Clinical trial results:
A Phase II Study to Evaluate Safety and Efficacy to a Third Vaccination in Immunocompromised Patients with Inadequate Humoral Response after Primary mRNA SARS-CoV-2 (Covid-19) Vaccination

Summary

EudraCT number	2021-002693-10
Trial protocol	AT
Global end of trial date	21 February 2022

Results information

Result version number	v1 (current)
This version publication date	17 April 2026
First version publication date	17 April 2026

Trial information

Trial identification

Sponsor protocol code	VAC3_SARS-CoV2_seroconversion_study

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Waehringer Guertel 18-20, Vienna, Austria,
Public contact	Clinical Trials Office , Medical University of Vienna, 0043 14040043010, daniela.sieghart@meduniwien.ac.at
Scientific contact	Clinical Trials Office , Medical University of Vienna, 0043 14040043010, daniela.sieghart@meduniwien.ac.at

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	23 February 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 February 2022
Global end of trial reached?	Yes
Global end of trial date	21 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study aims to investigate A) the humoral and cellular immune responses after a second boost vaccination against SARS-CoV-2 in adult patients treated with immunosuppressive therapy who did not show response to the first two vaccinations with an mRNA vaccine.
To assess the immunogenicity to a third vaccination mRNA-SARS-CoV-2 vaccine (Biontech/Pfizer or Moderna) compared to a vector SARS-CoV-2 (AstraZeneca) vaccination as a second boost in patients with immunosuppressive therapy.
B) To compare the immunogenicity to a third vaccination with a mRNA-SARS-CoV-2 vaccine as a second boost in immunocompromised patients and healthy controls who developed insufficient titres of antibodies (< 1500 U/ml) after the standard vaccination by measuring quantitative antibody levels by spike-protein-based assay. The level of antibody increase will be compared between the two groups.

Protection of trial subjects:

As the intervention was minimal (one time vaccination), no specific measures were performed.

Background therapy:

Patient groups were on their standard immunosuppressive treatment, NSAIDs were allowed wen required.

Evidence for comparator:

Some evidence suggested that a heterologous vaccination strategy might be more efficient in nonimmunocompromised healthy volunteers (Munro et al Lancet 2021, Atmar et al NEJM, 2022), thus warranting a trial in a very difficult to vacciate patient cohort.

Actual start date of recruitment	21 June 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	Austria: 218
Worldwide total number of subjects	218
EEA total number of subjects	218

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)	155
From 65 to 84 years	62
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

For A) The trial started on July 22, 2021, with the inclusion of the first patient. The last patient finalized the 4-week follow-up on October 8, 2021.
For B) The first participant was enrolled on 28 September 2021 and the last completed the 4-week follow-up on 22 December 2021.
For both parts: All recruitment was performed in Vienna, Austria.

Pre-assignment

Screening details:

For A) Adults (age ≥ 18 years) under immunosuppressive treatment without measurable SARS-CoV-2 spike protein-specific antibodies at least 4 weeks after their second COVID-19 vaccination were included.
For B) Adults (age>18 years) with a diagnosis of an IMIDs and HCs, both with anti-RBD antibody levels<1500 BAU after primary vaccination.

Period 1

Period 1 title	Vaccination
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

In this trial, laboratory assessors and patients were blinded to the type of vaccine used. Blinding of vaccines was ensured by the Central Pharmacy of the Vienna General Hospital, where dose aliquots were prearranged in syringes without reference to the vaccine type used.

Arms

Are arms mutually exclusive?	Yes
Arm title	A) mRNA

Arm description:

Vaccination with a third dose of mRNA vaccine without detectable antibodies.

Arm type	Active comparator
Investigational medicinal product name	BNT162b2
Investigational medicinal product code	
Other name	Comirnaty
Pharmaceutical forms	Powder and solvent for suspension for injection in multidose container
Routes of administration	Intramuscular use

Dosage and administration details:

BNT162b2 i.m. once.

Investigational medicinal product name	mRNA-1273
Investigational medicinal product code	
Other name	Elasomeran
Pharmaceutical forms	Powder and solvent for solution for injection in multidose container
Routes of administration	Intramuscular use

Dosage and administration details:

mRNA-1273 containing 100 µg mRNA i.m. once.

Arm title	A) Vector

Arm description:

Vaccination with a third dose of vector vaccine without detectable antibodies.

Arm type	Experimental

Investigational medicinal product name	ChAdOx1 nCoV-19
Investigational medicinal product code	
Other name	AZD1222
Pharmaceutical forms	Solution for injection in multidose container
Routes of administration	Intramuscular use

Dosage and administration details:

I.m. administration with the predefined dose per manfacturer.

Arm title	B) IMID

Arm description:

Immunosuppressed patients with detectable antibodies received a third vaccination with an mRNA vaccine.

Arm type	Active comparator
Investigational medicinal product name	BNT162b2
Investigational medicinal product code	
Other name	Comirnaty
Pharmaceutical forms	Powder and solvent for suspension for injection in multidose container
Routes of administration	Intramuscular use

Dosage and administration details:

BNT162b2 i.m. once.

Investigational medicinal product name	mRNA-1273
Investigational medicinal product code	
Other name	Elasomeran
Pharmaceutical forms	Powder and solvent for solution for injection in multidose container
Routes of administration	Intramuscular use

Dosage and administration details:

mRNA-1273 containing 100 µg mRNA i.m. once.

Arm title	B) HC

Arm description:

Healthy controls with detectable anti-RBD antibodies receiving a third mRNA vaccination

Arm type	Experimental
Investigational medicinal product name	BNT162b2
Investigational medicinal product code	
Other name	Comirnaty
Pharmaceutical forms	Powder and solvent for suspension for injection in multidose container
Routes of administration	Intramuscular use

Dosage and administration details:

BNT162b2 i.m. once.

Investigational medicinal product name	mRNA-1273
Investigational medicinal product code	
Other name	Elasomeran
Pharmaceutical forms	Powder and solvent for solution for injection in multidose container
Routes of administration	Intramuscular use

Dosage and administration details:

mRNA-1273 containing 100 µg mRNA i.m. once.

Number of subjects in period 1[1]	A) mRNA	A) Vector	B) IMID
Started	26	25	60
Completed	24	22	56
Not completed	2	3	4
Consent withdrawn by subject	2	3	-
Development of COVID19	-	-	1
Lost to follow-up	-	-	3

Number of subjects in period 1[1]	B) HC
Started	48
Completed	47
Not completed	1
Consent withdrawn by subject	-
Development of COVID19	1
Lost to follow-up	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The difference is due to a relevant percentage of individuals being screen failures (most likely due to detectable antibodies at screening in part A) and thus no being vaccinated in the trial. These individuals would have skewed baseline characteristics and were thus not included.

Period 2

Period 2 title	B) Follow-up
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	B) HC

Arm description:

Follow-up period including Healthy controls

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	B) IMID Patients

Arm description:

Follow-up of IMID patients

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2[2]	B) HC	B) IMID Patients
Started	47	56
Completed	42	50
Not completed	5	6
Consent withdrawn by subject	-	1
Development of COVID19	2	2
Lost to follow-up	3	3

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Only patients from Part B) were included into the B) Follow-up period.

Baseline characteristics

Reporting groups	
Reporting group title	A) mRNA
Reporting group description:	
Vaccination with a third dose of mRNA vaccine without detectable antibodies.	
Reporting group title	A) Vector
Reporting group description:	
Vaccination with a third dose of vector vaccine without detectable antibodies.	
Reporting group title	B) IMID
Reporting group description:	
Immunosuppressed patients with detectable antibodies received a third vaccination with an mRNA vaccine.	
Reporting group title	B) HC
Reporting group description:	
Healthy controls with detectable anti-RBD antibodies receiving a third mRNA vaccination	

Reporting group values	A) mRNA	A) Vector	B) IMID
Number of subjects	26	25	60
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	63.4	61.2	57.6
standard deviation	± 11.4	± 14.9	± 16.2
Gender categorical Units: Subjects			
Female	11	8	45
Male	15	17	15

Reporting group values	B) HC	Total	
Number of subjects	48	159	
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	48.1		
standard deviation	± 14.3	-	
Gender categorical			
Units: Subjects			
Female	26	90	
Male	22	69	

End points

End points reporting groups

Reporting group title	A) mRNA
Reporting group description:	
Vaccination with a third dose of mRNA vaccine without detectable antibodies.	
Reporting group title	A) Vector
Reporting group description:	
Vaccination with a third dose of vector vaccine without detectable antibodies.	
Reporting group title	B) IMID
Reporting group description:	
Immunosuppressed patients with detectable antibodies received a third vaccination with an mRNA vaccine.	
Reporting group title	B) HC
Reporting group description:	
Healthy controls with detectable anti-RBD antibodies receiving a third mRNA vaccination	
Reporting group title	B) HC
Reporting group description:	
Follow-up period including Healthy controls	
Reporting group title	B) IMID Patients
Reporting group description:	
Follow-up of IMID patients	

Primary: Seroconversion

End point title	Seroconversion[1]
End point description:	
Rate of seroconversion after a third dose.	
End point type	Primary
End point timeframe:	
After 4 weeks.	

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: The study consists of two different arms representing different populations, with a different statistical primary outcome.

End point values	A) mRNA	A) Vector		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	22		
Units: Rate of Seroconverion				
Seroconversion	15	4		
No seroconversion	9	18		

Statistical analyses

Statistical analysis title	Rate of seroconversion
Comparison groups	A) mRNA v A) Vector
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.006
Method	Chi-squared

Primary: Anti-RBD antibody levels >1500 BAU/mL

End point title	Anti-RBD antibody levels >1500 BAU/mL[2]

End point description:

he primary endpoint was defined as the presence of antibody levels against the receptor-binding domain (RBD)>1500 BAU/mL in patients with IMIDs versus HCs.

End point type	Primary

End point timeframe:

4 weeks

Notes:

[2] - 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: The study consists of two different arms representing different populations, with a different statistical primary outcome.

End point values	B) IMID	B) HC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	47		
Units: AB level over threshold				
AB < 1500 BAU/ml	5	0		
AB > 1500 BAU/ml	51	47		

Statistical analyses

Statistical analysis title	Rate of individuals with anti-RBD antibodies>1500
Comparison groups	B) IMID v B) HC
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.101
Method	Chi-squared

Post-hoc: Relative antibody reduction

End point title	Relative antibody reduction

End point description:

End point type	Post-hoc

End point timeframe:

After 12 weeks of vaccination.

End point values	B) HC	B) IMID Patients		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	50		
Units: Relative reduction				
number (confidence interval 95%)	42 (33 to 52)	59 (43 to 69)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 12 week in Group B, up to 4 weeks in group A.

Adverse event reporting additional description:

Paper based diary for vaccine related AEs.

Assessment type	Systematic

Dictionary used

Dictionary name	ICD
Dictionary version	10

Reporting groups

Reporting group title	A) mRNA

Reporting group description:

Vaccination with a third dose of mRNA vaccine without detectable antibodies.

Reporting group title	A) Vector

Reporting group description:

Vaccination with a third dose of vector vaccine without detectable antibodies.

Reporting group title	B) IMID

Reporting group description:

Immunosuppressed patients with detectable antibodies received a third vaccination with an mRNA vaccine.

Reporting group title	B) HC

Reporting group description:

Healthy controls with detectable anti-RBD antibodies receiving a third mRNA vaccination

Serious adverse events	A) mRNA	A) Vector	B) IMID
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 26 (7.69%)	1 / 25 (4.00%)	1 / 60 (1.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Diarrhoea	Additional description: Patients hospitalized because of diarrhea after the inital 4 weeks observational period.		
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 26 (7.69%)	0 / 25 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary tract infection			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia	Additional description: Hospitalization after ERCP due to elevated serum Potassium after the inital 4 weeks observational period.		
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	B) HC		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 48 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Diarrhoea	Additional description: Patients hospitalized because of diarrhea after the inital 4 weeks observational period.		
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 48 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 48 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia	Additional description: Hospitalization after ERCP due to elevated serum Potassium after the inital 4 weeks observational period.		
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 48 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	A) mRNA	A) Vector	B) IMID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 26 (88.46%)	17 / 25 (68.00%)	51 / 60 (85.00%)
Nervous system disorders			
Fatigue			
subjects affected / exposed	10 / 26 (38.46%)	11 / 25 (44.00%)	33 / 60 (55.00%)
occurrences (all)	10	11	33
Headache			
subjects affected / exposed	8 / 26 (30.77%)	9 / 25 (36.00%)	20 / 60 (33.33%)
occurrences (all)	8	9	20
General disorders and administration site conditions			
Pain at injection site			
subjects affected / exposed	9 / 26 (34.62%)	5 / 25 (20.00%)	43 / 60 (71.67%)
occurrences (all)	9	5	43
Redness at vaccination site			
subjects affected / exposed	9 / 26 (34.62%)	5 / 25 (20.00%)	11 / 60 (18.33%)
occurrences (all)	9	5	11
Swelling at vaccination site			
subjects affected / exposed	9 / 26 (34.62%)	5 / 25 (20.00%)	8 / 60 (13.33%)
occurrences (all)	9	5	8
Itching at vaccination site			
subjects affected / exposed	4 / 26 (15.38%)	3 / 25 (12.00%)	6 / 60 (10.00%)
occurrences (all)	4	3	6
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 26 (11.54%)	2 / 25 (8.00%)	5 / 60 (8.33%)
occurrences (all)	3	2	5
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	9 / 26 (34.62%)	7 / 25 (28.00%)	19 / 60 (31.67%)
occurrences (all)	9	7	19
Arthralgia			
subjects affected / exposed	4 / 26 (15.38%)	7 / 25 (28.00%)	12 / 60 (20.00%)
occurrences (all)	4	7	12

Non-serious adverse events	B) HC		
Total subjects affected by non-serious			

adverse events subjects affected / exposed	42 / 48 (87.50%)		
Nervous system disorders Fatigue subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	 24 / 48 (50.00%) 24 16 / 48 (33.33%) 16		
General disorders and administration site conditions Pain at injection site subjects affected / exposed occurrences (all) Redness at vaccination site subjects affected / exposed occurrences (all) Swelling at vaccination site subjects affected / exposed occurrences (all) Itching at vaccination site subjects affected / exposed occurrences (all)	 36 / 48 (75.00%) 36 3 / 48 (6.25%) 3 2 / 48 (4.17%) 2 4 / 48 (8.33%) 4		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	 5 / 48 (10.42%) 5		
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all)	 19 / 48 (39.58%) 19 7 / 48 (14.58%) 7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/36097029

http://www.ncbi.nlm.nih.gov/pubmed/36109141

http://www.ncbi.nlm.nih.gov/pubmed/36706534