Clinical trial results:
Immunogenicity and Safety of Quadrivalent Recombinant Influenza Vaccine (RIV4) in Children and Adolescents Aged 9 to 17 Years and Adults Aged 18 to 49 Years

Summary

EudraCT number	2022-000577-11
Trial protocol	ES PL DK CZ
Global end of trial date	27 October 2023

Results information

Result version number	v1 (current)
This version publication date	10 May 2024
First version publication date	10 May 2024

Trial information

Trial identification

Sponsor protocol code	VAP00027

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05513053
WHO universal trial number (UTN)	U1111-1260-4678

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur Inc.
Sponsor organisation address	Discovery Drive, Swiftwater, Pennsylvania, United States, 18370-0187
Public contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002418-PIP01-18
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	13 December 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 October 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferior hemagglutination inhibition (HAI) immune response of quadrivalent recombinant influenza vaccine (RIV4) for the 4 strains in participants aged 9 to 17 years vs participants aged 18 to 49 years.

Protection of trial subjects:

Vaccinations were performed by qualified and trained study personnel. Participants with allergy to any of the vaccine components were not vaccinated. After vaccination, participants were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment were also available on site in case of any immediate allergic reactions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 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	Czechia: 62
Country: Number of subjects enrolled	Poland: 91
Country: Number of subjects enrolled	Spain: 81
Country: Number of subjects enrolled	United States: 1074
Worldwide total number of subjects	1308
EEA total number of subjects	234

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)	200
Adolescents (12-17 years)	448

Adults (18-64 years)	660
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 36 investigational sites in 4 countries between 27 Oct 2022 to 27 Oct 2023.

Pre-assignment

Screening details:

A total of 1308 participants were enrolled in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Participants aged 9 to 17 years

Arm description:

Participants received a single intramuscular (IM) injection of RIV4 0.5 milliliter (mL) on Day 1.

Arm type	Experimental
Investigational medicinal product name	RIV4 season/2022-2023/NH
Investigational medicinal product code	
Other name	Supemtek, Flublok Quadrivalent
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

RIV4 0.5 mL was administered as a single IM injection in the deltoid muscle.

Arm title	Cohort 2: Participants aged 18 to 49 years

Arm description:

Participants received a single IM injection of RIV4 0.5 mL on Day 1.

Arm type	Experimental
Investigational medicinal product name	RIV4 season/2022-2023/NH
Investigational medicinal product code	
Other name	Supemtek, Flublok Quadrivalent
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

RIV4 0.5 mL was administered as a single IM injection in the deltoid muscle.

Number of subjects in period 1	Cohort 1: Participants aged 9 to 17 years	Cohort 2: Participants aged 18 to 49 years
Started	648	660
Completed	629	635
Not completed	19	25
Consent withdrawn by subject	2	9

Adverse event, non-fatal	-	2
Lost to follow-up	9	11
Withdrawal by parent/guardian	2	-
Protocol deviation	6	3

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: Participants aged 9 to 17 years
Reporting group description: Participants received a single intramuscular (IM) injection of RIV4 0.5 milliliter (mL) on Day 1.	
Reporting group title	Cohort 2: Participants aged 18 to 49 years
Reporting group description: Participants received a single IM injection of RIV4 0.5 mL on Day 1.	

Reporting group values	Cohort 1: Participants aged 9 to 17 years	Cohort 2: Participants aged 18 to 49 years	Total
Number of subjects	648	660	1308
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	13.0	34.3	
standard deviation	± 2.49	± 9.21	-
Gender Categorical Units: Subjects			
Female	312	395	707
Male	336	265	601
Race Units: Subjects			
American Indian or Alaska Native	5	1	6
Asian	1	6	7
Black or African American	157	98	255
Native Hawaiian or Other Pacific Islander	1	3	4
White	467	536	1003
Not Reported	0	2	2
Unknown	1	1	2
Multiple	16	13	29

End points

End points reporting groups

Reporting group title	Cohort 1: Participants aged 9 to 17 years
Reporting group description: Participants received a single intramuscular (IM) injection of RIV4 0.5 milliliter (mL) on Day 1.	
Reporting group title	Cohort 2: Participants aged 18 to 49 years
Reporting group description: Participants received a single IM injection of RIV4 0.5 mL on Day 1.	
Subject analysis set title	Cohort 1: Participants aged 9 to 17 years (Per Protocol)
Subject analysis set type	Per protocol
Subject analysis set description: Participants received a single IM injection of RIV4 0.5 mL on Day 1.	
Subject analysis set title	Cohort 2: Participants aged 18 to 49 years (Per Protocol)
Subject analysis set type	Per protocol
Subject analysis set description: Participants received a single IM injection of RIV4 0.5 mL on Day 1.	
Subject analysis set title	Cohort 1: Participants aged 9 to 17 years (Safety)
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received a single IM injection of RIV4 0.5 mL on Day 1.	
Subject analysis set title	Cohort 2: Participants aged 18 to 49 years (Safety)
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received a single IM injection of RIV4 0.5 mL on Day 1.	

Primary: Geometric Mean Titers (GMTs) Against Influenza Vaccine Antibodies at Day 29

End point title	Geometric Mean Titers (GMTs) Against Influenza Vaccine Antibodies at Day 29
End point description: GMTs of anti-influenza antibodies were measured using individual hemagglutination inhibition (HAI) assay for 4 influenza virus strains: A/H1N1, A/H3N2, B/Victoria, and B/Yamagata lineages. Titers were expressed in terms of 1/dilution. Analysis was performed on the Per-protocol analysis set (PPAS)-subset of full analysis set (FAS) which included participants who received 1 dose of the study vaccine and had a post-vaccination blood sample.	
End point type	Primary
End point timeframe: Day 29	

End point values	Cohort 1: Participants aged 9 to 17 years (Per Protocol)	Cohort 2: Participants aged 18 to 49 years (Per Protocol)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	609	606		
Units: titer				
geometric mean (confidence interval 95%)				

A/H1N1	1946 (1795 to 2109)	982 (881 to 1094)		
A/H3N2	1975 (1771 to 2202)	604 (531 to 687)		
B/Victoria	405 (362 to 452)	258 (233 to 285)		
B/Yamagata	1941 (1779 to 2118)	1593 (1477 to 1717)		

Statistical analyses

Statistical analysis title	Statistical analysis for A/H1N1
Comparison groups	Cohort 1: Participants aged 9 to 17 years (Per Protocol) v Cohort 2: Participants aged 18 to 49 years (Per Protocol)
Number of subjects included in analysis	1215
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio
Point estimate	1.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.73
upper limit	2.27

Statistical analysis title	Statistical analysis for A/H3N2
Comparison groups	Cohort 1: Participants aged 9 to 17 years (Per Protocol) v Cohort 2: Participants aged 18 to 49 years (Per Protocol)
Number of subjects included in analysis	1215
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio
Point estimate	3.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.76
upper limit	3.87

Statistical analysis title	Statistical analysis for B/Victoria
Comparison groups	Cohort 1: Participants aged 9 to 17 years (Per Protocol) v Cohort 2: Participants aged 18 to 49 years (Per Protocol)

Number of subjects included in analysis	1215
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio
Point estimate	1.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.35
upper limit	1.82

Statistical analysis title	Statistical analysis for B/Yamagata
Comparison groups	Cohort 1: Participants aged 9 to 17 years (Per Protocol) v Cohort 2: Participants aged 18 to 49 years (Per Protocol)
Number of subjects included in analysis	1215
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.09
upper limit	1.37

Primary: Percentage of Participants With Seroconversion for Influenza Vaccine Antibodies at Day 29

End point title	Percentage of Participants With Seroconversion for Influenza Vaccine Antibodies at Day 29

End point description:

Anti-influenza antibodies were measured using HAI assay for 4 influenza virus strains: A/H1N1, A/H3N2, B/Victoria, and B/Yamagata lineages. Seroconversion was defined as either a pre-vaccination titer less than (<) 1:10 (1/dilution) at Day 1 and a post-vaccination titer greater than or equal to (>=) 1: 40 (1/dilution) at Day 29 or a pre-vaccination titer >= 1:10 at Day 1 and a >= 4-fold increase in post-vaccination titer. Analysis was performed on the PPAS-subset of FAS which included participants who received 1 dose of the study vaccine and had a post-vaccination blood sample. Here 'n'= number of participants with available data for a particular category.

End point type	Primary

End point timeframe:

Day 29

End point values	Cohort 1: Participants aged 9 to 17 years (Per Protocol)	Cohort 2: Participants aged 18 to 49 years (Per Protocol)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	609	606		
Units: percentage of participants				
number (confidence interval 95%)				
A/H1N1 (n = 609, 606)	78.3 (74.8 to 81.5)	76.4 (72.8 to 79.7)		
A/H3N2 (n = 609, 606)	86.5 (83.6 to 89.1)	87.1 (84.2 to 89.7)		
B/Victoria (n = 609, 605)	76.8 (73.3 to 80.1)	73.6 (69.8 to 77.0)		
B/Yamagata (n = 609, 606)	77.2 (73.6 to 80.5)	62.9 (58.9 to 66.7)		

Statistical analyses

Statistical analysis title	Statistical analysis for A/H1N1
Comparison groups	Cohort 1: Participants aged 9 to 17 years (Per Protocol) v Cohort 2: Participants aged 18 to 49 years (Per Protocol)
Number of subjects included in analysis	1215
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Percent Difference
Point estimate	1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.78
upper limit	6.62

Statistical analysis title	Statistical analysis for B/Victoria
Comparison groups	Cohort 1: Participants aged 9 to 17 years (Per Protocol) v Cohort 2: Participants aged 18 to 49 years (Per Protocol)
Number of subjects included in analysis	1215
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Percent Difference
Point estimate	3.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.57
upper limit	8.14

Statistical analysis title	Statistical analysis for B/Yamagata
Comparison groups	Cohort 1: Participants aged 9 to 17 years (Per Protocol) v Cohort 2: Participants aged 18 to 49 years (Per Protocol)
Number of subjects included in analysis	1215
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Percent Difference
Point estimate	14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.17
upper limit	19.3

Statistical analysis title	Statistical analysis for A/H3N2
Comparison groups	Cohort 1: Participants aged 9 to 17 years (Per Protocol) v Cohort 2: Participants aged 18 to 49 years (Per Protocol)
Number of subjects included in analysis	1215
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Percent Difference
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.41
upper limit	3.23

Secondary: GMTs Against Influenza Vaccine Antibodies at Day 1

End point title	GMTs Against Influenza Vaccine Antibodies at Day 1

End point description:

GMTs of anti-influenza antibodies were measured using HAI assay for 4 influenza virus strains: A/H1N1, A/H3N2, B/Victoria, and B/Yamagata lineages. Titers were expressed in terms of 1/dilution. Analysis was performed on the PPAS-subset of FAS which included participants who received 1 dose of the study vaccine and had a post-vaccination blood sample. Here 'n'= number of participants with available data for a particular category.

End point type	Secondary

End point timeframe:

Pre-vaccination on Day 1

End point values	Cohort 1: Participants aged 9 to 17 years (Per Protocol)	Cohort 2: Participants aged 18 to 49 years (Per Protocol)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	609	606		
Units: titer				
geometric mean (confidence interval 95%)				
A/H1N1 (n = 609, 606)	154 (137 to 173)	74.9 (65.8 to 85.1)		
A/H3N2 (n = 609, 606)	111 (95.4 to 128)	29.0 (25.7 to 32.8)		
B/Victoria (n = 609, 605)	48.1 (43.0 to 53.8)	37.3 (34.0 to 40.9)		
B/Yamagata (n = 609, 606)	272 (243 to 305)	300 (269 to 335)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Detectable HAI Titers >=10 and >=40 (1/Dilution) for Influenza Vaccine Antibodies at Days 1 and 29

End point title	Percentage of Participants With Detectable HAI Titers >=10 and >=40 (1/Dilution) for Influenza Vaccine Antibodies at Days 1 and 29

End point description:

Antibody titers were measured using HAI assay for 4 influenza virus strains: A/H1N1, A/H3N2, B/Victoria, and B/Yamagata lineages. Percentage of participants with antibody titers >=10 and >=40 against influenza vaccine antibodies at Day 1 and Day 29 were reported in this outcome measure. Analysis was performed on the PPAS-subset of FAS which included participants who received 1 dose of the study vaccine and had a post-vaccination blood sample. Here 'n'= number of participants with available data for a particular category.

End point type	Secondary

End point timeframe:

Pre-vaccination on Day 1 and 28 days post-vaccination on Day 29

End point values	Cohort 1: Participants aged 9 to 17 years (Per Protocol)	Cohort 2: Participants aged 18 to 49 years (Per Protocol)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	609	606		
Units: percentage of participants				
number (confidence interval 95%)				
Titer >=10: A/H1N1: Day 1 (n = 609, 606)	97.0 (95.4 to 98.2)	89.8 (87.1 to 92.1)		
Titer >=10: A/H1N1: Day 29 (n = 609, 606)	100 (99.4 to 100)	99.3 (98.3 to 99.8)		

Titer >=40: A/H1N1: Day 1 (n = 609, 606)	87.2 (84.3 to 89.7)	71.8 (68.0 to 75.3)		
Titer >=40: A/H1N1: Day 29 (n = 609, 606)	99.7 (98.8 to 100)	97.5 (96.0 to 98.6)		
Titer >=10: A/H3N2: Day 1 (n = 609, 606)	89.2 (86.4 to 91.5)	77.7 (74.2 to 81.0)		
Titer >=10: A/H3N2: Day 29 (n = 609, 606)	100 (99.4 to 100)	99.7 (98.8 to 100)		
Titer >=40: A/H3N2: Day 1 (n = 609, 606)	74.7 (71.1 to 78.1)	45.0 (41.0 to 49.1)		
Titer >=40: A/H3N2: Day 29 (n = 609, 606)	99.0 (97.9 to 99.6)	95.0 (93.0 to 96.6)		
Titer >=10: B/Victoria: Day 1 (n = 609, 605)	92.1 (89.7 to 94.1)	91.7 (89.2 to 93.8)		
Titer >=10: B/Victoria: Day 29 (n = 609, 606)	99.5 (98.6 to 99.9)	99.8 (99.1 to 100)		
Titer >=40: B/Victoria: Day 1 (n = 609, 605)	61.4 (57.4 to 65.3)	59.8 (55.8 to 63.8)		
Titer >=40: B/Victoria: Day 29 (n = 609, 606)	95.6 (93.6 to 97.1)	97.0 (95.3 to 98.2)		
Titer >=10: B/Yamagata: Day 1 (n = 609, 606)	97.9 (96.4 to 98.9)	99.5 (98.6 to 99.9)		
Titer >=10: B/Yamagata: Day 29 (n = 609, 606)	100 (99.4 to 100)	100 (99.4 to 100)		
Titer >=40: B/Yamagata: Day 1 (n = 609, 606)	93.1 (90.8 to 95.0)	95.2 (93.2 to 96.8)		
Titer >=40: B/Yamagata: Day 29 (n = 609, 606)	99.5 (98.6 to 99.9)	100 (99.4 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titer Ratio (GMTR) of Influenza Vaccine Antibodies

End point title	Geometric Mean Titer Ratio (GMTR) of Influenza Vaccine Antibodies

End point description:

GMTR was the ratio of the individual titers post-vaccination over pre-vaccination. The GMTs were measured using HAI assay for 4 influenza virus strains: A/H1N1, A/H3N2, B/Victoria, and B/Yamagata lineages. Titers were expressed in terms of 1/dilution. Analysis was performed on the PPAS-subset of FAS which included participants who received 1 dose of the study vaccine and had a post-vaccination blood sample. Here 'n'= number of participants with available data for a particular category.

End point type	Secondary

End point timeframe:

Pre-vaccination on Day 1 and 28 days post-vaccination on Day 29

End point values	Cohort 1: Participants aged 9 to 17 years (Per Protocol)	Cohort 2: Participants aged 18 to 49 years (Per Protocol)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	609	606		
Units: ratio				

geometric mean (confidence interval 95%)				
A/H1N1 (n = 609, 606)	12.7 (11.1 to 14.5)	13.1 (11.4 to 15.0)		
A/H3N2 (n = 609, 606)	17.9 (15.7 to 20.3)	20.8 (18.4 to 23.6)		
B/Victoria (n = 609, 605)	8.41 (7.55 to 9.37)	6.91 (6.25 to 7.64)		
B/Yamagata (n = 609, 606)	7.13 (6.46 to 7.87)	5.31 (4.79 to 5.88)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Immediate Unsolicited Adverse Events (AEs)

End point title	Number of Participants With Immediate Unsolicited Adverse Events (AEs)

End point description:

An AE was any untoward medical occurrence in a clinical investigation participant temporally associated with the use of study intervention, whether or not considered related to the study intervention. An unsolicited AE was an observed AE that did not fulfill the conditions of solicited reactions, that is, prelisted in the case report form (CRF) in terms of diagnosis and/or onset window post-vaccination. All participants were observed for 30 minutes after vaccination, and any unsolicited AEs occurred during that time were recorded as immediate unsolicited AEs. Analysis was performed on the Safety analysis set which included participants who received 1 dose of the study vaccine.

End point type	Secondary

End point timeframe:

Within 30 minutes post-vaccination on Day 1

End point values	Cohort 1: Participants aged 9 to 17 years (Safety)	Cohort 2: Participants aged 18 to 49 years (Safety)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	641	658		
Units: participants	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Solicited Injection Site Reactions and Systemic Reactions

End point title	Number of Participants With Solicited Injection Site Reactions and Systemic Reactions

End point description:

A solicited reaction was an expected adverse reaction (sign or symptom) observed and reported under

the conditions (nature and onset) prelisted in the protocol and CRF and considered as related to the study intervention administered. An injection site reaction was an AR at and around the injection site and were commonly inflammatory reactions. Solicited systemic reactions were systemic AEs and those occurring during the specified collection period were always considered related to the intervention even if there was evidence of alternative etiology. Analysis was performed on the Safety analysis set which included participants who received 1 dose of the study vaccine. Only those participants with data available at a specified timepoint were analyzed. Here 'n'= number of participants with available data for a particular category.

End point type	Secondary

End point timeframe:

From Day 1 up to 8 days post-vaccination

End point values	Cohort 1: Participants aged 9 to 17 years (Safety)	Cohort 2: Participants aged 18 to 49 years (Safety)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	618	635		
Units: participants				
Solicited injection site reaction (n=618, 635)	220	259		
Solicited systemic reaction (n=615, 635)	182	230		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Unsolicited AEs

End point title	Number of Participants With Unsolicited AEs

End point description:

An AE was any untoward medical occurrence in a clinical investigation participant temporally associated with the use of study intervention, whether or not considered related to the study intervention. An unsolicited AE was an observed AE that did not fulfill the conditions of solicited reactions, that is, prelisted in the CRF in terms of diagnosis and/or onset window post-vaccination. Analysis was performed on the Safety analysis set which included participants who received 1 dose of the study vaccine.

End point type	Secondary

End point timeframe:

From Day 1 up to 28 days post-vaccination (up to Day 29)

End point values	Cohort 1: Participants aged 9 to 17 years (Safety)	Cohort 2: Participants aged 18 to 49 years (Safety)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	641	658		
Units: participants	93	119		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Medically Attended Adverse Events (MAAEs)

End point title	Number of Participants With Medically Attended Adverse Events (MAAEs)

End point description:

An MAAE was a new onset or a worsening of a condition that prompted the participant or participant's parent/guardian to seek unplanned medical advice at a physician's office or emergency department. Analysis was performed on the Safety analysis set which included participants who received 1 dose of the study vaccine.

End point type	Secondary

End point timeframe:

From Day 1 up to 28 days post-vaccination (up to Day 29)

End point values	Cohort 1: Participants aged 9 to 17 years (Safety)	Cohort 2: Participants aged 18 to 49 years (Safety)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	641	658		
Units: participants	27	35		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Serious Adverse Events (SAEs) And Adverse Events of Special Interest (AESI)

End point title	Number of Participants With Serious Adverse Events (SAEs) And Adverse Events of Special Interest (AESI)

End point description:

An SAE was any untoward medical occurrence that at any dose resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or was an important medical event. An AESI was defined as one of scientific and medical concern specific to the Sponsor's study intervention, events for which ongoing monitoring and rapid communication by the investigator to the sponsor was done. Analysis was performed on the Safety analysis set which included participants who received 1 dose of the study vaccine.

End point type	Secondary

End point timeframe:

From Day 1 up to 6 months post-vaccination (up to Day 181)

End point values	Cohort 1: Participants aged 9 to 17 years (Safety)	Cohort 2: Participants aged 18 to 49 years (Safety)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	641	658		
Units: participants				
SAE	3	7		
AESI	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From Day 1 up to 6 months post-vaccination (up to Day 181)	
Adverse event reporting additional description:	
Analysis was performed on the Safety analysis set.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups	
Reporting group title	Cohort 1: Participants aged 9 to 17 years
Reporting group description:	
Participants received a single IM injection of RIV4 0.5 mL on Day 1.	
Reporting group title	Cohort 2: Participants aged 18 to 49 years
Reporting group description:	
Participants received a single IM injection of RIV4 0.5 mL on Day 1.	

Serious adverse events	Cohort 1: Participants aged 9 to 17 years	Cohort 2: Participants aged 18 to 49 years	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 641 (0.47%)	7 / 658 (1.06%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastric Cancer Recurrent			
subjects affected / exposed	0 / 641 (0.00%)	1 / 658 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Intentional Overdose			
subjects affected / exposed	0 / 641 (0.00%)	1 / 658 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			

subjects affected / exposed	0 / 641 (0.00%)	1 / 658 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Fracture			
subjects affected / exposed	1 / 641 (0.16%)	0 / 658 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 641 (0.00%)	1 / 658 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Obstructive Pancreatitis			
subjects affected / exposed	0 / 641 (0.00%)	1 / 658 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Failure			
subjects affected / exposed	0 / 641 (0.00%)	1 / 658 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Major Depression			
subjects affected / exposed	0 / 641 (0.00%)	1 / 658 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal Ideation			
subjects affected / exposed	2 / 641 (0.31%)	1 / 658 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Kidney Infection			

subjects affected / exposed	0 / 641 (0.00%)	1 / 658 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort 1: Participants aged 9 to 17 years	Cohort 2: Participants aged 18 to 49 years	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	263 / 641 (41.03%)	336 / 658 (51.06%)	
Nervous system disorders			
Headache			
subjects affected / exposed	114 / 641 (17.78%)	152 / 658 (23.10%)	
occurrences (all)	121	153	
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	100 / 641 (15.60%)	106 / 658 (16.11%)	
occurrences (all)	100	106	
Injection Site Pain			
subjects affected / exposed	212 / 641 (33.07%)	255 / 658 (38.75%)	
occurrences (all)	212	256	
Chills			
subjects affected / exposed	45 / 641 (7.02%)	40 / 658 (6.08%)	
occurrences (all)	45	40	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	119 / 641 (18.56%)	129 / 658 (19.60%)	
occurrences (all)	119	129	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported