Clinical trial results:
An International Multicentre, Phase 2, Randomised, Adaptive Protocol to determine the need for, optimal timing of and immunogenicity of administering a booster mRNA vaccination dose against SARS-CoV-2 in the general population (18+ years) already vaccinated against SARS-CoV-2
(EU-COVAT-2 BOOSTAVAC)

Summary

EudraCT number	2021-004889-35
Trial protocol	IE NO DE ES BE
Global end of trial date	23 April 2024

Results information

Result version number	v1 (current)
This version publication date	11 April 2026
First version publication date	11 April 2026

Trial information

Trial identification

Sponsor protocol code	UCDCRC/21/10

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University College Dublin
Sponsor organisation address	Centre for Experimental Pathogen Host Research, Belfield Campus, Dublin, Ireland, D04 V1W8
Public contact	Department of Infectious Diseases, University College Dublin, paddy.mallon@ucd.ie
Scientific contact	Department of Infectious Diseases, University College Dublin, paddy.mallon@ucd.ie

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	28 January 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 April 2024
Global end of trial reached?	Yes
Global end of trial date	23 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the need for, optimal timing of, and immune response after administering a mRNA booster vaccination dose against SARS-CoV-2 in the general population (18+ years) already vaccinated with the mRNA vaccines.

Protection of trial subjects:

The trial was conducted in accordance with the valid versions of the trial protocol and the internationally recognised Good Clinical Practice Guidelines (ICH-GCP), including archiving of essential documents.

The participants volunteering for this trials were not considered to be at additional risk related to the vaccine selected as the intervention. Participants in this study were exposed to some general risks associated with the study procedures. The participants underwent additional blood sampling, which can be uncomfortable but rarely results in any relevant harm or discomfort. Collection of other samples where indicated, saliva or urine, were considered not to cause any significant harm. These risks are almost always short lived and do not result in any long-term effects.

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stressrelated reactions (e.g. dizziness, palpitations, increases in heart rate, alterations in blood pressure, paraesthesia, hypoaesthesia and sweating) may occur in association with the vaccination process itself. Events of anaphylaxis have been reported following vaccination with COMIRNATY®. Appropriate medical treatment and supervision was always available in case of an anaphylactic reaction following the administration of the vaccine.
Cases of myocarditis and pericarditis have been observed following vaccination with COMIRNATY®. These cases have primarily occurred within 14 days following vaccination.
Solicited AEs, including local and systemic manifestations as well as of symptoms of myocarditis and pericarditis, were collected by the participants in a study diary.

Participants' identities were protected at all times and personal health information held securely. No directly identifiable data was stored in the clinical trial database, and the participant lists were stored separately, secured, at the local study sites.

Background therapy:

Standard of care as per country guidelines

Evidence for comparator: -

Actual start date of recruitment	09 March 2022
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	Norway: 6
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	Sweden: 29

Country: Number of subjects enrolled	Belgium: 37
Country: Number of subjects enrolled	Germany: 51
Country: Number of subjects enrolled	Ireland: 111
Worldwide total number of subjects	255
EEA total number of subjects	255

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)	208
From 65 to 84 years	46
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The first participant was recruited on March 09, 2022, the last one on September 19, 2023.
Total recruitment time: 559 days.
A total of 255 participant were recruited in 14 centres across Europe. The planned sample size of 500 participants was not reached
The last participant completed the study on April 23, 2024
Total study duration: 776 days.

Pre-assignment

Screening details:

Potential participants were recruited from a European Volunteer Registry for vaccine trials, local site database or local advertising.
Elegible participants included adults who had received more than 3 doses of mRNA vaccine as primary vaccination for COVID-19 at least 3 but no more than 7 months prior to enrolment (consent)

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm 2: booster at month 0

Arm description:

Participants randomised to Arm 2 received IMP at the baseline visit.

Arm type	Active comparator
Investigational medicinal product name	COVID-19 Vaccine, mRNA
Investigational medicinal product code	
Other name	COMIRNATY
Pharmaceutical forms	Dispersion for injection
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

Subjects randomised to an intervention will receive a single dose of either Pfizer BNT162b2 or one of the Pfizer Bivalent COVID-19 Vaccines (COMIRNATY® Original/Omicron BA.1 or Original/Omicron BA.4-5) or COMIRNATY® Omicron XBB.1.5, at month 0, 2, 4 or 6 after enrolment as per the allocated study arm.

The choice of Pfizer vaccine administered will be determined by what is recommended within the country and/or what is used as standard clinical care at the study site and will be administered at the clinical site by trained study healthcare personnel.

The vaccine should be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm.
Pharmaceutical form: Concentrate for dispersion for injection
Dosage: 1 dose (day 1 at the allocated visit: month 0, 2, 4, or 6)

Arm title	Arm 3: booster at month 2

Arm description:

Participants randomised to Arm 3 received IMP at the follow-up visit at month 2

Arm type	Active comparator

Investigational medicinal product name	COVID-19 Vaccine, mRNA
Investigational medicinal product code	
Other name	COMIRNATY
Pharmaceutical forms	Dispersion for injection
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

Subjects randomised to an intervention will receive a single dose of either Pfizer BNT162b2 or one of the Pfizer Bivalent COVID-19 Vaccines (COMIRNATY® Original/Omicron BA.1 or Original/Omicron BA.4-5) or COMIRNATY® Omicron XBB.1.5, at month 0, 2, 4 or 6 after enrolment as per the allocated study arm.

The choice of Pfizer vaccine administered will be determined by what is recommended within the country and/or what is used as standard clinical care at the study site and will be administered at the clinical site by trained study healthcare personnel.

The vaccine should be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm.
Pharmaceutical form: Concentrate for dispersion for injection
Dosage: 1 dose (day 1 at the allocated visit: month 0, 2, 4, or 6)

Arm title	Arm 4: booster at month 4

Arm description:

Participants randomised to Arm 4 received IMP at the follow-up visit at month 4

Arm type	Active comparator
Investigational medicinal product name	COVID-19 Vaccine, mRNA
Investigational medicinal product code	
Other name	COMIRNATY
Pharmaceutical forms	Dispersion for injection
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

Subjects randomised to an intervention will receive a single dose of either Pfizer BNT162b2 or one of the Pfizer Bivalent COVID-19 Vaccines (COMIRNATY® Original/Omicron BA.1 or Original/Omicron BA.4-5) or COMIRNATY® Omicron XBB.1.5, at month 0, 2, 4 or 6 after enrolment as per the allocated study arm.

The choice of Pfizer vaccine administered will be determined by what is recommended within the country and/or what is used as standard clinical care at the study site and will be administered at the clinical site by trained study healthcare personnel.

The vaccine should be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm.
Pharmaceutical form: Concentrate for dispersion for injection
Dosage: 1 dose (day 1 at the allocated visit: month 0, 2, 4, or 6)

Arm title	Arm 5: booster at month 6

Arm description:

Participants randomised to Arm 5 received IMP at the follow-up visit at month 6

Arm type	Active comparator
Investigational medicinal product name	COVID-19 Vaccine, mRNA
Investigational medicinal product code	
Other name	COMIRNATY
Pharmaceutical forms	Dispersion for injection
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

Subjects randomised to an intervention will receive a single dose of either Pfizer BNT162b2 or one of the Pfizer Bivalent COVID-19 Vaccines (COMIRNATY® Original/Omicron BA.1 or Original/Omicron BA.4-5) or COMIRNATY® Omicron XBB.1.5, at month 0, 2, 4 or 6 after enrolment as per the allocated study arm.

The choice of Pfizer vaccine administered will be determined by what is recommended within the country and/or what is used as standard clinical care at the study site and will be administered at the clinical site by trained study healthcare personnel.

The vaccine should be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm.
Pharmaceutical form: Concentrate for dispersion for injection
Dosage: 1 dose (day 1 at the allocated visit: month 0, 2, 4, or 6)

Arm title	Arm 1: control
Arm description:	
Participants randomised to arm 1 (control) did not receive vaccination as part of the study	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Arm 2: booster at month 0	Arm 3: booster at month 2	Arm 4: booster at month 4
Started	51	53	50
Completed	48	48	46
Not completed	3	5	4
Consent withdrawn by subject	3	2	2
Physician decision	-	1	1
Lost to follow-up	-	2	1
Protocol deviation	-	-	-

Number of subjects in period 1	Arm 5: booster at month 6	Arm 1: control
Started	51	50
Completed	48	45
Not completed	3	5
Consent withdrawn by subject	2	4
Physician decision	-	-
Lost to follow-up	-	1
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Arm 2: booster at month 0
Reporting group description:	
Participants randomised to Arm 2 received IMP at the baseline visit.	
Reporting group title	Arm 3: booster at month 2
Reporting group description:	
Participants randomised to Arm 3 received IMP at the follow-up visit at month 2	
Reporting group title	Arm 4: booster at month 4
Reporting group description:	
Participants randomised to Arm 4 received IMP at the follow-up visit at month 4	
Reporting group title	Arm 5: booster at month 6
Reporting group description:	
Participants randomised to Arm 5 received IMP at the follow-up visit at month 6	
Reporting group title	Arm 1: control
Reporting group description:	
Participants randomised to arm 1 (control) did not receive vaccination as part of the study	

Reporting group values	Arm 2: booster at month 0	Arm 3: booster at month 2	Arm 4: booster at month 4
Number of subjects	51	53	50
Age categorical Units: Subjects			
18-49 years	17	18	17
50-59 years	20	20	19
≥60 years	14	15	14
Age continuous Units: years			
arithmetic mean	52	54	51
standard deviation	± 14	± 14	± 15
Gender categorical Units: Subjects			
Female	33	34	29
Male	18	19	21
Race Units: Subjects			
White	49	53	48
Asian	1	0	1
Other	1	0	1
Is the participant immunocompromised? Units: Subjects			
Yes	50	47	49
No	1	6	1
Prior SARS-CoV-2 Infection Units: Subjects			
Yes	28	26	25
No	20	27	23
Unknown	2	0	2

Missing	1	0	0
Number of pre-study vaccination Units: Subjects			
3 prior vaccines	12	12	9
>3 vaccines	39	41	41
BNT162b2 (Comirnaty)			
Type of vaccine recieved pre-study entry			
Units: Subjects			
Yes	24	32	21
No	27	21	29
Last vaccination to randomisation Units: day			
arithmetic mean	163	152	154
standard deviation	± 63	± 40	± 42
Anti-RBD titres			
Anti-RBD titres at study entry			
Units: IU/mL			
median	8278	8271	13521
inter-quartile range (Q1-Q3)	3876 to 15647	4112 to 18862	5627 to 29280

Reporting group values	Arm 5: booster at month 6	Arm 1: control	Total
Number of subjects	51	50	255
Age categorical Units: Subjects			
18-49 years	18	18	88
50-59 years	19	18	96
≥60 years	14	14	71
Age continuous Units: years			
arithmetic mean	51	54	
standard deviation	± 15	± 14	-
Gender categorical Units: Subjects			
Female	30	28	154
Male	21	22	101
Race Units: Subjects			
White	50	49	249
Asian	1	1	4
Other	0	0	2
Is the participant immunocompromised? Units: Subjects			
Yes	51	48	245
No	0	2	10
Prior SARS-CoV-2 Infection Units: Subjects			
Yes	29	22	130
No	17	26	113
Unknown	2	1	7
Missing	3	1	5
Number of pre-study vaccination			

Units: Subjects			
3 prior vaccines	14	12	59
>3 vaccines	37	38	196
BNT162b2 (Comirnaty)			
Type of vaccine recieved pre-study entry			
Units: Subjects			
Yes	31	33	141
No	20	17	114
Last vaccination to randomisation Units: day			
arithmetic mean	150	150	
standard deviation	± 33	± 39	-
Anti-RBD titres			
Anti-RBD titres at study entry			
Units: IU/mL			
median	12441	10373	
inter-quartile range (Q1-Q3)	4746 to 19261	4107 to 17530	-

End points

End points reporting groups

Reporting group title	Arm 2: booster at month 0
Reporting group description:	
Participants randomised to Arm 2 received IMP at the baseline visit.	
Reporting group title	Arm 3: booster at month 2
Reporting group description:	
Participants randomised to Arm 3 received IMP at the follow-up visit at month 2	
Reporting group title	Arm 4: booster at month 4
Reporting group description:	
Participants randomised to Arm 4 received IMP at the follow-up visit at month 4	
Reporting group title	Arm 5: booster at month 6
Reporting group description:	
Participants randomised to Arm 5 received IMP at the follow-up visit at month 6	
Reporting group title	Arm 1: control
Reporting group description:	
Participants randomised to arm 1 (control) did not receive vaccination as part of the study	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
All randomised participants with available anti-RBD antibody titre at baseline and at Day 14 post booster, analyzed according to intention-to-treat principle.	

Primary: Composite primary endpoint

End point title	Composite primary endpoint[1]
End point description:	
The primary endpoint comprised a composite endpoint of either an increase in anti-RBD antibody titre to ≥500 IU/mL at day 14 post booster vaccine in those with anti-RBD antibody titre of ≤500 IU/mL immediately before booster vaccination or a 2-fold increase in anti-RBD antibody titre at day 14 following booster dose vaccination in those with anti-RBD titre of ≥500 IU/mL immediately before booster vaccination, as measured by quantitative immunoassay targeting the anti-RBD antibody.	
End point type	Primary
End point timeframe:	
From baseline to 14-days post booster 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: Trial participants in Arm 1 (control arm - no vaccine group) were offered the booster dose at the end of the study but they were not followed up as the vaccine was administered after study completion. Hence they were excluded in the statistical analysis.	

End point values	Arm 2: booster at month 0	Arm 3: booster at month 2	Arm 4: booster at month 4	Arm 5: booster at month 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	47	48	44
Units: Subjects	29	35	23	26

Attachments (see zip file)	Statistical Analysis and Justification/Statistical analysis and

Statistical analyses

Statistical analysis title	Primary analysis of the schedule-response relation

Statistical analysis description:

Since the primary endpoint was analysed using one-sample one-sided hypothesis testing , results presented here points to further analyses that were done if efficacy was met (in the main primary analysis), and this was to determine the optimal timing of a booster dose, by modelling the schedule-response relationship using a logistic regression with fractional polynomials

Comparison groups	Arm 2: booster at month 0 v Arm 3: booster at month 2 v Arm 4: booster at month 4 v Arm 5: booster at month 6
Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.48 [3]
Method	Regression, Logistic

Notes:

[2] - Logistic regression with fractional polynomials to determine trend. Schedule-response relationship by randomisation group.
[3] - The p-value indicates whether the slope is 0 (i.e. no effect of time)

Secondary: 2-fold increase in RBD antibody titre

End point title	2-fold increase in RBD antibody titre[4]

End point description:

This endpoint describes subjects who received booster vaccination at each specific time point that achieve a 2-fold in-crease in RBD antibody titre 14 days after the booster vaccine

End point type	Secondary

End point timeframe:

14 days after the booster vaccine

Notes:

[4] - 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: Trial participants in Arm 1 (control arm - no vaccine group) were offered the booster dose at the end of the study but they were not followed up as the vaccine was administered after study completion. Hence they were excluded in the statistical analysis.

End point values	Arm 2: booster at month 0	Arm 3: booster at month 2	Arm 4: booster at month 4	Arm 5: booster at month 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	47	48	44
Units: Subjects	29	35	23	26

Statistical analyses

Statistical analysis title	2-fold increase in anti-RBD titre

Statistical analysis description:

Determining the optimal timing of a booster dose, by modelling the schedule-response relationship using a logistic regression with fractional polynomials (for time point of last vaccine dose) according to the randomisation group

Comparison groups	Arm 2: booster at month 0 v Arm 3: booster at month 2 v Arm 4: booster at month 4 v Arm 5: booster at month 6

Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.48 [6]
Method	Regression, Logistic

Notes:

[5] - Testing for slope using a logistic regression with the best fitting fractional polynomial

[6] - The p-value indicates whether the slope is 0 (i.e. no effect of time)

Secondary: Post anti-RBD ≥ 500 IU/mL

End point title	Post anti-RBD ≥ 500 IU/mL[7]

End point description:

This endpoint describes subjects who received the booster vaccination at each specific time point that achieve an anti-RBD antibody titre 500 IU/mL 14 days after the booster vaccine (regardless of the titre level before booster vaccination),

End point type	Secondary

End point timeframe:

From baseline to Day 14 post booster

Notes:

[7] - 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: Trial participants in Arm 1 (control arm - no vaccine group) were offered the booster dose at the end of the study but they were not followed up as the vaccine was administered after study completion. Hence they were excluded in the statistical analysis.

End point values	Arm 2: booster at month 0	Arm 3: booster at month 2	Arm 4: booster at month 4	Arm 5: booster at month 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	47	48	45
Units: Subjects	50	47	48	45

Statistical analyses

Statistical analysis title	Post anti-RBD titre > 500 IU/mL

Statistical analysis description:

Determining the optimal timing of a booster dose, by modelling the schedule-response relationship using a logistic regression with fractional polynomials (for time point of last vaccine dose) according to the randomisation group

Comparison groups	Arm 2: booster at month 0 v Arm 3: booster at month 2 v Arm 4: booster at month 4 v Arm 5: booster at month 6
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	= 1 [9]
Method	Regression, Logistic

Notes:

[8] - Testing for slope using a logistic regression with the best fitting fractional polynomial

[9] - The p value indicates whether the slope is 0. The titre outcomes at each booster point were not estimable hence the p value =1

Secondary: 2-fold increase in anti-S1 titre

End point title	2-fold increase in anti-S1 titre[10]

End point description:

This endpoint describes subjects with 2-fold RBD antibody titre increase following booster vaccination measured by quantitative immunoassay targeting the spike 1 (S1) antibodies at 14 days after booster vaccine

End point type	Secondary

End point timeframe:

From baseline to Day 14 after booster

Notes:

[10] - 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: Trial participants in Arm 1 (control arm - no vaccine group) were offered the booster dose at the end of the study but they were not followed up as the vaccine was administered after study completion. Hence they were excluded in the statistical analysis.

End point values	Arm 2: booster at month 0	Arm 3: booster at month 2	Arm 4: booster at month 4	Arm 5: booster at month 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	47	48	44
Units: Subjects	31	32	27	27

Statistical analyses

Statistical analysis title	2-fold increase in anti-S1 titre

Statistical analysis description:

Determining the optimal timing of a booster dose, by modelling the schedule-response relationship using a logistic regression with fractional polynomials (for time point of last vaccine dose) according to the randomisation group

Comparison groups	Arm 5: booster at month 6 v Arm 2: booster at month 0 v Arm 3: booster at month 2 v Arm 4: booster at month 4
Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	other[11]
P-value	= 0.67 [12]
Method	Regression, Logistic

Notes:

[11] - Testing for slope using a logistic regression with the best fitting fractional polynomial.

[12] - The p value indicates whether the slope is 0 (i.e no effect of time)

Secondary: 2-fold increase in anti-NC titre

End point title	2-fold increase in anti-NC titre[13]

End point description:

This endpoint describes subjects with 2-fold RBD antibody titre increase following booster vaccination measured by quantitative immunoassay targeting the nucleocapsid (NC) antibodies at 14 days after booster vaccine

End point type	Secondary

End point timeframe:

From baseline to Day 14 after booster

Notes:

[13] - 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: Trial participants in Arm 1 (control arm - no vaccine group) were offered the booster dose at the end of the study but they were not followed up as the vaccine was administered after study completion. Hence they were excluded in the statistical analysis.

End point values	Arm 2: booster at month 0	Arm 3: booster at month 2	Arm 4: booster at month 4	Arm 5: booster at month 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	47	48	44
Units: Subjects	9	9	1	4

Statistical analyses

Statistical analysis title	2-fold increase in anti-NC titre

Statistical analysis description:

Determining the optimal timing of a booster dose, by modelling the schedule-response relationship using a logistic regression with fractional polynomials (for time point of last vaccine dose) according to the randomisation group

Comparison groups	Arm 3: booster at month 2 v Arm 4: booster at month 4 v Arm 5: booster at month 6 v Arm 2: booster at month 0
Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	other[14]
P-value	= 0.038 [15]
Method	Regression, Logistic

Notes:

[14] - Testing for slope using a logistic regression with the best fitting fractional polynomial

[15] - The p value indicates whether the slope is 0. (i.e no effect of time)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs: within 7 days after booster dose.
Unsolicited AEs: until the end of trial.
SAEs: up to 3 months post-booster or until study completion, whichever occurs first.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	Arm 1: Control

Reporting group description:

Participants in this group received no booster vaccination

Reporting group title	Arm 2: Booster at month 0

Reporting group description:

Participants in this group received a booster vaccination at month 0 (baseline), immediately after enrolment

Reporting group title	Arm 3: Booster at month 2

Reporting group description:

Participants in this group received a booster vaccination at month 2 after enrolment

Reporting group title	Arm 4: Booster at month 4

Reporting group description:

Participants in this group received a booster vaccination at month 4 after enrolment.

Reporting group title	Arm 5: Booster at month 6

Reporting group description:

Participants in this group received a booster vaccination at month 6 after enrolment

Serious adverse events	Arm 1: Control	Arm 2: Booster at month 0	Arm 3: Booster at month 2
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 55 (1.82%)	1 / 52 (1.92%)	3 / 51 (5.88%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
Leg amputation			
subjects affected / exposed	0 / 55 (0.00%)	0 / 52 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal transplant			

subjects affected / exposed	0 / 55 (0.00%)	0 / 52 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 55 (0.00%)	0 / 52 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 52 (0.00%)	0 / 51 (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			
Vestibular neuronitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 52 (0.00%)	0 / 51 (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
Atypical pneumonia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 52 (0.00%)	0 / 51 (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
Orchitis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 52 (1.92%)	0 / 51 (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	Arm 4: Booster at month 4	Arm 5: Booster at month 6	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 49 (2.04%)	1 / 48 (2.08%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Surgical and medical procedures			
Leg amputation			

subjects affected / exposed	0 / 49 (0.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal transplant			
subjects affected / exposed	0 / 49 (0.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 49 (0.00%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Vestibular neuronitis			
subjects affected / exposed	0 / 49 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 49 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 48 (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	Arm 1: Control	Arm 2: Booster at month 0	Arm 3: Booster at month 2
Total subjects affected by non-serious adverse events subjects affected / exposed	27 / 55 (49.09%)	43 / 52 (82.69%)	42 / 51 (82.35%)
Nervous system disorders			
Headache	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	2 / 55 (3.64%)	13 / 52 (25.00%)	10 / 51 (19.61%)
occurrences (all)	2	18	11
General disorders and administration site conditions			
Fatigue	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	3 / 55 (5.45%)	14 / 52 (26.92%)	11 / 51 (21.57%)
occurrences (all)	3	23	15
Asthenia	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	0 / 55 (0.00%)	1 / 52 (1.92%)	2 / 51 (3.92%)
occurrences (all)	0	1	2
Influenza like illness	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	0 / 55 (0.00%)	0 / 52 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Injection site discomfort	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	0 / 55 (0.00%)	20 / 52 (38.46%)	27 / 51 (52.94%)
occurrences (all)	0	22	27
Injection site erythema	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	0 / 55 (0.00%)	5 / 52 (9.62%)	5 / 51 (9.80%)
occurrences (all)	0	5	5
Injection site induration	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	0 / 55 (0.00%)	7 / 52 (13.46%)	2 / 51 (3.92%)
occurrences (all)	0	9	2
Injection site pain	Additional description: Non serious adverse event above 5 % reported		
subjects affected / exposed	0 / 55 (0.00%)	2 / 52 (3.85%)	1 / 51 (1.96%)
occurrences (all)	0	2	1
Injection site pruritus	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	0 / 55 (0.00%)	3 / 52 (5.77%)	2 / 51 (3.92%)
occurrences (all)	0	3	2
Injection site swelling	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	0 / 55 (0.00%)	8 / 52 (15.38%)	7 / 51 (13.73%)
occurrences (all)	0	10	7
Malaise	Additional description: Non serious adverse event above 5% reported		

subjects affected / exposed	0 / 55 (0.00%)	3 / 52 (5.77%)	1 / 51 (1.96%)
occurrences (all)	0	3	1
Pyrexia	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	2 / 55 (3.64%)	1 / 52 (1.92%)	5 / 51 (9.80%)
occurrences (all)	2	1	5
Chills	Additional description: Non serious adverse events above 5% reported		
subjects affected / exposed	0 / 55 (0.00%)	4 / 52 (7.69%)	1 / 51 (1.96%)
occurrences (all)	0	4	1
Blood and lymphatic system disorders			
Lymphadenopathy	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	1 / 55 (1.82%)	2 / 52 (3.85%)	3 / 51 (5.88%)
occurrences (all)	1	3	3
Immune system disorders			
Seasonal allergy	Additional description: Non serious adverse events above 5% reported		
subjects affected / exposed	1 / 55 (1.82%)	3 / 52 (5.77%)	2 / 51 (3.92%)
occurrences (all)	1	3	2
Gastrointestinal disorders			
Diarrhoea	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	1 / 55 (1.82%)	5 / 52 (9.62%)	1 / 51 (1.96%)
occurrences (all)	1	5	1
Nausea	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	0 / 55 (0.00%)	0 / 52 (0.00%)	2 / 51 (3.92%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Cough	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	4 / 55 (7.27%)	4 / 52 (7.69%)	8 / 51 (15.69%)
occurrences (all)	5	4	8
Nasal congestion	Additional description: Non serious adverse events above 5% reported		
subjects affected / exposed	1 / 55 (1.82%)	3 / 52 (5.77%)	0 / 51 (0.00%)
occurrences (all)	1	3	0
Oropharyngeal pain	Additional description: Non serious adverse events above 5% reported		
subjects affected / exposed	2 / 55 (3.64%)	9 / 52 (17.31%)	7 / 51 (13.73%)
occurrences (all)	2	9	7
Rhinorrhoea	Additional description: Non serious adverse events above 5% reported		
subjects affected / exposed	0 / 55 (0.00%)	2 / 52 (3.85%)	5 / 51 (9.80%)
occurrences (all)	0	2	5

Skin and subcutaneous tissue disorders			
Hyperhidrosis	Additional description: Non serious adverse events above 5% reported		
subjects affected / exposed	0 / 55 (0.00%)	1 / 52 (1.92%)	1 / 51 (1.96%)
occurrences (all)	0	2	1
Psychiatric disorders			
Insomnia	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	0 / 55 (0.00%)	1 / 52 (1.92%)	1 / 51 (1.96%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	0 / 55 (0.00%)	4 / 52 (7.69%)	3 / 51 (5.88%)
occurrences (all)	0	4	4
Joint swelling	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	0 / 55 (0.00%)	0 / 52 (0.00%)	3 / 51 (5.88%)
occurrences (all)	0	0	3
Myalgia	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	0 / 55 (0.00%)	6 / 52 (11.54%)	8 / 51 (15.69%)
occurrences (all)	0	6	8
Pain in extremity			
subjects affected / exposed	0 / 55 (0.00%)	6 / 52 (11.54%)	1 / 51 (1.96%)
occurrences (all)	0	6	1
Infections and infestations			
Bronchitis	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	3 / 55 (5.45%)	0 / 52 (0.00%)	1 / 51 (1.96%)
occurrences (all)	3	0	1
COVID-19	Additional description: Non serious adverse events above 5% reported		
subjects affected / exposed	8 / 55 (14.55%)	8 / 52 (15.38%)	5 / 51 (9.80%)
occurrences (all)	8	8	5
Nasopharyngitis	Additional description: Non serious adverse events above 5% reported		
subjects affected / exposed	5 / 55 (9.09%)	12 / 52 (23.08%)	6 / 51 (11.76%)
occurrences (all)	5	13	6
Pharyngitis	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	1 / 55 (1.82%)	3 / 52 (5.77%)	0 / 51 (0.00%)
occurrences (all)	1	3	0
Sinusitis	Additional description: Non serious adverse event above 5% reported		

subjects affected / exposed	1 / 55 (1.82%)	0 / 52 (0.00%)	3 / 51 (5.88%)
occurrences (all)	1	0	3
Upper respiratory tract infection	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	3 / 55 (5.45%)	1 / 52 (1.92%)	2 / 51 (3.92%)
occurrences (all)	3	1	2

Non-serious adverse events	Arm 4: Booster at month 4	Arm 5: Booster at month 6	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 49 (89.80%)	37 / 48 (77.08%)	
Nervous system disorders			
Headache	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	9 / 49 (18.37%)	5 / 48 (10.42%)	
occurrences (all)	10	5	
General disorders and administration site conditions			
Fatigue	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	10 / 49 (20.41%)	14 / 48 (29.17%)	
occurrences (all)	15	18	
Asthenia	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	1 / 49 (2.04%)	3 / 48 (6.25%)	
occurrences (all)	2	5	
Influenza like illness	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	2 / 49 (4.08%)	3 / 48 (6.25%)	
occurrences (all)	2	3	
Injection site discomfort	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	27 / 49 (55.10%)	19 / 48 (39.58%)	
occurrences (all)	27	21	
Injection site erythema	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	9 / 49 (18.37%)	4 / 48 (8.33%)	
occurrences (all)	9	4	
Injection site induration	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	8 / 49 (16.33%)	7 / 48 (14.58%)	
occurrences (all)	8	7	
Injection site pain	Additional description: Non serious adverse event above 5 % reported		
subjects affected / exposed	2 / 49 (4.08%)	4 / 48 (8.33%)	
occurrences (all)	2	5	
Injection site pruritus	Additional description: Non serious adverse event above 5% reported		

subjects affected / exposed	6 / 49 (12.24%)	5 / 48 (10.42%)	
occurrences (all)	6	5	
Injection site swelling	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	10 / 49 (20.41%)	10 / 48 (20.83%)	
occurrences (all)	10	10	
Malaise	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	1 / 49 (2.04%)	2 / 48 (4.17%)	
occurrences (all)	1	2	
Pyrexia	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	4 / 49 (8.16%)	3 / 48 (6.25%)	
occurrences (all)	5	3	
Chills	Additional description: Non serious adverse events above 5% reported		
subjects affected / exposed	2 / 49 (4.08%)	2 / 48 (4.17%)	
occurrences (all)	2	2	
Blood and lymphatic system disorders			
Lymphadenopathy	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	2 / 49 (4.08%)	2 / 48 (4.17%)	
occurrences (all)	2	2	
Immune system disorders			
Seasonal allergy	Additional description: Non serious adverse events above 5% reported		
subjects affected / exposed	1 / 49 (2.04%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Diarrhoea	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	3 / 49 (6.12%)	1 / 48 (2.08%)	
occurrences (all)	3	1	
Nausea	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	6 / 49 (12.24%)	1 / 48 (2.08%)	
occurrences (all)	7	1	
Respiratory, thoracic and mediastinal disorders			
Cough	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	3 / 49 (6.12%)	4 / 48 (8.33%)	
occurrences (all)	3	4	
Nasal congestion	Additional description: Non serious adverse events above 5% reported		
subjects affected / exposed	0 / 49 (0.00%)	0 / 48 (0.00%)	
occurrences (all)	0	0	

Oropharyngeal pain	Additional description: Non serious adverse events above 5% reported		
subjects affected / exposed	6 / 49 (12.24%)	3 / 48 (6.25%)	
occurrences (all)	6	3	
Rhinorrhoea	Additional description: Non serious adverse events above 5% reported		
subjects affected / exposed	2 / 49 (4.08%)	2 / 48 (4.17%)	
occurrences (all)	2	2	
Skin and subcutaneous tissue disorders			
Hyperhidrosis	Additional description: Non serious adverse events above 5% reported		
subjects affected / exposed	1 / 49 (2.04%)	3 / 48 (6.25%)	
occurrences (all)	1	3	
Psychiatric disorders			
Insomnia	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	3 / 49 (6.12%)	2 / 48 (4.17%)	
occurrences (all)	3	2	
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	5 / 49 (10.20%)	1 / 48 (2.08%)	
occurrences (all)	5	1	
Joint swelling	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	1 / 49 (2.04%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
Myalgia	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	5 / 49 (10.20%)	11 / 48 (22.92%)	
occurrences (all)	5	11	
Pain in extremity			
subjects affected / exposed	1 / 49 (2.04%)	3 / 48 (6.25%)	
occurrences (all)	1	3	
Infections and infestations			
Bronchitis	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	2 / 49 (4.08%)	1 / 48 (2.08%)	
occurrences (all)	2	1	
COVID-19	Additional description: Non serious adverse events above 5% reported		
subjects affected / exposed	5 / 49 (10.20%)	7 / 48 (14.58%)	
occurrences (all)	5	7	
Nasopharyngitis	Additional description: Non serious adverse events above 5% reported		

subjects affected / exposed	5 / 49 (10.20%)	7 / 48 (14.58%)	
occurrences (all)	5	10	
Pharyngitis	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	0 / 49 (0.00%)	0 / 48 (0.00%)	
occurrences (all)	0	0	
Sinusitis	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	1 / 49 (2.04%)	2 / 48 (4.17%)	
occurrences (all)	1	2	
Upper respiratory tract infection	Additional description: Non serious adverse event above 5% reported		
subjects affected / exposed	1 / 49 (2.04%)	2 / 48 (4.17%)	
occurrences (all)	1	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 December 2021	Version 2.0, dated 16-Dec-2021 and approved in Feb 2022. The first BOOSTAVAC study protocol was developed and approved during the last quarter of 2021, however, a protocol amendment was required soon after the first approval and prior to inclusion of any participant into the study, to adapt the study to the rapidly changing clinical and regulatory environment surrounding the pandemic, which included a change in vaccination guidelines to recommend a third dose vaccine. As such the protocol was amended from a 3rd to 4th dose booster vaccination.
02 May 2022	Version 3.0, dated 02-May-2022 and first approved in Jul 2022: Further adjustments to the study protocol were necessary in response to feedback from regulatory reviews across Europe
26 September 2022	Version 4.0, dated 26-Sep-2022 and first approved in Nov 2022: An expansion of the entry criteria was implemented to enable individuals to participate regardless of the number of prior vaccinations, provided that they had received at least three doses of mRNA COVID-19 vaccines.
14 September 2023	Version 5.0, dated 14-Sep-2023, first approved in Oct 2023: Addition of the new adapted Comirnaty vaccine targeting the Omicron XBB.1.5 subvariant, revised AEs and revised study timelines

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.

The study only included 255 participants (of originally planned size of 500) with statistical power reduced from 93% to 70%.

Notes: