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# Vaccinations following CAR-T cell therapy: summary of reported cases and state-of-the-art review of current recommendations

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## Abstract

**Introduction:** Chimeric antigen receptor T-cell (CAR-T) therapy is a modern breakthrough technology used in the treatment of B-lineage lymphoid malignancies. These malignancies include acute lymphoblastic leukemia, non-Hodgkin lymphoma, and plasma cell disorders. CAR-T therapy combines cellular therapy, gene therapy, and individualized therapy. The objective of this paper was to review the latest clinical knowledge, and summarize the reported data pertaining to vaccinations in patients after CAR-T therapy.

**Material and methods:** We carried out a review of published original studies as indexed in PubMed, and a review of abstracts presented during major hematology meetings.

**Results:** Overall, 22 original studies were reviewed and considered suitable for analysis regarding the efficacy of vaccinations for patients who had received CAR-T therapy. Data was divided into three groupings: the efficacy of vaccination against coronavirus disease 2019 (COVID-19)/severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); the efficacy of vaccination against influenza; and the efficacy of post-CAR-T immunization persistence of vaccination performed before CAR-T therapy. Humoral and cellular response to SARS-CoV-2 vaccination was positive for 36.5% and 72.2% of patients, respectively. The positive response to the influenza vaccine was 40% when administered prior to CAR-T therapy, as opposed to 31% after. Seroprotection for vaccine-preventable infections within 3–6 months after CAR-T was comparable to that of the general population, although it was determined to be less effective against specific pathogens (S. pneumoniae, B. pertussis, H. influenzae) in most patients.

**Conclusions:** In cases of incomplete immune reconstitution, there is a high likelihood of a limited response to vaccination. Regarding the SARS-CoV-2/COVID-19 vaccine, T-cell-induced protection is relatively significant. Therefore, B-cell aplasia is not a contraindication for vaccination in CAR-T patients. The consensus of European Society of Blood and Marrow Transplantation/European Hematology Association experts is that vaccination after CAR-T therapy is beneficial in order to reduce the rates of infection, and eventually to improve clinical course.

**Key words:** CAR-T, vaccination, acute lymphoblastic leukemia, non-Hodgkin lymphoma, multiple myeloma, SARS-CoV-2, COVID-19, influenza

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## Introduction

Chimeric antigen receptor T-cells (CAR-T) therapy is a modern breakthrough technology used in the treatment of B-lineage lymphoid malignancies including acute lymphoblastic leukemia, non-Hodgkin lymphoma, and plasma cell disorders. CAR-T therapy combines cellular therapy, gene therapy, and individualized therapy. This treatment has been shown to be highly effective and safe for patients with an otherwise resistant, relapsing or refractory stage [1–5]. Even so, various complications can occur.

Approximately three to six months after commencing CAR-T therapy, the immune recovery of T-cells has been observed, while humoral response obviously occurs much later [6, 7]. Nevertheless, in the majority of patients who have achieved remission, B-lineage suppression and hypogammaglobulinemia were present. This condition results from expected activity of anti-CD19 CAR-T cells [8, 9]. Prevention of infections is of great importance in these patients [10, 11]. Supplementation of immunoglobulins is also important, especially in children [12].

Thus far, little is known about the use of vaccinations and the respective immune response in this cohort of patients. Therefore, the objective of this paper was to review the current clinical knowledge and to summarize reported data on vaccinations in patients after CAR-T therapy.

## Material and methods

### Design of study

Analysis and summary of available original data on the efficacy of vaccinations in patients after therapy with CAR-T cells, reported up to 28 February 2022.

### Source data

Review of published original reports indexed in PubMed and review of abstracts presented during meetings of American Society of Hematology (ASH), American Society of Transplantation and Cellular Therapy (ASTCT), Center for International Blood and Marrow Transplant Research (CIBMTR) Tandem Meetings and European Society of Blood and Marrow Transplantation (EBMT) up to 28 February 2022 (including the 2022 ASTCT and EBMT meetings, because these abstracts were already available online). No vaccination issues were presented at the 4th European CAR T-cell Meeting (10–12 February 2022).

### Inclusion criteria

We included patients after CAR-T therapy, and original data on humoral or cellular response to vaccination performed 1) after, and 2) before, the application of CAR-T therapy. Only studies reporting data of at least three patients after CAR-T therapy, with available information on their response to vaccination, were included in our analysis.

### Literature search and selection

A literature search was conducted by two researchers (TS, JSa), and checked by all other study group members. The key words used in data search were: 'chimeric receptor antigen' or 'CAR-T' or 'CAR T-cell' as well as 'vaccination' or 'vaccine'. The following data was retrieved from these reports: vaccination target disease, number of patients included, analysis of their response to vaccination, time elapsed between CAR-T infusion and vaccination, type of response to vaccination (humoral or cellular), and the response rate.

### Definitions

- CAR-T — lymphocytes T with chimeric antigen receptor directed against B-cell antigens (CD19, BCMA).
- BCMA — B-cell maturation antigen, analyzed in patients with multiple myeloma.
- CAR-T products (registered up to the end of 2021): tisagenlecleucel, axicabtagene ciloleucel, brexucabtagene autoleucel, idecabtagene vicleucel, and lisocabtagene maraleucel.
- Vaccination response — both humoral and cellular response. Humoral response to vaccination was measured by the presence of specific antibodies. Cellular response was measured by the presence of specific T-cells.
- Immune reconstitution — absolute number of CD4 T-cells >0.2 × $10^9$/L, number of CD19 or CD20 positive B-cells >0.2 × $10^9$/L, without concomitant cytotoxic or immunosuppressive therapy.

### Statistical analysis

Chi-square test of the Fisher exact test was used to analyze the differences of categorical variables between groups. Odds ratio (OR) and 95% confidence intervals (CI) were determined, if p-value was significant (<0.05).

## Results

### Reported data

Overall, 22 original studies were deemed suitable for analysis of the efficacy of vaccinations in patients who had been administered CAR-T therapy (Table I).

According to the objective and design of our study, data were grouped and analyzed in three topics:

- efficacy of vaccination against coronavirus disease 2019 (COVID-19)/severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2);
- efficacy of vaccination against influenza;
- efficacy of post-CAR-T immunization persistence of vaccination performed before CAR-T therapy.

**Table I.** Potentially relevant and selected for analysis original reports on vaccination after chimeric antigen receptor T-cell (CAR-T) therapy

| Source | Period analyzed | CAR-T reports | Vaccination after CAR-T | Potentially relevant | Selected for analysis |
|---|---|---|---|---|---|
| PubMed | Up to 28.02.2022 | 6,135 | 148 | 10 | 10 |
| ASH 2021 | 63rd Annual Meeting, 11–14 December 2021, Atlanta, USA | 388 | 15 | 7 | 7 |
| ASTCT 2022 | 2022 Tandem Meetings, 23–26 April 2022, Salt Lake City, USA | 108 | 7 | 7 | 4 |
| EBMT 2022 | 48th Annual Meeting, 20–23 March 2022, Prague, Czech Republic | 44 | 2 | 1 | 1 |

ASH — American Society of Hematology; ASTCT — American Society of Transplantation and Cellular Therapy; EBMT — European Society of Blood and Marrow Transplantation

## Vaccination against COVID-19/ /SARS-CoV-2

A total of eight published studies and 11 meeting reports were found relevant for this topic (Table II) [6, 13–19]. Overall response to the SARS-CoV-2 vaccination was positive for 88/241 (36.5%) patients in criteria of humoral response, and for 26/36 (72.2%) patients in criteria of cellular response. Thus, patients after CAR-T therapy produced a better cellular than humoral response after vaccination against SARS-CoV-2, with OR = 4.5 (95% CI = 2.1–9.8), $p$ <0.001 (Fisher exact test).

## Vaccination against influenza

Only one study has been published [20], with 18 vaccinated patients including five prior to and 13 after the administration of CAR-T therapy. The time between vaccination and CAR-T therapy was 14–29 days prior (n = 5) or 13–57 months following the infusion (n = 13). In this study, commercially available inactivated influenza vaccines were used in adult patients. Response to vaccination was measured in the pre-CAR-T cohort 90 days following CAR-T therapy, and in the post-CAR-T patients approximately 90 days after vaccination. Humoral immunogenicity was analyzed and response to vaccination was defined by hemagglutination inhibition (HAI) titer. Seroprotection against influenza was defined as an HAI titer ≥40. Response to vaccination was 2/5 (40%) before, and 4/13 (31%) after CAR-T.

## Response to vaccine-preventable infections after CAR-T therapy

In two studies, the proportion of patients with antibody levels above a threshold value was analyzed for seroprotection for vaccine-preventable infections (Table III). Overall humoral response within 3–6 months was comparable to the general population. However, seroprotection for specific pathogens (*Streptococcus pneumoniae, Bordetella pertussis, Hemophilus influenzae*) was found to be lacking in most patients. Additionally, even with these different patient cohorts, it was clear that protective seroconversion decreased between the third and the sixth month after CAR-T therapy. Walti et al. [21] underscored that CD19-CAR-T cell recipients had better seroprotection than BCMA-CAR-T cell patients. Neither total IgG concentration over 4 g/L, nor immunoglobulin supplementation, was associated with improved seroprotective IgG titers [21]. Prophylactic immunoglobulin replacement therapy did not confer immunization protection (ASH #3857).

# Discussion

From the introduction of CAR-T technology into the treatment of patients with B-cell-lineage acute lymphoblastic leukemia, then in non-Hodgkin lymphoma and multiple myeloma, the question of how to prevent infections before, during, and after CAR-T infusion has been a vital topic in patient management [11, 22–24], although there is a lack of evidence [10]. As a consequence of the COVID-19 pandemic, a new generation of vaccines was developed, and a universal vaccination program was introduced worldwide. By 1 March 2022, almost 5 billion people had been vaccinated with at least one dose of the SARS-CoV-2/ /COVID-19 vaccine, 63.8% of the entire world population (https://ourworldindata.org). Data on vaccination in CAR-T patients is very limited, but more and more studies have been presented at hematology, transplantation and cellular therapy forums.

In our study, we have summarized the available data regarding the response to vaccinations in patients who had been administered CAR-T therapy. The overall humoral response to SARS-CoV-2/COVID-19 vaccine, based upon 18 studies, was 36.5%. A similar percentage was found in a small cohort of patients vaccinated against influenza. On the other hand, cellular response to the SARS-CoV-2/ /COVID-19 vaccine was much better, and reached 72.2%. The importance of this result, based on three small studies, cannot be overstated [10, 25].

**Table II.** Summary of reported data in abstracts and full papers on vaccination against coronavirus disease 2019 (COVID-19)/severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

| Source | Patients included | Patients analyzed | Time of vaccination after CAR-T (median, range) | Final response | Follow-up |
|---|---|---|---|---|---|
| ASH #254 | 23 | 20 | 401 (113–819) days | 6/20 (30%) | No COVID-19 infection after 77 days (range: 49–127) |
| ASH #754 | 47 | 47 | NA | 11/47 (23.4%) | Booster vaccination 5 months after initial vaccination |
| ASH #1750 | 17 | 17 | 250 (32–881) days | 13/17 (76.4%) | MM higher titer response than NHL |
| ASH #1757 | 12 | 12 | 40.6 months (1,230 days) | 8/12 (66.7%) | Vaccine-specific antibody was strongly associated with level of circulating B cells |
| ASH #2504 | 8 | 8 | >12 months | 1/8 (12.5%) | Treatment with CAR-T was associated with lower immune response than HCT |
| ASH #2537 | 7 | 7 | >12 months | 1/7 (14.3%) | Treatment with CAR-T was associated with lower B titers |
| EBMT #P113 | 8 | 8 | 48 months | 8/8 (100%) | Cellular response |
| ASTCT #475 | 6 | 6 | Within 12 months after CAR-T therapy | 0/6 (0%) | No CAR-T recipients responded to first dose |
| ASTCT #264 | 11 prior<br>22 post CAR-T | 10 prior<br>22 post | NA | 5/10 (prior)<br>50% (n = 11/22 post) developed positive anti-S IgG<br>59% (n = 13/22 post) developed S-specific T cells | Antibody responses appeared more frequently later after CAR-T cell therapy |
| ASTCT #239 | 104 | 17 | 250 (32–881) days | 13/17 (76.4%) | More patients with MM had a higher titer response to vaccine (>250 U/mL) compared to NHL counterparts |
| ASTCT #476 | 11 prior | 3 | 250 (32–881) days | 1 (33.3%) | At days 30 and 100 post HCT/CAR-T, pre-cellular therapy titers were low in most patients and decreased soon post therapy |
| Ram et al. [13] | 6 | 6 | NA | 1 (16.6%) humoral<br>5 (83.3%) cellular | Humoral and cellular response was measured |
| Dahiya et al. [14] | 18 | 18 | 33 (24–447) days | 1 (5.5%) | Antibody response to common pathogens (e.g. influenza, Epstein-Barr virus, and tetanus toxoid) was preserved |
| Abid et al. [15] | 10 | 10 | | 4 (40%) | After third dose |
| Ram et al. [16] | 14 | 14 | 9 (3–17) months | 5/14 (36%) | Humoral immune response |
| Dhakal et al. [17] | 14 | 14 | 24 (8–31) months | 21% (3/14) | Humoral immune response |
| Greenberger et al. [18] | 12 | 12 | NA | BCMA– or CD138-CAR T: 80% (4/5)<br>CD19 + CAR-T: 14% (1/7) | Humoral immune response |
| Gastinne et al. [19] | 23 | 20 | 13 (4–27) months | 30% (6/20) | Humoral immune response |
| Tamari et al. [6] | 7 | 7 | 218 (66–825) days | 2 (28.5%) | Humoral immune response |
| TOTAL | 372 | 241 | | 88/241 (36.5%) humoral<br>26/36 (72.2%) cellular | Humoral and cellular response was measured |

CAR-T — chimeric antigen receptor T-cell; ASH — American Society of Hematology; MM — multiple myeloma; NHL — non-Hodgkin lymphoma; HCT — hematopoietic cell transplantation; EBMT — European Society of Blood and Marrow Transplantation; ASTCT — American Society of Transplantation and Cellular Therapy; NA — not applicable; IgG — immunoglobulin G; BCMA — B-cell maturation antigen

**Table III.** Seropositivity for routine immunization analyzed after chimeric antigen receptor T-cell (CAR-T) therapy

| Vaccine-preventable infection | Bansal et al. (ASH #3857) | Walti et al. [21] |
|---|---|---|
| Time | +3 months | +6 months |
| Number of patients | 87 | 65 |
| *Streptococcus pneumoniae* | 14% | 0% |
| *Bordetella pertusis* | NA | 0% |
| *Hemophilus influenzae* | NA | 15% |
| Hepatitis B | 71% | 39% |
| Hepatitis A | 64% | 43% |
| Mumps | 86% | 50% |
| Measles | 86% | 80% |
| Rubella | 95% | 90% |
| *Varicella zoster virus* (VZV) | 98% | 90% |
| Tetanus | 100% | 89% |
| Diphtheria | NA | 89% |
| Polio | NA | 89% |

ASH — American Society of Hematology; NA — not applicable

Importantly, it seems that the interval between the infusion of CAR-T cells and the day of vaccination did not influence the humoral response. Moreover, no development of lymphopenia $<1 \times 10^9$/L was observed. We speculate that the development of specific T-cell responses in CAR-T recipients was essential, and more data will provide more information about the humoral and cellular efficacy of vaccination in this context. In the CAR-T cohort patients, despite severe humoral immune deficiency, strong CD4+ T cell responses were observed, suggestive of a sufficient protective immunity (ASH #1757). Therefore, following anti-CD19 or anti-BCMA-CAR-T therapy, patients were able to develop seroprotection which was comparable to that obtained in the general population, despite hypogammaglobulinemia [21]. Nevertheless, exceptions for several specific pathogens, such as pneumococcus, were almost the rule. Also, in BCMA-CAR-T treated patients, lower pathogen-specific antibodies rates were found [2]. This underscores the need for vaccination, as well as for immunoglobulin replacement in these cohorts.

Obviously, the risk factors for a poor response to vaccination in CAR-T recipients are lymphopenia, hypogammaglobulinemia, and B-cell aplasia. Different information was available about other factors which contributed to the response to the vaccination. Compared to NHL, patients with MM had a higher response to the vaccine (>250 U/mL) (ASH #1750). Vaccination prior to CAR-T therapy results in low (if any) antibody titers in most patients, and to a decrease in these titers soon after therapy (ASTCT #476). Importantly, responses appear similar in those vaccinated <6 months vs ≥6 months after treatment (ASTCT #475), which justifies the indication for the SARS-CoV-2/COVID-19 vaccination as soon as three months after CAR-T infusion. With respect to the SARS-CoV-2/COVID-19 vaccination, response in seropositivity seemed to be higher with the mRNA-1273 vaccine, and therefore resulted in a higher spike of mRNA content, as well as a longer duration of response compared to the BNT162b2 vaccine [6, 16–19, 26].

Some authors have emphasized the necessity of an additional booster (third) dose of the SARS-CoV-2/COVID-19 vaccine, approximately five months after the initial vaccination, in order to allow better immune reconstitution prior to vaccination (ASH #754, ASTCT #476). It has previously been shown that a third dose of the anti-COVID-19 vaccine in patients after CAR-T therapy B-cell aplasia is safe, although a humoral response is achieved in a limited number of patients [13]. There is data showing that none of the CAR-T recipients with complete B-cell aplasia exhibited an anti-vaccine humoral response, although cellular response was achieved in 83% of these patients [13]. The third dose of the anti-SARS-CoV-2 mRNA vaccine resulted in lower antibody response in males and corticosteroid recipients. The type of vaccine and the strategy of vaccination had no impact [15].

Data indicates the added rationale for active immunization of CAR-T recipients by the administration of vaccinations. We should clearly keep in mind that there are contraindications for vaccinations with killed or inactivated vaccine in patients with concurrent immunosuppressive or cytotoxic therapy; and contraindications for live and non-live adjuvant vaccines in the period <2 years post allogeneic HCT, and up to eight months after the last dose of immunoglobulin replacement therapy [27–30].

**Table IV.** Eligibility criteria for vaccination in patients receiving CD19-targeted chimeric antigen receptor T-cell (CAR-T) therapy (adapted from [25])

| Type of vaccination | Before CAR-T therapy | After CAR-T therapy |
|---|---|---|
| Influenza vaccine | Preferably vaccinate 2 weeks prior to lymphodepleting therapy | Patients should be vaccinated >3 months after CAR-T |
| | Low likelihood of serological response when B-cell aplasia | Immunological reconstitution is irrelevant |
| SARS-CoV-19 | Preferably vaccinate prior to CAR-T therapy | Patients should be vaccinated >3 months after CAR-T |
| | Low likelihood of serological response when B-cell aplasia | Immunological reconstitution is irrelevant |
| Inactivated/killed vaccines | | Patients should be vaccinated >6 months after CAR-T and >2 months after immunoglobulin replacement therapy |
| Live and non-live adjuvant vaccines | | Patients should be vaccinated >1 year after CAR-T |
| | | Full immunological reconstitution is mandatory |

SARS-CoV-2 — severe acute respiratory syndrome coronavirus 2

The EBMT/European Haematology Association (EHA) cooperative group of experts announced recommendations pertaining to the management of patients undergoing therapy with CAR-T [12]. Their update [25] includes recommendations for patient vaccinations (Table IV). These guidelines are applicable to both adults and children [10, 25].

Based on the initial published data on vaccination against influenza after CAR-T infusion [20], in cases of incomplete immune reconstitution there is a high likelihood of a lower response to vaccination [10]. However, this might not be the case for the SARS-CoV-2/COVID-19 vaccine-induced protection, as it strongly relies on T-cell-mediated immunity. In this case, B-cell aplasia is not a contraindication for vaccination [10, 25]. On the other hand, the T-cell threshold has not been determined. In order to gain more knowledge, monitoring of post-vaccination response is necessary. The consensus view of EBMT/EHA experts is that vaccination in patients after CAR-T therapy is beneficial in order to reduce the rates of infection, and to eventually improve the clinical course [25]. Nevertheless, the use of these guidelines must adhere to specific national schedules. Furthermore, an individualized approach based on a patient's infection history together with laboratory assessments of their humoral and/or cellular immunity is necessary.

Novel active or passive immunization strategies are needed for this population. Further research is expected. Predictors of response to vaccination, including determination of the vaccine's efficacy and safety, optimal timing of vaccination, additional or booster doses of the vaccine, and passive immune and pharmacological prophylaxis and treatment, all need to be determined in CAR-T patients.

## List of analyzed meeting abstracts

- ASH #254. Thomas Gastinne, Amandine Le Bourgeois, Marianne Coste-Burel et al. Antibody response after one and/or two doses of BNT162b2 anti-SARS-CoV-2 mRNA vaccine in patients treated by CAR T-cells therapy. American Society of Hematology 63rd Annual Meeting, Atlanta, 11–14 December 2021. Blood 2021; 138 (Suppl) 1: abstract 254.
- ASH #754. Sabine Haggenburg, Birgit I Lissenberg-Witte, Robert S Van Binnendijk et al. For better or for worse: COVID-19 vaccination during or early after (immuno-) chemotherapy or hematopoietic progenitor cell transplantation. American Society of Hematology 63rd Annual Meeting, Atlanta, 11–14 December 2021. Blood 2021; 138, (Suppl) 1: abstract 754.
- ASH #1750. Julia E Wiedmeier, Madiha Iqbal, Javier Muñoz et al. Response to COVID-19 vaccination post-CAR T therapy in patients with non-Hodgkin lymphoma and multiple myeloma. American Society of Hematology 63rd Annual Meeting, Atlanta, 11–14 December 2021. Blood 2021; 138 (Suppl 1): abstract 1750.
- ASH #1757. Kalpana Parvathaneni, Kyabeth Toress-Rodriguez, Wenzhao Meng et al. Adoptive immune responses to SARS-CoV-2 vaccination in CART19 treated patients. American Society of Hematology 63rd Annual Meeting, Atlanta, 11–14 December 2021. Blood 2021; 138 (Suppl 1): abstract 1757.
- ASH #2504. Ning Dong, Akriti G Jain, Elaine S Tan et al. Immunogenicity of SARS-CoV-2 mRNA 1273 vaccine in patients with lymphoid malignancies. American Society of Hematology 63rd Annual Meeting, Atlanta, 11–14 December 2021. Blood 2021; 138 (Suppl 1): abstract 2504.
- ASH #2537. Lauren C Shapiro, Radhika Gali, Astha Thakkar et al. Seroconversion rates after

COVID-19 vaccination amongst patients with hematologic malignancies: results of a rapid vaccination and evaluation program in a minority rich, ethnically diverse inner city cohort. American Society of Hematology 63rd Annual Meeting, Atlanta, 11–14 December 2021. Blood 2021; 138 (Suppl 1): abstract 2537.

- ASH #3857. Radhika Bansal, Paschalis Vergidis, Pritish K Tosh et al. Vaccine titers in lymphoma patients receiving chimeric antigen receptor T cell therapy. American Society of Hematology 63rd Annual Meeting, Atlanta, 11–14 December 2021. Blood 2021; 138 (Suppl 1): abstract 3857.
- EBMT #P113. A Jarisch, E Wiercinska, S Huenecke et al. Humoral and T cell immune responses to anti-SARS-CoV-2 vaccines in pediatric & patients with anti-CD19 CAR-T-induced B-cell aplasia. European Society of Blood and Marrow Transplantation 48th Annual Meeting, 19–23 March 2022, abstract P113.
- ASTCT #475. Marcie L Riches, Joshua A Hill, Michael Martens et al. Humoral Immunogenicity of SARS-CoV-2 vaccination in the first year after hematopoietic cell transplant or chimeric antigen receptor T cell therapy: a CIBMTR and BMT CTN study. Tandem Meetings/American Society of Transplantation and Cellular Therapy 2022 Annual Meeting, Salt Lake City, 23–26 April 2022; abstract 475.
- ASTCT #264. Michael A Gonzalez, Jim Boonyaratanakornkit, Atif Bhatti et al. Comparison of humoral and T-cell response after SARS-CoV-2 vaccination among patients before and after chimeric antigen receptor-modified T cell (CAR-T cell) therapy. Tandem Meetings/ /American Society of Transplantation and Cellular Therapy 2022 Annual Meeting, Salt Lake City, 23–26 April 2022; abstract 264.
- ASTCT #239. Julia Erin Wiedmeier-Nutor, Madiha Iqbal, Javier Muñoz et al. Response to COVID-19 vaccination post-CAR T therapy in patients with non-Hodgkin lymphoma and multiple myeloma. Tandem Meetings/American Society of Transplantation and Cellular Therapy 2022 Annual Meeting, Salt Lake City, 23–26 April 2022; abstract 239.
- ASTCT #476. Gunjan L Shah, David J Chung, Roni Tamari et al. Humoral response to COVID-19 vaccination given pre-cellular therapy wanes in patients after cellular therapy: an argument for full reimmunization. Tandem Meetings/American Society of Transplantation and Cellular Therapy 2022 Annual Meeting,. Salt Lake City, 23–26 April 2022; abstract 476.

## Authors' contributions

JS — design of study; JS, TS, JSa — literature search and analysis of data; JS, TS, JSa, MW, DR — writing manuscript; all authors — critical revision and final approval.

## Conflict of interest

None.


## Financial support

None.


## Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform requirements for manuscripts submitted to biomedical journals.

## References


1. Maude SL, Laetsch T, Buechner J, et al. Tisagenlecleucel in children and young adults with B-cell lymphoblastic leukemia. N Engl J Med. 2018; 378(5): 439–448, doi: 10.1056/nejmoa1709866.
2. Neelapu SS, Locke FL, Bartlett NL, et al. Axicabtagene ciloleucel CAR T-cell therapy in refractory large B-cell lymphoma. N Engl J Med. 2017; 377(26): 2531–2544, doi: 10.1056/NEJMoa1707447, indexed in Pubmed: 29226797.
3. Schuster SJ, Schwartz JD, Geoffrion D, et al. JULIET Investigators. Tisagenlecleucel in diffuse large B-cell lymphoma. N Engl J Med. 2019; 380(16): 1585–1586, doi: 10.1056/NEJMc1901464, indexed in Pubmed: 30995382.
4. Raje N, Berdeja J, Lin Yi, et al. Anti-BCMA CAR T-cell therapy bb2121 in relapsed or refractory multiple myeloma. N Engl J Med. 2019; 380(18): 1726–1737, doi: 10.1056/NEJMoa1817226, indexed in Pubmed: 31042825.
5. Bembnista E. Implementation of CAR-T technology into clinical practice: challenge for cell bank. Acta Haematol Pol. 2021; 52(4): 263–267, doi: 10.5603/AHP.2021.0051.
6. Tamari R, Politikos I, Knorr DA, et al. Predictors of humoral response to SARS-CoV-2 vaccination after hematopoietic cell transplantation and CAR T-cell therapy. Blood Cancer Discov. 2021; 2(6): 577–585, doi: 10.1158/2643-3230.BCD-21-0142, indexed in Pubmed: 34778798.
7. Wang Y, Li C, Xia J, et al. Humoral immune reconstitution after anti-BCMA CAR T-cell therapy in relapsed/refractory multiple myeloma. Blood Adv. 2021; 5(23): 5290–5299, doi: 10.1182/bloodadvances.2021004603, indexed in Pubmed: 34587230.
8. Anagnostou T, Riaz I, Hashmi S, et al. Anti-CD19 chimeric antigen receptor T-cell therapy in acute lymphocytic leukaemia: a systematic review and meta-analysis. Lancet Haematol. 2020; 7(11): e816–e826, doi: 10.1016/s2352-3026(20)30277-5.
9. Awasthi R, Pacaud L, Waldron E, et al. Tisagenlecleucel cellular kinetics, dose, and immunogenicity in relation to clinical factors in relapsed/refractory DLBCL. Blood Adv. 2020; 4(3): 560–572, doi: 10.1182/bloodadvances.2019000525, indexed in Pubmed: 32045475.
10. Hill JA, Seo S. How I prevent infections in patients receiving CD19-targeted chimeric antigen receptor T cells for B-cell malignancies. Blood. 2020; 136(8): 925–935, doi: 10.1182/blood.2019004000.
11. Styczyński J. Infections following CAR-T cells therapy: current state-of-the-art review and recommendations. Acta Haematol Pol. 2020; 51(1): 11–16, doi: 10.2478/ahp-2020-0004.

12. Yakoub-Agha I, Chabannon C, Bader P, et al. Management of adults and children undergoing chimeric antigen receptor T-cell therapy: best practice recommendations of the European Society for Blood and Marrow Transplantation (EBMT) and the Joint Accreditation Committee of ISCT and EBMT (JACIE). Haematologica. 2020; 105(2): 297–316, doi: 10.3324/haematol.2019.229781, indexed in Pubmed: 31753925.
13. Ram R, Freund T, Halperin T, et al. Immunogenicity of a third dose of the BNT162b2 mRNA Covid-19 vaccine in patients with impaired B cell reconstitution after cellular therapy — a single center prospective cohort study. Transplant Cell Ther. 2022; 28(5): 278.e1–278.e4, doi: 10.1016/j.jtct.2022.02.012, indexed in Pubmed: 35182795.
14. Dahiya S, Luetkens T, Lutfi F, et al. Impaired immune response to COVID-19 vaccination in patients with B-cell malignancies after CD19 CAR T-cell therapy. Blood Adv. 2022; 6(2): 686–689, doi: 10.1182/bloodadvances.2021006112, indexed in Pubmed: 34941995.
15. Abid M, Rubin M, Ledeboer N, et al. Efficacy of a third SARS-CoV-2 mRNA vaccine dose among hematopoietic cell transplantation, CAR T cell, and BiTE recipients. Cancer Cell. 2022; 40(4): 340–342, doi: 10.1016/j.ccell.2022.02.010.
16. Ram R, Freund T, Halperin T, et al. Safety and immunogenicity of the BNT162b2 mRNA COVID-19 vaccine in patients after allogeneic HCT or CD19-based CART therapy — a single-center prospective cohort study. Transplant Cell Ther. 2021; 27(9): 788–794, doi: 10.1016/j.jtct.2021.06.024, indexed in Pubmed: 34214738.
17. Dhakal B, Abedin S, Fenske T, et al. Response to SARS-CoV-2 vaccination in patients after hematopoietic cell transplantation and CAR T-cell therapy. Blood. 2021; 138(14): 1278–1281, doi: 10.1182/blood.2021012769, indexed in Pubmed: 34339501.
18. Greenberger LM, Saltzman LA, Senefeld JW, et al. Anti-spike antibody response to SARS-CoV-2 booster vaccination in patients with B cell-derived hematologic malignancies. Cancer Cell. 2021; 39(10): 1297–1299, doi: 10.1016/j.ccell.2021.09.001, indexed in Pubmed: 34509182.
19. Gastinne T, Bourgeois ALe, Coste-Burel M, et al. Safety and antibody response after one and/or two doses of BNT162b2 Anti-SARS-CoV-2 mRNA vaccine in patients treated by CAR T cells therapy. Br J Haematol. 2021; 196(2): 360–362, doi: 10.1111/bjh.17818.
20. Walti CS, Loes AN, Shuey K, et al. Humoral immunogenicity of the seasonal influenza vaccine before and after CAR-T-cell therapy: a prospective observational study . J Immunother Cancer. 2021; 9(10): e003428, doi: 10.1136/jitc-2021-003428.
21. Walti CS, Krantz EM, Maalouf J, et al. Antibodies against vaccine-preventable infections after CAR-T cell therapy for B cell malignancies. JCI Insight. 2021; 6(11), doi: 10.1172/jci.insight.146743, indexed in Pubmed: 33914708.
22. Styczyński J. Where dreams come true: CAR-T cell therapy in Poland! Acta Haematol Pol. 2020; 51(1): 1, doi: 10.2478/ahp-2020-0001.
23. Styczyński J. A brief history of CAR-T cells: from laboratory to the bedside. Acta Haematol Pol. 2020; 51(1): 2–5, doi: 10.2478/ahp-2020-0002.
24. Gil L, Łojko-Dankowska A, Matuszak M, et al. CAR-T cell therapy — toxicity and its management. Acta Haematol Pol. 2020; 51(1): 6–10, doi: 10.2478/ahp-2020-0003.
25. Hayden PJ, Roddie C, Bader P, et al. Management of adults and children receiving CAR T-cell therapy: 2021 best practice recommendations of the European Society for Blood and Marrow Transplantation (EBMT) and the Joint Accreditation Committee of ISCT and EBMT (JACIE) and the EHA(EHA). Ann Oncol. 2022; 33(3): 259–275, doi: 10.1016/j.annonc.2021.12.003, indexed in Pubmed: 34923107.
26. Abbas MA, Abid MB. SARS-CoV-2 vaccine response in CAR T-cell therapy recipients: a systematic review and preliminary observations. Hematol Oncol. 2022; 40(2): 287–291, doi: 10.1002/hon.2957, indexed in Pubmed: 34911142.
27. Cordonnier C, Mikulska M, Einarsdottir S, et al. 2017 ECIL 7 vaccine guidelines. Lancet Infect Dis. 2019; 19(7): 694–695, doi: 10.1016/s1473-3099(19)30277-4.
28. Mikulska M, Cesaro S, Lavallade Hde, et al. Vaccination of patients with haematological malignancies who did not have transplantations: guidelines from the 2017 European Conference on Infections in Leukaemia (ECIL 7). Lancet Infect Dis. 2019; 19(6): e188–e199, doi: 10.1016/s1473-3099(18)30601-7.
29. Ljungman P, de la Camara R, Robin C, et al. 2017 European Conference on Infections in Leukaemia group. Guidelines for the management of cytomegalovirus infection in patients with haematological malignancies and after stem cell transplantation from the 2017 European Conference on Infections in Leukaemia (ECIL 7). Lancet Infect Dis. 2019; 19(8): e260–e272, doi: 10.1016/S1473-3099(19)30107-0, indexed in Pubmed: 31153807.
30. Cordonnier C, Einarsdottir S, Cesaro S, et al. Vaccination of haemopoietic stem cell transplant recipients: guidelines of the 2017 European Conference on Infections in Leukaemia (ECIL 7). Lancet Infect Dis. 2019; 19(6): e200–e212, doi: 10.1016/s1473-3099(18)30600-5.