

Supplementary Information:

Seroconversion rates after the second COVID-19 vaccination in patients with systemic light chain (AL) amyloidosis

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SUPPLEMENTAL TABLES

Table S1: Detailed comparison of positive and negative anti-SARS-CoV-2-S1 antibody cohorts after COVID-19 vaccination

	Positive antibody result (N=102)	Negative antibody result (N=15)	P-value*
Age, y	64 [44, 84]	65 [55, 82]	
Male Sex	56 (55 %)	10 (67 %)	
Lambda subtype	85 (83 %)	11 (73 %)	
Underlying clonal disease			
MGCS	30 (29 %)	4 (27 %)	
Smoldering myeloma	64 (63 %)	11 (73 %)	
Multiple myeloma	8 (8 %)	0 (0 %)	
Interval between initial diagnosis of AL amyloidosis and first vaccination, y	3.9 [0.01, 22.2]	2 [0.06, 8.3]	
BMPC infiltration at first diagnosis in %	10.0 [3, 75]¶	11 [4, 30]	
>2 organ involved	51 (50 %)	6 (40 %)	
Cardiac involvement	75 (74 %)	11 (73 %)	
Renal involvement	61 (60 %)	11 (73 %)	
Hepatic involvement	20 (20 %)	2 (13 %)	
Neuropathic involvement	25 (25 %)	6 (40 %)	
Gastrointestinal involvement	21 (21 %)	3 (20 %)	

	Positive antibody result (N=102)	Negative antibody result (N=15)	P-value*
Soft tissue involvement	41 (40 %)	7 (47 %)	
On active therapy at time of vaccination	36 (35 %)	9 (60 %)	
Interval between last treatment and first vaccination (patients with current or prior treatment), days	248 [0, 6790]	1.50 [0, 646]	0.03
Prior autoHCT	26 (25 %)	3 (20 %)	
Prior alloHCT	2 (2 %)	0 (0 %)	
Lines of treatment	2 [0, 8]	2 [0, 7]	
Disease in hematologic remission (CR or VGPR)	67 (66 %)	6 (40 %)	
Prior/current Daratumumab	47 (46 %)	9 (60 %)	
Prior/current Proteasom inhibitors	85 (83 %)	11 (73 %)	
Prior/current IMiDs	39 (38 %)	5 (33 %)	
Prior/current Melphalan	50 (49 %)	9 (60 %)	
WBC, /nl	6.69 [2.77, 14.9]	6.97 [4.05, 14.1]	
Lymphocyte count, /nL	1.5 [0.05, 4.4]	1.6 [0.3, 4.6]	
IgG in g/L	7.4 [0.8, 29.1] [†]	5.1 [1.9, 9.1] [†]	0.03
IgA in g/L	1.1 [0.08, 11.3] [‡]	0.5 [0.2, 2.2] [‡]	
IgM in g/L	0.4 [0.08, 7.1] [§]	0.3 [0.1, 0.8] [§]	
dFLC in mg/L	13.2 [0.300, 443]	17.8 [1.50, 460]	
GFR in mL/min	56.8 [5.4, 107]	49.8 [3.2, 89.7]	
Total serum protein in g/L	64.4 [49.6, 82.0]	56.1 [38.4, 67.9]	0.001
Daily Proteinuria in g/d	0.14 [0.1, 16.7] ^{††}	3.3 [0.1, 15.7] ^{††}	0.04
Serum Albumin in g/L	43.3 [23.3, 65.7]	35.9 [24.7, 46.0]	0.001
Patients on dialysis	9 (9 %)	2 (13 %)	
Vaccines			
AZD122 (AstraZeneca)	13 (13 %)	2 (13 %)	
BNT162b2 (BioNTech)	81 (79 %)	13 (87 %)	
Heterologous vaccines	4 (4 %)	0 (0 %)	
mRNA-1273 (Moderna)	4 (4 %)	0 (0 %)	
Interval between V1 and V2, days	41.0 [14.0, 89.0]	29.0 [18.0, 63.0]	

Data are number of patients (%) or median [range]. Percentages and median with ranges in brackets were calculated for all 102 patients with positive antibody results and all 15 patients with negative antibody results unless otherwise stated in numbers section. P values to test for differences between patients with positive and negative antibody results were calculated by use of Fisher's Exact test for categorical characteristics and the Mann-Whitney test for continuous characteristics. *For reasons of readability, only statistically significant P values (P < 0.05) are displayed.

Laboratory values were measured at the time of antibody measurement post V2 (+/- 3 months).

¶ 1 patient with positive antibody results not available

† 6 patients with positive antibody results and 3 patients with negative antibody results not available

‡ 18 patients with positive antibody results and 4 patients with negative antibody results not available

§ 20 patients with positive antibody results and 4 patients with negative antibody results not available

†† 15 patients with positive antibody results and 5 patients with negative antibody results not available

The diagnosis of multiple myeloma was defined as the presence of a clonal bone marrow plasma cell percentage $\geq 10\%$ or a biopsy-proven plasmacytoma and additionally the presence of at least one feature of end-organ damage (CRAB: hypercalcemia, renal failure, anemia, and bone lesions) that can be attributed to the malignant disease.

MGCS, monoclonal gammopathy of clinical significance; BMPC, bone marrow plasma cell; autoHCT, autologous hematopoietic cell transplantation; alloHCT, allogeneic hematopoietic cell transplantation; CR, complete remission; VGPR, very good partial response; IMiDs, immunomodulatory drugs; dFLC, difference between serum free light chains; GFR, glomerular filtration rate; V1, first vaccination; V2, second vaccination

Supplemental Table S2: anti-SARS-CoV-2-S1 antibody responses after the second COVID-19 vaccination based on the different vaccine regimens

Patient cohorts based on antibody levels	BNT162b2 (BioNTech) (N=94)	mRNA-1273 (Moderna) (N=4)	AZD122 (AstraZeneca) (N=15)	Heterologous vaccines (N=4)
High responder	35 (37.2%)	2 (50%)	0 (0%)	4 (100%)
Low responder	46 (48.9%)	2 (50%)	13 (86.7%)	0 (0%)
Non-responder	13 (13.8%)	0 (0%)	2 (13.3%)	0 (0%)

Table S3: Univariate analysis for a failure of seroconversion after two COVID-19 vaccinations

Characteristic	N	OR	95% CI	p-value
Age, per 10 years	117	1.10	0.55, 2.19	0.8
Sex	117			
Female		[Reference]		
Male		1.64	0.54, 5.59	0.4
BMPC infiltration at first diagnosis in %	116	1.00	0.94, 1.05	>0.9
>2 organ involved	117			
no		[Reference]		
yes		0.67	0.21, 1.98	0.5
Lines of treatment, per line	117	1.18	0.84, 1.60	0.3

Characteristic	N	OR	95% CI	p-value
Interval between last treatment and first vaccination	117			
>3 months		[Reference]		
<3 months		4.69	1.37, 21.7	0.024
untreated		4.58	0.20, 47.3	0.2
Disease in hematologic remission (CR or VGPR)	117			
no		[Reference]		
yes		0.35	0.11, 1.04	0.063
Prior/current Daratumumab	117			
no		[Reference]		
yes		1.76	0.59, 5.58	0.3
Lymphocyte count, per /nL	117	0.92	0.43, 1.74	0.8
IgG, per g/L	108	0.81	0.64, 0.98	0.049
IgA, per g/L	95	0.42	0.13, 0.94	0.085
IgM, per g/L	93	0.27	0.02, 1.21	0.2
GFR	117			
<60 mL/min		[Reference]		
>60 mL/min		0.72	0.23, 2.15	0.6
dFLC, per mg/L	117	1.00	1.00, 1.01	0.10
Total serum protein, per decrease of 1 g/L	117	1.15	1.07, 1.26	<0.001
Daily proteinuria, per g/d	97	1.25	1.07, 1.49	0.006
Serum albumin, per decrease of 1 g/L	117	1.19	1.09, 1.32	<0.001

Statistically significant results ($P < 0.05$) are bold. For continuous variables, OR is calculated for the increase per unit of the variable if not otherwise stated.

OR, Odds Ratio; CI, Confidence Interval; BMPC, bone marrow plasma cell; CR, complete remission; VGPR, very good partial response; GFR, glomerular filtration rate; dFLC, difference between serum free light chains

Table S4: Multivariate analysis for a failure of seroconversion after two COVID-19 vaccinations (full case analysis, n=108)

Characteristic	OR	95% CI	P-value
Age, per 10 years	1.01	0.91, 1.13	0.8
Dosing interval between both COVID-19 vaccinations, per day	0.93	0.87, 1.00	0.052
Vaccine regimen			
mRNA-based homolog/heterolog	[Reference]		
Vector-based homolog	2.09	0.20, 18.3	0.5
Serum albumin, per decrease 1 g/L	1.25	1.12, 1.44	<0.001
Lymphocyte count, per /nl	0.69	0.28, 1.50	0.4
GFR			
<60 mL/min	[Reference]		
>60 mL/min	0.47	0.10, 1.86	0.3
Interval between last treatment and first vaccination			
>3 months	[Reference]		
<3 months	6.53	1.25, 53.0	0.044
untreated	6.15	0.21, 115	0.2

Statistically significant results ($P < 0.05$) are bold. For continuous variables, OR is calculated for the increase per unit of the variable if not otherwise stated.

OR, Odds Ratio; CI, Confidence Interval; GFR, glomerular filtration rate

Table S5: Multivariate linear censored regression model (tobit model) of log₁₀-transformed anti-SARS-CoV-2-S1 antibody levels after two COVID-19 vaccinations (n=117)

	Regression coefficient	Lower 95% CI	Upper 95% CI	Fold change (FC)*	Lower 95% CI (FC)*	Upper 95% CI (FC)*	P-value
Age, per 10 years	-0.01	-0.32	0.29	0.97	0.48	1.97	0.940
Dosing interval between both COVID-19 vaccinations, per day	0.03	0.01	0.05	1.07	1.01	1.12	0.014
Homologous vector-based vaccination	-1.48	-2.37	-0.60	0.03	0.004	0.25	0.001
No treatment within 3 months prior vaccination	0.59	0.10	1.09	3.93	1.27	12.18	0.018
Albumin (serum), per 1 g/L	0.07	0.03	0.11	1.18	1.07	1.29	<0.001
Lymphocyte count, per 1/nl	0.06	-0.22	0.34	1.15	0.60	2.19	0.680
GFR >60 mL/min	0.49	0.01	0.96	3.08	1.03	9.23	0.044

Only data for variables that were included in the final model are shown. In the model, the dependent variable (anti-SARS-CoV-2-S1 antibody level) was log₁₀-transformed for normalization. Censoring was applied due to technical detection limits of the anti-SARS-CoV-2-S1 assay (censoring: left=log₁₀(0.01), right=log₁₀(150)). Left- and right-censoring was necessary for 3 and 37 patients, respectively.

* Fold change (FC) is calculated via 10^{^(Regression coefficient)} and expresses the multiplicative change per one unit of the corresponding variable.