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Original Article

Safety and efficacy of COVID-19 vaccines in children and adolescents with cancer

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ABSTRACT

Background. Children with cancer have a higher morbidity and mortality due to COVID-19. Vaccination of children with cancer is important. In this study, we aimed to investigate the effectiveness and side effects of the COVID-19 vaccines in children and adolescents with cancer.

Methods. Fifty-eight patients from four centers were included in the study. Antibodies to the SARS-CoV-2 spike protein levels were measured. Vaccine-related complaints were recorded.

Results. There were 33 male and 25 female patients. The mean age was 16.9±2.3 years. In 58.6% of cases, the diagnosis was hematological malignancies. Twenty patients were currently under treatment, while 38 had completed the treatment. Forty-eight patients received chemotherapy ± radiotherapy, 13 received immunotherapy, and 3 underwent stem cell transplantation. CoronoVac© and BNT162b2© vaccines were administered in 24% and 76%, respectively. The mean antibody level was lower in patients who received CoronaVac© than that of BNT162b2©, although the difference was not significant. The levels were within the protective limits in both groups. No significant difference was found in antibody levels according to diagnostic subgroups, treatment status, type of treatment, line of treatment, disease status and time between vaccines and measurement of antibody level. The most common side effects were pain at the injection site (37.9%) and malaise/weakness (17.2%), which were similar for both vaccines.

Conclusions. Our study showed that both mRNA and inactivated vaccines elicit an immune response in children with cancer. However, the seroconversion rate is significantly higher in mRNA vaccines. Side effects were similar to those seen in healthy children.

Key Words: cancer, COVID-19, vaccines, immunization.

As of the end of 2022, there are approximately a total of 650 million confirmed cases of coronavirus disease 2019 (COVID-19) and more than 6 million deaths reported by the World Health Organisation (WHO) globally.[1] In Türkiye, more than 17.000.000 cases of COVID-19 and 100.000 deaths have been reported.[2] At the beginning of the COVID-19 pandemic, the infection occurred infrequently in children, and most of them were asymptomatic or mildly symptomatic. However, new variants of the virus have resulted in significant changes in the clinical epidemiology of pediatric COVID-19. It was observed that the new variants affect a larger portion of the young population and that 18.8% of all COVID-19 infections were seen in children and adolescents.[3,4] Although

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the clinical signs in children became similar to those in adults, the frequency of serious and critical disease and the mortality rate due to COVID-19 remained low. Adults with cancer are reported to have a higher risk for COVID-19 and have more severe disease and higher mortality than the general population.[5] More than 25% of patients with cancer who catch the virus have died from the COVID-19 infection, while 0.9% of the normal population with COVID-19 have died.[1,5] At the end of 2022, there were 1814 children with cancer and laboratory confirmed COVID-19 infection reported from 51 countries.[6] Children with cancer are reported to have more severe and critical disease and a higher mortality rate (20% and 3.8%) due to COVID-19 than children without a cancer diagnosis (%12 and 1.9%).[4,6,7] Although several pharmacological agents are available, including antivirals (such as antiretrovirals, which are used for HIV infections, remdesivir, which was used in the Ebola epidemic), immunomodulatories, and monoclonal antibodies, a specific drug to cure COVID-19 has yet to be found.[3,8] It is now well established that vaccination is an optimal strategy to prevent infection or at least reduce its severity.[4]

Active immunization against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been shown to be highly effective at reducing the incidence, preventing severe illness and death from COVID-19. As of the end the 2022, approximately 50 vaccines were approved by at least one country, and at least one COVID-19 vaccine was approved in 201 countries.[9] On December 11, 2021, the U.S. Food and Drug Administration (FDA) approved an emergency use authorization for mRNA vaccine (PfizerBioNTech/Comirnaty) as a 2-dose series for the prevention of symptomatic COVID-19 in individuals aged ≥16 years.[9,10] Vaccination programs have been started by prioritizing high-risk groups in adults around the world[9] since December 2020 and in our country since January 2021[11]. In July 2021, the European Medicine Agency approved the use of the vaccine at the age of 12-17. Following this the age of immunization expanded to include age >5 years.[12] In the pediatric age, immunization is offered by a messenger RNA vaccine shot in the muscle of the upper arm. The schedule consists of a 2-dose primary series in children 5–11 years, with a booster dose in adolescents.[10,12-14] In our country, children over the age of 15 and between the ages of 12 and 15 with chronic diseases have been included in the vaccination program since 18 August 2021. Finally, as of September 6, the vaccination program has been expanded to include those over the age of 12 with the consent of the family. Three vaccines are in use in our country: mRNA BNT162b2© (Pfizer/BioNTech), inactivated CoronaVac© (Sinovac) and the inactivated Turkovac© (T.C. TUSEB).[11] After the experiences in adults, good efficacy and an acceptable security profile and effectiveness were demonstrated in children who received the COVID-19 vaccination.[13] Among children and adolescents, the safety of current COVID-19 vaccines is acceptable, and studies have suggested that mRNA vaccines can provide high protection against COVID-19 infection in pediatric age groups.[13,15]

Patients with cancer are at increased risk for greater morbidity and mortality due to COVID-19 infection.[5,6] Several studies have provided satisfactory evidence on the protective role of COVID-19 vaccines in patients with malignant disease.[16] In addition, COVID-19 vaccines are found to be safe and well tolerated in adults with cancer.[17] Based on this evidence, it was recommended that adults with cancer should receive the recommended dose and schedule of one of the COVID-19 vaccines. Among adults with cancer who were receiving active systemic chemotherapy, most exhibited an adequate antibody response to vaccines, although their antibody titers were lower than those of healthy controls, especially in cases with hematological malignancies.[16,17]

However, studies evaluating the immunogenicity and safety of COVID-19 vaccines in children with cancer are limited.[18,19] There are concerns regarding the protection of children with cancer through the standard

vaccination program and the safety of vaccines. In this regard, we performed this study to investigate the effectiveness and side effects of the COVID-19 vaccines.

Patients and Methods

The study included a total of 58 patients from four pediatric cancer centers. These patients had received at least two doses of the COVID-19 vaccine and had a minimum of 15 days since their previous immunization. The study protocol was approved by the Institutional Ethics Committee of Hacettepe University (2022/10-06). Written informed consent was obtained from the participants and/or their parents. Vaccine-related complaints observed by patients and parents were asked and recorded. A 5 ml venous blood sample was drawn from patients. The whole blood was allowed to clot by leaving it undisturbed at room temperature. This usually took 15–30 minutes. The clot was removed by centrifuging at 1,000– 2,000 g for 10 minutes. Following centrifugation, the serum was transferred into a clean polypropylene tube and stored at –20°C. Quantitative determination of antibodies to the SARS-CoV-2 spike protein levels was performed with Roche Elecsys© Anti-SARS-CoV-2S kit by electro chemiluminescence immunoassay method. The relationship between antibody response and vaccine type, diagnosis, disease status, treatment process, and treatment type were investigated.

Statistical analyzes were performed using IBM SPSS Statistics version 23.0. software. Categorical variables were recorded as numbers and percentages, and continuous variables were recorded as means ± standard deviations (SD) and median (interqunartile range) as appropriate. Compliance with normal distribution was examined with the Shapiro-Wilk test. The Mann-Whitney U test was used to compare the antibody levels between two vaccine groups. Antibody levels according to diagnostic groups (hematological malignancies and solid tumors), type of treatment (chemotherapy, chemoradiotherapy, immunotherapy ± chemotherapy), line of treatment (first line / second line or more), treatment status (completed / continued), disease status (active / remission), time between two vaccines (3-6 weeks / more than 6 weeks), and time between the last vaccine dose to the time point of measurement of antibody levels (less than 90 days/between 90 to180 days / between 180 to 270 days) were also compared. The comparison between two and three groups were performed with Mann-Whitney U and Kruskal Wallis tests, respectively. Frequencies of side effects in different groups were compared with Fisher's exact test. The *p*-value of less than 0.05 was considered significant.

Results

There were 33 male and 25 female patients with a mean age of 16.9±2.3 (12-21) years. The most common diagnoses were hematological malignancies (2 leukemia, 30 lymphomas and 2 Langerhans cell histiocytosis) in 34 patients (58.6%), followed by bone and soft tissue sarcomas in 13 (22.5%) (Table I). Twenty patients were currently on-treatment and they were vaccinated at the midpoint of the time between two courses (7-15 day before and after treatment). Patients taking oral agents did not interrupt their treatment. Treatment of 38 cases was completed (within the last 6 months in 13 patients, between 6 months and 1 year in 8 patients, and more than 1 year ago in 17 patients). Fifty-six patients recieved chemotherapy, 25 of those also received radiotherapy. In total, 12 patients received immunotherapy alone or in combination with chemotherapy. Seven patients received their vaccines with nivolumab (3), bevacizumab (1), entrectinib (1), sirolimus (1) and denosumab (1), and five patients received brentixumab (2), temsirolimus (1), nivolumab (1) and rituximab (1) before vaccination. Three cases underwent stem cell transplantation and have been followed in remission for 2-5 years before vaccination. Because of relapsed / refractory disease, twelve patients took second or more advanced line treatment. CoronoVac© and BNT162b2© COVID-19 vaccines were

administered in 24% and 76% of patients, respectively. At the time of the study, 86% of the patients were vaccinated with two doses, while only 13.8% received three doses. Antibody levels were lower than 300 U/ml in 35.7% and 6.8% of cases vaccinated with CoronoVac© and BNT162b2©, respectively (p: 0.015). The median time between the last dose of vaccine and measurements of antibody levels was 60 (15-270) days. The time between the last dose of vaccine and antibody measurement was less then 90 days in 35 (31.6%) cases, between 90 and 180 days in 17 (29.6%) cases, and between 180 and 270 days in 6 (17%) cases. Although levels in the third group (1204±1166.2 U/ml) was lower than that of second (1974.9±884.5 U/ml) and first group (2225.1±666.8 U/ml), the difference was not significant. When evaluated according to the vaccine type, the mean antibody level was found to be lower in those who received CoronaVac© compared to those who received BNT162b2© (1649.85±1143.04 vs 2172.22±682.10 U/ml). However, the difference was not statistically significant. It was determined that the mean antibody level during the treatment was within the protective limits for the infection (1890.93±972.47 U/ml), but it was lower than the antibody level in the patients whose treatment was discontinued (2128.21±756.57 U/ml) (p>0.05). No significant difference was found in antibody levels according to diagnostic subgroups, treatment status, type of treatment, line of treatment, disease status, and time between vaccines and measurement of antibody level.

The most common side effect was pain at the injection site (51.7%), followed by swelling/redness at the injection site (24.1%) and malaise/fatigue (18.9%). Although some side effects such as lymphadenopathy and headache, were seen only with BNT162b2© vaccine, there was no significant difference in the frequency of side effects in vaccine types (Table I). Side effects were not different between patients whose were on-treatment and off-treatment.

Discussion

Immunosuppressive diseases, cancer or treatment with anticancer drugs, and stem cell transplantation have suppressive effects on humoral, cell-mediated immunity and neutrophil function. It is known that children with cancer have an increased the risk of severe infections and complications caused by viral agents, such as adenovirus, respiratory syncytial virus, influenza and other agents.[20] Substantial evidence revealed that children with cancer have a higher risk for COVID-19 infection, and more severe disease and mortality. It was reported that almost 22% of the children with cancer had severe/critical disease and 18% necessitated intensive care.[5-7] Vaccination of patients with cancer became more important since they have higher morbidity and mortality due to the infection.[18,19] There have been numerous studies including meta-analyses in adults with a high number of patients. However, studies evaluating the immunogenicity and safety of vaccines in children with cancer are limited, although experts recommend them. The number of patients in those studies are small and the results are contradictory.[21-29]

The effectiveness of vaccines in children with cancer has been evaluated by measuring the T cell and/or most often B cell immune response, and/or by determining the rate of getting SARS-CoV-2 infection. We investigated immune response by measuring spike antibody levels and found that COVID-19 vaccines elicited an effective immune response. Miao et al.[21] compared the frequency of COVID-19 infection in vaccinated and unvaccinated children with cancer and showed that vaccination reduced the rate of infection and significantly improved clinical outcomes. In another study, none of the study subjects developed clinical disease at 12 weeks' follow-up after administration of the second dose of vaccine.[22] Revon-Riviere et al.[23] reported that 9 of 10 (90%) adolescent and young adult patients who were under cancer treatment had positive serology one month after the second vaccine injection; in addition, none

Table I. Characteristics of patients according to vaccine type.

Feature of Patients	Whole group	Type of Vaccine	
		m-RNA (BNT162b2©)	Inactivated (CoronaVac©)
Total number	58	44	14
Sex (M/F)	33/25	31/13	2/12
Age (median/range)	16.9±2.3 (12-21)	16.8±3.1 (12-21)	17.1±2.8 (12-21)
Diagnosis			
Hematological			
Leukemia	2 (3.4%)	-	2 (14.3%)
Hodgkin lymphoma	16 (24.1%)	10 (22.7%)	6 (42.8%)
Non-Hodgkin lymphoma	14 (31.8%)	12 (27.3%)	2 (14.3%)
Histiocytosis	2 (3.4%)	2 (4.5%)	-
Solid Tumors			
Central nervous system tumors	5 (8.6%)	4 (9.1%)	1 (7.1%)
Bone sarcomas	7 (20.5%)	6 (13.6%)	1 (7.1%)
Soft tissue sarcomas	6 (10.4%)	5 (11.3%)	1 (7.1%)
Germ cell tumors	3 (5.2%)	3 (6.8%)	-
Others	3 (5.2%)	2 (4.5%)	1 (7.1%)
Treatment Status			
On-treatment	20 (34.5%)	16 (36.4%)	4 (28.6%)
Off-treatment	38 (65.5%)	28 (63.3%)	10 (71.4%)
Type of treatment			
Chemotherapy	31 (53.4%)	23 (52.3%)	8 (57.1%)
Chemotherapy+radiotherapy	25 (43.1%)	20 (45.4%)	5 (35.7%)
Immunotherapy±chemotherapy	12 (20.6%)	8 (18.2%)	3 (21.4%)
Autologous haematopoietic stem cell transplantation	3 (51.7%)	3 (6.8%)	
Line of treatment			
First line	46 (79.3%)	35 (79.5%)	11 (78.6%)
Second line	8 (13.7%)	6 (13.6%)	2 (14.3%)
≥Third line	4 (6.9%)	3 (6.8%)	1 (7.1%)
Antibody level (U/ml)			
Mean±SD	2046.13±836.54	2172.22±682.10	1649.85±1143.04
Range	50-2500	136-2500	50-2340
Median (Interquartile range)	2500 (412.25)	2500 (2271.75)	2500 (252)
Side effects			
Arm pain	30 (51.7%)	22 (50%)	8 (57%)
Reaction in injection site	14 (24.1%)	9 (20.5)	5 (35.7%)
Malaise/fatigue	11 (18.9%)	9 (20.5)	2 (14.3%)
Myalgia	8 (13.7%)	7 (15.9%)	1 (7.1%)
Headache	5 (8.6%)	5 (11.4%)	-
Fever	6 (10.3%)	4 (9.0%)	1 (7.1%)
Lymphadenopathy	3 (5.1%)	3 (6.8%)	-
Bone and joint pain	2 (34.5%)	2 (4.5%)	1 (7.1%)

SD: standard deviation.

of the them developed COVID-19 infection. Lehrnbecher et al.[25] showed that seroconversion was achieved in 9 out of 11 (82%) adolescents with cancer after completion of two doses of vaccine and remained at effective levels for six months. Although we did not follow-up the antibody levels longitudinally, the median time between the last dose of the vaccine and measurements of antibody level was 60 days and reached to 270 days. Similar to most published reports, we evaluated the immunogenicity of the vaccine after two doses and found adequate antibody response. However, there are studies showing a significant increase in both the percentage of responsive patients and antibody titers after the 3rd dose.[25,26] It was found that detectable antibodies against SARS-CoV-2 were 76.2% (16/21) and 90% (18/20) after 2 and 3 doses, respectively.[25] Poparn et al.[22] compared the immune response to BNT162b2 mRNA vaccine in on-therapy and off-therapy pediatric cancer cases and found that the antibody levels were significantly low in the on-therapy group. Conversly, we did not find a significant difference between the antibody levels of patients receiving treatment and patients whose treatment was completed. Although the majority of the studies in the literature, including ours, showed COVID-19 vaccines provide adequate immune protection in children with cancer[21-26], the opposite results have rarely been reported. In a recent study, it was reported that only 36.4% of 11 cases showed adequate B-cell responses, while 77.8% showed adequate T-cell response.[27]

There are a some studies that include a healthy control group and children with cancer comparing the immune response to the COVID-19, but the results are contradictory.[27-29] Ma et al.[28] reported that 68.4% of children with cancer became seropositive after two doses of vaccine, but the seroconversion rate was significantly lower than that of healthy controls (86.5%). Additionally, antibody titers were found to be significantly lower in the patient group than in healthy children. In contrast, Martin et al.[29] reported that pediatric patients with cancer had similar immunoglobulin titers, antibody binding capacity, and effector function assay activity after vaccination against COVID-19 compared with healthy controls. Although we did not have a control group, we found that the effectiveness of the vaccines were similar to that reported in healthy children. In a meta-analysis of 88 articles on pediatric vaccination, the seroconversion rates after the second and third doses of the vaccines were found to be 96.5% and 99.8%, respectively.[15] In another systematic analysis it was reported that mRNA vaccines were found to be 91%–100% efficacious in preventing COVID-19 among children and adolescents.[13]

Vaccine studies in pediatric cancer patients in the literature have mostly been carried out with mRNA vaccines.[22-29] In a study conducted in China, it was shown that the inactivated vaccine was effective in children with hematology/oncology diseases.[21] We could not find any study comparing the different vaccine types in children with cancer. We compared an inactivated (CoronaVac) and a mRNA vaccine (BNT162b2) and showed that the mean antibody levels were within the protective limits in both groups.

Overall, COVID-19 vaccines were reported to be well tolerated. Approximately 50% of our patients had mild/moderate side effects. Pain and local reactions in the injection site were the most common complications reported in the literature similar to our study.[22,23,27] Although we did not have a healthy control group, we found that the frequency and distribution of side effects in our patients were not much different from those in studies conducted on healthy children. In a meta-analysis including 88 articles, the five adverse events with the highest incidence rates were tenderness (53%), injection site pain (51%), fatigue / asthenia / tiredness (24%), headache (20%), and myalgia / muscle pain (15%).[15] Ma et al.[28] showed that adverse events of the vaccines reported during follow-up were graded as I and II, and all adverse events were either self-limited or medically well-managed. The frequency and severity of side effects were

not found to be different between children with cancer and healthy children.

Our study has some limitations. Due to the lack of a control group, we did not have the opportunity to compare the results with healthy children. Since the vaccination process is not prospective, that is, the study was conducted on vaccinated patients, the number of doses, the time between doses, and the time of measurement of the antibody level were heterogeneous. In addition, we did not continue to monitor antibody levels, and hence we could not determine how long the immune protection provided by the vaccine lasted.

In conclusion, despite these limitations, our study provided some important implications. We showed that the seroprotective level of COVID-19 vaccines in children with cancer who receive anticancer treatment are effective but low compared with patients who completed the treatment. Both mRNA and inactivated vaccines produce immune responses, although antibody titers were lower with the inactivated vaccine than the mRNA vaccine.

Ethical approval

The study was conducted with the approval of the Ethics Committee of the Hacettepe University, (2022/10-06).

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: NK,TK, MC; data collection: NK, İK, ŞY, ÖV, OSD; analysis and interpretation of results: NK, TK; draft manuscript preparation: NK, TK. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

1. World Health Organization (WHO). Coronavirus disease (COVID-19) pandemic: WHO Coronavirus (COVID-19) Dashboard. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019 (Accessed on March 23, 2023).
2. Republic of Türkiye Ministry of Health. COVID-19 information platform. Available at: https://covid19.saglik.gov.tr/TR-66935/genel-koronavirus-tablosu.html (Accessed on March 23, 2023).
3. Habet V, Oliveira CR. Clinical epidemiology of pediatric Coronavirus disease 2019 and its postacute sequelae. Semin Respir Crit Care Med 2023; 44: 66-74. https://doi.org/10.1055/s-0042-1759566
4. Gupta SL, Tyagi R, Dhar A, Oswal N, Khandelwal A, Jaiswal RK. Children's SARS-CoV-2 infection and their vaccination. Vaccines (Basel) 2023; 11: 418. https://doi.org/10.3390/vaccines11020418
5. Saini KS, Tagliamento M, Lambertini M, et al. Mortality in patients with cancer and coronavirus disease 2019: a systematic review and pooled analysis of 52 studies. Eur J Cancer 2020; 139: 43-50. https://doi.org/10.1016/j.ejca.2020.08.011
6. Mukkada S, Bhakta N, Chantada GL, et al. Global characteristics and outcomes of SARS-CoV-2 infection in children and adolescents with cancer (GRCCC): a cohort study. Lancet Oncol 2021; 22: 1416-1426. https://doi.org/10.1016/S1470-2045(21)00454-X
7. Kebudi R, Kurucu N, Tuğcu D, et al. COVID-19 infection in children with cancer and stem cell transplant recipients in Turkey: a nationwide study. Pediatr Blood Cancer 2021; 68: e28915. https://doi.org/10.1002/pbc.28915
8. National Institutes of Health. COVID-19 treatment guidelines panel. Coronavirus disease 2019 (COVID-19) treatment guidelines. Available at: https://www.covid19treatmentguidelines.nih.gov (Accessed on March 23, 2023).

9. Basta NE, Moodie EMM on behalf of the VIPER (Vaccines, Infectious disease Prevention, and Epidemiology Research) Group COVID-19 Vaccine Development and Approvals Tracker Team. COVID-19 vaccine development and approvals tracker. 2020. Available at: https://covid19.trackvaccines.org

10. National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases. CDC COVID-19 Science Briefs. Atlanta (GA): Centers for Disease Control and Prevention (US); 2020-2021 Sep 15. Available at: https://www.ncbi.nlm.nih.gov/books/NBK570439/

11. Republic of Türkiye Ministry of Health. COVID-19 vaccines information platform. Available at: https://covid19asi.saglik.gov.tr/TR-77706/covid-19-asisi-ulusal-uygulama-stratejisi.html (Accessed on March 23, 2023).

12. Hause AM, Baggs J, Marquez P, et al. COVID-19 vaccine safety in children aged 5-11 Years - United States, November 3-December 19, 2021. MMWR Morb Mortal Wkly Rep 2021; 70: 1755-1760. https://doi.org/10.15585/mmwr.mm705152a1

13. Tian F, Yang R, Chen Z. Safety and efficacy of COVID-19 vaccines in children and adolescents: a systematic review of randomized controlled trials. J Med Virol 2022; 94: 4644-4653. https://doi.org/10.1002/jmv.27940

14. Bozzola E, Caffarelli C, Santamaria F, Corsello G. The year 2021 in COVID-19 pandemic in children. Ital J Pediatr 2022; 48: 161. https://doi.org/10.1186/s13052-022-01360-0

15. Gao P, Kang LY, Liu J, Liu M. Immunogenicity, effectiveness, and safety of COVID-19 vaccines among children and adolescents aged 2-18 years: an updated systematic review and meta-analysis. World J Pediatr 2023; 19: 1041-1054. https://doi.org/10.1007/s12519-022-00680-9

16. Kuderer NM, Hill JA, Carpenter PA, Lyman GH. Challenges and opportunities for COVID-19 vaccines in patients with cancer. Cancer Invest 2021; 39: 205-213. https://doi.org/10.1080/07357907.2021.1885596

17. 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: 1133-1140. https://doi.org/10.1001/jamaoncol.2021.2155

18. Caniza MA, Homsi MR, Bate J, et al. Answers to common questions about COVID-19 vaccines in children with cancer. Pediatr Blood Cancer 2022; 69: e29985. https://doi.org/10.1002/pbc.29985

19. Furlong E, Kotecha RS, Conyers R, et al. COVID-19 vaccination in children and adolescents aged 5 years and older undergoing treatment for cancer and non-malignant haematological conditions: Australian and New Zealand Children's Haematology/Oncology Group consensus statement. Med J Aust 2022; 216: 312-319. https://doi.org/10.5694/mja2.51444

20. Kaltsas A, Sepkowitz K. Community acquired respiratory and gastrointestinal viral infections: challenges in the immunocompromised host. Curr Opin Infect Dis 2012; 25: 423-430. https://doi.org/10.1097/QCO.0b013e328355660b

21. Miao J, Zhang JY, Liang J, et al. Efficacy of inactivated SARS-CoV-2 vaccination in pediatric hematology/oncology patients: a real-world study. World J Pediatr 2023; 19: 1017-1021. https://doi.org/10.1007/s12519-023-00737-3

22. Poparn H, Srichumpuang C, Sosothikul D, et al. Immune response after 2 doses of BNT162b2 mRNA COVID-19 vaccinations in children and adolescents with cancer and hematologic diseases. Asian Pac J Cancer Prev 2022; 23: 2049-2055. https://doi.org/10.31557/APJCP.2022.23.6.2049

23. Revon-Riviere G, Ninove L, Min V, et al. The BNT162b2 mRNA COVID-19 vaccine in adolescents and young adults with cancer: a monocentric experience. Eur J Cancer 2021; 154: 30-34. https://doi.org/10.1016/j.ejca.2021.06.002

24. Donze C, Ninove L, de Lamballerie X, Saultier P, Andre N. Six-month BNT162b2 vaccine efficacy in adolescents and young adults with cancer. Pediatr Blood Cancer 2022; 69: e29547. https://doi.org/10.1002/pbc.29547

25. Lehrnbecher T, Sack U, Speckmann C, et al. Longitudinal immune response to 3 doses of messenger RNA vaccine against Coronavirus disease 2019 (COVID-19) in pediatric patients receiving chemotherapy for cancer. Clin Infect Dis 2023; 76: e510-e513. https://doi.org/10.1093/cid/ciac570

26. Schmidt KLJ, Dautzenberg NMM, Hoogerbrugge PM, et al. Immune response following BNT162b2 mRNA COVID-19 vaccination in pediatric cancer patients. Cancers (Basel) 2023; 15: 2562. https://doi.org/10.3390/cancers15092562

27. D'Souza AM, Thomas M, Gnanamony M, Nguyen TH, de Alarcon PA. SARS-CoV-2 vaccination response in pediatric oncology patients. Pediatr Blood Cancer 2024; 71: e30785. https://doi.org/10.1002/pbc.30785

28. Ma Y, Chen B, Wang Y, et al. Reducedhumoral response against variants of concern in childhood solid cancer patients compared to adult patients and healthy children after SARS-CoV-2 vaccination. Front Immunol 2023; 14: 1110755. https://doi.org/10.3389/fimmu.2023.1110755

29. Martin SD, Nziza N, Miozzo P, et al. Humoral profiling of pediatric patients with cancer reveals robust immunity following anti-SARS-CoV-2 vaccination superior to natural infection. Pediatr Blood Cancer 2023; 70: e30473. https://doi.org/10.1002/pbc.30473