Received: 14 June 2023 | Revised: 2 October 2023 | Accepted: 28 December 2023

DOI: 10.1111/ajco.14047

ORIGINAL ARTICLE

WILEY

Response to COVID-19 vaccination in patients on cancer therapy: Analysis in a SARS-CoV-2-naïve population

George Cavic[1] | Andrew A. Almonte[1] | Sarah M. Hicks[2] | Teresa Neeman[3] | Jo-Wai Wang[1] | Sue Brew[4] | Philip Y. Choi[2,5] | Ian Cockburn[2] | Elizabeth E. Gardiner[2] | Desmond Yip[5,6,7] | Aude M. Fahrer[1,8] | Yada Kanjanapan[5,6]

[1]Research School of Biology, Australian National University, Canberra, Australia

[2]John Curtin School of Medical Research, Australian National University, Canberra, Australia

[3]Biological Data Science Institute, Australian National University, Canberra, Australia

[4]Medical Oncology Clinical Trials Unit, The Canberra Hospital, Canberra, Australia

[5]Department of Medical Oncology, The Canberra Hospital, Canberra, Australia

[6]ANU Medical School, Australian National University, Canberra, Australia

[7]Department of Haematology, The Canberra Hospital, Canberra, Australia

[8]Faculty of Science and Technology, University of Canberra, Canberra, Australia

Correspondence
Yada Kanjanapan, The Canberra Hospital, Yamba Dr, Garran, ACT 2605, Canberra, Australia.
Email: yada.kanjanapan@act.gov.au

Funding information
Australian Government Research Training Program Scholarship; Canberra Hospital Radiation Oncology Private Practice Fund; The Canberra Hospital Private Practice Fund; John James Foundation

Abstract

Background: Cancer patients have increased morbidity and mortality from COVID-19, but may respond poorly to vaccination. The Evaluation of COVID-19 Vaccination Efficacy and Rare Events in Solid Tumors (EVEREST) study, comparing seropositivity between cancer patients and healthy controls in a low SARS-CoV-2 community-transmission setting, allows determination of vaccine response with minimal interference from infection.

Methods: Solid tumor patients from The Canberra Hospital, Canberra, Australia, and healthy controls who received COVID-19 vaccination between March 2021 and January 2022 were included. Blood samples were collected at baseline, pre-second vaccine dose and at 1, 3 (primary endpoint), and 6 months post-second dose. SARS-CoV-2 anti-spike-RBD (S-RBD) and anti-nucleocapsid IgG antibodies were measured.

Results: Ninety-six solid tumor patients and 20 healthy controls were enrolled, with median age 62 years, and 60% were female. Participants received either AZD1222 (65%) or BNT162b2 (35%) COVID-19 vaccines. Seropositivity 3 months post vaccination was 87% (76/87) in patients and 100% (20/20) in controls ($p = .12$). Seropositivity was observed in 84% of patients on chemotherapy, 80% on immunotherapy, and 96% on targeted therapy (differences not satistically significant). Seropositivity in cancer patients increased from 40% (6/15) after first dose, to 95% (35/37) 1 month after second dose, then dropped to 87% (76/87) 3 months after second dose.

Conclusion: Most patients and all controls became seropositive after two vaccine doses. Antibody concentrations and seropositivity showed a decrease between 1 and 3 months post vaccination, highlighting need for booster vaccinations. SARS-CoV-2 infection amplifies S-RBD antibody responses; however, cannot be adequately identified using nucleocapsid serology. This underlines the value of our COVID-naïve population in studying vaccine immunogenicity.

George Cavic, Andrew A. Almonte, and Sarah M. Hicks contributed equally to the manuscript, and Elizabeth E. Gardiner, Desmond Yip, Aude M. Fahrer, and Yada Kanjanapan contributed equally to the manuscript.

KEYWORDS
COVID-19 vaccine, SARS-CoV-2, seroconversion, serology, solid tumor

1 | INTRODUCTION

Cancer patients have increased risk of morbidity and mortality from COVID-19.[1] The extent to which COVID-19 vaccination protects cancer patients, especially those receiving immunosuppressive anti-neoplastic therapy, is important knowledge in protecting this vulnerable population. While numerous studies have examined the efficacy of COVID-19 vaccination in cancer patients, the majority have been conducted in settings of prevalent community transmission of SARS-CoV-2, where immunity generated from recovery from COVID-19 can confound assessment of vaccine efficacy.

Canberra, Australia, had only 2167 reported cases of COVID-19 in a population of approximately 460,000 up to the December 19, 2021.[2] SARS-CoV-2 vaccination in Australia commenced in February 2021, initially in high-risk groups, with eligibility expanded to include all adults by August 2021. This study prospectively assessed the immunogenic response to COVID-19 vaccination in cancer patients receiving active systemic therapy, compared to a control cohort of healthy volunteers, in a high vaccination and low community transmission setting.

2 | MATERIALS AND METHODS

The Evaluation of COVID-19 Vaccination Efficacy and Rare Events in Solid Tumors (EVEREST) study is a single-center, prospective study conducted through the Canberra Hospital and Australian National University (ANU), Canberra, Australia. The study was approved by the ACT Health Human Research Ethics Committee (HREC) (2021.ETH.00062). Study participants in the patient cohort had solid tumors and were receiving systemic anti-cancer treatment within 2 weeks of their first or second COVID-19 vaccination doses. The healthy control cohort had no history of malignancy within the past 5 years. Participants were recruited between September 6 and December 18, 2021, before, or within 90 days of receiving two doses of BNT162b2 (Pfizer) or AZD1222 (AstraZeneca) COVID-19 vaccines. Those with a past laboratory-confirmed diagnosis of COVID-19 were excluded.

Blood collection at up to five separate timepoints (Figure S1) was undertaken. Timepoint (TP) 1 was the baseline sample prior to any COVID-19 vaccination. TP2 was collected after the first vaccine, up to 2 weeks before the second vaccine dose. TP3 was collected 30 days after the second vaccine; TP4, 90 days after the second vaccine dose. During the study, an amendment was made to collect TP4 up to 2 weeks before the administration of a third vaccine dose, in response to changing public health guidelines by the Australian Technical Advisory Group on Immunisation (ATAGI), which allowed immunocompromised individuals (including cancer patients) to receive a third primary dose of vaccination from 2 months after their second dose. TP5 was 180 days post second vaccine dose. As booster vaccination was available to the general population at 3–6 months following the primary vaccination course, TP5 was amended to allow collection up to 2 weeks prior to the booster dose (third dose for the healthy cohort and fourth dose for the patient cohort). A 2-week window before and after the participant's estimated date for sample collection was allowed for TP3–5.

Enzyme-linked immunosorbent assays (ELISA) for SARS-CoV-2 spike receptor binding domain (S-RBD) and nucleocapsid were conducted as described by Hicks et al.[3] In brief, white 96-well Maxisorp microtiter plates (Nunc, 436110) were coated overnight at 4°C with 100 μL of 500 ng/mL recombinant S-RBD (GenScript Biotech, Z03483) or Nucleocapsid (GenScript Biotech, Z03480) protein—both derived from the Wuhan strain of the virus. Serial dilutions of the National Institutes of Health (NIH) standard plasma (Frederick National Laboratory) were included on each plate to allow conversion of relative fluorescence units (RFU) to binding antibody units (BAU)/mL. In a departure from normal handling of this standard for other studies, Australian quarantine regulations required that the NIH standard was heat-inactivated (56°C for 30 min) and refrozen prior to shipment. Extended transport times resulted in the standard being thawed prior to receipt. Whilst this was regrettable, the BAU values we obtained from participant samples were very much in-line with other published studies, suggesting that this did not substantially impact the titer of the standard. Participant plasma from EDTA collection tubes were heat-inactivated at 56°C for 1 h. Plasma was diluted at 1/100 (for all samples on both S-RBD and nucleocapsid ELISAs) and 1/1000 (for some S-RBD samples only).

A four-parameter logistic regression model was used to construct standard curves for each ELISA plate using the RFU values obtained from serially diluted NIH standard controls. These curves were used to estimate a subject's anti-RBD and anti-nucleocapsid antibody concentration in BAU/mL. All subject samples were run in duplicate, and the resulting RFU values were averaged before being evaluated with their respective curves. BAU/mL values of samples tested in more than one assay were averaged. Twenty-five samples from healthy donors collected before December 2019 (pre-2020 controls) under protocols approved by the ANU HREC (2016/317) were included in the assay to determine the seropositive threshold. The threshold used to establish seropositivity was defined as 3 standard deviations above the geometric mean of the BAU/mL values obtained from these samples. The threshold values, represented by horizontal lines in Figure 1, were 17.25 BAU/mL for S-RBD and 45.36 BAU/mL for nucleocapsid (used to screen for patients with exposure to SARS-CoV-2).

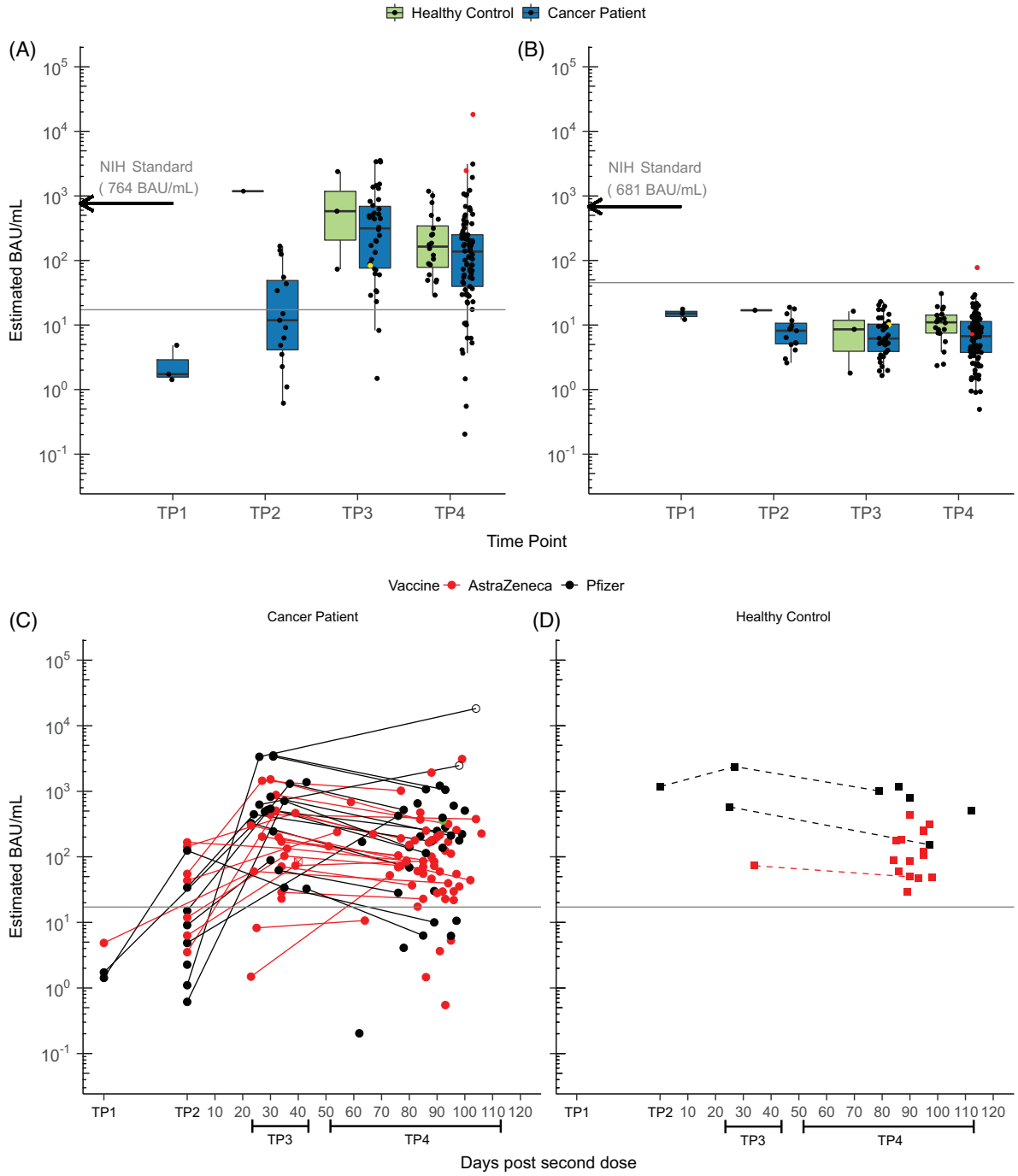

FIGURE 1 Anti-S-RBD and anti-nucleocapsid antibody responses in cancer patients and healthy controls. (A and B) Responses of cancer patients versus controls against (A) S-RBD (induced by vaccination) or (B) nucleocapsid (induced by infection). Median and interquartile range (IQR) are shown for healthy controls (green) and cancer patients (blue). Black dots represent patients included in the median and IQR calculations. (C and D) Responses against S-RBD resolved by time after second vaccine dose, by vaccine type, and linking samples taken from the same individual, for (C) cancer patients and (D) healthy controls. Points and lines colored according to vaccine type received; AstraZeneca (AZD1222) shown in red, Pfizer (BNT162b2) in black, one patient who received one of each vaccine in green—first dose AZD1222, second dose BNT162b2. Antibody response was measured by ELISA and converted to binding antibody units (BAU) per mL using the NIH standard. The threshold for seropositivity (shown by horizontal black lines in each graph) was calculated as 3 standard deviations above the geometric mean of 25 pre-2020 (negative control) sera; 17.25 BAU/mL for S-RBD (A, C, and D) and 45.36 BAU/mL for nucleocapsid (B). Two patients who were infected with SARS-CoV-2 before TP4 are shown as red dots in (A) and (B) and as open circles in (C). One patient who received three doses of vaccine before TP3 is shown as a yellow dot in (A) and (B), and as an open square in (C). TPs analyzed include: before first dose (TP1), between first and second doses (TP2), approximately 1 month after second dose (TP3: patients—median 31 days, range 23–43; controls—median 27 days, range 25–34), approximately 3 months after second dose (TP4: patients—median 88 days, range 51–106; controls—median 90 days, range 85–112). Cancer patients ($n = 96$), healthy controls ($n = 20$).

2.1 | Statistical analyses

Demographic data for participants were summarized by cohort. Baseline disease characteristics were summarized for the patient cohort. Differences in seroconversion rates between groups were evaluated using a two-sided Fisher's exact test. Differences in mean S-RBD antibody concentration (BAU/mL) between groups at TP3 and TP4 were assessed using a linear mixed model with timepoint and cohort as fixed effects and participant ID as a random effect. Statistical analyses were performed with RStudio (v. 4.1.2). A *p*-value less than .05 was considered statistically significant.

3 | RESULTS

3.1 | Participant demographics

A total of 102 patients and 22 controls were enrolled. Of these, 96 cancer patients and 20 control participants were included in our analyses, with data cutoff on March 2, 2022 (Figure S2). Participants had a median age of 62 years, with 60% being female, and received AZD1222 (AstraZeneca; 65%) or BNT162b2 (Pfizer; 35%) COVID-19 vaccines as first dose (Table S1). Demographic summary statistics were similar between cohorts. The cancer patient cohort received chemotherapy (60%), immunotherapy (15%), and targeted therapy (40%), with treatment categories being non-mutually exclusive (Table S2).

3.2 | Seroconversion 3 months post two vaccine doses

Eighty-seven patients and 20 control participants were eligible for the primary analysis of seroconversion at 3 months following two vaccine doses (TP4). The anti-S-RBD antibody seropositivity rate was 87% (76/87, 95% confidence interval [CI]: 79%–94%) in cancer patients and 100% (20/20, 95% CI: 83%–100%) in the control cohort ($p = .12$; Table 1).

Within the patient cohort, the anti-S-RBD antibody seropositivity rate at TP4 was 84% (43/51) for patients on any chemotherapy, 80% (8/10) for patients primarily on immunotherapy, and 96% (25/26) for patients on targeted therapy (Table 1). Differences were not statistically significant compared to the controls. Details of patient participants that did not seroconvert are shown in Table S3.

3.3 | Anti-S-RBD antibody

Anti-S-RBD concentrations at the defined study timepoints are shown in Table 2 and Figure 1A. Mean anti-S-RBD concentrations were numerically higher in healthy controls compared to cancer patients at both TP3 (410.2 vs. 206.1 BAU/mL) and TP4 (169.6 vs. 94.4 BAU/mL; Table 2); however, the differences were not significant. Similarly, no differences between cancer patients and healthy controls were observed when dividing cohorts by vaccine type (Table S4). The seropositivity rate in cancer patients was 40% (6/15) after one vaccine dose, and 95% (35/37) 1 month after the second vaccine dose, compared to the 87% (76/87) at the 3-month primary endpoint (Figure 1A). Thus, we see a general trend of a rise in antibody concentrations between TP2 and TP3, and a fall between TP3 and TP4 (Figure 1A).

TABLE 1 Comparison of seropositivity between controls, patients, and divisions of patients based on treatment type.

		Seropositive			
	Total *N*	*n*	%	95% Confidence interval	*p*-Value[a]
Controls	20	20	100	[83–100]	
Patients	87	76	87	[79–94]	.121
Patients by therapy[b]					
Chemotherapy	51	43	84	[71–93]	.095
Immunotherapy	10	8	80	[44–97]	.103
Targeted therapy	26	25	96	[80–100]	1.000

[a]Two-sided Fisher's exact test; all comparisons made to control cohort.
[b]Patient participants divided into primary treatment groups. These groups are defined as "Chemotherapy" = any patient who received chemotherapy; "Immunotherapy" = received immunotherapy, but no chemotherapy; "Targeted therapy" = received targeted therapy, but did not receive chemotherapy nor immunotherapy.

3.4 | Anti-nucleocapsid antibody

Anti-nucleocapsid antibody concentrations remained below the seropositive threshold for all except one participant. Only two patients reported RT-PCR-confirmed infection with COVID-19 during the study's sample collection period, both 15 days before the primary endpoint sample was taken. Both patients showed a rise in anti-S-RBD (red dots in Figure 1A and open circles in Figure 1C); however, only one patient was found to be seropositive for anti-nucleocapsid antibodies (red dot in Figure 1B and open circle in Figure S3C).

3.5 | Responses to different vaccines

We provide data delineated by primary vaccine course (AZD12221 shown in red or BNT162b2 shown in black; Figure 1C,D). However, as the Australian immunization guidelines initially reserved Pfizer vaccination for people under 60 years of age, any analysis of differences in vaccine response would be inherently confounded by age.

TABLE 2 Comparison of anti-S-RBD antibody concentration between patients and controls at TP3 and TP4.

Timepoint	Participant	*n*	Antibody (BAU/mL)[a]	(95% CI)	Ratio	(95% CI)
TP3	Cancer patient	37	206.1	[135.9–312.7]	.503	[.139–1.82]
	Healthy control	3	410.2	[121.4–1386.3]		
TP4	Cancer patient	87	94.4	[67–133.2]	.557	[.247–1.254]
	Healthy control	20	169.6	[81.3–354.1]		

Abbreviations: BAU, binding antibody units; CI, confidence interval.
[a]Geometric mean.

4 | DISCUSSION

A lower seropositivity rate of 87% in cancer patients, compared to 100% among controls, was observed 3 months following two doses of SARS-CoV-2 vaccine, although the difference did not reach statistical significance in this study. Anti-S-RBD concentrations were also numerically lower at 94.4 BAU/mL in cancer patients compared to 169.6 BAU/mL with controls. Importantly, our observations were made in a predominantly COVID-19-naïve population.

A number of studies observed lower antibody response following COVID-19 vaccination among solid organ cancer patients receiving chemotherapy.[4–7] Thakkar et al. reported that among 242 solid tumor patients, those who received chemotherapy had significantly lower spike-IgG seropositivity of 92% compared to 99% in patients who did not receive chemotherapy.[5] In the same series, patients on immunotherapy and hormonal therapy achieved 97% and 100% seropositivity rates, respectively.[5] The impact from combination therapy remains unclear. Massarweh et al. reported the RBD-IgG seropositivity to be lowest with combination of chemotherapy and immunotherapy at 14%, compared with chemotherapy alone at 29%, immunotherapy 22%, and biologics at 11%, although differences were nonsignificant on multivariate analysis.[8] Similarly, a meta-analysis of COVID-19 vaccination in cancer patients receiving immune checkpoint inhibitors found they had superior seroconversion compared with patients treated with chemotherapy, and no significant difference in seroconversion rate compared with healthy controls.[9] We observed seroconversion to be highest in patients on targeted therapy alone (96%), compared with chemotherapy (84%) or immunotherapy (80%). Our sample size may have limited the ability to detect any statistically significant difference. However, a large series of 503 solid tumor patients found comparable anti-S1 IgG response among immunotherapy- (99.2%), chemotherapy- (97.4%), and chemoimmunotherapy (100%)-treated patients at 28 days after the second vaccination.[10] Different timings of antibody measurement in relation to vaccine dosing may also partly account for the discordant findings.

The majority of analyses on early timepoints (within 1 month post vaccination) found comparable antibody responses among cancer patients and controls.[10–12] One of the larger series of 503 solid tumor patients reported from the Netherlands found the 28-day anti-S antibody response in each of patient cohort (immunotherapy, chemotherapy, or chemoimmunotherapy) to be non-inferior to the control cohort of individuals without cancer.[10] Another study similarly found 95% and 100% seropositivity among solid cancer patients and controls, respectively, at 2 weeks post two-dose BNT162b2 vaccination.[11] These observations suggest most cancer patients, even those on active anticancer therapy, are capable of mounting an initial antibody response to vaccination.

When considering later timepoints, however, an inferior humoral response to COVID-19 vaccination among solid tumor patients compared with the general population can be more clearly appreciated. Similar to our findings, Grinshpun et al. reported seroconversion of 87.2% among 172 cancer patients with no history of COVID-19, compared with 100% among controls, at a median of 77 days from two-dose vaccination ($p < .001$).[13] The CANVAX cohort also found significantly lower antibody titers among cancer patients compared with healthy controls, at a median of 79 days following the first vaccine dose.[4]

Decline in SARS-CoV-2 antibody level over time (without interval booster vaccination) has been a consistent finding across studies,[14–18] including ours. Ehmsen et al. reported a drop in anti-S IgG seropositivity rate from 93% at 36 days after vaccination to 86% at 3 months, among 201 patients with solid cancers.[15] The peak anti-S-RBD level occurred at a median of 42 days post second vaccine dose, with antibody levels significantly decreased at 4–6 months (median 145.5 days) among 291 cancer patients.[14] Solid tumor patients had higher peak and sustained antibody levels compared with haematological cancer patients.[14,15] Observations in our cancer patient cohort were similar, with a 95% seroconversion rate at 1 month and 88% at 3 months post two-dose COVID-19 vaccination, contrasted with 100% seroconversion at 1 and 3 months post two-dose COVID-19 vaccination in controls (Figure 1A,C). These observations highlight need for additional protective measures in this vulnerable population.[17,18]

While it is useful to account for possible background COVID-19 infection using an anti-nucleocapsid ELISA, this will not capture all cases of previous infection. Several studies used anti-nucleocapsid antibody assessment as an indicator of past infection with SARS-CoV-2,[4,14,19] given that the nucleocapsid protein is present on the viral particle but is not a component of most COVID-19 vaccines. While anti-nucleocapsid is a useful surrogate for previous COVID-19 infection, it is notable that only one of two patients with PCR-confirmed positive COVID-19 in our cohort was seropositive for nucleocapsid. We hypothesize that this is due to the short timeframe between SARS-CoV-2 infection and sample collection for anti-nucleocapsid antibody. When the first COVID-19 infection occurs after vaccination, anti-nucleocapsid antibody concentration is expected to

rise more slowly than anti-S-RBD antibody concentrations. This is due to generation of anti-nucleocapsid antibodies by a primary immune response, while the anti-S-RBD response is a tertiary immune response (as vaccines targeting S-protein previously primed this response). This is important as the undetected COVID infections will result in substantially higher apparent antibody responses to COVID vaccines.

The major limitation of our study was the sample size, which may have restricted the ability to demonstrate statistical significance. However, our use of the NIH standard in calculation of the anti-S-RBD levels allows for incorporation of our data in future meta-analyses. We were also unable to differentiate results by COVID-19 vaccine type; however, as BNT162b2 (Pfizer) was initially reserved for people under 60 years of age in Australia, any analysis of differences in vaccine response would be inherently confounded by age.

5 | CONCLUSIONS

Two doses of AZD1222 (AstraZeneca) or BNT162b2 (Pfizer) COVID-19 vaccine achieved seroconversion in 87% of cancer patients compared with 100% of control participants, at 3 months post vaccination. Both seroconversion rate and mean anti-S-RBD antibody concentrations were numerically lower among cancer patients compared with controls, although the difference did not reach statistical significance in our cohort. Antibody concentrations and seroconversion rates showed a decrease between 1 and 3 months post vaccination, highlighting the role for subsequent booster vaccinations to maintain antibody response. Our data indicate that reliance on anti-nucleocapsid antibody assays is not sufficient to exclude participants with previous COVID infection. Our study, conducted at a time of limited SARS-CoV-2 community transmission, provides a robust assessment of the humoral response from vaccination without the confounding impact of natural immunity due to infection.

ACKNOWLEDGMENTS

We wish to acknowledge funding support from the Canberra Hospital Private Practice Fund, Canberra Hospital Radiation Oncology Private Practice Fund, and John James Foundation, which made the study possible. We thank the patients and volunteers who participated in the study. We also wish to thank the medical and professional staff of the Canberra Hospital whose dedication and effort made this possible. George Cavic, Andrew A. Almonte, and Sarah M. Hicks were supported by the Australian Government Research Training Program (AGRTP) Scholarship.

Open access publishing facilitated by Australian National University, as part of the Wiley - Australian National University agreement via the Council of Australian University Librarians.

CONFLICT OF INTEREST STATEMENT

The authors declare they have no conflicts of interest.

ETHICS STATEMENT

Ethics approval for this study was provided by the ACT Health Human Research Ethics Committee (2021.ETH.00062). This applies to all data shown, unless explicitly stated otherwise in the text. Informed consent was obtained from study participants, in line with the approved ethics protocol by staff of the Canberra Hospital.

DATA AVAILABILITY STATEMENT

Data are available upon reasonable request from the corresponding author.

ORCID


George Cavic https://orcid.org/0000-0003-2657-8129

REFERENCES

1. Khoury E, Nevitt S, Madsen WR, Turtle L, Davies G, Palmieri C. Differences in outcomes and factors associated with mortality among patients with SARS-CoV-2 infection and cancer compared with those without cancer: a systematic review and meta-analysis. *JAMA Netw Open*. 2022;5(5):e2210880.
2. ACT COVID-19 statistics. Australian Capital Territory Government; updated 2023. (Accessed 1 Oct 2023) http://www.covid19.act.gov.au/updates/act-covid-19-statistics
3. Hicks SM, Pohl K, Neeman T, et al. A dual-antigen enzyme-linked immunosorbent assay allows the assessment of severe acute respiratory syndrome coronavirus 2 antibody seroprevalence in a low-transmission setting. *J Infect Dis*. 2021;223(1):10-14.
4. Naranbhai V, Pernat CA, Gavralidis A, et al. Immunogenicity and reactogenicity of SARS-CoV-2 vaccines in patients with cancer: the CANVAX cohort study. *J Clin Oncol*. 2022;40(1):12-23.
5. Thakkar A, Gonzalez-Lugo JD, Goradia N, et al. Seroconversion rates following COVID-19 vaccination among patients with cancer. *Cancer Cell*. 2021;39(8):1081-1090.e2.
6. Goshen-Lago T, Waldhorn I, Holland R, et al. Serologic status and toxic effects of the SARS-CoV-2 BNT162b2 vaccine in patients undergoing treatment for cancer. *JAMA Oncol*. 2021;7(10):1507-1513.
7. Palich R, Veyri M, Marot S, et al. Weak immunogenicity after a single dose of SARS-CoV-2 mRNA vaccine in treated cancer patients. *Ann Oncol*. 2021;32(8):1051-1053.
8. Massarweh A, Eliakim-Raz N, Stemmer A, et al. Evaluation of seropositivity following BNT162b2 messenger RNA vaccination for SARS-CoV-2 in patients undergoing treatment for cancer. *JAMA Oncol*. 2021;7(8):1133-1140.
9. Ruiz JI, Lopez-Olivo MA, Geng Y, Suarez-Almazor ME. COVID-19 vaccination in patients with cancer receiving immune checkpoint inhibitors: a systematic review and meta-analysis. *J Immunother Cancer*. 2023;11(2):e006246.
10. Oosting SF, van der Veldt AAM, GeurtsvanKessel CH, 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*. 2021;22(12):1681-1691.
11. Monin L, Laing AG, Munoz-Ruiz M, et al. Safety and immunogenicity of one versus two doses of the COVID-19 vaccine BNT162b2 for patients with cancer: interim analysis of a prospective observational study. *Lancet Oncol*. 2021;22(6):765-778.
12. Fendler A, Shepherd STC, Au L, et al. Adaptive immunity and neutralizing antibodies against SARS-CoV-2 variants of concern following vaccination in patients with cancer: the CAPTURE study. *Nature Cancer*. 2021;2(12):1305-1320.

13. Grinshpun A, Rottenberg Y, Ben-Dov IZ, Djian E, Wolf DG, Kadouri L. Serologic response to COVID-19 infection and/or vaccine in cancer patients on active treatment. *ESMO Open*. 2021;6(6):100283.
14. Figueiredo JC, Merin NM, Hamid O, et al. Longitudinal SARS-CoV-2 mRNA vaccine-induced humoral immune responses in patients with cancer. *Cancer Res*. 2021;81(24):6273-6280.
15. Ehmsen S, Asmussen A, Jeppesen SS, et al. Antibody and T cell immune responses following mRNA COVID-19 vaccination in patients with cancer. *Cancer Cell*. 2021;39(8):1034-1036.
16. Trontzas IP, Vathiotis I, Economidou C, et al. Assessment of seroconversion after SARS-CoV-2 vaccination in patients with lung cancer. *Vaccines (Basel)*. 2022;10(4):618.
17. Nelli F, Fabbri A, Onorato A, et al. Six-month immunogenicity of COVID-19 mRNA-BNT162b2 vaccine in actively treated cancer patients: updated results of the Vax-On study. *Ann Oncol*. 2022;33(3):352-354.
18. Eliakim-Raz N, Massarweh A, Stemmer A, Stemmer SM. Durability of response to SARS-CoV-2 BNT162b2 vaccination in patients on active anticancer treatment. *JAMA Oncol*. 2021;7(11):1716-1718.
19. Addeo A, Shah PK, Bordry N, et al. Immunogenicity of SARS-CoV-2 messenger RNA vaccines in patients with cancer. *Cancer Cell*. 2021;39(8):1091-1098.e2.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Cavic G, Almonte AA, Hicks SM, et al. Response to COVID-19 vaccination in patients on cancer therapy: Analysis in a SARS-CoV-2-naïve population. *Asia-Pac J Clin Oncol*. 2024;1-7. https://doi.org/10.1111/ajco.14047