Heliyon 8 (2022) e10583

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

A retrospective study to evaluate the efficacy and safety of SARS-CoV-2 vaccine in patients with advanced genitourinary cancers

Haoran Li *, Kamal Kant Sahu, Shruti Adidam Kumar, Blake Nordblad, Nicolas Sayegh, Nishita Tripathi, Vinay Mathew Thomas, Sumati Gupta, Benjamin L. Maughan, Neeraj Agarwal, Umang Swami

Division of Oncology, Internal Medicine, Huntsman Cancer Institute, University of Utah Health Care, Salt Lake City, 84112, Utah, United States

ARTICLE INFO

Keywords:
COVID-19
Vaccination
Cancer
Prostate cancer
Kidney cancer
Bladder cancer

ABSTRACT

Background: COVID-19 vaccination is one of the pivotal key tools against the ongoing pandemic, but its acceptance relies on efficacy and safety data among various populations, including patients with cancers. However, there is limited data on seroconversion rates, efficacy, and safety of the COVID-19 vaccine in patients with cancer. Breakthrough infections after vaccination have also been reported, which could further strengthen the refusal behavior of specific populations to be immunized. Our objective was to investigate the efficacy and safety of COVID-19 vaccination in real-world patients with advanced genitourinary cancers.

Methods and results: A retrospective study of the 738 patients with advanced metastatic genitourinary malignancy was conducted at our genitourinary oncology clinic from October 2020 to September 2021, out of which 462 patients (62.6%) were vaccinated. During the study period, two vaccinated, and six unvaccinated patients tested positive for SARS-CoV-2 (breakthrough infection rate: 0.4% vs. 2.2%, $p = 0.027$). Vaccine protection against infection was 81.8% (95% CI: 0.04–0.98). One vaccinated and 4 unvaccinated patients were hospitalized due to COVID-19 (0.2% vs. 1.4%, $p = 0.048$). Vaccine effectiveness in preventing hospitalization was 85.7% (95% CI: 0.02–1.33). Within one month of vaccination, 1.5% of patients (n = 7) had emergency visits, 0.8% (n = 4) were hospitalized for any reason, and of these, 3 (0.6%) experienced a delay in the receipt of their cancer therapy.

Conclusion: In our hypothesis-generating data among patients with advanced genitourinary cancers, COVID-19 vaccination was efficacious and safe and was rarely associated with treatment disruptions. These data should help improve the acceptance of the COVID-19 vaccine in the general population and patients with cancer. The vaccine effectiveness in our patients is comparable with existing published data without cancer.

1. Introduction

As of March 31, 2022, more than 80 million coronavirus disease-19 (COVID-19) cases and 1 million COVID-19-related deaths have been reported in the United States alone. Clinical presentations of COVID-19 range from asymptomatic or a mild flu-like illness to severe multiorgan failure, including acute respiratory failure syndrome (ARDS), causing increased mortality, especially in those with underlying malignancies [1]. Patients with underlying malignancies may have atypical presentations and are less likely to present with the typical COVID-19 symptoms of dry cough, fever, and malaise. A significant proportion of patients with cancer may not have a documented history of confirmed COVID-19 and can be established to have prior infection only by serologic positivity for SARS-CoV-2 virus IgG [2]. Also, patients with cancer and COVID-19 have higher rates of mechanical ventilation and mortality [3, 4, 5].

Three vaccines were approved by Food and Drug Administration (FDA) under emergency use authorization (EUA), each having a proven safety and efficacy in the large, randomized phase 3 trials [6, 7, 8]. As patients with cancer were excluded from pivotal trials leading to vaccine approval, additional studies were needed to explore the efficacy and safety of vaccines in cancer patients [9, 10]. Among the various cancers, most vaccine efficacy and safety data came from hematological malignancies [11, 12]. In addition, vaccine hesitancy posed an additional challenge to cancer care. There is a scarcity of data on the efficacy and safety of the covid-19 vaccine in patients with solid cancers.

* Corresponding author.
E-mail address: haoran.li@hci.utah.edu (H. Li).

https://doi.org/10.1016/j.heliyon.2022.e10583
Received 14 April 2022; Received in revised form 25 July 2022; Accepted 5 September 2022

Furthermore, vaccine hesitancy in this population is an area of unmet need that deserves immediate attention. Availability of data on the efficacy and safety of the COVID-19 vaccine will likely ease concerns among patients with advanced solid tumors, diminish vaccine hesitancy, and improve acceptability.

We hypothesized that receipt of the COVID-19 vaccine is efficacious and safe in patients with advanced genitourinary malignancies.

2. Methods

2.1. Participants and design

Patients with advanced genitourinary cancers who were seen from October 2020 to September 2021 were retrospectively enrolled in the study. We included patients with metastatic renal, bladder, and prostate cancers to minimize heterogeneity in the study population. Patients were excluded if: 1, the patient received a vaccine that is not approved by FDA; 2, the respiratory specimen was collected <14 days after completing the primary series; 3, the patient recently tested positive for COVID-19 (<45 days); or 4, patients with localized cancer. Percentages of various treatment ('ongoing treatment') that the patients were undergoing during our study, including chemotherapy, hormone therapy, immunotherapy, or active surveillance, was calculated and used for descriptive analysis.

2.2. Definition of vaccine efficacy and safety

Vaccine efficacy was evaluated by assessing the incidence of breakthrough infections. Infection was defined by whether the SARS-CoV-2 RNA or antigen was detected ≥14 days after completing the primary series of an FDA-authorized SARS-CoV-2 vaccine. Testing was done in patients who reported symptoms/concerns for COVID 19 infection. Vaccine efficacy was calculated as (infection rate among the unvaccinated group – infection rate among the vaccinated group)/infection rate among the unvaccinated group. The second measure of efficacy was vaccine efficacy against hospitalization due to COVID-19 infection.

Safety was evaluated by assessing the incidence of vaccine-related adverse events and delays in receiving cancer treatment due to the vaccine. For patients with active treatment plans, treatment disruption was defined as the experience of vaccination-associated side effects within 30 days of receipt of the vaccine, which led to a delay in cancer treatment by more than seven days.

2.3. Statistical analysis

Descriptive data were presented in this analysis as mean with standard deviation or as median with interquartile range (IQR). Discrete variables were compared using Pearson's chi-square or Fisher's exact tests. Vaccine efficacy was analyzed using the Clopper–Pearson method with a corresponding 95% confidence interval (CI). All statistical analysis was performed using SPSS. A two-sided p-value < 0.05 was considered statistically significant.

3. Results

3.1. Patient characteristics

Our retrospective study included patients between October 2020 and September 2021, and 1554 patients with genitourinary malignancies were screened for inclusion. Among them, 738 patients were diagnosed with metastatic disease from prostate cancer, bladder cancer, and kidney cancer and were included in this study. The rest of the patients were excluded from the study for various reasons mentioned in the exclusion criteria. Out of the 738 patients in our study, 462 received at least one dose of the SARS-CoV-2 vaccine. The vaccination rate was 62.6%. The vaccines our patients received were Pfizer-BioNTech (also marketed as Comirnaty), Moderna (also marketed as SpikeVax), and Janssen COVID-19 vaccine as approved by FDA. Charts were then reviewed to look for a history of COVID 19 infection >14 days after vaccination.

Patient demographics are summarized in Table 1. The median age of patients was older in the vaccinated group than in the unvaccinated group (72 vs. 70, $p < 0.01$). Most were male in both groups (93.1% and 91.7%, $p = 0.48$). Metastatic prostate cancer was the most common diagnosis, accounting for 75.5 % in vaccinated group and 67.0% in unvaccinated group ($p = 0.012$), followed by metastatic bladder cancer (12.1% vs. 18.5%, $p = 0.017$), and metastatic kidney cancer (12.5% vs. 14.5%, $p = 0.45$). Fewer vaccinated patients received active surveillance than unvaccinated patients during this period (5.2% vs. 13.4%, $p < 0.01$). There was no statistically significant difference between patients who received current chemotherapy (10.6% vs. 7.2%, $p = 0.13$) and immunotherapy (11% vs. 9.4%, $p = 0.45$) between the two groups. A statistically significant difference was noted in those receiving hormone therapy between the two groups (75.5% vs. 66.7%, $p < 0.01$). We also calculated the time interval between cancer diagnosis and the most recent follow-up. Interestingly, compared to unvaccinated patients, vaccinated patients with prostate cancer had longer time intervals significantly since diagnosis (65.6 months vs. 53.2 months, $p < 0.01$). In addition, more patients (1.9%) in the vaccinated group were infected by COVID-19 before vaccination, while COVID-19 infected only one patient (0.3%) in the unvaccinated group before December 2020 ($p = 0.07$). The synopsis of the study is depicted in Figure 1.

3.2. Vaccination efficacy

At the end of our study period, two vaccinated, and six unvaccinated patients had tested positive for SARS-CoV-2 (infection rate: 0.4% vs. 2.2%, $p = 0.027$) (Figure 2). Vaccine protection against infection was 81.8% (95% CI: 0.04–0.98). Only 1 vaccinated and 4 unvaccinated patients were hospitalized due to COVID-19 (0.2% vs. 1.4%, $p = 0.048$). Vaccine effectiveness in preventing hospitalization was 85.7% (95% CI: 0.02–1.33). Among breakthrough infection cases, both patients' ages were 56 and 67 years, respectively. Both patients were male and had a diagnosis of metastatic prostate cancer. One patient had concurrent advanced esophageal carcinoma. The median time from completion of the vaccine series to infection was 21.5 weeks (range: 21–22). Concurrent treatments include hormone therapy (n = 2), chemotherapy (n = 1), and radiation (n = 1). Both patients received the Pfizer-BioNTech vaccine. They both developed symptoms, and one was hospitalized due to COVID-19.

Table 1. Characteristics of patients with advanced genitourinary malignancies.

Variables	Vaccinated (n = 462)	Unvaccinated (n = 276)	p value
Age, median (IQR)	72 (66–77)	70 (64–76)	<0.01
Gender, male (%)	430 (93.1%)	253 (91.7%)	0.48
Diagnosis, n (%)			
Metastatic prostate cancer	349 (75.5%)	185 (67.0%)	0.012
Metastatic bladder cancer	56 (12.1%)	51 (18.5%)	0.017
Metastatic kidney cancer	58 (12.5%)	40 (14.5%)	0.45
Ongoing treatment, n (%)			
Surveillance	24 (5.2%)	37 (13.4%)	<0.01
Chemotherapy	49 (10.6%)	20 (7.2%)	0.13
Hormone therapy	349 (75.5%)	184 (66.7%)	<0.01
Immunotherapy	51 (11.0%)	26 (9.4%)	0.49
Time interval since diagnosis, median months (IQR)			
Metastatic prostate cancer	65.6 (30–143.5)	53.2 (23.7–109.2)	<0.01
Metastatic bladder cancer	23.7 (11–45.3)	15.1 (7.5–38)	0.12
Metastatic kidney cancer	47.2 (31.8–89.6)	34.4 (14.8–60.6)	0.21
Previous COVID infection, n (%)	9 (1.9%)	1 (0.3%)	0.07

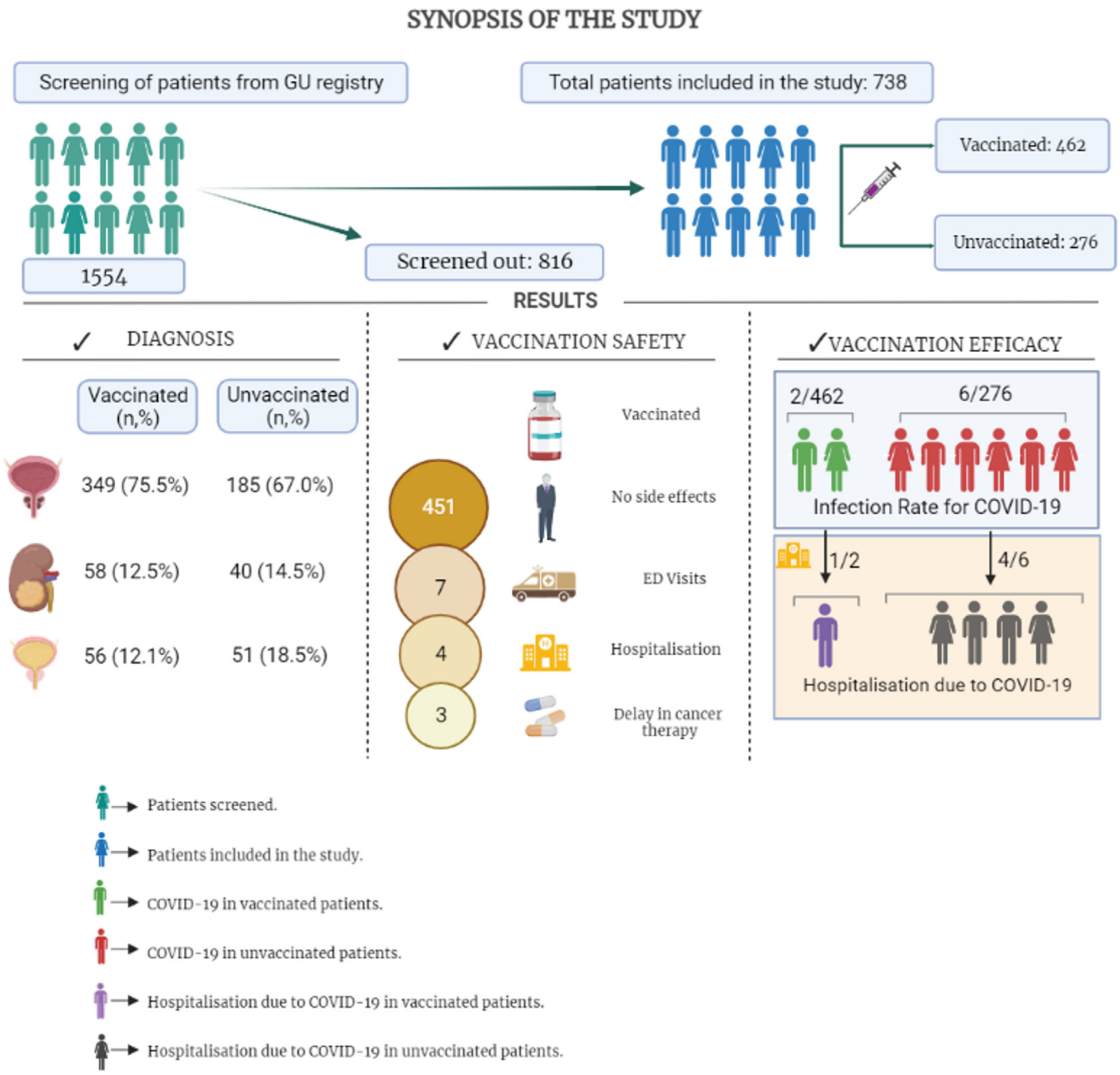

Figure 1. A pictorial description of the patients with cancer types, vaccination percentage, infection rates, emergency department visits, and hospitalization rates.

3.3. Safety of vaccination

Among 462 patients who received at least one dose of SARS-CoV-2 vaccines, 451 (97.6%) reported no severe side effects after vaccination. Within one month of vaccination, 1.5% of patients (n = 7) had emergency room visits, and 0.8% (n = 4) were hospitalized for any reason (Figure 2). Of them, 3 (0.6%) experienced a delay in receiving their cancer therapy. Hospitalizations due to any causes are summarized in Table 2.

4. Discussion

Our data provide a real-world experience of managing patients with cancer during the COVID-19 pandemic. This study also highlighted that vaccinating patient with advanced genitourinary cancers leads to minimal treatment interruptions, lesser breakthrough infections, and no significant vaccine-related side effects. These observations from our study on genitourinary cancers may be extrapolated to other solid cancers, which could further improve vaccine acceptance rates amongst unvaccinated patients. We found that COVID-19 vaccines effectively prevent COVID-19 infection in patients with metastatic genitourinary cancers. Our findings are comparable to published data in cancer patients, albeit lower than in healthy volunteers [13].

Before the emergence of the Omicron variant, breakthrough infections in vaccinated patients were rare, especially within five months of vaccination. Patients with breakthrough infections may have symptoms similar to those of unvaccinated but generally milder. In addition, the heterogenicity within cancer biology poses a challenge when the data are interpreted for clinical applicability. For example, patients with hematologic cancers may not mount an appropriate immune response despite receipt of the entire course of vaccination [14, 15].

Mutated variants of SARS-CoV-2, such as the Delta and Omicron variants, have disproportionately affected unvaccinated populations

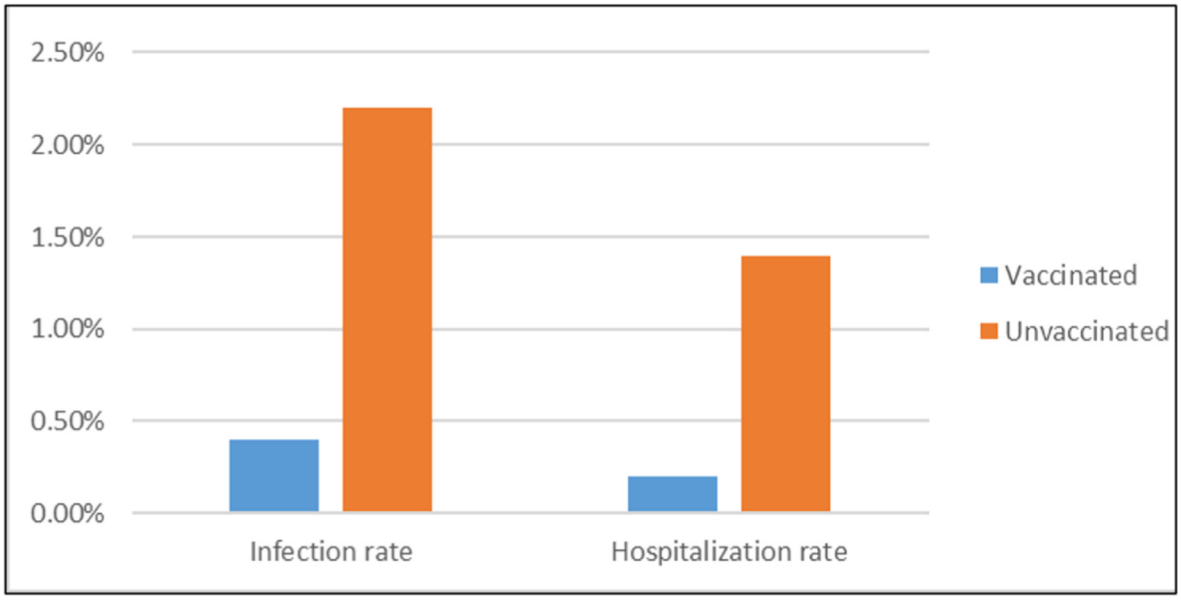

Figure 2. Infection and hospitalization rate in vaccinated versus unvaccinated patients.

Table 2. Patients hospitalized for possible COVID-19 vaccine side effects.

Patients	Age	Gender	Diagnosis	Cancer treatment	Vaccine type	Dose series	Symptoms	Admission diagnosis	Treatment disruption
Pt 1	56	Female	Kidney cancer	Immunotherapy	Pfizer-BioNTech	3	Diarrhea	Autoimmune colitis	Yes
Pt 2	58	Male	Kidney cancer	Radiation	Janssen	1	Altered mental status	Pulmonary embolism	Yes
Pt 3	74	Female	Kidney cancer	None	Pfizer-BioNTech	2	Fatigue	Neuropathy	No
Pt 4	82	Male	Prostate cancer	Hormone therapy	Pfizer-BioNTech	1	Shortness of breath, palpitation	New onset atrial fibrillation	Yes

[16]. Broad acceptance of vaccination can be the critical approach to truncate the emergence of new variants. Still, vaccine acceptance will heavily rely on safety data among various populations, including cancer patients who are receiving treatment and are perceived vulnerable to infection. One major concern amongst cancer patients is the impact of vaccination on anti-cancer therapy. Questions such as, "Will vaccination jeopardize cancer treatment?" often arise when a vaccine is offered. As a result, many patients postponed COVID vaccination while on cancer treatment. Although COVID-19 vaccines are universally recommended for cancer patients, there is limited research that could reliably correlate the seroconversion rates amongst patients with cancer [17, 18]. Ariamanesh et al. reported a higher seroconversion in younger patients with cancer than 60 years (90.9%, 90%, and 79% in patients $<$40 years, 40–60 years, and $>$60 years; respectively, $p = .042$) [19]. Multiple studies suggest that patients with solid malignancies are likely to have a higher seroconversion than patients with hematologic malignancies [13, 19, 20, 21]. Joudi et al. reported an excellent immune response (93.3%) to vaccination with minimal side effects (local pain and fever in 22.3% and 24.3% of patients, respectively) in their cohort of 160 patients with breast cancer. Following vaccination, the prevalence of COVID-19 infection reduced with time (0.7%, 0%, and 0%, respectively, for the first, second, and third months of follow-up) [21]. These real-world observations support the results presented in our study.

Cancer patients were among the first groups of people eligible to be vaccinated. In many states, they received the COVID-19 vaccine as early as December 2020. Since then, mounting evidence has demonstrated a declining antibody titer and waning protection in early vaccine recipients [22]. As a result, Food and Drug Administration (FDA), under emergency use authorization (EUA), issued recommendations for a single booster dose of the COVID-19 vaccine, including Pfizer-BioNTech, Moderna mRNA, and the Janssen vaccine. The initial vaccine booster recommendation was limited to specific individuals with immunocompromised status, which is defined differently across states [23]. Utah has one of the highest COVID-19 infection rates per capita in the United States due to low vaccination rates among eligible people. The data presented in this analysis provide an overview of unvaccinated patients with underlying active metastatic cancer. Unvaccinated patients were significantly younger than those who were vaccinated. They also had shorter time intervals from the diagnosis of advanced cancer. More unvaccinated patients were under active surveillance. However, unvaccinated patients had similar COVID-19 infection rates before December 2020. A likely explanation for this observation could be that unvaccinated patients might have practiced other measures to avoid exposure to the virus despite vaccine hesitancy. Overall, unvaccinated patients had more significant COVID-19 infections than their vaccinated counterparts.

Multiple tools have been developed to identify at-risk patients without cancer and predict adverse outcomes associated with COVID-19 infection [24, 25, 26]. Active cancer is associated with a more severe disease once COVID-19 infection is acquired. Nevertheless, the heterogenicity of cancer makes such a scoring system less feasible to be used in patients with cancer.

Real-world data is needed to determine who is at risk of developing breakthrough infection and should be prioritized for a third vaccine dose. In patients with cancer, the integrity of the immune systems depends on age, type of cancer, treatments received, and other comorbidities. The National Comprehensive Cancer Network (NCCN) recommends that all patients with cancer should be vaccinated with full primary vaccine series and additional booster doses [27, 28].

4.1. Limitations of the study

We have identified several limitations of our study. The patient population in the study included patients with active or newly diagnosed cancer and hence likely had frequent visits to health care facilities in a year. Our study included only a selected patient population with robust immunosuppression secondary to cancer or chemotherapy. Hence, data interpretation from this study should not be generalized to all patients with cancer (active or cured) in general. This study was conducted before the Omicron variant became the dominant cause of COVID-19 infection, which caused more breakthrough infections in vaccinated people. Despite truncated vaccine effectiveness against Omicron, the vaccine's safety profile demonstrated in our study is still acceptable and reassuring.

5. Conclusion

In summary, our hypothesis-generating data suggest that among the patients with advanced genitourinary malignancies, COVID-19 vaccination is efficacious and safe, associated with low breakthrough infection rates, an acceptable safety profile, and minimal risk disruptions of ongoing cancer treatment. This data provide real-world evidence that should help improve the acceptance of the SARS-CoV-2 vaccine amongst patients with advanced solid tumors, specifically genitourinary cancers. Further, more extensive prospective studies are needed to validate these results in patients with cancer.

Declarations

Author contribution statement

Haoran Li; Kamal Kant Sahu: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Blake Nordblad; Shruti Adidam Kumar: Analyzed and interpreted the data; Wrote the paper.

Nicolas Sayegh; Nishita Tripathi: Conceived and designed the experiments; Performed the experiments.

Vinay Mathew Thomas; Sumati Gupta: Contributed reagents, materials, analysis tools or data.

Benjamin L. Maughan; Neeraj Agarwal; Umang Swami: Conceived and designed the experiments; Wrote the paper.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability statement

Data will be made available on request.

Declaration of interest's statement

The authors declare the following conflict of interests:

Dr. Neeraj Agarwal (lifetime disclosures): Consultancy to Astellas, Astra Zeneca, Aveo, Bayer, Bristol Myers Squibb, Calithera, Clovis, Eisai, Eli Lilly, EMD Serono, Exelixis, Foundation Medicine, Genentech, Gilead, Janssen, Merck, MEI Pharma, Nektar, Novartis, Pfizer, Pharmacyclics, and Seattle Genetics. Research funding to Neeraj Agarwal's institution: Astellas, Astra Zeneca, Bavarian Nordic, Bayer, Bristol Myers Squibb, Calithera, Celldex, Clovis, Eisai, Eli Lilly, EMD Serono, Exelixis, Genentech, Gilead, Glaxo Smith Kline, Immunomedics, Janssen, Medivation, Merck, Nektar, New Link Genetics, Novartis, Pfizer, Prometheus, Rexahn, Roche, Sanofi, Seattle Genetics, Takeda, and Tracon.

Dr. Umang Swami: Dr. Swami reports consultancy to Astellas, Exelixis and Seattle Genetics and research funding to institute from Janssen, Exelixis and Astellas/Seattle Genetics.

Dr. Sumati Gupta: Dr. Sumati Gupta has received clinical trials support from Bristol Myers Squibb, Rexahn, Incyte, Novartis, LSK, Five Prime, Mirati, QED, Debiopharm, Merck, Pfizer, Astra Zeneca, Medimmune, Clovis, Immunocore, Seattle Genetics, Pfizer, LSK/Elevar therapeutics, Acrotech, Astra Zeneca, travel fund from QED and spouse has stock ownership in Salarius pharmaceutical.

Dr. Benjamin Maughan: Roche/Genentech, Pfizer, AVEO Oncology, Janssen Oncology, Astellas, Bristol-Myers Squibb, Clovis, Tempu, Merck, Exelixis, Bayer Oncology, Peloton Therapeutics (C/A), Exelixis, Bavarian-Nordic, Clovis, Genentech, Bristol-Myers Squibb (FR– institutional).

Additional information

No additional information is available for this paper.

References

[1] G. Onder, G. Rezza, S. Brusaferro, Case-fatality rate and Characteristics of patients dying in relation to COVID-19 in Italy, JAMA 323 (18) (2020) 1775–1776.
[2] S.A. Javadinia, M. Ariamanesh, M. Nabavifard, P. Porouhan, B. PeyroShabany, D. Fazilat-Panah, et al., Multicenter study of antibody seroprevalence against COVID-19 in patients presenting to Iranian cancer centers after one year of the COVID-19 pandemic, Cancer Invest. 40 (2) (2022) 115–123.
[3] S. Shahidsales, S.A. Aledavood, M. Joudi, F. Molaie, H. Esmaily, S.A. Javadinia, COVID-19 in cancer patients may be presented by atypical symptoms and higher mortality rate, a case-controlled study from Iran, Cancer Rep (Hoboken) 4 (5) (2021) e1378.
[4] T. Vidaurre, D. Enriquez-Vera, S. Bertani, Excess mortality in patients with cancer during the COVID-19 pandemic in Peru: an analysis of death registry data, Lancet Oncol. 23 (Suppl 1) (2022) S28.
[5] J.M. Unger, A. Moseley, B. Symington, M. Chavez-MacGregor, S.D. Ramsey, D.L. Hershman, Geographic distribution and survival outcomes for rural patients with cancer treated in clinical trials, JAMA Netw. Open 1 (4) (2018), e181235.
[6] F.P. Polack, S.J. Thomas, N. Kitchin, J. Absalon, A. Gurtman, S. Lockhart, et al., Safety and efficacy of the BNT162b2 mRNA covid-19 vaccine, N. Engl. J. Med. 383 (27) (2020) 2603–2615.
[7] L.R. Baden, H.M. El Sahly, B. Essink, K. Kotloff, S. Frey, R. Novak, et al., Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine, N. Engl. J. Med. 384 (5) (2021) 403–416.
[8] J. Sadoff, G. Gray, A. Vandebosch, V. Cárdenas, G. Shukarev, B. Grinsztejn, et al., Safety and efficacy of single-dose Ad26.COV2.S vaccine against covid-19, N. Engl. J. Med. 384 (23) (2021) 2187–2201.
[9] S.F. Oosting, A.A.M. van der Veldt, C.H. GeurtsvanKessel, R.S.N. Fehrmann, R.S. van Binnendijk, A.C. Dingemans, et al., 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) (2021) 1681–1691.
[10] I. Waldhorn, R. Holland, T. Goshen-Lago, Y. Shirman, M. Szwarcwort-Cohen, A. Reiner-Benaim, et al., Six-month efficacy and toxicity profile of BNT162b2 vaccine in cancer patients with solid tumors, Cancer Discov. 11 (10) (2021) 2430–2435.
[11] C. Perry, E. Luttwak, R. Balaban, G. Shefer, M.M. Morales, A. Aharon, et al., Efficacy of the BNT162b2 mRNA COVID-19 vaccine in patients with B-cell non-Hodgkin lymphoma, Blood Adv 5 (16) (2021) 3053–3061.
[12] C. Bagacean, R. Letestu, C. Al-Nawakil, S. Brichler, V. Lévy, N. Sritharan, et al., Humoral response to mRNA anti-COVID-19 vaccines BNT162b2 and mRNA-1273 in patients with chronic lymphocytic leukemia, Blood Adv 6 (1) (2022) 207–211.
[13] A.I. Yasin, S.G. Aydin, B. Sümbül, L. Koral, M. Şimşek, Ç. Geredeli, et al., Efficacy and safety profile of COVID-19 vaccine in cancer patients: a prospective, multicenter cohort study, Future Oncol. (2022).
[14] Y. Herishanu, I. Avivi, A. Aharon, G. Shefer, S. Levi, Y. Bronstein, et al., Efficacy of the BNT162b2 mRNA COVID-19 vaccine in patients with chronic lymphocytic leukemia, Blood 137 (23) (2021) 3165–3173.
[15] E. Terpos, S.V. Rajkumar, N. Leung, Neutralizing antibody testing in patients with multiple myeloma following COVID-19 vaccination, JAMA Oncol. (2021).
[16] B.A. Petros, J. Turcinovic, N.L. Welch, L.F. White, E.D. Kolaczyk, M.R. Bauer, et al., Early introduction and rise of the Omicron SARS-CoV-2 variant in highly vaccinated university populations, Clin. Infect. Dis. (2022).
[17] D.C. Guven, T.K. Sahin, S. Akın, F.M. Uckun, Impact of therapy in patients with hematologic malignancies on seroconversion rates after SARS-CoV-2 vaccination, Oncol. 27 (4) (2022) e357–e361.
[18] A. Thakkar, J.D. Gonzalez-Lugo, N. Goradia, R. Gali, L.C. Shapiro, K. Pradhan, et al., Seroconversion rates following COVID-19 vaccination among patients with cancer, Cancer Cell 39 (8) (2021) 1081, 90.e2.
[19] M. Ariamanesh, P. Porouhan, B. PeyroShabany, D. Fazilat-Panah, M. Dehghani, M. Nabavifard, et al., Immunogenicity and safety of the inactivated SARS-CoV-2

vaccine (BBIBP-CorV) in patients with malignancy, Cancer Invest. 40 (1) (2022) 26–34.
[20] S.A. Javadinia, K. Alizadeh, M.S. Mojadadi, F. Nikbakht, F. Dashti, M. Joudi, et al., COVID-19 vaccination in patients with malignancy; A systematic review and meta-analysis of the efficacy and safety, Front. Endocrinol. 13 (2022), 860238.
[21] M. Joudi, M. Moradi Binabaj, P. Porouhan, B. PeyroShabany, M. Tabasi, D. Fazilat-Panah, et al., A cohort study on the immunogenicity and safety of the inactivated SARS-CoV-2 vaccine (BBIBP-CorV) in patients with breast cancer; does trastuzumab interfere with the outcome? Front. Endocrinol. 13 (2022), 798975.
[22] J. Khoury, R. Najjar-Debbiny, A. Hanna, A. Jabbour, Y. Abu Ahmad, A. Saffuri, et al., COVID-19 vaccine - long term immune decline and breakthrough infections, Vaccine 39 (48) (2021) 6984–6989.
[23] P. Bergman, O. Blennow, L. Hansson, S. Mielke, P. Nowak, P. Chen, et al., Safety and efficacy of the mRNA BNT162b2 vaccine against SARS-CoV-2 in five groups of immunocompromised patients and healthy controls in a prospective open-label clinical trial, EBioMedicine 74 (2021), 103705.
[24] W. Liang, H. Liang, L. Ou, B. Chen, A. Chen, C. Li, et al., Development and validation of a clinical risk score to predict the occurrence of critical illness in hospitalized patients with COVID-19, JAMA Intern. Med. 180 (8) (2020) 1081–1089.
[25] E. Jimenez-Solem, T.S. Petersen, C. Hansen, C. Lioma, C. Igel, W. Boomsma, et al., Developing and validating COVID-19 adverse outcome risk prediction models from a bi-national European cohort of 5594 patients, Sci. Rep. 11 (1) (2021) 3246.
[26] L. Wynants, B. Van Calster, G.S. Collins, R.D. Riley, G. Heinze, E. Schuit, et al., Prediction models for diagnosis and prognosis of covid-19: systematic review and critical appraisal, BMJ 369 (2020) m1328.
[27] A.L. Schmidt, C. Labaki, C.Y. Hsu, Z. Bakouny, N. Balanchivadze, S.A. Berg, et al., COVID-19 vaccination and breakthrough infections in patients with cancer, Ann. Oncol. 33 (3) (2021) 340–346.
[28] A. Massarweh, N. Eliakim-Raz, A. Stemmer, A. Levy-Barda, S. Yust-Katz, A. Zer, et al., Evaluation of seropositivity following BNT162b2 messenger RNA vaccination for SARS-CoV-2 in patients undergoing treatment for cancer, JAMA Oncol. 7 (8) (2021) 1133–1140.