reference	Participants Cancer/Control	Vaccine Type	Cancer Type	Immune Response to Vaccine (%)			
				1st Cancer Group	2nd Cancer Group	Control Group	P-Values
Seropositivity (Anti-S IgG)							
Massarweh et al., 2021 [71]	102/78	BNT162b2	Solid tumors	90%	———	100%	———
Addeo et al., 2021 [72]	101/22	BNT162b2 and mRNA-1273	Solid tumors and hematological malignancy	98%	77%	———	0.002
Monin et al., 2021 [73]	95/56/54	BNT162b2	Solid tumors and hematological malignancy	37.5%	19%	94%	———
Goshen-Lago et al., 2021 [74]	232/261	BNT162b2	Solid tumors	29%	———	84%	<0.001
Palich et al., 2021 [75]	223/49	BNT162b2	Solid tumors	94%	———	100%	———
Thakkar et al., 2021 [76]	134/66	BNT162b2 and mRNA-1273	Solid tumors and hematological malignancy	98%	85%	———	0.001
Ehmsen et al., 2021 [77]	201/323	BNT162b2 and mRNA-1273	Solid tumors and hematological malignancy	93%	66%	———	0.004
Malard et al., 2021 [78]	195/30	BNT162b2	Hematological malignancy	———	46.7%	87%	0.0002
Van Oekelen et al., 2021 [79]	260/67	BNT162b2 and mRNA-1273	Hematological malignancy	———	84.2%	100%	———
Barrière et al., 2021	42/24	BNT162b2	Solid tumors	95.2%	———	100%	0.016
Lim et al., 2021 [80]	129/150	BNT162b2 and AZD1222	Hematological malignancy	———	68%	100%	———
Pimpinelli et al., 2021 [81]	92/36	BNT162b2	Hematological malignancy	83.7%	———	100%	0.036
Herishanu et al., 2021 [82]	52/52	BNT162b2	Hematological malignancy	———	52%	100%	<0.001
Parry et al., 2021 [83]	67/96	BNT162b2 and AZD1222	Hematological malignancy	———	75%	100%	<0.001
Molica et al., 2022 [84]	70/57	BNT162b2	Hematological malignancy	———	58.5%	100%	<0.001
Lasagna et al., 2022 [85]	142/100	BNT162b2	Solid tumors	51%	———	65%	0.035
Qin et al., 2023 [86]	95/30	BNT162b2	Hematological malignancy	———	68%	100%	<0.001

Note: 1st cancer group, Solid tumors; 2nd cancer group, hematological malignancy; Control, Healthy control: health workers who were vaccinated in the same hospital.

6. Discussion

Currently, there is no agreement on the precise status of SARS-CoV-2 vaccinations or the future of the following ten years. Policymakers frequently assert that seasonal fluctuations manage COVID-19 in a manner similar to the flu. However, what is this significance or interpretation? What level of disease control are we considering, and more importantly, what will be the repercussions? Initially, the vaccine trials aimed to determine whether the vaccine could effectively decrease the occurrence of new PCR-confirmed infections, lower the number of hospital admissions, or achieve both outcomes. Despite the availability of very effective vaccines in many Western European countries and the United States, there continues to be a significant number of daily infections in the population. Even though the relatively low number of infections compared to previous waves of illness prior to the vaccine's availability, there is still a significant impact on hospital admissions and fatalities [87]. Even in individuals with mild symptoms, the extensive spread of the virus among the population has considerable consequences for healthcare provision, the emergence of new worrisome variants, and the establishment of a substantial and enduring burden of long-term COVID [88]. Amidst the surges of Delta and Omicron infections, there was a notable rise in the number of cases affecting youngsters. Several countries have initiated vaccination programs targeting adolescents, with fewer programs specifically targeting children aged 5 to 12 years [89]. In the future, it will be necessary to exert substantial effort in order to enhance the efficiency of vaccination for particular age groups of children. This includes making decisions on the most effective way to incorporate a new vaccine into the current structure of pediatric immunization programs.

Now, the vaccine method primarily focuses on targeting the original Wuhan Hu-1 ancestral sequence, which is a single antigen in the extensive viral immunome [90]. This highly specialized strategy for avoiding safety measures may have associated drawbacks [91]. The question at hand is whether we possess the capability to promptly address emerging species of concern in the future. It's important to think of different ways to do things, like changing the strain of interest based on the season in current vaccine platforms, adding sequences from the strain of interest to multivalent vaccines, and using fully inactivated progenitor or strain of interest viruses or antigens to boost immunity. Furthermore, prioritizing epitope-based methods by adopting rational and neutralizing strategies is crucial [92–94]. Currently, there is limited space to provide a comparative assessment of these highly diversified options and their various outcomes.

Researchers are currently conducting ongoing research to assess the effectiveness of COVID-19 vaccines in individuals with cancer. Monin et al. [73] conducted a trial assessing the efficacy of the BNT162b2 COVID-19 vaccination in individuals with solid tumors, hematological malignancies, and healthy individuals. The initial findings indicated that only 38% of individuals with solid tumors and less than 20% of individuals with hematological malignancies had measurable levels of anti-S IgG antibodies 21 days after the initial dosage was administered. According to the study, 94% of the healthy individuals examined had a positive result for IgG antibodies. They also examined the effects of delivering an additional dose of the vaccination. The study found that 95% of solid cancer patients who received a booster shot three weeks after the initial immunization dosage showed positive anti-S IgG antibodies two weeks later. Conversely, just 30% of individuals who did not get an enhancement demonstrated seropositivity. A separate study found that only 29% of solid cancer patients who received systemic chemotherapy, immunotherapy, biological agents, or a combination of these treatments tested positive for antibodies after receiving the first dosage. Out of the healthy people examined, 84% had good results. However, after administering a second dosage, approximately 86% of the patients tested positive for antibodies approximately two weeks later [74].

Several studies have investigated the immune response to the COVID-19 vaccination in patient groups with either solid or hematologic malignancies. Patients with solid cancer had a seroconversion rate of 94% (relative to 100% in healthy individuals) following the administration of two doses of the COVID-19 vaccine. In addition, people receiving chemotherapy experienced significantly reduced levels of anti-spike antibodies [75]. In two more studies, it was shown that after the second dose of the vaccine, 90% [71] and 95% [95] of patients with solid tumors had a positive antibody response. This was different from the healthy control group, which had a 100% positive response. Persons with hematologic malignancies exhibit reduced rates of seroconversion in comparison to healthy people. A study found that the seroconversion rate reached 100% in healthy people two weeks after the second dose of the vaccine. Nevertheless, the rate of seroconversion in patients with multiple myeloma was 78.6%, whereas in patients with chronic myeloid leukemia (CML) and myeloproliferative neoplasms (MPNs), it reached

88% [81]. Further investigation revealed that among individuals with chronic lymphocytic leukemia (CLL), only 39.5% achieved seroconversion after receiving two doses of the vaccine, whereas the healthy control group had a 100% seroconversion rate [96]. Moreover, 84.2% of patients diagnosed with multiple myeloma demonstrated a favorable immune response, whereas the complete control group attained a response rate of 100% [79]. After receiving two vaccination doses, patients with hematologic malignancies showed lower antibody levels compared to healthy people [97,98].

Scientists have performed a comparative investigation to assess the immune response to vaccines in individuals with blood cancers and those with tumors affecting solid organs. A study has revealed that individuals diagnosed with hematologic cancer exhibit lower median levels of antibodies and lower rates of seroconversion [77] in comparison to those with solid organ cancer. After getting two doses of the vaccine, people with a hematological malignancy had lower rates of seroconversion (77% vs. 98%) and lower levels of antibodies. This was in opposition to patients with a solid tumor. Both of these findings exhibited statistical significance [72]. Thakkar et al. [76] did a study that found that individuals with a hematologic malignancy had considerably lower rates of seroconversion (85% versus 98%) compared to patients with a solid tumor. This disparity was especially evident in those receiving anti-CD20 treatment and stem cell transplantation. Although there is no precise threshold of anti-S IgG levels that guarantees effective viral suppression, most studies rely on measuring anti-spike antibodies as an indirect marker of immunity to COVID-19.

Researchers found a correlation between more than 30% of neutralizing antibodies (NAbs) and a concentration of anti-S IgG above 3,100 UA mL^{-1}, which is considered the threshold for positive NAbs [78]. In addition, just 46.7% of their group showed outcomes surpassing this criterion after receiving two immunization doses, while 87% of the control group did. Terpos et al. [98] defined a positive test as having a neutralizing antibody titre that exceeds 30%. Additionally, they stated that a result exceeding 50% indicated a clinically meaningful suppression of the virus. Additional investigation is necessary to determine specific standards for clinically meaningful neutralizing antibodies and anti-S IgG titers.

Researchers have conducted several inquiries to examine the impact of anticancer medications on the immune response to the COVID-19 vaccination. Scientists have shown that certain medications can counteract the immune response, while others can reduce the effectiveness of the vaccine. Studies have linked cytotoxic therapy to poor seroconversion rates [72,75,77]. Multiple studies have shown that anti-CD20 treatments have a low seroconversion rate [76,77,96,97]. This is because these treatments eliminate B-cells, which impair both T cell-dependent and T cell-independent responses and can persist for up to twelve months [99]. Individuals undergoing anti-CD20 treatment may benefit from receiving a supplementary injection six months following their previous dose, or they may choose to wait six months after the completion of their treatment before obtaining another injection [80]. Research indicates that the administration of anti-CD38 medicine has a detrimental impact on the immune response. Treatment for multiple myeloma commonly involves this approach.

7. Clinical Implications

In a situation where the coronavirus has spread throughout the world, cancer patients are considered one of the high-risk groups for COVID-19. In general, cancer, like hypertension, cardiovascular disease, obesity, and many other underlying diseases, is considered a risk factor for COVID-19. The fact is that cancer patients are more vulnerable to this disease than other groups due to systemic immunodeficiency. A strong immune system is very important to combat COVID-19 [100,101]. Since certain medications for cancer patients severely affect the functioning of their overall body system, these patients must be much more careful to avoid contracting the coronavirus. Even if the treatment process with chemotherapy or radiation drugs is over and the cancer patient has recovered and returned to normal life, it is still necessary to strictly follow health and self-care protocols to avoid contracting the coronavirus. Consequently, patients who have been treated for cancer in the past may have a weakened immune system, which can make them more susceptible to severe COVID-19.

People with immunodeficiency, whether congenital or due to cancer treatment, are at high risk of developing COVID-19. Meanwhile, vaccination with currently approved vaccines has been shown to often not provide adequate protection for these individuals. The coronavirus vaccine activates T cells not only against the SARS-CoV-2 spike protein, but also against many other components of the virus that counteract the development of resistance by mutations of the virus [102,103]. Peptides are short proteins that enter the immune system, specifically the T cells,

on the surface of tumor cells as well as in virus-infected cells. This enables the immune system to recognize and destroy foreign cells. Therefore, if these peptides are vaccinated with an appropriate immune stimulator, or so-called adjuvant, T cells can be activated specifically against tumor cells as well as against virus-infected cells. So, cancer vaccination may impose a double effect issue when considering the COVID-19 vaccine [104–106]. So far, it's not clear at which stage of cancer it might have an impact. This fact may be related to the availability of limited evidence. The research in this field is a very early stage and may need more comprehensive studies on a wider population. The relationship between cancer and COVID-19 is a complex one that can threaten a person even after the end of treatment. Cancer treatment temporarily reduces the ability of the immune system, affecting white blood cells and, of course, destroying cancer cells [107]. Over time, after the end of the course, the body rebuilds healthy cells and forms healthy tissue again. This allows the immune system to regain its strength; however, this important system in the body may never return to its original state, even after the end of treatment. For this reason, it is not yet clear which cancer survivors are at greater risk than others (even among those who have completed cancer treatment).

8. Conclusions

This pandemic has caused a worldwide disaster, but numerous vaccination initiatives have made significant advancements. The robust perception of numerous countries effectively refuted even the gloomiest forecasts regarding the vaccine's efficacy. Currently, we need reliable data to address upcoming uncertainties, including the effective early detection of newly identified species of concern, the optimization of future vaccine strategies in terms of structure, dosage, timing between doses, and methods for establishing safe immunity. Develop a long-lasting vaccination that can be effective for both children and adults. Additionally, outline the best approaches to stimulating cross-immunity that offers varying levels of protection, regardless of prior infection. Multiple investigations have shown that cancer patients have lower serologic response rates to the COVID-19 immunization compared to healthy controls, specifically in terms of their antibody response. Patients undergoing B-cell lowering therapy have exhibited a conspicuous lack of serologic responses, as anticipated. There is a limited amount of research that has investigated how cells react to stimuli, and the findings have been inconsistent. Several studies have been unable to distinguish between individuals with cancer and those who are healthy, thereby providing an explanation for this phenomenon. In order to address the outstanding matters pertaining to immunization, further investigation is necessary. Factors to consider include the frequency of breakthrough infections, the need to monitor the immune response, and its durability.

9. Future Perspective

Researchers have recognized mRNA vaccines as a highly auspicious framework for cancer therapy. mRNA vaccines work well to make antigen-presenting cells (APCs) express tumor antigens during the immunization process, whether they are alone or attached to a carrier. As a result, APC activation occurs, leading to the stimulation of both innate and adaptive immune responses. The mRNA cancer vaccine outperforms other traditional vaccination platforms in terms of its superior efficacy, safe delivery, rapid development capabilities, and cost-efficient production. Nevertheless, the instability, inherent immunogenicity, and ineffective in vivo administration of mRNA vaccines have limited their usage. Scientists have examined many modifications to the mRNA structure, such as improving codons, altering nucleotides, and utilizing self-amplifying mRNAs. They have also explored other techniques like lipid nanoparticles (LNPs), polymers, and peptides to tackle these issues. Enhancements in mRNA vaccine administration, coupled with the concurrent delivery of other immunotherapeutic agents such as checkpoint inhibitors, have significantly augmented the immune response against tumors. This has increased the likelihood of malignant cells being completely eradicated. The FDA recently authorized lipid nanoparticle (LNP)-loaded mRNA vaccines for the prevention of COVID-19. These vaccines have demonstrated potential in clinical studies against many aggressive solid tumors, indicating that mRNA vaccines are likely to advance rapidly in the field of cancer immunotherapy in the near future. This paper provides a thorough examination of the latest developments and existing challenges in the area of mRNA cancer vaccines. Additionally, it explores the prospective future uses of mRNA vaccines in cancer immunotherapies.

The remarkable effectiveness of mRNA vaccines in combating COVID-19 has generated much hope in the battle

against other life-threatening diseases, including cancer. Differences in the encoded proteins lead to specific molecular and cellular mechanisms in mRNA vaccines. The advancements in nanotechnology and molecular medicine have led to the creation of customized antigen-encoding mRNA vaccines. These vaccines possess the capacity to enhance the display of antigens, leading to efficient immune reactions and the prevention of unintended harmful effects. This review focuses on new findings about the influence of encoded antigens, cytokines, and other functional proteins on the mechanisms of mRNA vaccines. Moreover, we emphasize the significance of delivery methods and chemical modifications in enhancing the efficacy, durability, and specificity of mRNA translation. Furthermore, we investigate the potential obstacles and future prospects of mRNA vaccines as versatile tools in the battle against cancer.

Author Contributions

F.R., I.Z.A. and A.A.S.: Developed the concept, conducted the data analysis, wrote, and revised the first draft of the manuscript. S.T.N. and A.M.H.: Developed the concept, contributed to the draft review, editing, and validation. T.A.-H.: Developed the concept and participated in language editing. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declared no conflict of interest.

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