Clinical trial results:
Population-based prospective, clinical study on efficacy and safety of a booster COVID-19 vaccination

Summary

EudraCT number	2021-005094-28
Trial protocol	AT
Global end of trial date	11 July 2022

Results information

Result version number	v1 (current)
This version publication date	06 April 2023
First version publication date	06 April 2023

Trial information

Trial identification

Sponsor protocol code	VAC3_COVID-19_antibody_study_V1

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	Spitalgasse 23, Vienna, Austria, 1090
Public contact	Clinical Trials Office, Medical University of Vienna, 0043 014040067300, daniela.sieghart@meduniwien.ac.at
Scientific contact	Clinical Trials Office, Medical University of Vienna, 0043 014040043010, 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	Interim
Date of interim/final analysis	01 December 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 July 2022
Global end of trial reached?	Yes
Global end of trial date	11 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evidence of efficacy and safety of a third vaccination in real-live setting is still missing. The aim of this study is to provide scientific support to the vaccination campaign of the City of Vienna by performing a population-based study to generate evidence on efficacy and safety of a third vaccination against SARS-CoV-2 in a real world setting. The expected magnitude and broad range of this epidemiological study would enable us to take into account various factors associated with immune response as well as safety.

Protection of trial subjects:

Healthy participants were recruited after receiving the Covid-19 booster vaccination. The study was limited to questionaires and blood draws (3 times) at different time points. Blood draw was reduced to the minimal amount needed for analysis (max. 8ml) per visit. Blood was drawn by qualified nurses and doctors in a comfortable environment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 October 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 4955
Worldwide total number of subjects	4955
EEA total number of subjects	4955

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)	4507
From 65 to 84 years	443

85 years and over	5

Subject disposition

Recruitment

Recruitment details:

Recruitment start was on the 28th of October 2021 and recruitment end was on the 21st of January 2022.
4954 peolpe were recruited for trial participation at Austria's largest vaccination site, the Austria Center Vienna (n=4117) and at the AKH Vienna/the Medical University of Vienna (n=837).

Pre-assignment

Screening details:

In total, 4997 people were screened for potential participation in the clincial trial. The most frequent cause for screening failure was the violoation of protocol regarding standard vaccination (vaccines used, time between vaccinations, ...).

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

no blinding

Arms

Are arms mutually exclusive?	Yes
Arm title	BioNTech/Pfizer BI

Arm description:

Participants received BioNTech/Pfizer as their basic immunisation.

Arm type	Experimental
Investigational medicinal product name	Comirnaty consentrate for dispersion for injection
Investigational medicinal product code	BNT162B2
Other name	
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

30 µg dispersion for intramuscular use

Arm title	Moderna BI

Arm description:

Participants received Moderna as their basic immunisation

Arm type	Experimental
Investigational medicinal product name	Covid-19 vaccine Moderna dispersion for injection
Investigational medicinal product code	CX-024414
Other name	mRNA-1273
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

50 µg (half dose) for booster vaccination; intramuscular use

Arm title	Influenza combined

Arm description:

247 participants were vaccinated with influenza and SARS-CoV-2 in combination.

Arm type	Experimental

Investigational medicinal product name	Comirnaty concentrate for dispersion for injection
Investigational medicinal product code	BNT162B2
Other name	
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

30 µg, intramuscular use

Investigational medicinal product name	Influvac Tetra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

60 µg in total (15 µg each strain) for intramuscular use

Arm title	Influenza only

Arm description:

Participants received only an Influenza vaccination.

Arm type	Experimental
Investigational medicinal product name	Influvac Tetra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

60 µg in total (15 µg each strain) for intramuscular use

Arm title	AstraZeneca and mRNA BI

Arm description:

Subjects who received AstraZeneca Vaxzevria as their first vaccine, but mRNA (Moderna or BioNTech/Pfizer) as their second vaccine.

Arm type	Experimental
Investigational medicinal product name	Vaxzevria
Investigational medicinal product code	ChAdOx1-S
Other name	Covid-19 Vaccine AstraZeneca
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

0,5 mL dispersion for intramuscular use.

Investigational medicinal product name	Comirnaty consentrate for dispersion for injection
Investigational medicinal product code	BNT162B2
Other name	
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

30 µg dispersion for intramuscular use

Investigational medicinal product name	Covid-19 vaccine Moderna dispersion for injection
Investigational medicinal product code	CX-024414
Other name	mRNA-1273
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

50 µg (half dose) for booster vaccination; intramuscular use

Arm title	AstraZeneca Vaxzevria BI

Arm description:

Subjects received two doses of Vaxzevria as their basic immunisation.

Arm type	Experimental
Investigational medicinal product name	Vaxzevria
Investigational medicinal product code	ChAdOx1-S
Other name	Covid-19 Vaccine AstraZeneca
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

0,5 mL dispersion for intramuscular use.

Arm title	COVID-19 Vaccine Janssen BI

Arm description:

Subjects received COVID-19 Vaccine Janssen for their basic immunisation

Arm type	Experimental
Investigational medicinal product name	COVID-19 Vaccine Janssen suspension for injection
Investigational medicinal product code	Ad26.COV2-S.02
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

0,5 mL dispersion for intramuscular use.

Arm title	other

Arm description:

Subjects who received only one vaccine as their base immunization but were infected befor were also included in this study. Also some subjects received BioNTech and Moderna as their base immunization. On some subject data concerning the first two vaccination is missing.

Arm type	Experimental
Investigational medicinal product name	Comirnaty consentrate for dispersion for injection
Investigational medicinal product code	BNT162B2
Other name	
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

30 µg dispersion for intramuscular use

Investigational medicinal product name	Covid-19 vaccine Moderna dispersion for injection
Investigational medicinal product code	CX-024414
Other name	mRNA-1273
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

50 µg (half dose) for booster vaccination; intramuscular use

Investigational medicinal product name	Vaxzevria
Investigational medicinal product code	ChAdOx1-S
Other name	Covid-19 Vaccine AstraZeneca
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

0,5 mL dispersion for intramuscular use.

Number of subjects in period 1	BioNTech/Pfizer BI	Moderna BI	Influenza combined
Started	2779	385	247
Completed	2779	385	247

Number of subjects in period 1	Influenza only	AstraZeneca and mRNA BI	AstraZeneca Vaxzevria BI
Started	33	85	1246
Completed	33	85	1246

Number of subjects in period 1	COVID-19 Vaccine Janssen BI	other
Started	94	86
Completed	94	86

Period 2	
Period 2 title	4 weeks
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	BioNTech/Pfizer Booster
Arm description:	
Participants received a booster vaccination with BioNTech/Pfizer	
Arm type	Experimental
Investigational medicinal product name	Comirnaty consentrate for dispersion for injection
Investigational medicinal product code	BNT162B2
Other name	
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
30 µg dispersion for intramuscular use	
Arm title	Moderna Booster
Arm description:	
Participants received a booster vaccination with Moderna	
Arm type	Active comparator

Investigational medicinal product name	Covid-19 vaccine Moderna dispersion for injection
Investigational medicinal product code	CX-024414
Other name	mRNA-1273
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

50 µg (half dose) for booster vaccination; intramuscular use

Arm title	Influenza combined

Arm description:

247 participants were vaccinated with influenza and SARS-CoV-2 in combination.

Arm type	Experimental
Investigational medicinal product name	Comirnaty concentrate for dispersion for injection
Investigational medicinal product code	BNT162B2
Other name	
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

30 µg, intramuscular use

Investigational medicinal product name	Influvac Tetra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

60 µg in total (15 µg each strain) for intramuscular use

Arm title	Influenza only

Arm description:

Participants received only an Influenza vaccination.

Arm type	Experimental
Investigational medicinal product name	Influvac Tetra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

60 µg in total (15 µg each strain) for intramuscular use

Arm title	other Booster

Arm description:

Subjects boosted with other vaccine e. g. Astra Zeneca or Johnson&Johnson

Arm type	Experimental
Investigational medicinal product name	Vaxzevria
Investigational medicinal product code	ChAdOx1-S
Other name	Covid-19 Vaccine AstraZeneca
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

0,5 mL dispersion for intramuscular use.

Investigational medicinal product name	COVID-19 Vaccine Janssen suspension for injection
Investigational medicinal product code	Ad26.COV2-S.02
Other name	
Pharmaceutical forms	Injection

Routes of administration	Intramuscular use

Dosage and administration details:

0,5 mL dispersion for intramuscular use.

Number of subjects in period 2[1]	BioNTech/Pfizer Booster	Moderna Booster	Influenza combined
Started	3940	598	229
Completed	3940	598	229

Number of subjects in period 2[1]	Influenza only	other Booster
Started	31	10
Completed	31	10

Notes:

[1] - 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: Probands were lost to follow up in between Periods.

Period 3

Period 3 title	month 6
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	BioNTech/Pfizer Booster

Arm description:

Participants received a booster vaccination with BioNTech/Pfizer

Arm type	Experimental
Investigational medicinal product name	Comirnaty consentrate for dispersion for injection
Investigational medicinal product code	BNT162B2
Other name	
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

30 µg dispersion for intramuscular use

Arm title	Moderna Booster

Arm description:

Participants received a booster vaccination with Moderna

Arm type	Active comparator

Investigational medicinal product name	Covid-19 vaccine Moderna dispersion for injection
Investigational medicinal product code	CX-024414
Other name	mRNA-1273
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

50 µg (half dose) for booster vaccination; intramuscular use

Arm title	other Booster

Arm description:

Subjects boosted with other vaccine e. g. Astra Zeneca or Johnson&Johnson

Arm type	Experimental
Investigational medicinal product name	COVID-19 Vaccine Janssen suspension for injection
Investigational medicinal product code	Ad26.COV2-S.02
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

0,5 mL dispersion for intramuscular use.

Investigational medicinal product name	Vaxzevria
Investigational medicinal product code	ChAdOx1-S
Other name	Covid-19 Vaccine AstraZeneca
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

0,5 mL dispersion for intramuscular use.

Number of subjects in period 3[2][3]	BioNTech/Pfizer Booster	Moderna Booster	other Booster
Started	3155	525	10
Completed	3348	525	10

Joined	193	0	0
Transferred in from other group/arm	193	-	-

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: Probands were lost to follow up in between Periods.

[3] - The number of subjects transferring in and out of the arms in the period are not the same. It is expected the net number of transfers in and out of the arms in a period, will be zero.
Justification: Probands from the influenza combined arm (which ended in period 2) were transferred to the BnT arm for further analysis.

Baseline characteristics

Reporting groups	
Reporting group title	BioNTech/Pfizer BI
Reporting group description:	
Participants received BioNTech/Pfizer as their basic immunisation.	
Reporting group title	Moderna BI
Reporting group description:	
Participants received Moderna as their basic immunisation	
Reporting group title	Influenza combined
Reporting group description:	
247 participants were vaccinated with influenza and SARS-CoV-2 in combination.	
Reporting group title	Influenza only
Reporting group description:	
Participants received only an Influenza vaccination.	
Reporting group title	AstraZeneca and mRNA BI
Reporting group description:	
Subjects who received AstraZeneca Vaxzevria as their first vaccine, but mRNA (Moderna or BioNTech/Pfizer) as their second vaccine.	
Reporting group title	AstraZeneca Vaxzevria BI
Reporting group description:	
Subjects received two doses of Vaxzevria as their basic immunisation.	
Reporting group title	COVID-19 Vaccine Janssen BI
Reporting group description:	
Subjects received COVID-19 Vaccine Janssen for their basic immunisation	
Reporting group title	other
Reporting group description:	
Subjects who received only one vaccine as their base immunization but were infected befor were also included in this study. Also some subjects received BioNTech and Moderna as their base immunization. On some subject data concerning the first two vaccination is missing.	

Reporting group values	BioNTech/Pfizer BI	Moderna BI	Influenza combined
Number of subjects	2779	385	247
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2521	332	246
From 65-84 years	255	52	1
85 years and over	3	1	0
Gender categorical Units: Subjects			
Female	1605	228	141
Male	1174	156	106

unknown	0	1	0

Reporting group values	Influenza only	AstraZeneca and mRNA BI	AstraZeneca Vaxzevria BI
Number of subjects	33	85	1246
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	32	81	1126
From 65-84 years	1	4	120
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	19	31	737
Male	14	54	509
unknown	0	0	0

Reporting group values	COVID-19 Vaccine Janssen BI	other	Total
Number of subjects	94	86	4955
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	93	76	4507
From 65-84 years	1	9	443
85 years and over	0	1	5
Gender categorical Units: Subjects			
Female	44	53	2858
Male	50	33	2096
unknown	0	0	1

Subject analysis sets

Subject analysis set title	Infected
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with recorded Covid-19 breakthrough infection between week 4 and month 6.

Subject analysis set title	Non-infected
Subject analysis set type	Full analysis

Subject analysis set description:

Control group; participants without a recorded breakthrough infection between week 4 and month 6 (and negative for nucleocapsid antibodies; markers for infection).

Subject analysis set title	Homologous vaccination
Subject analysis set type	Per protocol

Subject analysis set description:

Patients who received a homologous vaccination schema (3x BNT162B2 or 3x mRNA-1273)

Subject analysis set title	Heterologous
Subject analysis set type	Full analysis

Subject analysis set description:

Participants receiving a heterologous vaccination schema (2x vector vaccination and 1x mRNA).

Subject analysis set title	Influenza only
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received only Influenza vaccine. Screening took place at baseline and week 4.

Subject analysis set title	Influenza combined
Subject analysis set type	Full analysis

Subject analysis set description:

Probands receiving Covid 19 booster at the same time as the influenza vaccine.

Reporting group values	Infected	Non-infected	Homologous vaccination
Number of subjects	1372	2386	2437
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1270	2102	2171
From 65-84 years	102	280	263
85 years and over	0	4	3
Gender categorical Units: Subjects			
Female	805	1445	1463
Male	567	941	974
unknown	0	0	0

Reporting group values	Heterologous	Influenza only	Influenza combined
Number of subjects	1213	33	247
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0

Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1101	32	246
From 65-84 years	112	1	1
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	727	19	141
Male	486	14	106
unknown	0	0	0

End points

End points reporting groups

Reporting group title	BioNTech/Pfizer BI
Reporting group description:	
Participants received BioNTech/Pfizer as their basic immunisation.	
Reporting group title	Moderna BI
Reporting group description:	
Participants received Moderna as their basic immunisation	
Reporting group title	Influenza combined
Reporting group description:	
247 participants were vaccinated with influenza and SARS-CoV-2 in combination.	
Reporting group title	Influenza only
Reporting group description:	
Participants received only an Influenza vaccination.	
Reporting group title	AstraZeneca and mRNA BI
Reporting group description:	
Subjects who received AstraZeneca Vaxzevria as their first vaccine, but mRNA (Moderna or BioNTech/Pfizer) as their second vaccine.	
Reporting group title	AstraZeneca Vaxzevria BI
Reporting group description:	
Subjects received two doses of Vaxzevria as their basic immunisation.	
Reporting group title	COVID-19 Vaccine Janssen BI
Reporting group description:	
Subjects received COVID-19 Vaccine Janssen for their basic immunisation	
Reporting group title	other
Reporting group description:	
Subjects who received only one vaccine as their base immunization but were infected befor were also included in this study. Also some subjects received BioNTech and Moderna as their base immunization. On some subject data concerning the first two vaccination is missing.	
Reporting group title	BioNTech/Pfizer Booster
Reporting group description:	
Participants received a booster vaccination with BioNTech/Pfizer	
Reporting group title	Moderna Booster
Reporting group description:	
Participants received a booster vaccination with Moderna	
Reporting group title	Influenza combined
Reporting group description:	
247 participants were vaccinated with influenza and SARS-CoV-2 in combination.	
Reporting group title	Influenza only
Reporting group description:	
Participants received only an Influenza vaccination.	
Reporting group title	other Booster
Reporting group description:	
Subjects boosted with other vaccine e. g. Astra Zeneca or Johnson&Johnson	
Reporting group title	BioNTech/Pfizer Booster
Reporting group description:	
Participants received a booster vaccination with BioNTech/Pfizer	
Reporting group title	Moderna Booster
Reporting group description:	
Participants received a booster vaccination with Moderna	

Reporting group title	other Booster
Reporting group description:	
Subjects boosted with other vaccine e. g. Astra Zeneca or Johnson&Johnson	
Subject analysis set title	Infected
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with recorded Covid-19 breakthrough infection between week 4 and month 6.	
Subject analysis set title	Non-infected
Subject analysis set type	Full analysis
Subject analysis set description:	
Control group; participants without a recorded breakthrough infection between week 4 and month 6 (and negative for nucleocapsid antibodies; markers for infection).	
Subject analysis set title	Homologous vaccination
Subject analysis set type	Per protocol
Subject analysis set description:	
Patients who received a homologous vaccination schema (3x BNT162B2 or 3x mRNA-1273)	
Subject analysis set title	Heterologous
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants receiving a heterologous vaccination schema (2x vector vaccination and 1x mRNA).	
Subject analysis set title	Influenza only
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received only Influenza vaccine. Screening took place at baseline and week 4.	
Subject analysis set title	Influenza combined
Subject analysis set type	Full analysis
Subject analysis set description:	
Probands receiving Covid 19 booster at the same time as the influenza vaccine.	

Primary: 6 months post booster vaccine

End point title	6 months post booster vaccine
End point description:	
End point type	Primary
End point timeframe:	
Due to feasibilty the final visits were scheduled in a time range of 6 months (± 25 days) after receiving the booster vaccine.	

End point values	Infected	Non-infected	Homologous vaccination	Heterologous
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1362	2276	1075	2267
Units: Weeks	1362	2276	1075	2267

Statistical analyses

Statistical analysis title	Association antibodies and break through infection

Statistical analysis description:

The association of anti-RBD-antibodies with incident break-through infections was modelled with Cox proportional hazards regression. Due to missing data, not all subject were included into the statistical analysis.

Comparison groups	Non-infected v Infected
Number of subjects included in analysis	3638
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	Regression, Cox
Parameter estimate	Cox proportional hazard

Statistical analysis title	Infection after hetero-/homologous immunisation

Statistical analysis description:

Infections in subjects with heterologous and homologous immunisation strategies were compared to each other. Due to missing data, not all subject were included into the statistical analysis.

Comparison groups	Homologous vaccination v Heterologous
Number of subjects included in analysis	3342
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	Regression, Cox
Parameter estimate	Cox proportional hazard

Primary: 4 weeks post influenza vaccine

End point title	4 weeks post influenza vaccine[1]

End point description:

End point type	Primary

End point timeframe:

For Influenza only arm 2 visits took place. Due to feasibility visits were scheduled within 28 ± 7 days.

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: This endpoint only applies to two of the arms.

End point values	Influenza combined	Influenza only	Influenza only	Influenza combined
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	229	32	32	229
Units: Weeks	229	32	32	229

Statistical analyses

Statistical analysis title	Influenza only vs. Influenza Covid combined

Statistical analysis description:

This analysis compared the effectiveness of different vaccination strategies. Subjects from the influenza only and influenza combined arms as well as 558 matched subjects from the boosster arm were included. The number of antibodies produced and adverse events were assessed.

Comparison groups	Influenza combined v Influenza only
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	Wilcoxon (Mann-Whitney)

Primary: Baseline

End point title	Baseline[2]

End point description:

At the baseline visit blood samples were drawn and antibody titers were measured. Antibodylevels were correlated with the vaccination strategy to find differences between those strategies.

End point type	Primary

End point timeframe:

Baseline visits took place from October 28th to January 21st.

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: Due to small sample sizes, not all arms were included in the statistic analysis.

End point values	BioNTech/Pfizer BI	Moderna BI	AstraZeneca Vaxzevria BI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2271	251	1246	
Units: visits	2271	251	1246	

Statistical analyses

Statistical analysis title	Antibody level comparison vector vs. mRNA

Statistical analysis description:

Due to small sample sizes of Janssen and AstraZeneca+mRNA, no analysis of these groups were conducted. Due to missing data, not all subjects were analysed.

Comparison groups	BioNTech/Pfizer BI v Moderna BI v AstraZeneca Vaxzevria BI
Number of subjects included in analysis	3768
Analysis specification	Pre-specified
Analysis type	equivalence[3]
P-value	≤ 0.001
Method	Regression, Linear

Notes:

[3] - Antibody levels from subjects vaccinated with vector vaccine (Vaxzevria) were compared to subjects who received mRNA vaccines (Moderna or BioNTech/Pfizer)

Primary: 4 weeks post booster vaccine

End point title	4 weeks post booster vaccine

End point description:

End point type	Primary

End point timeframe:

Due to feasibility visits were scheduled within 28 ± 7 days.

End point values	BioNTech/Pfizer Booster	Moderna Booster	Homologous vaccination	Heterologous
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	3288	550	2924	1171
Units: Weeks	3288	550	2924	1171

Statistical analyses

Statistical analysis title	homologous vs. heterologous vaccination

Statistical analysis description:

Due to missing data, not all subject were included into the statistical analysis.

Comparison groups	Homologous vaccination v Heterologous
Number of subjects included in analysis	4095
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.001
Method	Regression, Linear

Statistical analysis title	Moderna vs. BioNTech

Statistical analysis description:

Due to missing data, not all subject were included into the statistical analysis.

Comparison groups	Moderna Booster v BioNTech/Pfizer Booster
Number of subjects included in analysis	3838
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.001
Method	Regression, Linear

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected during the baseline visit until first follow-up visit 4 weeks after the booster vaccintion by questionnaire and interview. Severe adverse events (SAEs) were reported during the complete study period of 6 months.

Assessment type	Systematic

Dictionary used

Dictionary name	ICH E2A
Dictionary version	1

Reporting groups

Reporting group title	BioNTech Pfizer
Reporting group description: -	
Reporting group title	Moderna
Reporting group description: -	
Reporting group title	Influenza combined
Reporting group description: -	
Reporting group title	Influenza only
Reporting group description: -	
Reporting group title	other
Reporting group description: -	

Serious adverse events	BioNTech Pfizer	Moderna	Influenza combined
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 3996 (0.18%)	2 / 653 (0.31%)	0 / 247 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Intracranial haematoma	Additional description: intracranial bleeding and subarachnoidal bleeding		
subjects affected / exposed	1 / 3996 (0.03%)	0 / 653 (0.00%)	0 / 247 (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
Cardiac disorders			
Myocarditis	Additional description: Shortness of breath and heart burn three weeks after immunization. Diganosis: Myocarditis/Takotsubo Additional dysesthesia of left body - might be related to cardiac event.		
subjects affected / exposed	1 / 3996 (0.03%)	0 / 653 (0.00%)	0 / 247 (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
General disorders and administration site conditions			
Anaphylactic reaction	Additional description: Symptoms: hypertension, headache, nausea, chills, perioral numbness		

subjects affected / exposed	1 / 3996 (0.03%)	0 / 653 (0.00%)	0 / 247 (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
Ear and labyrinth disorders			
Vertigo	Additional description: Acute onset of vertigo and emesis, diagnosed with vertigo due to vestibular paroxysmia.		
subjects affected / exposed	1 / 3996 (0.03%)	0 / 653 (0.00%)	0 / 247 (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
Eye disorders			
Visual impairment	Additional description: Acute loss of vision in right eye, intermittend supraventricular Tachycarida and atherosclerosis diagnosed. Visual impairment due to macular disorder, surgery was performed.		
subjects affected / exposed	1 / 3996 (0.03%)	1 / 653 (0.15%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diverticulitis intestinal perforated	Additional description: Diverticulitis with acute perforation of the colon and putride peritonitis - immediate Sigmaresection was performed. Loss of blood - another acute surgery - no bleeding site found. Pain and neurological symptoms - guillian barre syndrome suspected.		
subjects affected / exposed	0 / 3996 (0.00%)	1 / 653 (0.15%)	0 / 247 (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
Diverticular bleeding	Additional description: Intestinal diverticular bleeding and haemorrhagic anaemia, sigmaresection performed.		
subjects affected / exposed	1 / 3996 (0.03%)	0 / 653 (0.00%)	0 / 247 (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
Psychiatric disorders			
Depression	Additional description: Patient with known depression had to be admitted to hospital to treat flair of disease; according to treating psychiatrist the event is not suspected to be related to vaccination.		
subjects affected / exposed	1 / 3996 (0.03%)	0 / 653 (0.00%)	0 / 247 (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

Serious adverse events	Influenza only	other	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)	0 / 13 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Vascular disorders			
Intracranial haematoma	Additional description: intracranial bleeding and subarachnoidal bleeding		
subjects affected / exposed	0 / 40 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocarditis	Additional description: Shortness of breath and heart burn three weeks after immunization. Diganosis: Myocarditis/Takotsubo Additional dysesthesia of left body - might be related to cardiac event.		
subjects affected / exposed	0 / 40 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Anaphylactic reaction	Additional description: Symptoms: hypertension, headache, nausea, chills, perioral numbness		
subjects affected / exposed	0 / 40 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo	Additional description: Acute onset of vertigo and emesis, diagnosed with vertigo due to vestibular paroxysmia.		
subjects affected / exposed	0 / 40 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Visual impairment	Additional description: Acute loss of vision in right eye, intermittend supraventricular Tachycarida and atherosclerosis diagnosed. Visual impairment due to macular disorder, surgery was performed.		
subjects affected / exposed	0 / 40 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diverticulitis intestinal perforated	Additional description: Diverticulitis with acute perforation of the colon and putride peritonitis - immediate Sigmaresection was performed. Loss of blood - another acute surgery - no bleeding site found. Pain and neurological symptoms - guillian barre syndrome suspected.		
subjects affected / exposed	0 / 40 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular bleeding	Additional description: Intestinal diverticular bleeding and haemorrhagic anaemia, sigmaresection performed.		

subjects affected / exposed	0 / 40 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression	Additional description: Patient with known depression had to be admitted to hospital to treat flair of disease; according to treating psychiatrist the event is not suspected to be related to vaccination.		
subjects affected / exposed	0 / 40 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	BioNTech Pfizer	Moderna	Influenza combined
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2946 / 3996 (73.72%)	523 / 653 (80.09%)	196 / 247 (79.35%)
General disorders and administration site conditions			
Body temperature increased	Additional description: Fever		
subjects affected / exposed	452 / 3996 (11.31%)	145 / 653 (22.21%)	39 / 247 (15.79%)
occurrences (all)	638	638	638
Fatigue			
subjects affected / exposed	1770 / 3996 (44.29%)	310 / 653 (47.47%)	120 / 247 (48.58%)
occurrences (all)	2208	2208	2208
Headache			
subjects affected / exposed	1164 / 3996 (29.13%)	222 / 653 (34.00%)	77 / 247 (31.17%)
occurrences (all)	1477	1477	1477
Chills			
subjects affected / exposed	375 / 3996 (9.38%)	113 / 653 (17.30%)	26 / 247 (10.53%)
occurrences (all)	488	488	488
Swelling	Additional description: Swelling around injection site		
subjects affected / exposed	716 / 3996 (17.92%)	165 / 653 (25.27%)	57 / 247 (23.08%)
occurrences (all)	944	944	944
Redness	Additional description: Redness around injection site		
subjects affected / exposed	558 / 3996 (13.96%)	141 / 653 (21.59%)	38 / 247 (15.38%)
occurrences (all)	742	742	742

Pain	Additional description: Pain around injection site		
subjects affected / exposed	2058 / 3996 (51.50%)	373 / 653 (57.12%)	152 / 247 (61.54%)
occurrences (all)	2596	2596	2596
Muscle Pain			
subjects affected / exposed	1023 / 3996 (25.60%)	200 / 653 (30.63%)	61 / 247 (24.70%)
occurrences (all)	1287	1287	1287
Joint pain			
subjects affected / exposed	626 / 3996 (15.67%)	127 / 653 (19.45%)	40 / 247 (16.19%)
occurrences (all)	794	794	794
Blood and lymphatic system disorders			
Lymph node swelling			
subjects affected / exposed	141 / 3996 (3.53%)	13 / 653 (1.99%)	5 / 247 (2.02%)
occurrences (all)	161	161	161
Ear and labyrinth disorders			
Acute hearing loss			
subjects affected / exposed	0 / 3996 (0.00%)	0 / 653 (0.00%)	0 / 247 (0.00%)
occurrences (all)	1	1	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	172 / 3996 (4.30%)	35 / 653 (5.36%)	10 / 247 (4.05%)
occurrences (all)	217	217	217

Non-serious adverse events	Influenza only	other	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 40 (37.50%)	8 / 13 (61.54%)	
General disorders and administration site conditions			
Body temperature increased	Additional description: Fever		
subjects affected / exposed	1 / 40 (2.50%)	1 / 13 (7.69%)	
occurrences (all)	638	638	
Fatigue			
subjects affected / exposed	6 / 40 (15.00%)	2 / 13 (15.38%)	
occurrences (all)	2208	2208	
Headache			
subjects affected / exposed	6 / 40 (15.00%)	4 / 13 (30.77%)	
occurrences (all)	1477	1477	
Chills			

subjects affected / exposed	0 / 40 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	488	488	
Swelling	Additional description: Swelling around injection site		
subjects affected / exposed	5 / 40 (12.50%)	1 / 13 (7.69%)	
occurrences (all)	944	944	
Redness	Additional description: Redness around injection site		
subjects affected / exposed	2 / 40 (5.00%)	3 / 13 (23.08%)	
occurrences (all)	742	742	
Pain	Additional description: Pain around injection site		
subjects affected / exposed	10 / 40 (25.00%)	3 / 13 (23.08%)	
occurrences (all)	2596	2596	
Muscle Pain			
subjects affected / exposed	1 / 40 (2.50%)	2 / 13 (15.38%)	
occurrences (all)	1287	1287	
Joint pain			
subjects affected / exposed	1 / 40 (2.50%)	0 / 13 (0.00%)	
occurrences (all)	794	794	
Blood and lymphatic system disorders			
Lymph node swelling			
subjects affected / exposed	0 / 40 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	161	161	
Ear and labyrinth disorders			
Acute hearing loss			
subjects affected / exposed	0 / 40 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 40 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	217	217	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 November 2021	We adapted the inclusion criteria according to the recommendation of the Austrian vaccination committee The wording of ICFs was adapted according to the recommendation of the data security manager and the legal office of the Medical University of Vienna. The submission of study results to the participants was describedin more detail.
31 March 2022	The numbers of trial subjects recruited at each site was adjusted. Information on blood group and sleeping quality/circadian rhythm will be collected during 3rd visit. We further specified the timing of study visits. Trial data will be merged with an Austrian epidemiologic database to verify information on Covid-19 infection and vaccination.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

1) It was a non-randomized study -> distribution of mRNA-1273 and BNT162b2 booster is not balanced, with more individuals boosted with BNT162b2.
2) Information gained during the study was partly self-reported by participants ; recall bias.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/36328594

http://www.ncbi.nlm.nih.gov/pubmed/36509374