Clinical trial results:
A Phase III, open-label, randomized, controlled, multicountry study to evaluate the immune response, safety and reactogenicity of an RSVPreF3 OA investigational vaccine when co-administered with FLU aQIV (inactivated influenza vaccine – adjuvanted) in adults aged 65 years and above.

Summary

EudraCT number	2022-000623-21
Trial protocol	ES BE
Global end of trial date	17 July 2023

Results information

Result version number	v1 (current)
This version publication date	15 March 2024
First version publication date	15 March 2024

Trial information

Trial identification

Sponsor protocol code	218350

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	GSK Response Center, GlaxoSmithKline, 44 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 44 8664357343, GSKClinicalSupportHD@gsk.com

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	15 November 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To demonstrate the non-inferiority of the FLU vaccine when co administered with the RSVPreF3 OA vaccine compared to the FLU vaccine administered alone.
• To demonstrate the non-inferiority of the RSVPreF3 OA vaccine when co-administered with the FLU vaccine compared to the RSVPreF3 OA vaccine administered alone.

Protection of trial subjects:

Study participants were observed closely for at least 30 minutes after the administration of the study interventions. Appropriate medical treatment was readily available during the observation period in case of anaphylaxis or syncope.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 October 2022
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	Belgium: 121
Country: Number of subjects enrolled	Finland: 110
Country: Number of subjects enrolled	France: 223
Country: Number of subjects enrolled	Spain: 444
Country: Number of subjects enrolled	United Kingdom: 147
Worldwide total number of subjects	1045
EEA total number of subjects	898

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)	0
From 65 to 84 years	1045
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All 1045 enrolled participants were randomized to Co-Ad and Control Groups and received at least 1 dose of study intervention and were included in the exposed set.

Pre-assignment

Screening details:

This study assessed the immunogenicity, safety and reactogenicity of the RSVPreF3 OA vaccine when co-administered with an adjuvanted quadrivalent influenza (FLU-aQIV [FLU]) vaccine, in adults aged 65 years old or above.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Co-Ad Group

Arm description:

Participants received one dose of FLU-aQIV vaccine and one dose of RSVPreF3 OA vaccine, both doses administered at Day 1, and were followed until end of study.

Arm type	Experimental
Investigational medicinal product name	FLU-aQIV vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose of FLU-aQIV vaccine administered intramuscularly.

Investigational medicinal product name	RSVPreF3 OA vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose of RSVPreF3 OA vaccine administered intramuscularly.

Arm title	Control Group

Arm description:

Participants received one dose of FLU-aQIV vaccine at Day 1, followed by one dose of RSVPreF3 OA vaccine at Day 31, and were followed until end of study.

Arm type	Active comparator
Investigational medicinal product name	FLU-aQIV vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose of FLU-aQIV vaccine administered intramuscularly.

Investigational medicinal product name	RSVPreF3 OA vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose of RSVPreF3 OA vaccine administered intramuscularly.

Number of subjects in period 1	Co-Ad Group	Control Group
Started	523	522
Completed	518	499
Not completed	5	23
Consent withdrawn by subject	1	10
Adverse event, non-fatal	-	8
Not specified	2	2
Lost to follow-up	2	3

Baseline characteristics

Reporting groups	
Reporting group title	Co-Ad Group
Reporting group description:	
Participants received one dose of FLU-aQIV vaccine and one dose of RSVPreF3 OA vaccine, both doses administered at Day 1, and were followed until end of study.	
Reporting group title	Control Group
Reporting group description:	
Participants received one dose of FLU-aQIV vaccine at Day 1, followed by one dose of RSVPreF3 OA vaccine at Day 31, and were followed until end of study.	

Reporting group values	Co-Ad Group	Control Group	Total
Number of subjects	523	522	1045
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	0	0	0
>=65 years	523	522	1045
Age continuous Units: years			
median	72.1	72.2	
standard deviation	± 5.4	± 5.2	-
Sex: Female, Male Units: Participants			
Female	255	275	530
Male	268	247	515
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	1	2	3
Asian	0	1	1
Black or African American	0	1	1
White	522	516	1038
Multiple	0	1	1
Other - Unspecified	0	1	1

End points

End points reporting groups

Reporting group title	Co-Ad Group
Reporting group description:	
Participants received one dose of FLU-aQIV vaccine and one dose of RSVPreF3 OA vaccine, both doses administered at Day 1, and were followed until end of study.	
Reporting group title	Control Group
Reporting group description:	
Participants received one dose of FLU-aQIV vaccine at Day 1, followed by one dose of RSVPreF3 OA vaccine at Day 31, and were followed until end of study.	

Primary: Titers for Hemagglutination Inhibition (HI) antibodies against 4 FLU vaccine strains expressed as group Geometric Mean Titers (GMTs) at 1 month after FLU vaccine dose

End point title	Titers for Hemagglutination Inhibition (HI) antibodies against 4 FLU vaccine strains expressed as group Geometric Mean Titers (GMTs) at 1 month after FLU vaccine dose
End point description:	
HI antibodies assessed were antibodies against the Flu A/Darwin/6/2021 H3N2, Flu A/Victoria/2570/2019 H1N1, Flu B/Austria/1359417/2021 Victoria, and Flu B/Phuket/3073/2013 Yamagata flu strains. Analysis was performed on Per Protocol Set for FLU analysis which included eligible participants who: received at least one control group intervention or all Co-Ad group interventions, had pre- and post-dose immunogenicity results, adhered to specified blood draw intervals, with immunogenicity data available for the specified analysis at the specified time point post-FLU vaccine dose, who lacked interfering medical conditions and avoided prohibited concomitant medication/vaccination.	
End point type	Primary
End point timeframe:	
At 1 month after the FLU vaccine dose (Day 31 for both groups)	

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	429	400		
Units: Titers				
geometric mean (confidence interval 95%)				
Flu A/Darwin/6/2021 H3N2 (N=429,400)	43.8 (38.9 to 49.4)	57.7 (51.0 to 65.3)		
Flu A/Victoria/2570/2019 H1N1 (N=420,396)	143.0 (128.6 to 159.0)	148.5 (133.2 to 165.6)		
Flu B/Austria/1359417/2021 Victoria (N=429,400)	613.9 (575.1 to 655.2)	597.5 (558.7 to 639.1)		
Flu B/Phuket/3073/2013 Yamagata (N=428,400)	406.2 (380.0 to 434.2)	421.0 (393.0 to 451.0)		

Statistical analyses

Statistical analysis title	HI GMTs against the Flu A/Darwin/6/2021 H3N2

Statistical analysis description:

To demonstrate the non-inferiority of the FLU vaccine when co administered with the RSVPreF3 OA vaccine compared to the FLU vaccine administered alone, in terms of HI GMTs against the Flu A/Darwin/6/2021 H3N2 strain, at 1 month post-FLU vaccine dose administration (Day 31 for both groups).

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	829
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	GMT Ratio
Point estimate	1.32
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	1.13
upper limit	1.53

Notes:

[1] - The non-inferiority is demonstrated if the upper limit (UL) of the 2-sided 95% confidence interval (CI) of the group GMT ratio (Control group divided by Co-Ad group) for HI antibody titers for the Flu strain is less than or equal (<=) 1.5.

Statistical analysis title	HI GMTs against the Flu A/Victoria/2570/2019 H1N1

Statistical analysis description:

To demonstrate the non-inferiority of the FLU vaccine when co administered with the RSVPreF3 OA vaccine compared to the FLU vaccine administered alone, in terms of HI GMTs against the Flu A/Victoria/2570/2019 H1N1 strain, at 1 month post-FLU vaccine dose administration (Day 31 for both groups).

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	829
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	GMT Ratio
Point estimate	1.04
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	0.91
upper limit	1.18

Notes:

[2] - The non-inferiority is demonstrated if the UL of the 2-sided 95% CI of the group GMT ratio (Control group divided by Co-Ad group) for HI antibody titers for the Flu strain is <=1.5.

Statistical analysis title	HI GMTs against the Flu B/Austria/1359417/2021

Statistical analysis description:

To demonstrate the non-inferiority of the FLU vaccine when co administered with the RSVPreF3 OA vaccine compared to the FLU vaccine administered alone, in terms of HI GMTs against the Flu B/Austria/1359417/2021 strain, at 1 month post-FLU vaccine dose administration (Day 31 for both groups).

Comparison groups	Co-Ad Group v Control Group

Number of subjects included in analysis	829
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	GMT Ratio
Point estimate	0.97
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	0.9
upper limit	1.06

Notes:

[3] - The non-inferiority is demonstrated if the UL of the 2-sided 95% CI of the group GMT ratio (Control group divided by Co-Ad group) for HI antibody titers for the Flu strain is <=1.5.

Statistical analysis title	HI GMTs against Flu B/Phuket/3073/2013 Yamagata

Statistical analysis description:

To demonstrate the non-inferiority of the FLU vaccine when co administered with the RSVPreF3 OA vaccine compared to the Flu vaccine administered alone, in terms of HI GMTs against the Flu B/Phuket/3073/2013 Yamagata strain, at 1 month post-FLU vaccine dose administration (Day 31 for both groups).

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	829
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	GMT Ratio
Point estimate	1.04
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	0.95
upper limit	1.13

Notes:

[4] - The non-inferiority is demonstrated if the UL of the 2-sided 95% CI of the group GMT ratio (Control group divided by Co-Ad group) for HI antibody titers for the Flu strain is <=1.5.

Primary: RSV-A neutralizing antibody titers expressed as GMTs

End point title	RSV-A neutralizing antibody titers expressed as GMTs

End point description:

RSV-A neutralizing antibodies were given as GMTs and expressed as Estimated Dilution 60 (ED60). Analysis was performed on Per Protocol Set for RSV OA analysis which included eligible participants who: received at least one control group intervention or all Co-Ad group interventions, had pre- and post-dose immunogenicity results, adhered to specified blood draw intervals, with immunogenicity data available for the specified analysis at the specified time point post-RSVPreF3 OA vaccine dose, who lacked interfering medical conditions and avoided prohibited concomitant medication/vaccination.

End point type	Primary

End point timeframe:

At 1 month after the RSVPreF3 OA dose (Day 31 for the Co-Ad Group and Day 61 for the Control Group)

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	471	373		
Units: Titers				
geometric mean (confidence interval 95%)	6673.4 (6057.2 to 7352.4)	6591.8 (5917.8 to 7342.6)		

Statistical analyses

Statistical analysis title	RSV-A Group GMT Ratio

Statistical analysis description:

To demonstrate the non-inferiority of the RSVPreF3 OA vaccine when co-administered with the FLU vaccine compared to the RSVPreF3 OA vaccine administered alone, in terms of RSV-A neutralizing antibody titers, at 1 month after the RSVPreF3 OA vaccine dose (Day 31 for the Co-Ad Group and Day 61 for the Control Group).

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	844
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	GMT Ratio
Point estimate	0.99
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	0.87
upper limit	1.12

Notes:

[5] - The non-inferiority is demonstrated if the UL of the 2-sided 95% CI of the GMT ratio (Control group divided by Co-Ad group) for RSV-A neutralizing antibody vaccine is <=1.5.

Primary: RSV-B neutralizing antibody titers expressed as GMTs

End point title	RSV-B neutralizing antibody titers expressed as GMTs

End point description:

RSV B neutralizing antibodies are given as GMTs and expressed as Estimated Dilution 60 (ED60). Analysis was performed on Per Protocol Set for RSV OA analysis which included eligible participants who: received at least one control group intervention or all Co-Ad group interventions, had pre- and post-dose immunogenicity results, adhered to specified blood draw intervals, with immunogenicity data available for the specified analysis at the specified time point post-RSVPreF3 OA vaccine dose, who lacked interfering medical conditions and avoided prohibited concomitant medication/vaccination.

End point type	Primary

End point timeframe:

At 1 month after the RSVPreF3 OA dose (Day 31 for the CoAd Group and Day 61 for the Control Group)

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	469	373		
Units: Titers				
geometric mean (confidence interval 95%)	7880.1 (7195.4 to 8629.8)	9134.1 (8255.9 to 10105.7)		

Statistical analyses

Statistical analysis title	RSV-B Group GMT Ratio

Statistical analysis description:

To demonstrate the non-inferiority of the RSVPreF3 OA vaccine when co-administered with the FLU vaccine compared to the RSVPreF3 OA vaccine administered alone, in terms of RSV-B neutralizing antibody titers, at 1 month after the RSVPreF3 OA vaccine dose (Day 31 for the CoAd Group and Day 61 for the Control Group).

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	842
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	GMT Ratio
Point estimate	1.16
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	1.03
upper limit	1.3

Notes:

[6] - The non-inferiority is demonstrated if the UL of the 2-sided 95% CI of the GMT ratio (Control group divided by Co-Ad group) for RSV-B neutralizing antibody vaccine is <=1.5.

Secondary: HI seroconversion rate (SCR) for 4 FLU vaccine strains

End point title	HI seroconversion rate (SCR) for 4 FLU vaccine strains

End point description:

SCR for HI antibody is defined as the percentage of participants who have either a HI predose titer less than (<) 1:10 and a post-dose titer greater than or equal to (>=) 1:40, or a pre-dose titer >= 1:10 and at least a 4-fold increase in post-dose titer. The assessed Flu strains were: Flu A/Darwin/6/2021 H3N2, Flu A/Victoria/2570/2019 H1N1, Flu B/Austria/1359417/2021 Victoria, and Flu B/Phuket/3073/2013 Yamagata.
Analysis was performed on Per Protocol Set for FLU analysis which included eligible participants who: received at least one control group intervention or all Co-Ad group interventions, had pre- and post-dose immunogenicity results, adhered to specified blood draw intervals, with immunogenicity data available for the specified analysis at the specified time point post-FLU vaccine dose, who lacked interfering medical conditions and avoided prohibited concomitant medication/vaccination.

End point type	Secondary

End point timeframe:

At 1 month after the FLU vaccine dose (Day 31 for both groups)

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	429	400		
Units: Percentage of participants				
number (confidence interval 95%)				
Flu A/Darwin/6/2021 H3N2 (N=429,400)	51.7 (46.9 to 56.6)	62.0 (57.0 to 66.8)		
Flu A/Victoria/2570/2019 H1N1 (N=420,396)	44.0 (39.2 to 48.9)	45.7 (40.7 to 50.8)		
Flu B/Austria/1359417/2021 Victoria (N=429,400)	17.2 (13.8 to 21.2)	17.5 (13.9 to 21.6)		
Flu B/Phuket/3073/2013 Yamagata (N=428,400)	18.5 (14.9 to 22.5)	19.3 (15.5 to 23.5)		

Statistical analyses

Statistical analysis title	SCR for Flu A/Darwin/6/2021 H3N2

Statistical analysis description:

To evaluate the non-inferiority of the FLU vaccine when co-administered with the RSVPreF3 OA vaccine compared to the FLU vaccine administered alone as measured by the difference of percentage of participants achieving seroconversion for HI antibody titers against Flu A/Darwin/6/2021 H3N2 strain at 1 month post-FLU vaccine dose administration (Day 31 for both groups).

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	829
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	Difference of Percentage
Point estimate	10.25
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	3.5
upper limit	16.9

Notes:

[7] - The non-inferiority is demonstrated if the UL of the 2-sided 95% CI on the group difference (Control group minus Co-Ad group) in terms of SCR is <=10% for anti-HI antibodies.

Statistical analysis title	SCR for Flu B/Austria/1359417/2021 Victoria

Statistical analysis description:

To evaluate the non-inferiority of the FLU vaccine when co-administered with the RSVPreF3 OA vaccine compared to the FLU vaccine administered alone as measured by the difference of percentage of participants achieving seroconversion for HI antibody titers against Flu B/Austria/1359417/2021 Victoria at 1 month post-FLU vaccine dose administration (Day 31 for both groups).

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	829
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference of Percentage
Point estimate	0.25

Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	-4.92
upper limit	5.46

Statistical analysis title	SCR for Flu B/Phuket/3073/2013 Yamagata

Statistical analysis description:

To evaluate the non-inferiority of the FLU vaccine when co-administered with the RSVPreF3 OA vaccine compared to the FLU vaccine administered alone as measured by the difference of percentage of participants achieving seroconversion for HI antibody titers against Flu B/Phuket/3073/2013 Yamagata strain at 1 month post-FLU vaccine dose administration (Day 31 for both groups).

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	829
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference of Percentage
Point estimate	0.79
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	-4.54
upper limit	6.17

Statistical analysis title	SCR for Flu A/Victoria/2570/2019 H1N1

Statistical analysis description:

To evaluate the non-inferiority of the FLU vaccine when co-administered with the RSVPreF3 OA vaccine compared to the FLU vaccine administered alone as measured by the difference of percentage of participants achieving seroconversion for HI antibody titers against Flu A/Victoria/2570/2019 H1N1 strain at 1 month post-FLU vaccine dose administration (Day 31 for both groups).

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	829
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	Difference of Percentage
Point estimate	1.66
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	-5.16
upper limit	8.47

Notes:

[8] - The non-inferiority is demonstrated if the UL of the 2-sided 95% CI on the group difference (Control group minus Co-Ad group) in terms of SCR is <=10% for anti-HI antibodies.

Secondary: RSV-A neutralization antibody titers expressed as mean geometric increase (MGI)

End point title	RSV-A neutralization antibody titers expressed as mean geometric increase (MGI)

End point description:

MGI was defined as the geometric mean of the within-participant ratios of the post-dose titer over the pre-dose titer.
Analysis was performed on Per Protocol Set for RSV OA analysis which included eligible participants who: received at least one control group intervention or all Co-Ad group interventions, had pre- and post-dose immunogenicity results, adhered to specified blood draw intervals, with immunogenicity data available for the specified analysis at the specified time point post-RSVPreF3 OA vaccine dose, who lacked interfering medical conditions and avoided prohibited concomitant medication/vaccination.

End point type	Secondary

End point timeframe:

At 1 month after the RSVPreF3 OA vaccine dose (Day 31 for the Co-Ad Group and Day 61 for the Control Group) compared to pre-vaccination (Day 1 for Co-Ad group and Day 31 for Control group)

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	471	373		
Units: Ratio				
geometric mean (confidence interval 95%)	8.50 (7.79 to 9.27)	7.58 (6.82 to 8.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: RSV-B neutralization antibody titers expressed as MGI

End point title	RSV-B neutralization antibody titers expressed as MGI

End point description:

MGI was defined as the geometric mean of the within-participant ratios of the post-dose titer over the pre-dose titer.
Analysis was performed on Per Protocol Set for RSV OA analysis which included eligible participants who: received at least one control group intervention or all Co-Ad group interventions, had pre- and post-dose immunogenicity results, adhered to specified blood draw intervals, with immunogenicity data available for the specified analysis at the specified time point post-RSVPreF3 OA vaccine dose, who lacked interfering medical conditions and avoided prohibited concomitant medication/vaccination.

End point type	Secondary

End point timeframe:

At 1 month after the RSVPreF3 OA vaccine dose (Day 31 for the Co-Ad Group and Day 61 for the Control Group) compared to pre-vaccination (Day 1 for Co-Ad group and Day 31 for Control group)

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	469	373		
Units: Ratio				
geometric mean (confidence interval 95%)	7.11 (6.55 to 7.72)	7.46 (6.74 to 8.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for HI antibodies against 4 FLU vaccine strains

End point title	Titers for HI antibodies against 4 FLU vaccine strains

End point description:

HI antibodies assessed were antibodies against the Flu A/Darwin/6/2021 H3N2, Flu A/Victoria/2570/2019 H1N1, Flu B/Austria/1359417/2021 Victoria, and Flu B/Phuket/3073/2013 Yamagata flu strains. HI antibodies were expressed as GMT, in titers.
Analysis was performed on Per Protocol Set for FLU analysis which included eligible participants who: received at least one control group intervention or all Co-Ad group interventions, had pre- and post-dose immunogenicity results, adhered to specified blood draw intervals, with immunogenicity data available for the specified analysis at the specified time point post-FLU vaccine dose, who lacked interfering medical conditions and avoided prohibited concomitant medication/vaccination

End point type	Secondary

End point timeframe:

At Day 1 (Baseline) and Day 31

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	469	449		
Units: Titers				
geometric mean (confidence interval 95%)				
Flu A/Darwin/6/2021 H3N2,Day1(N=469,449)	9.1 (8.4 to 9.8)	8.7 (8.1 to 9.4)		
Flu A/Darwin/6/2021 H3N2,Day31(N=442,400)	45.3 (40.6 to 50.5)	58.3 (51.6 to 65.8)		
Flu A/Victoria/2570/2019 H1N1,Day1(N=460,446)	40.0 (35.4 to 45.1)	43.2 (38.4 to 48.5)		
Flu A/Victoria/2570/2019 H1N1,Day31(N=440,399)	151.0 (136.4 to 167.2)	163.8 (147.5 to 181.9)		
FluB/Austria/1359417/2021Victoria,Day 1(N=469,449)	323.6 (300.4 to 348.5)	327.2 (303.6 to 352.7)		
FluB/Austria/1359417/2021Victoria,Day 31(N=442,400)	614.9 (575.5 to 657.0)	608.1 (566.8 to 652.5)		
Flu B/Phuket/3073/2013 Yamagata,Day1(N=468,449)	213.1 (198.5 to 228.7)	193.2 (179.9 to 207.5)		
Flu B/Phuket/3073/2013 Yamagata,Day31(N=442,400)	423.0 (394.6 to 453.5)	417.5 (387.9 to 449.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: HI seroprotection rate (SPR) for 4 FLU vaccine strains

End point title	HI seroprotection rate (SPR) for 4 FLU vaccine strains

End point description:

SPR for HI antibody was defined as the percentage of participants with a serum HI titer >= 1:40. The assessed Flu strains were: Flu A/Darwin/6/2021 H3N2, Flu A/Victoria/2570/2019 H1N1, Flu B/Austria/1359417/2021 Victoria, and Flu B/Phuket/3073/2013 Yamagata.
Analysis was performed on Per Protocol Set for FLU analysis which included eligible participants who: received at least one control group intervention or all Co-Ad group interventions, had pre- and post-dose immunogenicity results, adhered to specified blood draw intervals, with immunogenicity data available for the specified analysis at the specified time point post-FLU vaccine dose, who lacked interfering medical conditions and avoided prohibited concomitant medication/vaccination.

End point type	Secondary

End point timeframe:

At Day 1 (Baseline) and Day 31

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	469	449		
Units: Percentage of participants				
number (confidence interval 95%)				
Flu A/Darwin/6/2021 H3N2, Day1 (N=469, 449)	10.4 (7.8 to 13.6)	10.7 (8.0 to 13.9)		
Flu A/Darwin/6/2021 H3N2, Day31 (N=442,400)	63.6 (58.9 to 68.1)	71.0 (66.3 to 75.4)		
Flu A/Victoria/2570/2019 H1N1, Day1 (N=460,446)	60.0 (55.4 to 64.5)	64.3 (59.7 to 68.8)		
Flu A/Victoria/2570/2019 H1N1, Day31 (N=440,399)	92.0 (89.1 to 94.4)	95.2 (92.7 to 97.1)		
FluB/Austria/1359417/2021Victoria,Day 1(N=469,449)	99.6 (98.5 to 99.9)	100 (99.2 to 100)		
FluB/Austria/1359417/2021Victoria,Day 31(N=442,400)	100 (99.2 to 100)	100 (99.1 to 100)		
Flu B/Phuket/3073/2013 Yamagata,Day1(N=468,449)	99.8 (98.8 to 100.0)	98.9 (97.4 to 99.6)		
Flu B/Phuket/3073/2013 Yamagata,Day31(N=442,400)	100 (99.2 to 100)	100 (99.1 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: HI antibody titers for 4 FLU vaccine strains expressed as MGI

End point title	HI antibody titers for 4 FLU vaccine strains expressed as MGI

End point description:

MGI was defined as the geometric mean of the within-participant ratios of the post-dose titer over the pre-dose titer. The assessed Flu strains were: Flu A/Darwin/6/2021 H3N2, Flu A/Victoria/2570/2019 H1N1, Flu B/Austria/1359417/2021 Victoria, and Flu B/Phuket/3073/2013 Yamagata.
Analysis was performed on Per Protocol Set for FLU analysis which included eligible participants who: received at least one control group intervention or all Co-Ad group interventions, had pre- and post-dose

immunogenicity results, adhered to specified blood draw intervals, with immunogenicity data available for the specified analysis at the specified time point post-FLU vaccine dose, who lacked interfering medical conditions and avoided prohibited concomitant medication/vaccination.

End point type	Secondary

End point timeframe:

At 1 month after the FLU dose (Day 31 for both groups) compared to pre-vaccination (Day 1 for both groups)

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	429	400		
Units: Ratio				
geometric mean (confidence interval 95%)				
Flu A/Darwin/6/2021 H3N2 HI (N=429,400)	5.10 (4.60 to 5.66)	6.87 (6.12 to 7.71)		
Flu A/Victoria/2570/2019 H1N1 HI (N=420,396)	3.85 (3.40 to 4.35)	3.79 (3.34 to 4.31)		
Flu B/Austria/1359417/2021 Victoria HI (N=429,400)	1.89 (1.77 to 2.03)	1.84 (1.71 to 1.98)		
Flu B/Phuket/3073/2013 Yamagata HI (N=428,400)	1.94 (1.82 to 2.07)	2.11 (1.97 to 2.27)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants reporting each solicited administration site event after each vaccine dose administration

End point title	Percentage of participants reporting each solicited administration site event after each vaccine dose administration

End point description:

The solicited administration site events after vaccination include erythema, pain and swelling. Analysis was performed on Exposed set which included participants who received a study intervention and with the electronic diary completed post-each vaccination and for whom solicited administration event data was available for specific visit. The Control group received FLU vaccination at Day 1 and RSVPreF3 OA vaccination at Day 31; Co-Ad group received co-administered vaccine (RSVPreF3 OA + FLU) on Day 1. Analysis per group is based on the study intervention administered on specific visit.

End point type	Secondary

End point timeframe:

Within 7 days (the day of vaccination and 6 subsequent days) after each vaccine administration (vaccines administered at Day 1 for CoAd Group and at Day 1 and Day 31 for Control group)

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	516	513		
Units: Percentage of participants				
number (confidence interval 95%)				
Erythema, FLU dose given at Day 1 (N=516,513)	6.6 (4.6 to 9.1)	5.3 (3.5 to 7.6)		
Erythema, RSV dose given at Day 1 (N=516,0)	14.1 (11.3 to 17.5)	0 (0 to 0)		
Erythema, RSV dose given at Day 31 (N=0,451)	0 (0 to 0)	12.4 (9.5 to 15.8)		
Pain, FLU dose given at Day 1 (N=516,513)	51.7 (47.3 to 56.1)	44.8 (40.5 to 49.3)		
Pain, RSV dose given at Day 1 (N=516,0)	66.1 (61.8 to 70.2)	0 (0 to 0)		
Pain, RSV dose given at Day 31 (N=0,451)	0 (0 to 0)	58.8 (54.1 to 63.3)		
Swelling, FLU dose given at Day 1 (N=515,513)	5.2 (3.5 to 7.5)	6.0 (4.1 to 8.5)		
Swelling, RSV dose given at Day 1 (N=516,0)	10.5 (8.0 to 13.4)	0 (0 to 0)		
Swelling, RSV dose given at Day 31 (N=0,451)	0 (0 to 0)	8.4 (6.0 to 11.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants reporting each solicited systemic event after each dose administration

End point title	Percentage of participants reporting each solicited systemic event after each dose administration

End point description:

The solicited systemic events after vaccination include fever, headache, fatigue, myalgia and arthralgia. Analysis was performed on Exposed set which included participants who received a study intervention and with the electronic diary completed post-each vaccination and for whom solicited administration event data was available for specific visit. The Control group received FLU vaccination at Day 1 and RSVPreF3 OA vaccination at Day 31; Co-Ad group received co-administered vaccine (RSVPreF3 OA + FLU) on Day 1. Analysis per group is based on the study intervention administered on specific visit.

End point type	Secondary

End point timeframe:

Within 7 days (the day of vaccination and 6 subsequent days) after each vaccine administration (vaccines administered at Day 1 and Day 31 for Co-Ad Group and at Day 1 and Day 31 for Control group)

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	516	513		
Units: Percentage of participants				
number (confidence interval 95%)				

Arthralgia, Dosing at Day 1 (N=516,513)	25.8 (22.1 to 29.8)	15.6 (12.6 to 19.0)		
Arthralgia, Dosing at Day 31 (N=0,451)	0 (0 to 0)	17.1 (13.7 to 20.9)		
Fatigue, Dosing at Day 1 (N=516,513)	45.7 (41.4 to 50.1)	28.5 (24.6 to 32.6)		
Fatigue, Dosing at Day 31 (N=0, 451)	0 (0 to 0)	30.4 (26.2 to 34.9)		
Fever, Dosing at Day 1 (N=516,513)	2.1 (1.1 to 3.8)	0.6 (0.1 to 1.7)		
Fever, Dosing at Day 31 (N=0,451)	0 (0 to 0)	1.1 (0.4 to 2.6)		
Headache, Dosing at Day 1 (N=516,513)	32.2 (28.2 to 36.4)	19.3 (16.0 to 23.0)		
Headache, Dosing at Day 31 (N=0, 451)	0 (0 to 0)	23.9 (20.1 to 28.2)		
Myalgia, Dosing at Day 1 (N=516,513)	39.0 (34.7 to 43.3)	23.0 (19.4 to 26.9)		
Myalgia, Dosing at Day 31 (N=0,451)	0 (0 to 0)	31.9 (27.6 to 36.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants reporting unsolicited adverse events (AEs)

End point title	Percentage of participants reporting unsolicited adverse events (AEs)

End point description:

An unsolicited AEs is an AE that is not included in a list of solicited events using a Participant Electronic Diary. Unsolicited events must be spontaneously communicated by a participant who signs the informed consent. Unsolicited AEs include both serious, non-serious AEs and potential immune-mediated diseases (pIMDs).
Analysis was performed on Exposed set which included participants who received at least a study intervention and had data for the assessed timepoint and analysis.

End point type	Secondary

End point timeframe:

Within 30 days (the day of vaccination and 29 subsequent days) after each vaccine administration

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	523	522		
Units: Percentage of participants				
number (confidence interval 95%)	13.6 (10.8 to 16.8)	24.5 (20.9 to 28.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants reporting at least one Potential Immune-mediated Disease (pIMDs)

End point title	Percentage of participants reporting at least one Potential Immune-mediated Disease (pIMDs)

End point description:

pIMDs are a subset of AEs of special interest that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune etiology. The investigator must exercise his/her medical/scientific judgment to determine whether other diseases have an autoimmune origin (i.e., pathophysiology involving systemic or organ-specific pathogenic autoantibodies) and should also be recorded as a pIMD.
Analysis was performed on Exposed set which included participants who received at least a study intervention and had data for the assessed timepoint and analysis.

End point type	Secondary

End point timeframe:

From Day 1 until 6 months after last vaccination (Month 6 for the Co-Ad Group, Month 7 for the Control group)

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	523	522		
Units: Percentage of participants				
number (confidence interval 95%)	0 (0 to 0.7)	0.6 (0.1 to 1.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants reporting at least one Serious Adverse Event (SAEs)

End point title	Percentage of participants reporting at least one Serious Adverse Event (SAEs)

End point description:

An SAE is any untoward medical occurrence that results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, or results in disability/incapacity or is a congenital anomaly/birth defect in the offspring of a study participant.
Analysis was performed on Exposed set which included participants who received at least a study intervention and had data for the assessed timepoint and analysis.

End point type	Secondary

End point timeframe:

From Day 1 until 6 months after last vaccination (Month 6 for the Co-Ad Group, Month 7 for the Control group)

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	523	522		
Units: Percentage of participants				
number (confidence interval 95%)	4.0 (2.5 to 6.1)	6.9 (4.9 to 9.4)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs were collected during 7-day follow-up period after each vaccination. Unsolicited AEs were collected during 30-day follow-up period after each vaccination. SAEs and pIMDs were collected from Day 1 to 6 months after last vaccination.

Adverse event reporting additional description:

Solicited and unsolicited events were reported per participant at any dose for the assessed timeframe (within 30 days after any vaccine dose administration) according to occurrence of each event, as pre-specified in Statistical Analysis Plan.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	v26.0

Reporting groups

Reporting group title	Control Group

Reporting group description:

Participants received one dose of FLU-aQIV vaccine at Day 1, followed by one dose of RSVPreF3 OA vaccine at Day 31, and were followed until end of study.

Reporting group title	Co-Ad Group

Reporting group description:

Participants received one dose of FLU-aQIV vaccine and one dose of RSVPreF3 OA vaccine, both doses administered at Day 1, and were followed until end of study.

Serious adverse events	Control Group	Co-Ad Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 522 (6.90%)	21 / 523 (4.02%)	
number of deaths (all causes)	6	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Small intestine carcinoma			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adenocarcinoma gastric			
subjects affected / exposed	1 / 522 (0.19%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bladder neoplasm			

subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ocular melanoma			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal neoplasm			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Giant cell arteritis			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			

subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 522 (0.19%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary arterial hypertension			
subjects affected / exposed	2 / 522 (0.38%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	3 / 522 (0.57%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 0	
Hypercapnia			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Wound necrosis			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Posterior capsule rupture			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 522 (0.19%)	2 / 523 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 522 (0.19%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	1 / 522 (0.19%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			

subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 522 (0.19%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			

subjects affected / exposed	1 / 522 (0.19%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperparathyroidism			

subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Spinal stenosis			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	1 / 522 (0.19%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	3 / 522 (0.57%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 522 (0.19%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 522 (0.19%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 522 (0.19%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial disease carrier			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Complicated appendicitis			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 522 (0.00%)	2 / 523 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 522 (0.00%)	2 / 523 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superinfection			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal abscess			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infective exacerbation of bronchiectasis			

subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infected skin ulcer			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Control Group	Co-Ad Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	428 / 522 (81.99%)	427 / 523 (81.64%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	5 / 522 (0.96%)	2 / 523 (0.38%)	
occurrences (all)	5	2	
General disorders and administration site conditions			

Injection site erythema			
subjects affected / exposed	76 / 522 (14.56%)	83 / 523 (15.87%)	
occurrences (all)	84	83	
Injection site swelling			
subjects affected / exposed	61 / 522 (11.69%)	67 / 523 (12.81%)	
occurrences (all)	69	67	
Injection site pain			
subjects affected / exposed	349 / 522 (66.86%)	368 / 523 (70.36%)	
occurrences (all)	496	368	
Fatigue			
subjects affected / exposed	212 / 522 (40.61%)	236 / 523 (45.12%)	
occurrences (all)	286	237	
Administration site erythema			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	4 / 522 (0.77%)	1 / 523 (0.19%)	
occurrences (all)	5	1	
Pyrexia			
subjects affected / exposed	9 / 522 (1.72%)	14 / 523 (2.68%)	
occurrences (all)	9	14	
Asthenia			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Chills			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Inflammation			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Injection site haematoma			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Administration site pain			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	

Vessel puncture site swelling			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 522 (1.15%)	1 / 523 (0.19%)	
occurrences (all)	6	1	
Oropharyngeal pain			
subjects affected / exposed	3 / 522 (0.57%)	1 / 523 (0.19%)	
occurrences (all)	3	1	
Productive cough			
subjects affected / exposed	2 / 522 (0.38%)	1 / 523 (0.19%)	
occurrences (all)	2	1	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 522 (0.19%)	1 / 523 (0.19%)	
occurrences (all)	1	1	
Catarrh			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Lung disorder			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			

subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Psychiatric disorders			
Restlessness			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Occult blood positive			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 522 (0.57%)	1 / 523 (0.19%)	
occurrences (all)	3	1	
Limb injury			
subjects affected / exposed	3 / 522 (0.57%)	0 / 523 (0.00%)	
occurrences (all)	3	0	
Contusion			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Eye injury			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Fibula fracture			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Head injury			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Immunisation reaction			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Ligament sprain			

subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	2	0	
Muscle contusion			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Road traffic accident			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Vaccination complication			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness postural			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Presyncope			
subjects affected / exposed	2 / 522 (0.38%)	0 / 523 (0.00%)	
occurrences (all)	2	0	
Paraesthesia			
subjects affected / exposed	1 / 522 (0.19%)	1 / 523 (0.19%)	
occurrences (all)	1	1	
Headache			
subjects affected / exposed	164 / 522 (31.42%)	167 / 523 (31.93%)	
occurrences (all)	210	167	
Sciatica			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Syncope			

subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Hypochromic anaemia			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Neovascular age-related macular degeneration			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Glaucoma			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Oral disorder			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	1 / 522 (0.19%)	1 / 523 (0.19%)	
occurrences (all)	1	1	
Diarrhoea			
subjects affected / exposed	2 / 522 (0.38%)	0 / 523 (0.00%)	
occurrences (all)	2	0	
Abdominal pain			

subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Hiatus hernia			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Irritable bowel syndrome			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Melaena			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Odynophagia			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Oesophagitis			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Erythema			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Rash			

subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 522 (0.19%)	1 / 523 (0.19%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Haemarthrosis			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Groin pain			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Exostosis			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	2 / 522 (0.38%)	0 / 523 (0.00%)	
occurrences (all)	2	0	
Back pain			
subjects affected / exposed	3 / 522 (0.57%)	1 / 523 (0.19%)	
occurrences (all)	3	1	
Arthralgia			
subjects affected / exposed	133 / 522 (25.48%)	133 / 523 (25.43%)	
occurrences (all)	164	134	
Myalgia			
subjects affected / exposed	206 / 522 (39.46%)	201 / 523 (38.43%)	
occurrences (all)	263	203	
Rotator cuff syndrome			

subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Tenosynovitis stenosans			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Synovial cyst			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	15 / 522 (2.87%)	13 / 523 (2.49%)	
occurrences (all)	17	13	
COVID-19			
subjects affected / exposed	14 / 522 (2.68%)	11 / 523 (2.10%)	
occurrences (all)	14	11	
Bronchitis			
subjects affected / exposed	5 / 522 (0.96%)	4 / 523 (0.76%)	
occurrences (all)	5	4	
Respiratory tract infection			
subjects affected / exposed	7 / 522 (1.34%)	0 / 523 (0.00%)	
occurrences (all)	7	0	
Upper respiratory tract infection			
subjects affected / exposed	4 / 522 (0.77%)	3 / 523 (0.57%)	
occurrences (all)	4	3	
Rhinitis			
subjects affected / exposed	3 / 522 (0.57%)	2 / 523 (0.38%)	
occurrences (all)	3	2	
Pharyngitis			
subjects affected / exposed	1 / 522 (0.19%)	2 / 523 (0.38%)	
occurrences (all)	1	2	
Sinusitis			
subjects affected / exposed	1 / 522 (0.19%)	2 / 523 (0.38%)	
occurrences (all)	1	2	

Herpes zoster			
subjects affected / exposed	1 / 522 (0.19%)	1 / 523 (0.19%)	
occurrences (all)	1	1	
Lower respiratory tract infection			
subjects affected / exposed	2 / 522 (0.38%)	0 / 523 (0.00%)	
occurrences (all)	2	0	
Pneumonia			
subjects affected / exposed	1 / 522 (0.19%)	1 / 523 (0.19%)	
occurrences (all)	1	1	
Erysipelas			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Ear infection			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Diverticulitis			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Cellulitis			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Abscess oral			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	2 / 522 (0.38%)	0 / 523 (0.00%)	
occurrences (all)	2	0	
Herpes simplex			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Infected bite			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Localised infection			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	

Parotitis			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Post procedural infection			
subjects affected / exposed	1 / 522 (0.19%)	0 / 523 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Tooth infection			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Hyperlipidaemia			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Hyperglycaemia			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	
Folate deficiency			
subjects affected / exposed	0 / 522 (0.00%)	1 / 523 (0.19%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 December 2022	The purpose of this amendment was to promote from secondary objective to primary objective the non-inferiority of RSV-B neutralizing antibody titers, as measured by GMT, when RSVPreF3 OA is co-administered with FLU aQIV, compared to RSVPreF3 OA alone. In addition, the SAE definition of anomalies in offspring was added, laboratory blinding procedures were updated, and minor editorial changes were made for clarity.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported