Apendix: Methods, Suppl. Table 1 and Suppl. Fig. 1 and 2-3.

Materials and Methods

Patients and healthy controls

All participants gave their informed, written consent. The study has been performed according to the declaration of Helsinki. Sample collection and analysis were approved by the ethics committee of the Medical Center, University of Erlangen, Germany (protocol 118_20B, 174_20B, 19-336_1-B). Patients' characteristics are shown in Table 1. Healthy volunteers after two doses of BNT162b2 vaccination and convalescent patients were used as controls.

Detection of SARS-CoV-2 specific antibodies

Sera were analyzed for the presence of anti-SARS-CoV-2 antibodies with two independent fully automated commercial tests. First, anti-spike antibodies were measured with the LIAISON®SARS-CoV-2 trimericS IgG assay (DiaSorin, Saluggia, Italy) according to the manufactures' instruction. Antibody levels were quantified according to the WHO International Reference standard and listed as BAU/ml. An antibody level greater than or equal to 33.8 BAU/ml is considered as positive recording to manufactures' information. The second assay was a surrogate neutralization assay (iFlash-2019-nCoV NAb assay, Yhlo, Shenzen, China) detecting antibodies that are able to compete with receptor-binding domain (RBD) binding to the SARS-CoV-2 receptor ACE2. Activity is determined in AU/ml and a cut-off of >10 AU/ml is considered as positive as described in manufactures' instructions.[22]

Detection of SARS-CoV-2 specific T-cells

PBMCs from convalescent COVID-19 patients, patients before and after CAR-T cell therapy and vaccinated healthy volunteers were separated by density gradient centrifugation and stored in liquid nitrogen until further processing. T-cell recognition was accessed either by activation as measured by flow cytometry and by cytokine secretion as measured by IFN-γ ELISA or by IFN-γ ELISPOT. PBMCs were thawed and cultured in RPMI 1640 (Gibco, Thermo Fischer Scientific) with 10% Human Serum (Anprotec), 40 IU/mL penicillin, 40 µg/mL streptomycin, 2 mM Glutamine, 0.4% vitamin solution, 50 µM mercaptoethanol, 1% minimal essential media, and 1 mM sodium pyruvate (all Gibco, Thermo Fischer Scientific). Flow cytometric analysis was performed after 18 to 24 hours (37 °C, 5% CO_2) *in vitro* stimulation with 1 µg/ml Spike or Nucleocapsid PeptMix peptides (JPT) in the presence of 10 IU/ml recombinant human IL-2 (rhIL-2, Proleukin, Vevey, Switzerland).[23] Cytostim (Miltenyi-Biotec, Bergisch-Gladbach, Germany) was used as a positive control according to the manufacturers' instructions, unstimulated cells served as negative control. Supernatants of cultivated cells were collected and measured by IFN-γ ELISA according to the manufactures` instructions (Biolegend). In addition, T-cell

functionality was analyzed via an IFN-γ ELISPOT (T-SPOT.COVID, Oxford Immunotec, Abingdon, UK) according to the manufacturers' instructions. Cells were harvested, stained with 7AAD and anti-human anti-CD3 (clone UCHT1), anti-CD4 (SK3), anti-CD8 (RPA-T8), anti-CD69 (FN450; all BD Biosciences, Heidelberg, Germany), and anti-CD137 (4B4-1; Biolegend, San Diego, USA) monoclonal antibodies. Flow cytometry data were acquired on a LSRFortessa (BD Biosciences) and cells were analyzed for indicated antibodies with FlowJo software v10 (TreeStar, Ashland, Oregon, USA) and Kaluza software v2.1 (Beckmann Coulter, Krefeld, Germany). Doublets were excluded by FSC-A/FSC-H, lymphocytes were determined by FSC-A/SSC-A, T-cells were determined by CD3/SSC-A, dead cells were excluded by 7AAD, and activated T-cells were gated by CD137/CD69. Unstimulated and infection-naïve, unvaccinated controls were used to identify a threshold for a positive response using mean+3 SD for Spike or Nucleocapsid PeptMix peptides.[24] This resulted in a cut-off for positivity of >10 events out of 10^4 T-cells. Cytokine secretion data confirmed the cut-off. Only patients with positive T-cell responses measured by flow cytometry showed a positive signal in IFN-γ ELISA and/or IFN-γ ELISPOT. Gating strategy is shown in Suppl. Fig. 2.

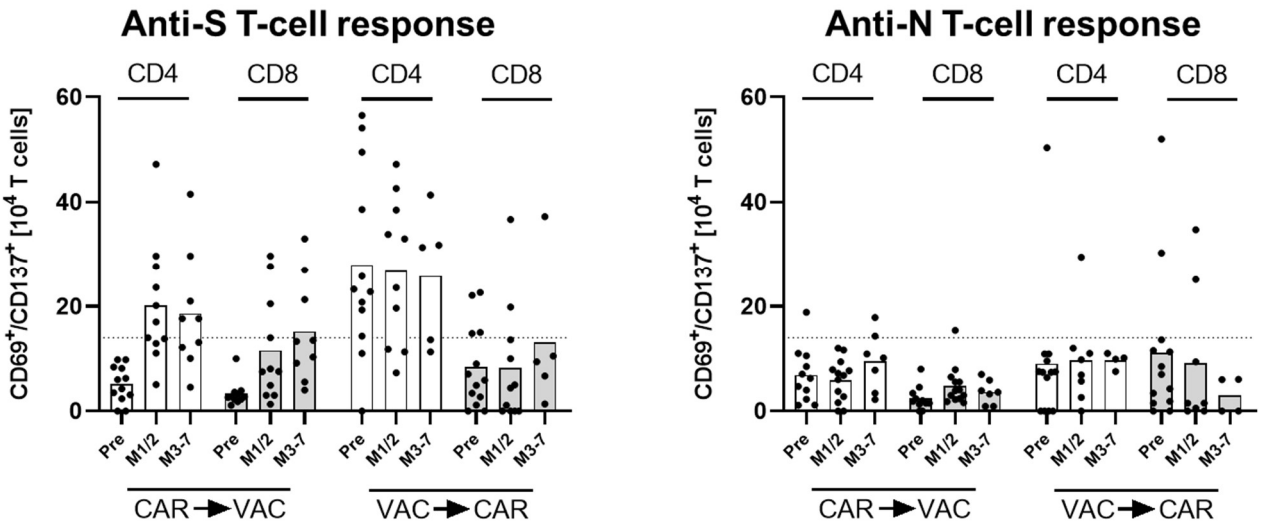
Statistical analyses

Data were analyzed with Graphpad Prism software (GraphPad San Diego, California, USA). Results were compared using nonparametric (Mann-Whitney-U or Wilcoxon) tests. A p-value of <0.05 was considered significant

	CAR -> VAC				VAC -> CAR			
	Humoral response, n=15 (%)		T-cell response, n=15 (%)		Humoral response, n=21 (%)		T-cell response, n=16 (%)	
	R (2; 13%)	NR (13; 87%)	R (13; 87%)	NR (2; 13%)	R (13; 62%)	NR (8; 38%)	R (14; 88%)	NR (2; 12%)
Patient characteristics								
Age, median (range)	65 (63-66)	66 (21-83)	66 (21-83)	58 (51-66)	60 (22-82)	70 (43-77)	64 (22-82)	65 (53-67)
Type of disease (DLBCL), n(%)	1 (50%)	9 (60%)	8 (62%)	2 (100%)	5 (38%)	6 (75%)	6 (43%)	1 (50%)
Patients in remission, n(%)	2 (100%)	13 (100%)	13 (100%)	2 (100%)	1 (13%)	1 (13%)	0 (0%)	1 (50%)
Refractory disease, n(%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (8%)	2 (25%)	1 (7%)	1 (50%)
Body Mass Index, median (range)	29 (19-40)	24 (13-34)	23 (19-40)	28 (24-31)	23 (21-29)	24 (18-33)	23 (21-29)	25 (23-27)
Ferritin, median (range)	354 (79-629)	569 (30-2442)	387 (30-2442)	1068 (562-1573)	955 (72-6512)	301 (36-1944)	324 (72-6512)	1328 (401-2255)
LDH, median (range)	197 (195-199)	208 (149-486)	23 (149-486)	178 (168-185)	215 (150-790)	193 (123-314)	202 (141-790)	318 (269-367)
CRP, median (range)	3.1 (3-3.1)	1.3 (0.1-26.1)	1.4 (0.1-26.1)	1.3 (1.2-1.3)	0.9 (0-10)	0.6 (0.4-3.2)	0.7 (0-10)	0.9 (0.7-1.2)
CD19.CAR-T cell therapy								
Tisagenlecleucel, n(%)	0 (0%)	6 (46%)	5 (38%)	1 (50%)	2 (15%)	2 (25%)	2 (14%)	1 (50%)
Axicabtagene ciloleucel, n(%)	1 (50%)	2 (15%)	2 (15%)	1 (50%)	3 (23%)	4 (50%)	5 (36%)	1 (50%)
other CAR product, n(%)	1 (50%)	5 (38%)	6 (46%)	0 (0%)	8 (62%)	2 (25%)	7 (50%)	0 (0%)
Corticosteroids, n(%)	1 (50%)	4 (31%)	3 (23%)	2 (100%)	5 (38%)	4 (50%)	7 (50%)	0 (0%)
CRS >=2, n(%)	1 (50%)	4 (31%)	4 (31%)	1 (50%)	4 (31%)	1 (13%)	3 (21%)	0 (0%)
ICANS >=2, n(%)	1 (50%)	1 (8%)	1 (8%)	1 (50%)	1 (8%)	2 (25%)	2 (14%)	0 (0%)
Severe Neutropenia, n(%)	0 (0%)	2 (15%)	1 (8%)	1 (50%)	4 (31%)	1 (13%)	3 (21%)	1 (50%)
anti-IL6R, n(%)	1 (50%)	10 (77%)	9 (69%)	1 (50%)	11 (85%)	5 (63%)	12 (86%)	1 (50%)
Type of vaccine (BNT162b2), n(%)	2 (100%)	8 (62%)	9 (69%)	1 (50%)	9 (69%)	7 (88%)	12 (86%)	2 (100%)
IgG, median (range)	7.2 (6.1-8.2)	3.7 (1.0-8.2)	3.2 (1.0-8.2)	3.2 (2.7-3.7)	5.6 (1.2-11.4)	4.9 (2.3-40.8)	5.2 (1.2-40.8)	3.9 (2-5.8)
mild AE, n(%)	1 (50%)	2 (15%)	3 (23%)	0 (0%)	6 (46%)	1 (13%)	6 (43%)	0 (0%)
moderate-severe AE, n(%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Timing of Vaccination, n(%)								
≥ 6 months	1 (50%)	8 (62%)	8 (62%)	1 (50%)	-	-	-	-
< 6 months	1 (50%)	5 (38%)	5 (38%)	1 (50%)	-	-	-	-
SARS-CoV-2 infection								
mild disease, n(%)	1 (50%)	3 (23%)	4 (31%)	0 (0%)	5 (38%)	1 (13%)	5 (36%)	0 (0%)
moderate-severe disease, n(%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Immune cells								
Detectable B-cells, n(%)	2 (100%)	0 (0%)	2 (15%)	0 (0%)	10 (77%)	5 (63%)	10 (71%)	2 (100%)
B cells absolute, median (range)	43 (29-56)	0	0 (0-56)	0	234 (0-4407)	2 (0-424)	76 (0-4407)	32 (1-63)
Detectable CAR T cells, n(%)	0 (0%)	10 (77%)	9 (60%)	1 (50%)	-	-	-	-
CAR T cells absolute, median (range)	0	3 (0-86)	3 (0-86)	1 (0-2)	-	-	-	-
T-cell count, median (range)	283 (232-334)	731 (303-1823)	534 (232-1823)	903 (657-1149)	515 (269-2709)	706 (212-888)	680 (212-2709)	821 (753-888)
CD4 T cell count, median (range)	189 (156-222)	194 (60-649)	194 (60-649)	217 (143-291)	321 (165-1664)	200 (73-561)	297 (112-1664)	197 (73-321)

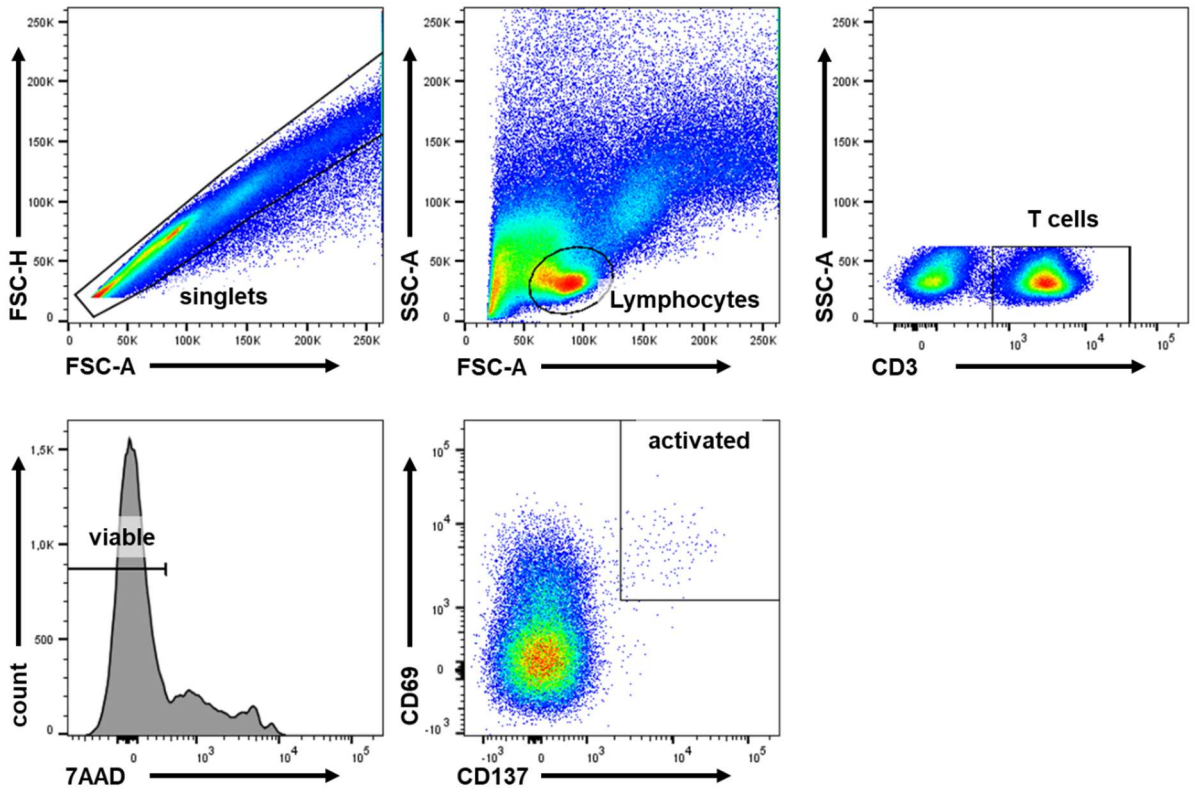
Suppl. Table 1: Comparison of characteristics in responders and non-responders to SARS-CoV-2 vaccination

Suppl. Fig 1



Suppl. Fig. 1: CD4 and CD8 T-cell immune responses to Spike and Nucleocapsid peptides in CAR T-cell patients. Patients after CAR T-cell therapy (CAR->VAC) before vaccination (Pre) and 1-2 months (M1/2) and 3-7 months (M3-7) after SARS-CoV-2 vaccination and patients after SARS-CoV-2 vaccination (VAC->CAR) before and 1-2 months (M1/2) and 3-7 months (M3-7) after CAR-T cell therapy were analyzed for anti-Spike (A) and anti-Nucleocapsid (B) specific T-cells by flow cytometry. Bars depict the mean of activated $CD69^+/CD137^+$ CD4 (white) and CD8 (grey) T cells, each symbol represent an individual subject. Dotted lines indicate the respective cut-off values.

Suppl. Fig. 2



Suppl. Fig. 2: Gating strategy of flow cytometry. PBMC from vaccinated healthy control were stimulated with 1 µg/ml Spike PeptMix peptides as indicated in the Methods. Doublets were excluded by FSC-A/FSC-H, lymphocytes were determined by FSC-A/SSC-A, T-cells were determined by CD3/SSC-A, dead cells were excluded by 7AAD, and activated T-cells were gated by CD137/CD69.