Clinical trial results:
Vaccine response against SARS-CoV-2 in patients with primary Sjögren's syndrome

Summary

EudraCT number	2021-001414-10
Trial protocol	NL
Global end of trial date	23 August 2022

Results information

Result version number	v1 (current)
This version publication date	08 January 2023
First version publication date	08 January 2023
Summary attachment (see zip file)	Final report VaccineSS study (Final report of VaccineSS study for METc dd 08-11-2022.pdf)

Trial information

Trial identification

Sponsor protocol code	202100076

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Medical Center Groningen
Sponsor organisation address	Hanzeplein 1, Groningen, Netherlands, 9713GZ
Public contact	Postdoctoral researcher, University Medical Center Groningen, g.m.p.j.verstappen@umcg.nl
Scientific contact	Postdoctoral researcher, University Medical Center Groningen, g.m.p.j.verstappen@umcg.nl

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to study protective antibody responses after SARS-CoV-2 vaccination in patients with pSS.

Protection of trial subjects:

This study investigates the immune response and AEs in patients with pSS compared with healthy individuals. If subjects had not participated in this study, they still would have received the vaccine against SARS-CoV-2 according to standard of care via their general practitioner or area health authority without additional testing. The participant burden (questionnaires, saliva collection and blood drawing) were kept to a minimum to answer all research questions.

Background therapy:

Background therapy was allowed, except for:
- current use of conventional or biological DMARDs (hydroxychloroquine was allowed)
- prednisone >10 mg/day
- previous use of DMARDs ≤6 months before inclusion (rituximab ≤12 months)

Evidence for comparator: -

Actual start date of recruitment	01 April 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 104
Worldwide total number of subjects	104
EEA total number of subjects	104

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	71
From 65 to 84 years	33
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with pSS who participated in the REgistry of Sjögren syndrome in Umcg – LongiTudinal (RESULT)-cohort were screened for in- and exclusion criteria. Potentially eligible patients received a letter with study information.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	pSS patients

Arm description:

Patients with primary Sjögren's syndrome

Arm type	patient group
Investigational medicinal product name	Comirnaty COVID-19 mRNA vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

A course of 2 doses (0.3 mL each)

Investigational medicinal product name	ChAdOx1-S COVID-19 vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

A course of 2 doses (0.5 mL each)

Investigational medicinal product name	Ad26.COV2-S COVID-19 vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single-dose of 0.5 mL

Investigational medicinal product name	Spikevax COVID-19 mRNA vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

A course of 2 doses (0.5 mL each)

Arm title	Healthy controls

Arm description: Female healthy controls	
Arm type	healthy control group
Investigational medicinal product name	Comirnaty COVID-19 mRNA vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: A course of 2 doses (0.3 mL each)	
Investigational medicinal product name	ChAdOx1-S COVID-19 vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: A course of 2 doses (0.5 mL each)	
Investigational medicinal product name	Ad26.COV2-S COVID-19 vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: Single-dose of 0.5 mL	
Investigational medicinal product name	Spikevax COVID-19 mRNA vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: A course of 2 doses (0.5 mL each)	

Number of subjects in period 1	pSS patients	Healthy controls
Started	70	34
Completed	67	33
Not completed	3	1
Consent withdrawn by subject	1	1
Protocol deviation	2	-

Baseline characteristics

End points

End points reporting groups

Reporting group title	pSS patients
Reporting group description: Patients with primary Sjögren's syndrome	
Reporting group title	Healthy controls
Reporting group description: Female healthy controls	

Primary: Absolute difference in protective antibody titers against SARS-CoV-2 between patients with pSS and healthy controls

End point title	Absolute difference in protective antibody titers against SARS-CoV-2 between patients with pSS and healthy controls[1]
End point description:	
End point type	Primary
End point timeframe: Day 28 after the second vaccination	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Because of an unequal distribution of vaccination products between arms (e.g., more Spikevax in the healthy control arm), statistical comparison of two arms is not valid. We did statistically compare the two arms for each vaccination product. For details we refer to: Verstappen GM, de Wolff L, Arends S, et al. Immunogenicity and safety of COVID-19 vaccination in patients with primary Sjögren's syndrome. RMD Open 2022;8:e002265. doi:10.1136/rmdopen-2022-002265

End point values	pSS patients	Healthy controls		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	29		
Units: AU/mL				
median (inter-quartile range (Q1-Q3))	97230 (60247 to 224608)	110710 (16771 to 280630)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

7 days after each vaccination. Periodic (quarterly) assessment of SAEs during follow-up specifically for ChAdOx1-S according to contract with AstraZeneca (one of the subsidising parties).

Adverse event reporting additional description:

One patient with an SAE was excluded from the primary and secondary analyses, because of a screening failure. This patient is however included in the current adverse events report, resulting in a total of 68 participants in the pSS group.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	pSS patients
Reporting group description: -	
Reporting group title	Healthy controls

Reporting group description: -

Serious adverse events	pSS patients	Healthy controls	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 68 (2.94%)	0 / 33 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Respiratory, thoracic and mediastinal disorders			
Chest pain			
subjects affected / exposed	1 / 68 (1.47%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 68 (1.47%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	pSS patients	Healthy controls	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 68 (76.47%)	17 / 33 (51.52%)	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	43 / 68 (63.24%)	15 / 33 (45.45%)	
occurrences (all)	63	18	
Pyrexia			
subjects affected / exposed	7 / 68 (10.29%)	4 / 33 (12.12%)	
occurrences (all)	8	4	
Chills			
subjects affected / exposed	17 / 68 (25.00%)	7 / 33 (21.21%)	
occurrences (all)	20	7	
Headache			
subjects affected / exposed	37 / 68 (54.41%)	12 / 33 (36.36%)	
occurrences (all)	49	13	
Myalgia			
subjects affected / exposed	28 / 68 (41.18%)	12 / 33 (36.36%)	
occurrences (all)	41	16	
Nausea			
subjects affected / exposed	10 / 68 (14.71%)	4 / 33 (12.12%)	
occurrences (all)	13	4	
Gastrointestinal disorders			
Burning mouth syndrome			
subjects affected / exposed	1 / 68 (1.47%)	0 / 33 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	13 / 68 (19.12%)	3 / 33 (9.09%)	
occurrences (all)	17	3	
Product issues			
Injection site rash			
subjects affected / exposed	10 / 68 (14.71%)	3 / 33 (9.09%)	
occurrences (all)	10	3	
Injection site oedema	Additional description: At the site of injection		

subjects affected / exposed	13 / 68 (19.12%)	4 / 33 (12.12%)	
occurrences (all)	14	5	
Injection site pain			
subjects affected / exposed	43 / 68 (63.24%)	16 / 33 (48.48%)	
occurrences (all)	61	24	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2021	- Addition of Spikevax to the investigational products - Addition of AstraZeneca as subsidising party and according to contract ChAdOx1-S COVID-19 vaccine SAE reporting during follow-up

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported