

Supplementary material

Immunogenicity and safety of COVID-19 vaccination in patients with primary Sjögren's syndrome

Supplementary Table 1 Baseline characteristics of subgroup of pSS patients and HC with blood and/or saliva sample

	pSS (n=31)	HC (n=11)
Gender - female	27 (87)	11 (100)
Age	59 (55-67)*	41 (32-56)*
<u>Type of vaccine</u>		
Pfizer/BioNtech	22 (71)	3 (27)
Moderna	3 (10)	1 (9)
AstraZeneca	6 (19)	3 (27)
Janssen	0	4 (36)
Hydroxychloroquine use	6 (19)	n/a
ESSDAI (total score)	2.0 (1.0-3.3) ^b	n/a
ESSDAI <5	23 (88)	
ESSDAI 5-14	3 (12)	
ESSDAI ≥14	0	
Physician GDA	2.0 (1.0-2.0) ^b	n/a
ESSPRI (total score)	6.3 (4.7-7.0)	n/a
Patient GDA	6.0 (5.0-7.0)	n/a
IgG (g/L)	13.1 (10.3-15.6) ^a	10.6 (9.4-12.5) ^c
Anti-SSA positive	24 (77%)	n/a
RF positive	16 (55%) ^a	n/a
Available data (n)		
RIVM S1/RBD antibody titers (post-vaccination)	28	10
IFN-γ ELIspot assay (pre- and post-vaccination)	24	5
Anti-SSA antibody titers (pre-vaccination)	26	n/a
Anti-SSA antibody titers (post-vaccination)	26	n/a
Saliva S1/RBD antibody titers (pre-vaccination)	27	9
Saliva S1/RBD antibody titers (post-vaccination)	26	9

Data presented as median (IQR) or n (%)

*Indicates significant difference ($p < 0.005$) between pSS and HC group

^a1-10%, ^b10-20%, ^c20-30%, ^d30-40% missing data

ESSDAI, Physician GDA and RF collected ≤ 1 year before first vaccination date

Abbreviations: ELIspot: enzyme-linked immune absorbent assay, ESSDAI: European League Against Rheumatism (EULAR) Sjögren's Syndrome Disease Activity Index, ESSPRI: EULAR Sjögren's Syndrome Patient Reported Index, GDA: global disease activity, HC: healthy controls, IFN: interferon, IgG: immunoglobulin G, n/a: not applicable, pSS: primary Sjögren's syndrome, RBD: receptor binding domain, RIVM: Dutch National Institute for Public Health and the Environment, S1: spike 1

Supplementary Table 2 Univariate and multivariate linear regression corrected for age to explore the difference in SARS-CoV-2 antibody titers* between pSS patients and HC for the Pfizer-BioNtech, AstraZeneca and Moderna vaccine types

PFIZER-BIONTECH			
	B-coefficient of pSS/HC group	95% CI	P-value
Univariate regression	0.114	-0.135 – 0.363	0.36
Multivariate regression corrected for age	0.108	-0.143 – 0.358	0.39
ASTRAZENECA			
	B-coefficient of pSS/HC group	95% CI	P-value
Univariate regression	-0.017	-0.519 – 0.485	0.94
Multivariate regression corrected for age	-0.011	-0.586 – 0.563	0.97
MODERNA			
	B-coefficient of pSS/HC group	95% CI	P-value
Univariate regression	0.216	-0.124 – 0.556	0.19
Multivariate regression corrected for age	0.205	-0.205 – 0.615	0.29

*Antibody titers were log-transformed to obtain a normal distribution of residuals

Abbreviations: CI: confidence interval, HC: healthy controls, pSS: primary Sjögren's syndrome, SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2

Supplementary Table 3 Univariate linear regression to explore the association between baseline characteristics and SARS-CoV-2 antibody titers* for the Pfizer-BioNTech and AstraZeneca vaccine types in pSS patients

PFIZER/BIONTECH		
	B-coefficient (95% CI)	P-value
Hydroxychloroquine use	-0.167 (-0.465 – 0.131)	0.27
ESSDAI	-0.007 (-0.060 – 0.045)	0.77
IgG	-0.006 (-0.026 – 0.014)	0.55
Lymphocyte count	0.175 (-0.126– 0.476)	0.25
ASTRAZENECA		
	B-coefficient (95% CI)	P-value
Hydroxychloroquine use	0.565 (-0.034 – 1.163)	0.06
ESSDAI	-0.077 (-0.236 – 0.083)	0.31
IgG	-0.030 (-0.099 – 0.039)	0.33
Lymphocyte count	-0.248 (-0.588 – 0.092)	0.13

*Antibody titers were log-transformed to obtain a normal distribution of residuals

ESSDAI and lymphocyte count collected ≤ 1 year before first vaccination date

Abbreviations: CI: confidence interval, ESSDAI: European League Against Rheumatism (EULAR) Sjögren's Syndrome Disease Activity Index, HC: healthy controls, IgG: immunoglobulin G pSS: primary Sjögren's syndrome, SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2

Supplementary Table 4 Correlation coefficients of T-cell response as measured with spike-specific IFN- γ producing SFCs with RIVM SARS-CoV-2 antibody titers (7 days after 2nd vaccination)

TOTAL GROUP (pSS+HC)	R	p-value
Anti-S1 IgG antibody titer (n=29)	0.451	0.01
Anti-RBD IgG antibody titer (n=29)	0.456	0.01
pSS		
Anti-S1 IgG antibody titer (n=24)	0.452	0.03
Anti-RBD IgG antibody titer (n=24)	0.451	0.03

Abbreviations: HC: healthy controls, IFN: interferon, IgG: Immunoglobulin G, pSS: primary Sjögren's syndrome, RBD: receptor binding domain, RIVM: Dutch National Institute for Public Health and the Environment, SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2, S1: spike 1, SFC: spot-forming cell,

Supplementary Table 5 Change in patient-reported and systemic disease activity and IgG levels in pSS patients after vaccination, split for Pfizer-BioNtech, AstraZeneca and Moderna vaccine types

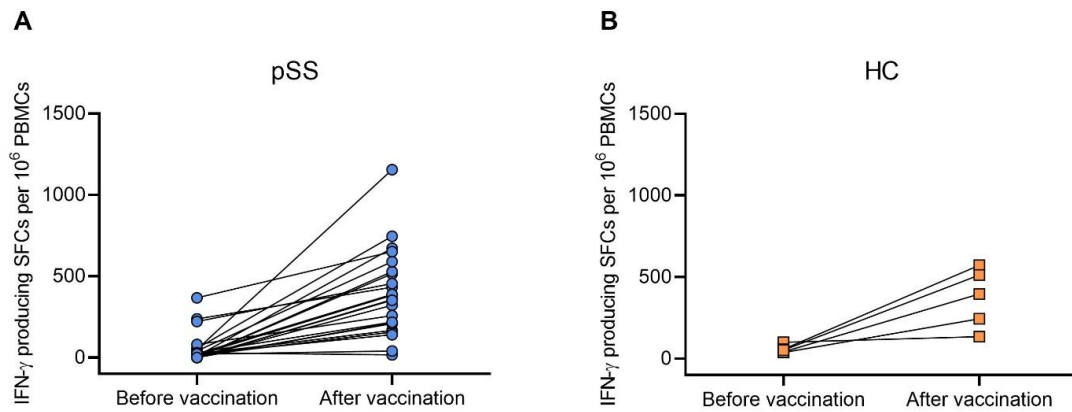
PFIZER-BIONTECH	Baseline	After vaccination	p-value
ESSPRI – total	6.0 (4.7-7.0) (n=47)	5.7 (3.8-6.8) (n=45)	0.22
ESSPRI – dryness	7.0 (4.0-7.0) (n=47)	6.0 (4.0-7.0) (n=46)	0.08
ESSPRI – fatigue	6.0 (4.0-8.0) (n=47)	6.5 (4.0-7.0) (n=46)	0.92
ESSPRI – pain	6.0 (4.0-7.0) (n=47)	5.0 (2.5-7.0) (n=45)	0.49
Patient GDA	6.0 (5.0-7.0) (n=47)	6.0 (4.0-7.0) (n=46)	0.33
ESSDAI	3.0 (1.0-4.8) (n=40)	3.0 (1.0-5.0) (n=23)	0.83
IgG	13.5 (10.3-19.0) (n=46)	13.0 (10.6-18.3) (n=45)	0.38
ASTRAZENECA			
ESSPRI – total	6.0 (5.0-7.5) (n=13)	5.0 (3.8-6.5) (n=12)	0.28
ESSPRI – dryness	7.0 (5.0-8.0) (n=13)	5.0 (4.5-7.5) (n=13)	0.25
ESSPRI – fatigue	6.0 (5.0-8.0) (n=13)	7.0 (4.3-7.8) (n=12)	1.00
ESSPRI – pain	7.0 (5.0-7.5) (n=13)	5.0 (3.0-6.5) (n=13)	0.30
Patient GDA	7.0 (5.5-8.0) (n=13)	6.0 (4.0-7.5) (n=13)	0.12
ESSDAI	3.0 (2.0-4.5) (n=13)	2.0 (1.5-4.3) (n=10)	0.66
IgG	12.1 (9.4-15.6) (n=10)	12.4 (7.9-13.4) (n=11)	0.74
MODERNA			
ESSPRI – total	7.0 (5.6-8.0) (n=6)	8.2 (5.2-8.5) (n=6)	0.59
ESSPRI – dryness	7.5 (5.8-8.0) (n=6)	7.5 (5.8-9.0) (n=6)	0.78
ESSPRI – fatigue	6.5 (4.8-8.0) (n=6)	7.5 (5.8-9.0) (n=6)	0.44
ESSPRI – pain	8.0 (6.3-8.0) (n=6)	8.0 (4.5-9.3) (n=6)	0.88
Patient GDA	6.5 (5.5-8.0) (n=6)	7.0 (5.3-8.3) (n=6)	1.00
ESSDAI	2.0 (0.0-3.5) (n=5)	2.5 (-) (n=2)	1.00
IgG	11.2 (10.3-14.9) (n=6)	11.0 (9.3-18.8) (n=6)	0.56

Data presented as median (IQR).

Baseline ESSDAI was collected within 1 year before the first vaccination and follow-up ESSDAI was collected within 6 months after vaccination

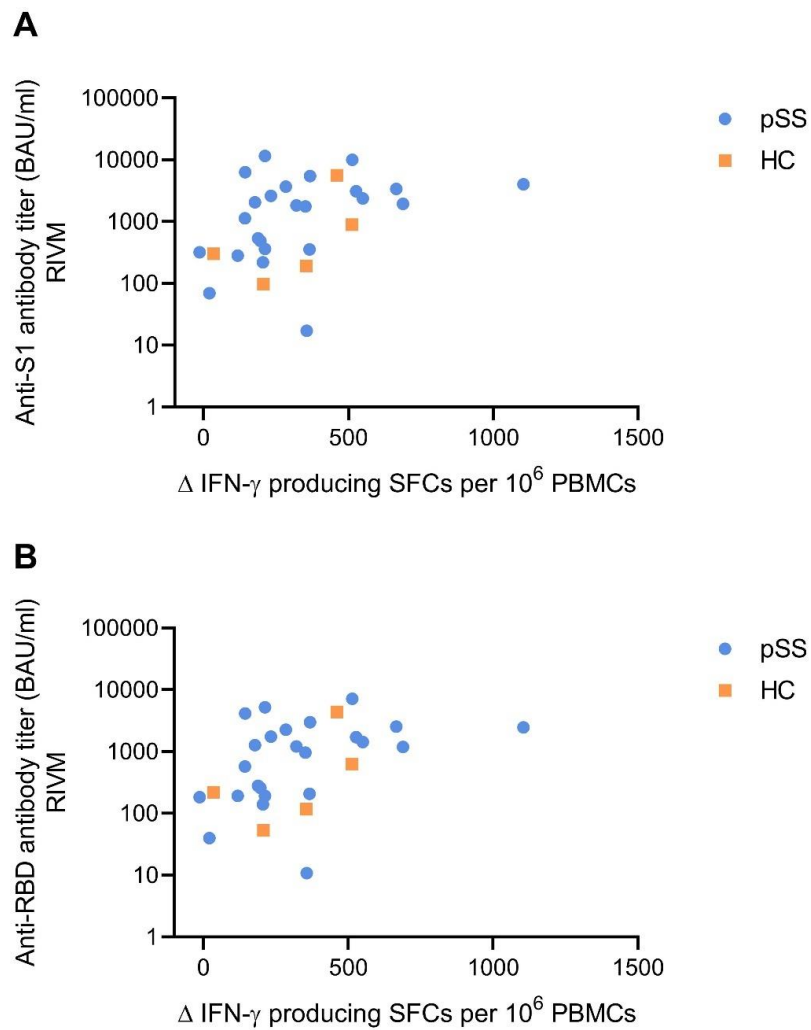
ESSPRI, patient GDA and IgG scores were collected at baseline and 28 days after the second vaccination

Abbreviations: ESSDAI: European League Against Rheumatism (EULAR) Sjögren's Syndrome Disease Activity Index, ESSPRI: EULAR Sjögren's Syndrome Patient Reported Index, GDA: global disease activity, IgG: immunoglobulin G, pSS: primary Sjögren's syndrome



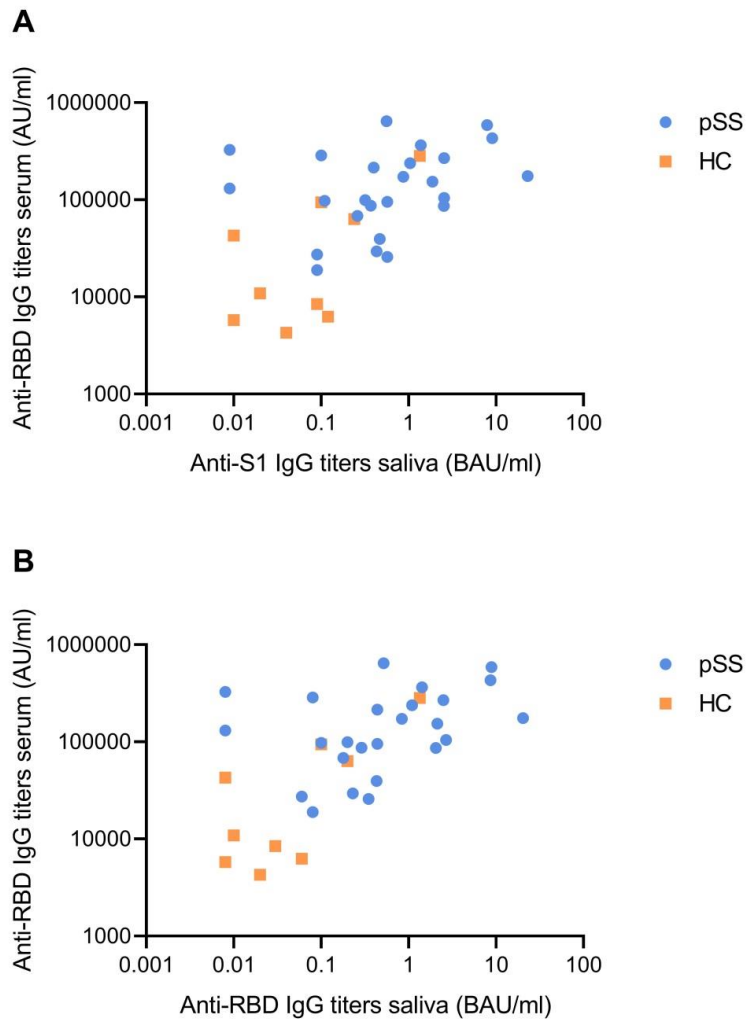
Supplementary Figure 1 Change in IFN- γ producing SFCs before and after vaccination in **A)** pSS patients and **B)** healthy controls

Abbreviations: HC: healthy controls, IFN: interferon, PBMC: peripheral blood mononuclear cell, pSS: primary Sjögren's syndrome, SFC: spot-forming cell



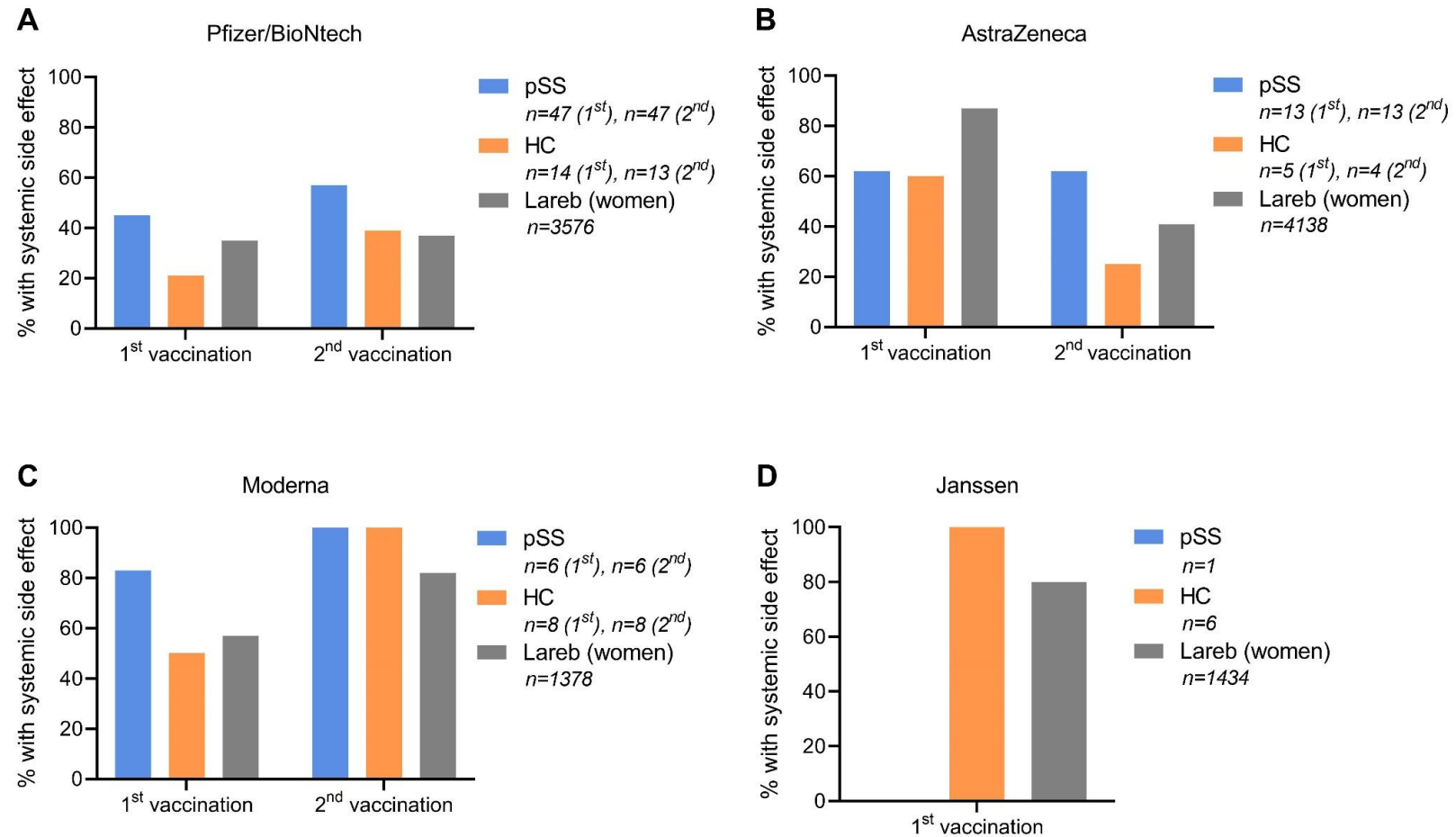
Supplementary Figure 2 Scatterplots of IFN- γ producing SFCs with **A)** anti-S1 antibody titers in RIVM blood samples (+7 days after second vaccination) **B)** anti-RBD antibody titers in RIVM blood samples (+7 days after second vaccination)

Abbreviations: HC: healthy controls, IFN: interferon, RIVM: Dutch National Institute for Public Health and the Environment, PBMC: peripheral blood mononuclear cell, pSS: primary Sjögren's syndrome, RBD: receptor binding domain, S1: spike 1, SFC: spot-forming cell



Supplementary Figure 3 Scatterplots of anti-RBD IgG titers in serum and **A**) anti-S1 IgG titers in saliva and **B**) anti-RBD IgG titers in saliva for patients with primary Sjögren's syndrome (pSS) and healthy controls (HC)

Abbreviations: HC: healthy controls, IgG: Immunoglobulin G, pSS: primary Sjögren's syndrome, RBD: receptor binding domain, S1: spike 1



Supplementary Figure 4 Systemic side effects after the 1st and 2nd vaccination for participants who received **A)** Pfizer-BioNtech **B)** AstraZeneca **C)** Moderna or **D)** Janssen

Abbreviations: HC: healthy controls, pSS: primary Sjögren's syndrome

