Clinical trial results:
A Phase 3, Randomized, Observer-blind, Controlled, Multicenter, Clinical Study to Evaluate Immunogenicity and Safety of an MF59-adjuvanted Quadrivalent Subunit Inactivated Influenza Vaccine in Comparison with a Licensed Quadrivalent Influenza Vaccine, in Adults 50 to 64 Years of Age

Summary

EudraCT number	2021-001721-40
Trial protocol	DE EE
Global end of trial date	14 October 2022

Results information

Result version number	v1 (current)
This version publication date	14 October 2023
First version publication date	14 October 2023

Trial information

Trial identification

Sponsor protocol code	V118_23

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05044195
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Seqirus UK Limited
Sponsor organisation address	The Point, 29 Market Street, Maidenhead, United Kingdom, SL6 8AA
Public contact	Clinical Trial Disclosures Manager, Seqirus UK Limited, Seqirus.ClinicalTrials@Seqirus.com
Scientific contact	Clinical Trial Disclosures Manager, Seqirus UK Limited, Seqirus.ClinicalTrials@Seqirus.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	09 December 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 January 2022
Global end of trial reached?	Yes
Global end of trial date	14 October 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Immunogenicity Objectives:

1. To demonstrate immunological noninferiority of aQIV versus a nonadjuvanted quadrivalent influenza comparator (QIV) in subjects 50-64 years of age, as measured by hemagglutination inhibition (HI) geometric mean titers (GMTs) and seroconversion rates (SCRs) for each vaccine strain, at 3 weeks after vaccination.
2. To demonstrate that aQIV induces a superior immune response compared with QIV in subjects 50-64 years of age as measured by HI GMTs at 3 weeks after vaccination for at least 2 of the 4 vaccine strains.

Protection of trial subjects:

This clinical study was designed, implemented, and reported in accordance with the ICH Harmonised Tripartite Guidelines for Good Clinical Practice (ICH E6(R2)), with applicable local regulations European Directive 2001/20/EC, United States (US) Code of Federal Regulations Title 21, and Japanese Ministry of Health, Labor, and Welfare, Seqirus codes on protection of human rights, and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 September 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Estonia: 787
Country: Number of subjects enrolled	Germany: 513
Country: Number of subjects enrolled	United States: 744
Worldwide total number of subjects	2044
EEA total number of subjects	1300

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)	2044
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled from 6 centers in Estonia, 11 centers in Germany, and 12 centers in the US.

Pre-assignment

Screening details:

All enrolled subjects were randomized in the study.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	aQIV

Arm description:

Adjuvanted QIV containing 2 influenza type A strains and 2 influenza type B strains

Arm type	Experimental
Investigational medicinal product name	Adjuvanted Quadrivalent Influenza Vaccine (aQIV)
Investigational medicinal product code	
Other name	Fluad Tetra
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Single intramuscular injection (0.5 mL dose) on Day 1

Arm title	Comparator QIV

Arm description:

Non-adjuvanted comparator QIV containing 2 influenza type A strains and 2 influenza type B strains

Arm type	Active comparator
Investigational medicinal product name	Non-adjuvanted Quadrivalent Influenza Vaccine (QIV)
Investigational medicinal product code	
Other name	Fluarix Quadrivalent
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Single intramuscular injection (0.5 mL dose) on Day 1

Number of subjects in period 1	aQIV	Comparator QIV
Started	1027	1017
Completed	982	989
Not completed	45	28
Adverse event, serious fatal	1	-

Consent withdrawn by subject	6	8
Adverse event, non-fatal	-	1
Other	3	2
Lost to follow-up	35	17

Baseline characteristics

Reporting groups	
Reporting group title	aQIV
Reporting group description:	
Adjuvanted QIV containing 2 influenza type A strains and 2 influenza type B strains	
Reporting group title	Comparator QIV
Reporting group description:	
Non-adjuvanted comparator QIV containing 2 influenza type A strains and 2 influenza type B strains	

Reporting group values	aQIV	Comparator QIV	Total
Number of subjects	1027	1017	2044
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1027	1017	2044
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	57.8	57.8	
standard deviation	± 4.17	± 4.21	-
Gender categorical Units: Subjects			
Female	635	615	1250
Male	392	402	794
Age group Units: Subjects			
50 to 59 years	609	596	1205
60 to 64 years	418	421	839
Ethnicity Units: Subjects			
Hispanic or Latino	14	12	26
Not Hispanic or Latino	1013	1001	2014
Unknown or Not Reported	0	4	4
Race Units: Subjects			
American Indian or Alaska Native	2	3	5
Asian	2	4	6
Black or African American	39	36	75
Native Hawaiian or Other Pacific Islander	1	1	2
White	982	972	1954

Other	1	1	2
Country Units: Subjects			
Estonia	391	396	787
Germany	259	254	513
United States	377	367	744
Received an influenza vaccination in the previous 3 influenza seasons Units: Subjects			
Yes	586	598	1184
No	441	419	860
Comorbidity Risk Score			
A subject's comorbidity risk score was obtained by adding scores for each applicable characteristic: age (<70; 70-74; 75-79; 80-89; ≥90 years); sex (female; male); number of outpatient visits during the previous year (0; 1-6; 7-12; ≥13); previous hospitalization due to pneumonia or influenza (no; yes); pre-existing comorbidity (pulmonary disease; heart disease; renal disease or renal transplant; dementia or stroke; nonhematological and hematological cancer). A cut-off score ≥50 defines higher probability of hospitalization due to pneumonia/influenza or death (Hak et al, J Infect Dis 2004).			
Units: Subjects			
<50	912	919	1831
≥50	115	98	213

End points

End points reporting groups

Reporting group title	aQIV
Reporting group description:	
Adjuvanted QIV containing 2 influenza type A strains and 2 influenza type B strains	
Reporting group title	Comparator QIV
Reporting group description:	
Non-adjuvanted comparator QIV containing 2 influenza type A strains and 2 influenza type B strains	
Subject analysis set title	FAS Immunogenicity
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The Full Analysis Set (FAS) Immunogenicity is defined as all enrolled subjects who were randomized, received study vaccination and provided immunogenicity data at any time point.	
Subject analysis set title	PPS Immunogenicity
Subject analysis set type	Per protocol
Subject analysis set description:	
The Per Protocol Set (PPS) Immunogenicity is defined as all subjects in the FAS Immunogenicity who: had both Day 1 and Day 22 immunogenicity assessment; correctly received the vaccine (ie, received the vaccine to which the subjects were randomized and at the scheduled time points); had no protocol deviations leading to exclusion as defined prior to unblinding/analysis; were not excluded due to other reasons defined prior to unblinding or analysis.	
Subject analysis set title	Solicited Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Solicited Safety Set is defined as all exposed subjects with any solicited AE data including temperature measurements or use of analgesics/antipyretics.	
Subject analysis set title	Unsolicited Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Unsolicited Safety Set is defined as all exposed subjects who provided unsolicited AE data.	

Primary: Immunogenicity Endpoint: Geometric Mean Titer (GMT) and GMT Ratio of Hemagglutination Inhibition (HI) Antibodies at Day 22 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains (PPS Immunogenicity)

End point title	Immunogenicity Endpoint: Geometric Mean Titer (GMT) and GMT Ratio of Hemagglutination Inhibition (HI) Antibodies at Day 22 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains (PPS Immunogenicity)
End point description:	
The GMT ratio is defined as the geometric mean of the postvaccination HI titer for Comparator QIV over the geometric mean of the postvaccination HI titer for aQIV. Adjusted GMTs are presented.	
End point type	Primary
End point timeframe:	
Day 22	

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	983	985		
Units: titer				
geometric mean (confidence interval 95%)				
A/H1N1	731.90 (689.39 to 777.04)	586.85 (552.83 to 622.96)		
A/H3N2	347.89 (324.78 to 372.64)	313.16 (292.42 to 335.36)		
B/Yamagata	154.40 (146.80 to 162.40)	145.74 (138.57 to 153.27)		
B/Victoria	144.41 (136.97 to 152.26)	143.32 (135.97 to 151.07)		

Statistical analyses

Statistical analysis title	GMT Ratio / A/H1N1
Statistical analysis description:	
GMT ratio of HI antibodies at Day 22 for the A/H1N1 vaccine strain	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1968
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	GMT ratio
Point estimate	0.802
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.738
upper limit	0.871

Notes:

[1] - Non-inferiority criteria for the GMT ratio: upper limit (UL) of the 95% confidence interval (CI) for the inter-group GMT ratio is ≤1.5 for each vaccine strain

Statistical analysis title	GMT Ratio / A/H3N2
Statistical analysis description:	
GMT ratio of HI antibodies at Day 22 for the A/H3N2 vaccine strain	
Comparison groups	Comparator QIV v aQIV
Number of subjects included in analysis	1968
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	GMT ratio
Point estimate	0.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.819
upper limit	0.989

Notes:

[2] - Non-inferiority criteria for the GMT ratio: UL of the 95% CI for the inter-group GMT ratio is ≤1.5 for each vaccine strain

Statistical analysis title	GMT Ratio / B/Yamagata

Statistical analysis description:

GMT ratio of HI antibodies at Day 22 for the B/Yamagata vaccine strain

Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1968
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	GMT ratio
Point estimate	0.944
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.012

Notes:

[3] - Non-inferiority criteria for the GMT ratio: UL of the 95% CI for the inter-group GMT ratio is ≤1.5 for each vaccine strain

Statistical analysis title	GMT Ratio / B/Victoria

Statistical analysis description:

GMT ratio of HI antibodies at Day 22 for the B/Victoria vaccine strain

Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1968
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	GMT ratio
Point estimate	0.992
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.923
upper limit	1.067

Notes:

[4] - Non-inferiority criteria for the GMT ratio: UL of the 95% CI for the inter-group GMT ratio is ≤1.5 for each vaccine strain

Primary: Immunogenicity Endpoint: Seroconversion Rate (SCR) and SCR Difference for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains (PPS Immunogenicity)

End point title	Immunogenicity Endpoint: Seroconversion Rate (SCR) and SCR Difference for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains (PPS Immunogenicity)

End point description:

The SCR defined as the percentage of subjects with either a prevaccination HI titer <1:10 and a postvaccination (Day 22) HI titer ≥1:40, or with either a prevaccination HI titer ≥1:10 and a ≥4-fold

increase in postvaccination HI titer.
The SCR difference is defined as the Comparator QIV SCR minus the aQIV SCR.

End point type	Primary

End point timeframe:

Day 1 to Day 22

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	983	985		
Units: percentage of participants				
number (confidence interval 95%)				
A/H1N1	81.2 (78.57 to 83.58)	76.8 (74.04 to 79.42)		
A/H3N2	63.6 (60.46 to 66.63)	61.8 (58.61 to 64.82)		
B/Yamagata	43.4 (40.27 to 46.60)	41.0 (37.92 to 44.19)		
B/Victoria	44.5 (41.39 to 47.74)	40.6 (37.52 to 43.76)		

Statistical analyses

Statistical analysis title	SCR Difference / A/H1N1

Statistical analysis description:

SCR difference at Day 22 for the A/H1N1 vaccine strain

Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1968
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	SCR difference
Point estimate	-4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.97
upper limit	-0.74

Notes:

[5] - Non-inferiority criteria for the SCR difference: UL of the 95% CI for the difference in SCR is ≤10% for each vaccine strain

Statistical analysis title	SCR Difference / A/H3N2

Statistical analysis description:

SCR difference at Day 22 for the A/H3N2 vaccine strain

Comparison groups	aQIV v Comparator QIV

Number of subjects included in analysis	1968
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	SCR difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.14
upper limit	2.48

Notes:

[6] - Non-inferiority criteria for the SCR difference: UL of the 95% CI for the difference in SCR is ≤10% for each vaccine strain

Statistical analysis title	SCR Difference / B/Yamagata

Statistical analysis description:

SCR difference at Day 22 for the B/Yamagata vaccine strain

Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1968
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	SCR difference
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.77
upper limit	2

Notes:

[7] - Non-inferiority criteria for the SCR difference: UL of the 95% CI for the difference in SCR is ≤10% for each vaccine strain

Statistical analysis title	SCR Difference / B/Victoria

Statistical analysis description:

SCR difference at Day 22 for the B/Victoria vaccine strain

Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1968
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	SCR difference
Point estimate	-3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.31
upper limit	0.45

Notes:

[8] - Non-inferiority criteria for the SCR difference: UL of the 95% CI for the difference in SCR is ≤10% for each vaccine strain

Primary: Immunogenicity Endpoint: GMT and GMT Ratio of HI Antibodies at Day 22 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains (FAS Immunogenicity)

End point title	Immunogenicity Endpoint: GMT and GMT Ratio of HI Antibodies at Day 22 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains (FAS Immunogenicity)

End point description:

The GMT ratio is defined as the geometric mean of the postvaccination HI titer for Comparator QIV over the geometric mean of the postvaccination HI titer for aQIV. Adjusted GMTs are presented.

End point type	Primary

End point timeframe:

Day 22

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1027	1016		
Units: titer				
geometric mean (confidence interval 95%)				
A/H1N1	729.17 (687.51 to 773.36)	589.07 (555.25 to 624.94)		
A/H3N2	347.09 (324.44 to 371.33)	315.69 (295.04 to 337.79)		
B/Yamagata	155.19 (147.67 to 163.09)	146.89 (139.74 to 154.40)		
B/Victoria	143.73 (136.44 to 151.42)	143.74 (136.42 to 151.45)		

Statistical analyses

Statistical analysis title	GMT Ratio / A/H1N1

Statistical analysis description:

GMT ratio of HI antibodies at Day 22 for the A/H1N1 vaccine strain

Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	2043
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	GMT ratio
Point estimate	0.808
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.745
upper limit	0.876

Statistical analysis title	GMT Ratio / A/H3N2

Statistical analysis description:	
GMT ratio of HI antibodies at Day 22 for the A/H3N2 vaccine strain	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	2043
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	GMT ratio
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.829
upper limit	0.998

Statistical analysis title	GMT Ratio / B/Yamagata
Statistical analysis description:	
GMT ratio of HI antibodies at Day 22 for the B/Yamagata vaccine strain	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	2043
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	GMT ratio
Point estimate	0.947
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.884
upper limit	1.014

Statistical analysis title	GMT Ratio / B/Victoria
Statistical analysis description:	
GMT ratio of HI antibodies at Day 22 for the B/Victoria vaccine strain	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	2043
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	GMT ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.931
upper limit	1.075

Secondary: Immunogenicity Endpoint: GMT and GMT Ratio of HI Antibodies at Day 181 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains (FAS Immunogenicity)

End point title	Immunogenicity Endpoint: GMT and GMT Ratio of HI Antibodies at Day 181 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains (FAS Immunogenicity)

End point description:

The GMT ratio is defined as the geometric mean of the postvaccination HI titer for Comparator QIV over the geometric mean of the postvaccination HI titer for aQIV. Adjusted GMTs are presented.

End point type	Secondary

End point timeframe:

Day 181

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1027	1016		
Units: titer				
geometric mean (confidence interval 95%)				
A/H1N1	351.73 (331.61 to 373.06)	306.11 (288.62 to 324.66)		
A/H3N2	165.17 (155.85 to 175.05)	157.34 (148.48 to 166.73)		
B/Yamagata	83.42 (79.81 to 87.20)	84.53 (80.87 to 88.36)		
B/Victoria	79.51 (75.81 to 83.40)	81.73 (77.92 to 85.72)		

Statistical analyses

Statistical analysis title	GMT Ratio / A/H1N1

Statistical analysis description:

GMT ratio of HI antibodies at Day 181 for the A/H1N1 vaccine strain

Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	2043
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.803
upper limit	0.944

Statistical analysis title	GMT Ratio / A/H3N2
Statistical analysis description: GMT ratio of HI antibodies at Day 181 for the A/H3N2 vaccine strain	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	2043
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.953
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.032

Statistical analysis title	GMT Ratio / B/Yamagata
Statistical analysis description: GMT ratio of HI antibodies at Day 181 for the B/Yamagata vaccine strain	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	2043
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	1.013
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.953
upper limit	1.077

Statistical analysis title	GMT Ratio / B/Victoria
Statistical analysis description: GMT ratio of HI antibodies at Day 181 for the B/Victoria vaccine strain	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	2043
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	1.028
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.963
upper limit	1.098

Secondary: Immunogenicity Endpoint: GMT of HI Antibodies on Day 1, Day 22, and Day 181 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains (FAS Immunogenicity)

End point title	Immunogenicity Endpoint: GMT of HI Antibodies on Day 1, Day 22, and Day 181 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains (FAS Immunogenicity)

End point description:

GMTs on Day 1 (prior to vaccination), Day 22 (3 weeks after vaccination), and Day 181 (6 months after vaccination) as determined by HI assay against each of the four vaccine strains. Unadjusted GMTs are presented.

End point type	Secondary

End point timeframe:

Day 1 to Day 181

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1027	1016		
Units: titer				
geometric mean (confidence interval 95%)				
A/H1N1 Day 1 GMT	54.37 (49.71 to 59.47)	50.41 (46.13 to 55.09)		
A/H1N1 Day 22 GMT	708.36 (666.39 to 752.98)	553.70 (519.14 to 590.56)		
A/H1N1 Day 181 GMT	330.76 (308.44 to 354.70)	276.24 (257.32 to 296.56)		
A/H3N2 Day 1 GMT	45.97 (42.06 to 50.25)	46.54 (42.63 to 50.81)		
A/H3N2 Day 22 GMT	323.40 (300.77 to 347.73)	292.50 (271.72 to 314.88)		
A/H3N2 Day 181 GMT	151.92 (141.27 to 163.37)	143.80 (133.33 to 155.09)		
B/Yamagata Day 1 GMT	38.50 (35.83 to 41.38)	38.33 (35.68 to 41.18)		
B/Yamagata Day 22 GMT	144.30 (136.02 to 153.08)	134.15 (126.31 to 142.48)		
B/Yamagata Day 181 GMT	76.87 (72.33 to 81.70)	77.34 (72.72 to 82.25)		
B/Victoria Day 1 GMT	36.24 (33.78 to 38.87)	37.06 (34.56 to 39.73)		
B/Victoria Day 22 GMT	134.45 (126.24 to 143.21)	132.45 (124.32 to 141.10)		
B/Victoria Day 181 GMT	74.17 (69.66 to 78.97)	75.99 (71.42 to 80.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: Geometric Mean Fold Increase (GMFI) for Day 22/Day 1 and Day 181/Day 1 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains (FAS Immunogenicity)

End point title	Immunogenicity Endpoint: Geometric Mean Fold Increase (GMFI) for Day 22/Day 1 and Day 181/Day 1 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains (FAS Immunogenicity)

End point description:

The GMFI is defined as the geometric mean of the fold increase of postvaccination HI titer over the prevaccination HI titer.

End point type	Secondary

End point timeframe:

Day 1 to Day 181

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1027	1016		
Units: fold increase				
geometric mean (confidence interval 95%)				
A/H1N1 Fold increase Day 22 HI Titer	13.07 (11.92 to 14.34)	11.00 (10.07 to 12.02)		
A/H1N1 Fold increase Day 181 HI Titer	6.22 (5.71 to 6.76)	5.47 (5.03 to 5.95)		
A/H3N2 Fold increase Day 22 HI Titer	7.09 (6.43 to 7.83)	6.31 (5.78 to 6.89)		
A/H3N2 Fold increase Day 181 HI Titer	3.29 (3.04 to 3.56)	3.08 (2.86 to 3.31)		
B/Yamagata Fold increase Day 22 HI Titer	3.77 (3.50 to 4.07)	3.50 (3.25 to 3.77)		
B/Yamagata Fold increase Day 181 HI Titer	2.03 (1.91 to 2.16)	2.01 (1.89 to 2.14)		
B/Victoria Fold increase Day 22 HI Titer	3.73 (3.45 to 4.02)	3.60 (3.33 to 3.88)		
B/Victoria Fold increase Day 181 HI Titer	2.06 (1.93 to 2.19)	2.05 (1.92 to 2.20)		

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: The Percentage of Subjects With a Titer ≥1:40 at Day 1, Day 22, and Day 181 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains (FAS Immunogenicity)

End point title	Immunogenicity Endpoint: The Percentage of Subjects With a Titer ≥1:40 at Day 1, Day 22, and Day 181 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains (FAS Immunogenicity)

End point description:

Percentage of subjects with a titer ≥1:40 on Day 1, Day 22, and Day 181 as determined by HI assay against each of the four vaccine strains

End point type	Secondary

End point timeframe:

Day 1 to Day 181

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1027	1016		
Units: percentage of participants				
number (confidence interval 95%)				
A/H1N1 HI Titer ≥1:40 at Day 1	65.2 (62.20 to 68.15)	64.2 (61.14 to 67.15)		
A/H1N1 HI Titer ≥1:40 at Day 22	99.7 (99.14 to 99.94)	99.2 (98.44 to 99.66)		
A/H1N1 HI Titer ≥1:40 at Day 181	98.2 (97.13 to 98.92)	96.3 (94.89 to 97.36)		
A/H3N2 HI Titer ≥1:40 at Day 1	60.3 (57.16 to 63.30)	61.7 (58.61 to 64.72)		
A/H3N2 HI Titer ≥1:40 at Day 22	97.5 (96.39 to 98.40)	97.3 (96.12 to 98.23)		
A/H3N2 HI Titer ≥1:40 at Day 181	92.0 (90.08 to 93.59)	89.9 (87.81 to 91.68)		
B/Yamagata HI Titer ≥1:40 at Day 1	60.8 (57.77 to 63.87)	61.9 (58.81 to 64.90)		
B/Yamagata HI Titer ≥1:40 at Day 22	95.9 (94.47 to 97.01)	94.6 (93.05 to 95.94)		
B/Yamagata HI Titer ≥1:40 at Day 181	83.9 (81.48 to 86.17)	84.0 (81.60 to 86.28)		
B/Victoria HI Titer ≥1:40 at Day 1	58.5 (55.42 to 61.57)	60.4 (57.30 to 63.43)		
B/Victoria HI Titer ≥1:40 at Day 22	94.4 (92.79 to 95.72)	93.3 (91.63 to 94.81)		
B/Victoria HI Titer ≥1:40 at Day 181	83.4 (80.90 to 85.66)	84.3 (81.84 to 86.48)		

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: SCR at Day 22 and Day 181 for the A/H1N1,

A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains (FAS Immunogenicity)

End point title	Immunogenicity Endpoint: SCR at Day 22 and Day 181 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains (FAS Immunogenicity)

End point description:

The SCR defined as the percentage of subjects with either a prevaccination HI titer <1:10 and a postvaccination (Day 22 or Day 181) HI titer ≥1:40, or with either a prevaccination HI titer ≥1:10 and a ≥4-fold increase in postvaccination HI titer.

End point type	Secondary

End point timeframe:

Day 1 to Day 181

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1027	1016		
Units: percentage of participants				
number (confidence interval 95%)				
A/H1N1 Day 22 SCR	80.8 (78.24 to 83.20)	77.1 (74.34 to 79.65)		
A/H1N1 Day 181 SCR	64.5 (61.46 to 67.55)	56.1 (52.94 to 59.24)		
A/H3N2 Day 22 SCR	63.4 (60.35 to 66.42)	61.8 (58.65 to 64.79)		
A/H3N2 Day 181 SCR	39.4 (36.28 to 42.54)	38.6 (35.51 to 41.72)		
B/Yamagata Day 22 SCR	42.9 (39.82 to 46.02)	41.1 (37.99 to 44.19)		
B/Yamagata Day 181 SCR	22.4 (19.82 to 25.16)	22.4 (19.86 to 25.19)		
B/Victoria Day 22 SCR	43.9 (40.86 to 47.08)	40.6 (37.50 to 43.68)		
B/Victoria Day 181 SCR	24.3 (21.64 to 27.13)	23.6 (20.97 to 26.38)		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Endpoint: Solicited Local and Systemic AEs for 7 Days Following Vaccination (Solicited Safety Set)

End point title	Safety Endpoint: Solicited Local and Systemic AEs for 7 Days Following Vaccination (Solicited Safety Set)

End point description:

Percentage of subjects with solicited local and systemic AEs occurring for 7 days following vaccination

End point type	Secondary

End point timeframe:

Day 1 through Day 7

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1020	1008		
Units: percentage of subjects				
number (not applicable)				
Any Solicited AEs	65.9	53.7		
Any Solicited Local AEs	49.8	30.4		
Any Solicited Systemic AEs	45.3	40.0		
Analgesic/Antipyretic Use	12.9	9.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Endpoint: All Unsolicited AEs for 21 Days Following Vaccination (Unsolicited Safety Set)

End point title	Safety Endpoint: All Unsolicited AEs for 21 Days Following Vaccination (Unsolicited Safety Set)

End point description:

The percentage of subjects with at least one unsolicited AE occurring 21 days following vaccination
The severity of AEs is based on the maximum severity associated with a Preferred Term for a reported AE. Related AEs include possibly related AEs, probably related AEs and AEs with missing relatedness assessment. The severity and relatedness of AEs were determined by the investigator. For the any AE summary by severity, a subject with multiple AEs is counted according to the highest severity of their reported AEs.

End point type	Secondary

End point timeframe:

Day 1 through Day 22

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1027	1016		
Units: percentage of subjects				
number (not applicable)				
Any AE	16.5	16.9		
Any AE (Mild)	11.3	11.3		
Any AE (Moderate)	5.0	4.9		
Any AE (Severe)	0.2	0.7		
Related AE	3.2	3.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Endpoint: Serious Adverse Events (SAEs), Adverse Events (AEs) Leading to Withdrawal From the Study, and Adverse Events of Special Interest (AESIs)

End point title	Safety Endpoint: Serious Adverse Events (SAEs), Adverse Events (AEs) Leading to Withdrawal From the Study, and Adverse Events of Special Interest (AESIs)

End point description:

The percentage of subjects with any SAE, AE leading to withdrawal, or AESI during the study period

End point type	Secondary

End point timeframe:

Day 1 through Day 271

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1027	1016		
Units: percentage of subjects				
number (not applicable)				
SAE	3.0	3.1		
Related SAE	0	0.1		
AE leading to study withdrawal	0	0.1		
AESI	0.2	0		
Death	0.1	0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Immunogenicity Endpoint: GMT and GMT Ratio of HI Antibodies at Day 22 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains by Age (Subgroup Analysis: 50 to 59 years) (FAS Immunogenicity)

End point title	Immunogenicity Endpoint: GMT and GMT Ratio of HI Antibodies at Day 22 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains by Age (Subgroup Analysis: 50 to 59 years) (FAS Immunogenicity)

End point description:

The GMT ratio is defined as the geometric mean of the postvaccination HI titer for Comparator QIV over the geometric mean of the postvaccination HI titer for aQIV. Subgroup analysis by age (50 to 59 years; 60 to 64 years). Adjusted GMTs for the 50 to 59 years age subgroup are presented.

End point type	Other pre-specified

End point timeframe:

Day 22

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	609	595		
Units: titer				
geometric mean (confidence interval 95%)				
A/H1N1 (50 to 59 years)	674.25 (622.70 to 730.07)	565.33 (521.77 to 612.53)		
A/H3N2 (50 to 59 years)	345.83 (317.55 to 376.63)	319.55 (293.19 to 348.27)		
B/Yamagata (50 to 59 years)	161.27 (150.98 to 172.25)	149.36 (139.72 to 159.67)		
B/Victoria (50 to 59 years)	167.60 (156.68 to 179.27)	165.81 (154.92 to 177.47)		

Statistical analyses

Statistical analysis title	GMT Ratio / A/H1N1 (50 to 59 years)
Statistical analysis description: GMT ratio of HI antibodies at Day 22 for the A/H1N1 vaccine strain	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1204
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.838
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.751
upper limit	0.936

Statistical analysis title	GMT Ratio / A/H3N2 (50 to 59 years)
Statistical analysis description: GMT ratio of HI antibodies at Day 22 for the A/H3N2 vaccine strain	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1204
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.924

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.821
upper limit	1.04

Statistical analysis title	GMT Ratio / B/Yamagata (50 to 59 years)
Statistical analysis description:	
GMT ratio of HI antibodies at Day 22 for the B/Yamagata vaccine strain	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1204
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.926
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.845
upper limit	1.015

Statistical analysis title	GMT Ratio / B/Victoria (50 to 59 years)
Statistical analysis description:	
GMT ratio of HI antibodies at Day 22 for the B/Victoria vaccine strain	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1204
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.989
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.901
upper limit	1.087

Other pre-specified: Immunogenicity Endpoint: GMT and GMT Ratio of HI Antibodies at Day 22 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains by Age (Subgroup Analysis: 60 to 64 years) (FAS Immunogenicity)

End point title	Immunogenicity Endpoint: GMT and GMT Ratio of HI Antibodies at Day 22 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains by Age (Subgroup Analysis: 60 to 64 years) (FAS Immunogenicity)

End point description:

The GMT ratio is defined as the geometric mean of the postvaccination HI titer for Comparator QIV over

the geometric mean of the postvaccination HI titer for aQIV. Subgroup analysis by age (50 to 59 years; 60 to 64 years). Adjusted GMTs for the 60 to 64 years age subgroup are presented.

End point type	Other pre-specified

End point timeframe:

Day 22

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	418	421		
Units: titer				
geometric mean (confidence interval 95%)				
A/H1N1 (60 to 64 years)	806.65 (740.51 to 878.70)	618.90 (567.97 to 674.41)		
A/H3N2 (60 to 64 years)	348.59 (312.82 to 388.45)	310.23 (278.52 to 345.54)		
B/Yamagata (60 to 64 years)	148.20 (137.62 to 159.59)	144.34 (134.10 to 155.36)		
B/Victoria (60 to 64 years)	119.64 (110.33 to 129.75)	121.16 (111.79 to 131.32)		

Statistical analyses

Statistical analysis title	GMT Ratio / A/H1N1 (60 to 64 years)

Statistical analysis description:

GMT ratio of HI antibodies at Day 22 for the A/H1N1 vaccine strain

Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	839
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.767
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.681
upper limit	0.864

Statistical analysis title	GMT Ratio / A/H3N2 (60 to 64 years)

Statistical analysis description:

GMT ratio of HI antibodies at Day 22 for the A/H3N2 vaccine strain

Comparison groups	aQIV v Comparator QIV

Number of subjects included in analysis	839
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.766
upper limit	1.033

Statistical analysis title	GMT Ratio / B/Yamagata (60 to 64 years)
Statistical analysis description:	
GMT ratio of HI antibodies at Day 22 for the B/Yamagata vaccine strain	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	839
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.974
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.879
upper limit	1.079

Statistical analysis title	GMT Ratio / B/Victoria (60 to 64 years)
Statistical analysis description:	
GMT ratio of HI antibodies at Day 22 for the B/Victoria vaccine strain	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	839
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	1.013
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.905
upper limit	1.133

Other pre-specified: Immunogenicity Endpoint: GMT and GMT Ratio of HI Antibodies at Day 22 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains by Influenza Vaccination History (Subgroup Analysis: yes) (FAS Immunogenicity)

End point title	Immunogenicity Endpoint: GMT and GMT Ratio of HI Antibodies at Day 22 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains by Influenza Vaccination History (Subgroup Analysis: yes) (FAS Immunogenicity)

End point description:

The GMT ratio is defined as the geometric mean of the postvaccination HI titer for Comparator QIV over the geometric mean of the postvaccination HI titer for aQIV. Subgroup analysis by influenza vaccination history (received at least one influenza vaccination within the previous 3 influenza seasons: yes; no). Adjusted GMTs for subjects who received at least one influenza vaccination within the previous 3 influenza seasons (yes) are presented.

End point type	Other pre-specified

End point timeframe:

Day 22

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	586	598		
Units: titer				
geometric mean (confidence interval 95%)				
A/H1N1 (previous influenza vaccination - yes)	648.75 (601.45 to 699.78)	547.54 (508.79 to 589.24)		
A/H3N2 (previous influenza vaccination - yes)	279.61 (257.70 to 303.38)	282.44 (260.95 to 305.71)		
B/Yamagata (previous influenza vaccination - yes)	116.48 (110.62 to 122.65)	110.37 (104.98 to 116.04)		
B/Victoria (previous influenza vaccination - yes)	101.89 (96.50 to 107.59)	101.59 (96.39 to 107.07)		

Statistical analyses

Statistical analysis title	GMT Ratio / A/H1N1 (yes)

Statistical analysis description:

GMT ratio of HI antibodies at Day 22 for the A/H1N1 vaccine strain (previous influenza vaccination - yes)

Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1184
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.844
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.761
upper limit	0.935

Statistical analysis title	GMT Ratio / A/H3N2 (yes)

Statistical analysis description:

GMT ratio of HI antibodies at Day 22 for the A/H3N2 vaccine strain (previous influenza vaccination - yes)

Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1184
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.904
upper limit	1.128

Statistical analysis title	GMT Ratio / B/Yamagata (yes)

Statistical analysis description:

GMT ratio of HI antibodies at Day 22 for the B/Yamagata vaccine strain (previous influenza vaccination - yes)

Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1184
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.948
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.883
upper limit	1.016

Statistical analysis title	GMT Ratio / B/Victoria (yes)

Statistical analysis description:

GMT ratio of HI antibodies at Day 22 for the B/Victoria vaccine strain (previous influenza vaccination - yes)

Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1184
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.997

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.926
upper limit	1.073

Other pre-specified: Immunogenicity Endpoint: GMT and GMT Ratio of HI Antibodies at Day 22 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains by Influenza Vaccination History (Subgroup Analysis: no) (FAS Immunogenicity)

End point title	Immunogenicity Endpoint: GMT and GMT Ratio of HI Antibodies at Day 22 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains by Influenza Vaccination History (Subgroup Analysis: no) (FAS Immunogenicity)

End point description:

The GMT ratio is defined as the geometric mean of the postvaccination HI titer for Comparator QIV over the geometric mean of the postvaccination HI titer for aQIV. Subgroup analysis by influenza vaccination history (received at least one influenza vaccination within the previous 3 influenza seasons: yes; no). Adjusted GMTs for subjects who did not receive at least one influenza vaccination within the previous 3 influenza seasons (no) are presented.

End point type	Other pre-specified

End point timeframe:

Day 22

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	441	418		
Units: titer				
geometric mean (confidence interval 95%)				
A/H1N1 (previous influenza vaccination - no)	755.46 (688.45 to 829.00)	582.90 (529.83 to 641.28)		
A/H3N2 (previous influenza vaccination - no)	389.77 (347.94 to 436.63)	312.38 (277.97 to 351.06)		
B/Yamagata (previous influenza vaccination - no)	188.78 (172.28 to 206.85)	178.45 (162.38 to 196.12)		
B/Victoria (previous influenza vaccination - no)	185.31 (168.62 to 203.65)	186.65 (169.30 to 205.78)		

Statistical analyses

Statistical analysis title	GMT Ratio / A/H1N1 (no)

Statistical analysis description:

GMT ratio of HI Antibodies at Day 22 for the A/H1N1 vaccine strain (previous influenza vaccination - no)

Comparison groups	aQIV v Comparator QIV

Number of subjects included in analysis	859
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.772
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.677
upper limit	0.88

Statistical analysis title	GMT Ratio / A/H3N2 (no)
Statistical analysis description:	
GMT ratio of HI Antibodies at Day 22 for the A/H3N2 vaccine strain (previous influenza vaccination - no)	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	859
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.801
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.683
upper limit	0.941

Statistical analysis title	GMT Ratio / B/Yamagata (no)
Statistical analysis description:	
GMT ratio of HI Antibodies at Day 22 for the B/Yamagata vaccine strain (previous influenza vaccination - no)	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	859
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.945
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.831
upper limit	1.076

Statistical analysis title	GMT Ratio / B/Victoria (no)

Statistical analysis description:	
GMT ratio of HI Antibodies at Day 22 for the B/Victoria vaccine strain (previous influenza vaccination - no)	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	859
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	1.007
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.881
upper limit	1.151

Other pre-specified: Immunogenicity Endpoint: GMT and GMT Ratio of HI Antibodies at Day 22 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains by Comorbidity Risk Score (Subgroup Analysis: <50) (FAS Immunogenicity)

End point title	Immunogenicity Endpoint: GMT and GMT Ratio of HI Antibodies at Day 22 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains by Comorbidity Risk Score (Subgroup Analysis: <50) (FAS Immunogenicity)
End point description:	
The GMT ratio is defined as the geometric mean of the postvaccination HI titer for Comparator QIV over the geometric mean of the postvaccination HI titer for aQIV. Subgroup analysis by comorbidity risk score (<50; ≥50). Adjusted GMTs for subjects with a comorbidity risk score <50 are presented.	
End point type	Other pre-specified
End point timeframe:	
Day 22	

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	912	918		
Units: titer				
geometric mean (confidence interval 95%)				
A/H1N1 (Comorbidity Risk Score <50)	715.26 (671.75 to 761.60)	586.42 (550.95 to 624.16)		
A/H3N2 (Comorbidity Risk Score <50)	337.43 (314.06 to 362.53)	314.75 (293.14 to 337.96)		
B/Yamagata (Comorbidity Risk Score <50)	150.17 (142.37 to 158.40)	145.98 (138.44 to 153.93)		
B/Victoria (Comorbidity Risk Score <50)	139.76 (132.15 to 147.82)	141.58 (133.93 to 149.68)		

Statistical analyses

Statistical analysis title	GMT Ratio / A/H1N1 (<50)
Statistical analysis description: GMT ratio of HI antibodies at Day 22 for the A/H1N1 vaccine strain (Comorbidity Risk Score <50)	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1830
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.752
upper limit	0.894

Statistical analysis title	GMT Ratio / A/H3N2 (<50)
Statistical analysis description: GMT ratio of HI antibodies at Day 22 for the A/H3N2 vaccine strain (Comorbidity Risk Score <50)	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1830
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.933
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.846
upper limit	1.029

Statistical analysis title	GMT Ratio / B/Yamagata (<50)
Statistical analysis description: GMT ratio of HI antibodies at Day 22 for the B/Yamagata vaccine strain (Comorbidity Risk Score <50)	
Comparison groups	aQIV v Comparator QIV

Number of subjects included in analysis	1830
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.972
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.904
upper limit	1.046

Statistical analysis title	GMT Ratio / B/Victoria (<50)
Statistical analysis description:	
GMT ratio of HI antibodies at Day 22 for the B/Victoria vaccine strain (Comorbidity Risk Score <50)	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	1830
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	1.013
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.938
upper limit	1.094

Other pre-specified: Immunogenicity Endpoint: GMT and GMT Ratio of HI Antibodies at Day 22 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains by Comorbidity Risk Score (Subgroup Analysis: ≥50) (FAS Immunogenicity)

End point title	Immunogenicity Endpoint: GMT and GMT Ratio of HI Antibodies at Day 22 for the A/H1N1, A/H3N2, B/Yamagata, and B/Victoria Vaccine Strains by Comorbidity Risk Score (Subgroup Analysis: ≥50) (FAS Immunogenicity)
End point description:	
The GMT ratio is defined as the geometric mean of the postvaccination HI titer for Comparator QIV over the geometric mean of the postvaccination HI titer for aQIV. Subgroup analysis by comorbidity risk score (<50; ≥50). Adjusted GMTs for subjects with a comorbidity risk score ≥50 are presented.	
End point type	Other pre-specified
End point timeframe:	
Day 22	

End point values	aQIV	Comparator QIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	98		
Units: titer				
geometric mean (confidence interval 95%)				
A/H1N1 (Comorbidity Risk Score ≥50)	812.59 (681.59 to 968.76)	573.86 (473.11 to 696.06)		
A/H3N2 (Comorbidity Risk Score ≥50)	453.60 (368.59 to 558.20)	333.16 (265.15 to 418.62)		
B/Yamagata (Comorbidity Risk Score ≥50)	198.10 (172.89 to 227.00)	153.05 (131.91 to 177.58)		
B/Victoria (Comorbidity Risk Score ≥50)	174.79 (151.43 to 201.74)	158.12 (135.26 to 184.85)		

Statistical analyses

Statistical analysis title	GMT Ratio / A/H1N1 (≥50)
Statistical analysis description: GMT ratio of HI antibodies at Day 22 for the A/H1N1 vaccine strain (Comorbidity Risk Score ≥50)	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.706
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.553
upper limit	0.902

Statistical analysis title	GMT Ratio / A/H3N2 (≥50)
Statistical analysis description: GMT ratio of HI antibodies at Day 22 for the A/H3N2 vaccine strain (Comorbidity Risk Score ≥50)	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.734

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.549
upper limit	0.982

Statistical analysis title	GMT Ratio / B/Yamagata (≥50)
Statistical analysis description:	
GMT ratio of HI antibodies at Day 22 for the B/Yamagata vaccine strain (Comorbidity Risk Score ≥50)	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.773
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.638
upper limit	0.935

Statistical analysis title	GMT Ratio / B/Victoria (≥50)
Statistical analysis description:	
GMT ratio of HI antibodies at Day 22 for the B/Victoria vaccine strain (Comorbidity Risk Score ≥50)	
Comparison groups	aQIV v Comparator QIV
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.905
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.739
upper limit	1.107

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
SAEs: Day 1 through Day 271; nonserious unsolicited AEs: Day 1 through Day 22	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	aQIV
Reporting group description:	
Adjuvanted QIV containing 2 influenza type A strains and 2 influenza type B strains	
Reporting group title	Comparator QIV
Reporting group description:	
Non-adjuvanted comparator QIV containing 2 influenza type A strains and 2 influenza type B strains	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No nonserious unsolicited AEs were reported at a frequency >5% in either vaccine group during the study.

Serious adverse events	aQIV	Comparator QIV	
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 1027 (3.02%)	31 / 1016 (3.05%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial adenocarcinoma			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Follicular lymphoma			

subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic neoplasm			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Huerthle cell carcinoma			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip and/or oral cavity cancer			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasmacytoma			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			

subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (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			
Adverse drug reaction			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 1027 (0.10%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia pain			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergy to metals			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst			

subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal prolapse			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (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			
Haemothorax			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary thrombosis			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conversion disorder			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Psychiatric decompensation			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (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			
Alcohol poisoning			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder injury			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb crushing injury			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Road traffic accident			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scapula fracture			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 1027 (0.19%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 1027 (0.10%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	1 / 1027 (0.10%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 1027 (0.00%)	2 / 1016 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Cerebellar stroke			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Middle ear adhesions			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum			
subjects affected / exposed	2 / 1027 (0.19%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Intestinal obstruction			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 1027 (0.10%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (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			
Osteoarthritis			
subjects affected / exposed	2 / 1027 (0.19%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			

subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess limb			
subjects affected / exposed	1 / 1027 (0.10%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	3 / 1027 (0.29%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			

subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 1027 (0.00%)	1 / 1016 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Ketoacidosis			
subjects affected / exposed	1 / 1027 (0.10%)	0 / 1016 (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: 5 %

Non-serious adverse events	aQIV	Comparator QIV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1027 (0.00%)	0 / 1016 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 November 2021	Version 1.0 to Version 2.0 The main reasons for the protocol amendment were the following: 1. Updating of the CI for secondary objectives 2a and 2b to reflect the correct alpha. 2. Conducting database lock and unblinding in two stages to allow expedited CSR reporting. A Blinding Maintenance Plan was prepared to ensure blinding of relevant laboratory and statistical personnel was maintained until their activities had been completed. 3. Clarification of Exclusion Criteria #7b and #9, based on regulatory agency feedback. 4. Clarifications of reporting requirements for solicited AEs that start during Day 1-7 and continue beyond Day 14. 5. Correction of how the FAS would be analyzed in case of vaccination errors, based on regulatory agency feedback.
11 July 2022	Version 2.0 to Version 3.0 The main reasons for the protocol amendment were the following: 1. Reclassification of the secondary objective of immunogenicity persistence at 9 months after vaccination (Day 271) as an exploratory objective in order to expedite the primary and secondary immunogenicity results and report them with the complete safety data to support timely license applications in different regions. 2. Improvement in the definition of previous influenza vaccination as a stratification factor to consider subjects who had received an influenza vaccination in the previous 3 influenza seasons as previously vaccinated subjects (Yes) in order to acknowledge variability in timing of the annual influenza vaccination campaigns. 3. Correction of an inconsistency in the assessment and reporting of local solicited reactions to consider local events as being present if they measured ≥25 mm to ensure consistency with the approved labeling information for aQIV (Fluad Quadrivalent/Quad/Tetra).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported