Clinical trial results:
Immunogenicity of COVID-19 vaccines in medical staff and special risk populations

Summary

EudraCT number	2021-001512-28
Trial protocol	DE
Global end of trial date	30 December 2021

Results information

Result version number	v1 (current)
This version publication date	03 August 2023
First version publication date	03 August 2023

Trial information

Trial identification

Sponsor protocol code	COVIM

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Charité - Universitätsmedizin Berlin
Sponsor organisation address	Charitéplatz 1, Berlin, Germany, 10117
Public contact	Med. Klinik m. S. Infektiologie, Charité - Universitätsmedizin Berlin, 49 30450653034, leif-erik.sander@charite.de
Scientific contact	Med. Klinik m. S. Infektiologie, Charité - Universitätsmedizin Berlin, 49 30450653034, leif-erik.sander@charite.de

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	Interim
Date of interim/final analysis	01 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 November 2021
Global end of trial reached?	Yes
Global end of trial date	30 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Determination of immunogenicity of SARS-CoV-2 vaccines in healthy individuals compared to special risk populations

Protection of trial subjects:

The study was conducted according the declaration of Helsiniki.

Background therapy:

Despite the available immunogenicity, safety and efficacy data from randomized controlled trials, key questions regarding the newly approved SARS-CoV-2 vaccines remain unanswered. Immunogenicity and safety of SARS-CoV-2 vaccines in individuals with varying degrees of immunodeficiency is unknown. These risk populations include patients with chronic kidney failure and hemodialysis, kidney transplant recipients, patients with neuroimmunological diseases such as MS and NMOSD with and without B cell depleting therapies, patients with hemato-oncological malignancies including B cell malignancies, patients with rheumatic and autoimmune diseases and patients with primary immunodeficiencies. The identification of immunological correlates of protection for COVID-19 vaccines is of critical importance to determine vaccine success in such risk populations and for the design and evaluation of new vaccines.

Evidence for comparator: -

Actual start date of recruitment	01 May 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 1889
Worldwide total number of subjects	1889
EEA total number of subjects	1889

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)	1396
From 65 to 84 years	408
85 years and over	85

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 26 sites in Germany. First Patient, first Visit: 26-MAY-2021, Last Patient, last Visit: 30-DEC-2021

Pre-assignment

Screening details:

Planned recruitment: approximately 3050 participants in a total of eight cohorts vaccinated with different SARS-CoV-2 vaccines in specific at-risk populations.
-> Total number of recruited participants: 1889
There are no specific sex distribution as no sex specific differences. Participants were not randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	BNPL

Arm description:

Haemato-oncological participants and participants with B-cell neoplasia (BNPL)

Arm type	vaccination
Investigational medicinal product name	Tozinameran
Investigational medicinal product code	
Other name	Comirnaty; COVID-19 mRNA vaccine (nucleoside-modified)
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Injection

Dosage and administration details:

2 doses

Investigational medicinal product name	CO-VID-19 Vac-ci-ne Jans-sen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Injection

Dosage and administration details:

1 dose

Investigational medicinal product name	COVID-19 mRNA vaccine Moderna (CX-024414)
Investigational medicinal product code	SUB207171
Other name	COVID-19 Vaccine Moderna
Pharmaceutical forms	Dispersion for injection
Routes of administration	Injection

Dosage and administration details:

2 doses

Investigational medicinal product name	COVID-19 vaccine AstraZeneca (ChAdOx1 nCoV-19)
Investigational medicinal product code	SUB207764
Other name	Vaxzevria (CO-VID-19 Vac-ci-ne Astra-Zene-ca)
Pharmaceutical forms	Suspension for injection
Routes of administration	Injection

Dosage and administration details: 2 doses	

Arm title	Participants with haemodialysis (HD)
Arm description: Participants with chronic kidney failure undergoing a haemodialysis (HD)	
Arm type	Vaccination cohort
Investigational medicinal product name	Tozinameran
Investigational medicinal product code	
Other name	Comirnaty; COVID-19 mRNA vaccine (nucleoside-modified)
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Injection
Dosage and administration details: 2 doses	
Investigational medicinal product name	CO-VID-19 Vac-ci-ne Jans-sen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Injection
Dosage and administration details: 1 dose	
Investigational medicinal product name	COVID-19 mRNA vaccine Moderna (CX-024414)
Investigational medicinal product code	SUB207171
Other name	COVID-19 Vaccine Moderna
Pharmaceutical forms	Dispersion for injection
Routes of administration	Injection
Dosage and administration details: 2 doses	
Investigational medicinal product name	COVID-19 vaccine AstraZeneca (ChAdOx1 nCoV-19)
Investigational medicinal product code	SUB207764
Other name	Vaxzevria (CO-VID-19 Vac-ci-ne Astra-Zene-ca)
Pharmaceutical forms	Suspension for injection
Routes of administration	Injection
Dosage and administration details: 2 doses	
Arm title	health care workers (HCW)
Arm description: Healthy health care workers at one of the participating trial centers (HCW)	
Arm type	Vaccination cohort
Investigational medicinal product name	Tozinameran
Investigational medicinal product code	
Other name	Comirnaty; COVID-19 mRNA vaccine (nucleoside-modified)
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Injection
Dosage and administration details: 2 doses	
Investigational medicinal product name	CO-VID-19 Vac-ci-ne Jans-sen
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Injection
Dosage and administration details: 1 dose	
Investigational medicinal product name	COVID-19 mRNA vaccine Moderna (CX-024414)
Investigational medicinal product code	SUB207171
Other name	COVID-19 Vaccine Moderna
Pharmaceutical forms	Dispersion for injection
Routes of administration	Injection
Dosage and administration details: 2 doses	
Investigational medicinal product name	COVID-19 vaccine AstraZeneca (ChAdOx1 nCoV-19)
Investigational medicinal product code	SUB207764
Other name	Vaxzevria (CO-VID-19 Vac-ci-ne Astra-Zene-ca)
Pharmaceutical forms	Suspension for injection
Routes of administration	Injection
Dosage and administration details: 2 doses	
Arm title	Patients with IBD
Arm description: Patients with inflammatory bowel disease (IBD)	
Arm type	vaccination cohort
Investigational medicinal product name	Tozinameran
Investigational medicinal product code	
Other name	Comirnaty; COVID-19 mRNA vaccine (nucleoside-modified)
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Injection
Dosage and administration details: 2 doses	
Investigational medicinal product name	CO-VID-19 Vac-ci-ne Jans-sen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Injection
Dosage and administration details: 1 dose	
Investigational medicinal product name	COVID-19 mRNA vaccine Moderna (CX-024414)
Investigational medicinal product code	SUB207171
Other name	COVID-19 Vaccine Moderna
Pharmaceutical forms	Dispersion for injection
Routes of administration	Injection
Dosage and administration details: 2 doses	
Investigational medicinal product name	COVID-19 vaccine AstraZeneca (ChAdOx1 nCoV-19)
Investigational medicinal product code	SUB207764
Other name	Vaxzevria (CO-VID-19 Vac-ci-ne Astra-Zene-ca)
Pharmaceutical forms	Suspension for injection
Routes of administration	Injection
Dosage and administration details: 2 doses	
Arm title	NEUR

Arm description:	
Participants with neuroimmunological diseases such as MS and NMOSD (NEUR)	
Arm type	Vaccination cohort
Investigational medicinal product name	Tozinameran
Investigational medicinal product code	
Other name	Comirnaty; COVID-19 mRNA vaccine (nucleoside-modified)
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Injection
Dosage and administration details:	
2 doses	
Investigational medicinal product name	CO-VID-19 Vac-ci-ne Jans-sen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Injection
Dosage and administration details:	
1 dose	
Investigational medicinal product name	COVID-19 mRNA vaccine Moderna (CX-024414)
Investigational medicinal product code	SUB207171
Other name	COVID-19 Vaccine Moderna
Pharmaceutical forms	Dispersion for injection
Routes of administration	Injection
Dosage and administration details:	
2 doses	
Investigational medicinal product name	COVID-19 vaccine AstraZeneca (ChAdOx1 nCoV-19)
Investigational medicinal product code	SUB207764
Other name	Vaxzevria (CO-VID-19 Vac-ci-ne Astra-Zene-ca)
Pharmaceutical forms	Suspension for injection
Routes of administration	Injection
Dosage and administration details:	
2 doses	
Arm title	Participants with NTX
Arm description:	
Participants with history of kidney transplantation (NTX)	
Arm type	vaccination cohort
Investigational medicinal product name	Tozinameran
Investigational medicinal product code	
Other name	Comirnaty; COVID-19 mRNA vaccine (nucleoside-modified)
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Injection
Dosage and administration details:	
2 doses	
Investigational medicinal product name	CO-VID-19 Vac-ci-ne Jans-sen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Injection
Dosage and administration details:	
1 dose	

Investigational medicinal product name	COVID-19 mRNA vaccine Moderna (CX-024414)
Investigational medicinal product code	SUB207171
Other name	COVID-19 Vaccine Moderna
Pharmaceutical forms	Dispersion for injection
Routes of administration	Injection

Dosage and administration details:
2 doses

Investigational medicinal product name	COVID-19 vaccine AstraZeneca (ChAdOx1 nCoV-19)
Investigational medicinal product code	SUB207764
Other name	Vaxzevria (CO-VID-19 Vac-ci-ne Astra-Zene-ca)
Pharmaceutical forms	Suspension for injection
Routes of administration	Injection

Dosage and administration details:
2 doses

Arm title	Participants with PID

Arm description:
Participants with primary immunodeficiency (PID)

Arm type	vaccination cohort
Investigational medicinal product name	Tozinameran
Investigational medicinal product code	
Other name	Comirnaty; COVID-19 mRNA vaccine (nucleoside-modified)
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Injection

Dosage and administration details:
2 doses

Investigational medicinal product name	CO-VID-19 Vac-ci-ne Jans-sen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Injection

Dosage and administration details:
1 dose

Investigational medicinal product name	COVID-19 mRNA vaccine Moderna (CX-024414)
Investigational medicinal product code	SUB207171
Other name	COVID-19 Vaccine Moderna
Pharmaceutical forms	Dispersion for injection
Routes of administration	Injection

Dosage and administration details:
2 doses

Investigational medicinal product name	COVID-19 vaccine AstraZeneca (ChAdOx1 nCoV-19)
Investigational medicinal product code	SUB207764
Other name	Vaxzevria (CO-VID-19 Vac-ci-ne Astra-Zene-ca)
Pharmaceutical forms	Suspension for injection
Routes of administration	Injection

Dosage and administration details:
2 doses

Arm title	RHEU

Arm description:
Participants with rheumatic and autoimmune diseases under immunosuppression (RHEU)

Arm type	vaccination cohort

Investigational medicinal product name	Tozinameran
Investigational medicinal product code	
Other name	Comirnaty; COVID-19 mRNA vaccine (nucleoside-modified)
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Injection
Dosage and administration details: 2 doses	
Investigational medicinal product name	CO-VID-19 Vac-ci-ne Jans-sen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Injection
Dosage and administration details: 1 dose	
Investigational medicinal product name	COVID-19 mRNA vaccine Moderna (CX-024414)
Investigational medicinal product code	SUB207171
Other name	COVID-19 Vaccine Moderna
Pharmaceutical forms	Dispersion for injection
Routes of administration	Injection
Dosage and administration details: 2 doses	
Investigational medicinal product name	COVID-19 vaccine AstraZeneca (ChAdOx1 nCoV-19)
Investigational medicinal product code	SUB207764
Other name	Vaxzevria (CO-VID-19 Vac-ci-ne Astra-Zene-ca)
Pharmaceutical forms	Suspension for injection
Routes of administration	Injection
Dosage and administration details: 2 doses	
Arm title	Participants older than 70 years SEN
Arm description: Participants ≥70 years-of age, with none of the medical conditions specified above (SEN)	
Arm type	vaccination cohort
Investigational medicinal product name	Tozinameran
Investigational medicinal product code	
Other name	Comirnaty; COVID-19 mRNA vaccine (nucleoside-modified)
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Injection
Dosage and administration details: 2 doses	
Investigational medicinal product name	CO-VID-19 Vac-ci-ne Jans-sen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Injection
Dosage and administration details: 1 dose	
Investigational medicinal product name	COVID-19 mRNA vaccine Moderna (CX-024414)
Investigational medicinal product code	SUB207171
Other name	COVID-19 Vaccine Moderna
Pharmaceutical forms	Dispersion for injection
Routes of administration	Injection

Dosage and administration details: 2 doses	
Investigational medicinal product name	COVID-19 vaccine AstraZeneca (ChAdOx1 nCoV-19)
Investigational medicinal product code	SUB207764
Other name	Vaxzevria (CO-VID-19 Vac-ci-ne Astra-Zene-ca)
Pharmaceutical forms	Suspension for injection
Routes of administration	Injection
Dosage and administration details: 2 doses	

Number of subjects in period 1	BNPL	Participants with haemodialysis (HD)	health care workers (HCW)
Started	81	87	669
Completed	65	79	595
Not completed	16	8	74
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	2	4	2
Exclusion criteria occur after recruitment	-	-	1
personal reason/ discontinuation recommendation d.	-	4	64
discontinuation recommendation by investigator	14	-	-
missing data	-	-	3
lost contact	-	-	4
Protocol deviation	-	-	-

Number of subjects in period 1	Patients with IBD	NEUR	Participants with NTX
Started	93	252	147
Completed	69	203	124
Not completed	24	49	23
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	1	5	2
Exclusion criteria occur after recruitment	-	-	-
personal reason/ discontinuation recommendation d.	19	39	14
discontinuation recommendation by investigator	-	-	-
missing data	3	-	-
lost contact	1	2	5
Protocol deviation	-	3	1

Number of subjects in period 1	Participants with PID	RHEU	Participants older than 70 years SEN
Started	139	114	307

Completed	103	98	299
Not completed	36	16	8
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	2	-	-
Exclusion criteria occur after recruitment	-	2	-
personal reason/ discontinuation recommendation d.	33	3	7
discontinuation recommendation by investigator	-	-	-
missing data	1	8	-
lost contact	-	3	-
Protocol deviation	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	BNPL
Reporting group description:	
Haemato-oncological participants and participants with B-cell neoplasia (BNPL)	
Reporting group title	Participants with haemodialysis (HD)
Reporting group description:	
Participants with chronic kidney failure undergoing a haemodialysis (HD)	
Reporting group title	health care workers (HCW)
Reporting group description:	
Healthy health care workers at one of the participating trial centers (HCW)	
Reporting group title	Patients with IBD
Reporting group description:	
Patients with inflammatory bowel disease (IBD)	
Reporting group title	NEUR
Reporting group description:	
Participants with neuroimmunological diseases such as MS and NMOSD (NEUR)	
Reporting group title	Participants with NTX
Reporting group description:	
Participants with history of kidney transplantation (NTX)	
Reporting group title	Participants with PID
Reporting group description:	
Participants with primary immunodeficiency (PID)	
Reporting group title	RHEU
Reporting group description:	
Participants with rheumatic and autoimmune diseases under immunosuppression (RHEU)	
Reporting group title	Participants older than 70 years SEN
Reporting group description:	
Participants ≥70 years-of age, with none of the medical conditions specified above (SEN)	

Reporting group values	BNPL	Participants with haemodialysis (HD)	health care workers (HCW)
Number of subjects	81	87	669
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	63.33	60.01	40.27

standard deviation	± 12.02	± 14.44	± 12.74

Gender categorical Units: Subjects			
Female	34	27	465
Male	47	60	204
no. of vaccine doses Units: Subjects			
0 does	1	1	0
1 dose	1	0	8
2 doses	39	66	360
3 doses	38	18	301
4 doses	2	0	0
Not recorded	0	2	0
BMI			
body mass idex			
Units: kg/ m2			
arithmetic mean	25.66	26.15	24.11
standard deviation	± 4.14	± 6.8	± 4.28

Reporting group values	Patients with IBD	NEUR	Participants with NTX
Number of subjects	93	252	147
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	39.73	44.93	51.83
standard deviation	± 11.97	± 12.64	± 15.70
Gender categorical Units: Subjects			
Female	40	182	60
Male	53	70	87
no. of vaccine doses Units: Subjects			
0 does	1	2	0
1 dose	1	10	5
2 doses	87	188	69
3 doses	3	51	65
4 doses	0	1	7

Not recorded	1	0	1

BMI			
body mass idex			
Units: kg/ m2			
arithmetic mean	25.12	24.44	24.82
standard deviation	± 5.55	± 4.64	± 4.71

Reporting group values	Participants with PID	RHEU	Participants older than 70 years SEN
Number of subjects	139	114	307
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	45.67	57.34	81.03
standard deviation	± 14.6	± 13.9	± 6.65
Gender categorical			
Units: Subjects			
Female	78	62	214
Male	61	52	93
no. of vaccine doses			
Units: Subjects			
0 does	0	0	0
1 dose	3	1	0
2 doses	107	50	40
3 doses	28	58	267
4 doses	0	5	0
Not recorded	1	0	0
BMI			
body mass idex			
Units: kg/ m2			
arithmetic mean	24.7	25.99	24.82
standard deviation	± 5.16	± 5.42	± 4.04

Reporting group values	Total		
Number of subjects	1889		
Age categorical			
Units: Subjects			
In utero	0		

Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	1162		
Male	727		
no. of vaccine doses			
Units: Subjects			
0 does	5		
1 dose	29		
2 doses	1006		
3 doses	829		
4 doses	15		
Not recorded	5		
BMI			
body mass idex			
Units: kg/ m2			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	BNPL
Reporting group description:	
Haemato-oncological participants and participants with B-cell neoplasia (BNPL)	
Reporting group title	Participants with haemodialysis (HD)
Reporting group description:	
Participants with chronic kidney failure undergoing a haemodialysis (HD)	
Reporting group title	health care workers (HCW)
Reporting group description:	
Healthy health care workers at one of the participating trial centers (HCW)	
Reporting group title	Patients with IBD
Reporting group description:	
Patients with inflammatory bowel disease (IBD)	
Reporting group title	NEUR
Reporting group description:	
Participants with neuroimmunological diseases such as MS and NMOSD (NEUR)	
Reporting group title	Participants with NTX
Reporting group description:	
Participants with history of kidney transplantation (NTX)	
Reporting group title	Participants with PID
Reporting group description:	
Participants with primary immunodeficiency (PID)	
Reporting group title	RHEU
Reporting group description:	
Participants with rheumatic and autoimmune diseases under immunosuppression (RHEU)	
Reporting group title	Participants older than 70 years SEN
Reporting group description:	
Participants ≥70 years-of age, with none of the medical conditions specified above (SEN)	

Primary: change of immunogenicity of Covid 19 vaccination

End point title	change of immunogenicity of Covid 19 vaccination[1]
End point description:	
presence of anti SARS-CoV-2 specific antibodies after first vaccination	
End point type	Primary
End point timeframe:	
six months up to max. 9 months after first vaccination	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: HCW vs RAID OR = 0.014 , OR lower CI = 0.000755, OR upper CI = 0.0733
(RAID is defined as participants with rheumatic and autoimmune diseases under immunosuppression including participants with inflammatory bowel diseases (IBD) or rheumatological disorders (RHEU). These two cohorts are separately characterized in baseline characteristics, but analysed as one new cohort RAID

End point values	BNPL	Participants with haemodialysis (HD)	health care workers (HCW)	NEUR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	65	526	171
Units: subjects				
number of subjects	36	56	525	110

End point values	Participants with NTX	Participants with PID	Participants older than 70 years SEN	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	86	275	
Units: subjects				
number of subjects	55	62	260	

Statistical analyses

Statistical analysis title	HCW vs. NTX
Comparison groups	health care workers (HCW) v Participants with NTX
Number of subjects included in analysis	625
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.00319
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.000175
upper limit	0.016

Statistical analysis title	HCW vs HD
Comparison groups	health care workers (HCW) v Participants with haemodialysis (HD)
Number of subjects included in analysis	591
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.00782

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.00782
upper limit	0.0622

Statistical analysis title	HCW vs PID
Comparison groups	Participants with PID v health care workers (HCW)
Number of subjects included in analysis	612
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.00457
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.000197
upper limit	0.027

Statistical analysis title	HCW vs BNPL
Comparison groups	BNPL v health care workers (HCW)
Number of subjects included in analysis	589
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.00442
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.000217
upper limit	0.0285

Statistical analysis title	HCW vs. NEUR
Comparison groups	NEUR v health care workers (HCW)

Number of subjects included in analysis	697
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.00414
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.000229
upper limit	0.0201

Statistical analysis title	HCW vs Eldery
Comparison groups	health care workers (HCW) v Participants older than 70 years SEN
Number of subjects included in analysis	801
Analysis specification	Pre-specified
Analysis type	equivalence
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.0511
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.00282
upper limit	0.255

Adverse events

Adverse events information	
Timeframe for reporting adverse events: overall trial	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	5

Reporting groups	
Reporting group title	NEUR
Reporting group description: -	
Reporting group title	BNPL
Reporting group description: -	
Reporting group title	HCW Healthy1 health care workers
Reporting group description: -	
Reporting group title	kidney failure under haemodialysis (HD)
Reporting group description: -	
Reporting group title	NTX kidney transplantation
Reporting group description: Participants with history of kidney transplantation (NTX)	
Reporting group title	SEN ≥70 years-of age
Reporting group description: Participants ≥70 years-of age, with none of the medical conditions specified above (SEN)	
Reporting group title	inflammatory bowel diseases IBD
Reporting group description: -	
Reporting group title	primary immunodeficiency PID
Reporting group description: -	
Reporting group title	RHEU
Reporting group description: -	

Serious adverse events	NEUR	BNPL	HCW Healthy1 health care workers
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 252 (0.79%)	1 / 81 (1.23%)	1 / 669 (0.15%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
other, Hodgkin's disease unclassifiable			
subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
other. V.a. malignoma of lung			

subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Retinal vascular disorder			
subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 252 (0.40%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
heart failure, Death			
subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemia			
subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death NOS			
subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Pregnancy loss			
subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	1 / 669 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

Bronchospasm			
subjects affected / exposed	0 / 252 (0.00%)	1 / 81 (1.23%)	0 / 669 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
shingles			
subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 252 (0.40%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	kidney failure under haemodialysis (HD)	NTX kidney transplantation	SEN ≥70 years-of age
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 87 (1.15%)	0 / 147 (0.00%)	6 / 307 (1.95%)
number of deaths (all causes)	0	0	5
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
other, Hodgkin's disease unclassifiable			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	1 / 307 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
other. V.a. malignoma of lung			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	1 / 307 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Vascular disorders			
Retinal vascular disorder			

subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	1 / 307 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
heart failure, Death			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	1 / 307 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Ischaemia			
subjects affected / exposed	1 / 87 (1.15%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death NOS			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	1 / 307 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Reproductive system and breast disorders			
Pregnancy loss			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

shingles			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	1 / 307 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Serious adverse events	inflammatory bowel diseases IBD	primary immunodeficiency PID	RHEU
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 93 (1.08%)	0 / 139 (0.00%)	0 / 114 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
other, Hodgkin's disease unclassifiable			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
other. V.a. malignoma of lung			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Retinal vascular disorder			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
heart failure, Death			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemia			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death NOS			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Pregnancy loss			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
shingles			
subjects affected / exposed	1 / 93 (1.08%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	NEUR	BNPL	HCW Healthy1 health care workers
Total subjects affected by non-serious adverse events			
subjects affected / exposed	82 / 252 (32.54%)	5 / 81 (6.17%)	6 / 669 (0.90%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
carcinoma, colon (chemotherapy)			
subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
shunt insufficiency			
subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	0	0	0
peripheral artery disease			
subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Elective surgery			
subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	1 / 669 (0.15%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 252 (2.38%)	0 / 81 (0.00%)	1 / 669 (0.15%)
occurrences (all)	9	0	1
flu like symptoms			
subjects affected / exposed	11 / 252 (4.37%)	0 / 81 (0.00%)	1 / 669 (0.15%)
occurrences (all)	11	0	1

fever			
subjects affected / exposed	5 / 252 (1.98%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	5	0	0
Injection site reaction			
subjects affected / exposed	14 / 252 (5.56%)	0 / 81 (0.00%)	1 / 669 (0.15%)
occurrences (all)	15	0	1
Chills			
subjects affected / exposed	3 / 252 (1.19%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	3	0	0
Intestinal diverticulitis			
subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Irregular menstruation			
subjects affected / exposed	2 / 252 (0.79%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	0	0	0
Investigations			
GGT increased			
subjects affected / exposed	0 / 252 (0.00%)	2 / 81 (2.47%)	0 / 669 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 252 (4.37%)	0 / 81 (0.00%)	2 / 669 (0.30%)
occurrences (all)	12	0	2
Vertigo			
subjects affected / exposed	3 / 252 (1.19%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	3	0	0
worsening existing symptoms (MS, spasm)			

subjects affected / exposed	5 / 252 (1.98%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	5	0	0
Tingling (leg, finger)			
subjects affected / exposed	3 / 252 (1.19%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	3	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 252 (0.79%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal disorders			
Gastrointestinal pain			
subjects affected / exposed	4 / 252 (1.59%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	4	0	0
Diarrhea			
subjects affected / exposed	1 / 252 (0.40%)	0 / 81 (0.00%)	1 / 669 (0.15%)
occurrences (all)	1	0	1
Nausea and Vomiting			
subjects affected / exposed	0 / 252 (0.00%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Muscle and joint pain			
subjects affected / exposed	6 / 252 (2.38%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	6	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	8 / 252 (3.17%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	9	0	0
Urinary tract infection			
subjects affected / exposed	6 / 252 (2.38%)	0 / 81 (0.00%)	0 / 669 (0.00%)
occurrences (all)	6	0	0
SARS-COV 19 test positive			
subjects affected / exposed	3 / 252 (1.19%)	1 / 81 (1.23%)	0 / 669 (0.00%)
occurrences (all)	3	1	0
reactivation Herpes (simplex vs. labialis)			
subjects affected / exposed	0 / 252 (0.00%)	1 / 81 (1.23%)	0 / 669 (0.00%)
occurrences (all)	0	1	0

Metabolism and nutrition disorders			
Hyperglycemia			
subjects affected / exposed	0 / 252 (0.00%)	2 / 81 (2.47%)	0 / 669 (0.00%)
occurrences (all)	0	2	0
Hypothyroidism			
subjects affected / exposed	0 / 252 (0.00%)	1 / 81 (1.23%)	0 / 669 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	kidney failure under haemodialysis (HD)	NTX kidney transplantation	SEN ≥70 years-of age
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 87 (3.45%)	3 / 147 (2.04%)	6 / 307 (1.95%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
carcinoma, colon (chemotherapy)			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	1 / 307 (0.33%)
occurrences (all)	0	0	1
Vascular disorders			
shunt insufficiency			
subjects affected / exposed	1 / 87 (1.15%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	1	0	0
peripheral artery disease			
subjects affected / exposed	1 / 87 (1.15%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
Elective surgery			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	2 / 307 (0.65%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
flu like symptoms			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
fever			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			

subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
Intestinal diverticulitis			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	1 / 307 (0.33%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Irregular menstruation			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	1 / 87 (1.15%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	1	0	0
Investigations			
GGT increased			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
worsening existing symptoms (MS, spasm)			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
Tingling (leg, finger)			

subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Gastrointestinal pain			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
Diarrhea			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
Nausea and Vomiting			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Muscle and joint pain			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 87 (0.00%)	3 / 147 (2.04%)	2 / 307 (0.65%)
occurrences (all)	0	3	2
SARS-COV 19 test positive			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
reactivation Herpes (simplex vs. labialis)			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperglycemia			

subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 87 (0.00%)	0 / 147 (0.00%)	0 / 307 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	inflammatory bowel diseases IBD	primary immunodeficiency PID	RHEU
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 93 (4.30%)	1 / 139 (0.72%)	17 / 114 (14.91%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
carcinoma, colon (chemotherapy)			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
shunt insufficiency			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences (all)	0	0	0
peripheral artery disease			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Elective surgery			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	3 / 114 (2.63%)
occurrences (all)	0	0	3
flu like symptoms			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	1 / 114 (0.88%)
occurrences (all)	0	0	2
fever			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	2 / 114 (1.75%)
occurrences (all)	0	0	2
Injection site reaction			

subjects affected / exposed	1 / 93 (1.08%)	0 / 139 (0.00%)	9 / 114 (7.89%)
occurrences (all)	1	0	12
Chills			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	1 / 114 (0.88%)
occurrences (all)	0	0	1
Intestinal diverticulitis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Irregular menstruation			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	2 / 114 (1.75%)
occurrences (all)	0	0	2
Epistaxis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences (all)	0	0	0
Investigations			
GGT increased			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 93 (1.08%)	0 / 139 (0.00%)	2 / 114 (1.75%)
occurrences (all)	1	0	2
Vertigo			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences (all)	0	0	0
worsening existing symptoms (MS, spasm)			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences (all)	0	0	0
Tingling (leg, finger)			

subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Gastrointestinal pain			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences (all)	0	0	0
Diarrhea			
subjects affected / exposed	1 / 93 (1.08%)	0 / 139 (0.00%)	1 / 114 (0.88%)
occurrences (all)	1	0	1
Nausea and Vomiting			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	2 / 114 (1.75%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Muscle and joint pain			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	3 / 114 (2.63%)
occurrences (all)	0	0	3
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 93 (0.00%)	1 / 139 (0.72%)	1 / 114 (0.88%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	1 / 93 (1.08%)	0 / 139 (0.00%)	1 / 114 (0.88%)
occurrences (all)	1	0	1
SARS-COV 19 test positive			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	0 / 114 (0.00%)
occurrences (all)	0	0	0
reactivation Herpes (simplex vs. labialis)			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	2 / 114 (1.75%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Hyperglycemia			

subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	1 / 114 (0.88%)
occurrences (all)	0	0	1
Hypothyroidism			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	1 / 114 (0.88%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 June 2021	new Protocol Version 1.3: - Increase in the number of patients (from 2250 to 2900), - additional samples and investigations in the MS/NMOSD cohort and adding another secondary endpoint for the RAID and the MS/NMOSD cohort (Effects of vaccination on underlying chronic disease measured by disease activity scores) - Performance of SARS-CoV-2 antigen test instead of PCR test possible - Harmonization of the information on the questionnaires - Completion of the responsible laboratories for assessments -Adding an unscheduled visit after any booster vaccination following second vaccination and modification in the schedule of assessments to make it more flexible due to different vaccination schedules -Exceptions in AE- and SAE-reporting
16 August 2021	new Protocol Version 1.4: - Adjustment of the primary endpoint (immunogenicity of COVID-19 vaccination) to make the timing of measurement of it more flexible. It is measured between six and up to max. nine months after primary vaccination. - Correction of the time of Visit 4 (6 months ± 2 weeks instead of 24 ± 2 weeks after first vaccination). - Increase in number of patients in elderly cohort (from 150 to 300, total number of patients from 2900 to 3050) - Adding further secondary endpoints related to unscheduled visit after any booster vaccination. - Accordingly, secondary endpoints were added for the monthly data locks - Adding an optional visit 9 months ± 2 weeks after first vaccination - Secondary endpoints were added accordingly
22 August 2021	new Protocol Version 1.5: -Possibility of including individuals incapable of giving consent in cohort 8 (Elderly). - Correction of the duration of individual study participation (8 months ± 2 weeks instead of 9 months ± 2 weeks
09 December 2021	new Protocol Version 1.6: - Termination of the COVIM-Boost sub-study by 31.12.2021 Due to the dynamic pandemic development and changing COVID-19 vaccination recommendations, adjustments are always necessary, which influence the study implementation. These changes have to be implemented quickly; therefore it was decided to conduct COVIM-Boost as an independent study under the conditions of § 4 para. 7a MedBVSV in the form of an observational study. - Correction of an inclusion criterion related to the adjustment of the primary endpoint (inclusion up to months instead of six months after primary vaccination possible, see Protocol Amendment Version 1.4/16th August 2021) - Removal of the interim analysis 4 months after study, as this was not reasonably possible due to the recruitment status at the time indicated. - It was clarified for the MS/NMOSD cohort in the schedule of assessments when the expanded disability status scale (EDSS) survey is to be conducted. - Correction of the number of aliquots to be sent to the Central Laboratory of the University of Cologne

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported