Clinical trial results:
A Phase 3, Randomized, Double-blind Trial to Evaluate the Safety of a 20-Valent Pneumococcal Conjugate Vaccine in Healthy Infants

Summary

EudraCT number	2019-003307-35
Trial protocol	HU DE GR FI CZ
Global end of trial date	31 August 2022

Results information

Result version number	v1 (current)
This version publication date	10 February 2023
First version publication date	10 February 2023

Trial information

Trial identification

Sponsor protocol code	B7471013

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04379713
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002330-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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 September 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the safety profile of 20-Valent Pneumococcal Conjugate Vaccine (20vPnC).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 May 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 79
Country: Number of subjects enrolled	Canada: 189
Country: Number of subjects enrolled	Chile: 30
Country: Number of subjects enrolled	Czechia: 29
Country: Number of subjects enrolled	Germany: 49
Country: Number of subjects enrolled	Spain: 320
Country: Number of subjects enrolled	Finland: 17
Country: Number of subjects enrolled	Greece: 31
Country: Number of subjects enrolled	Hungary: 262
Country: Number of subjects enrolled	Puerto Rico: 19
Country: Number of subjects enrolled	United States: 478
Worldwide total number of subjects	1503
EEA total number of subjects	708

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)	1503
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 1511 subjects were enrolled and randomised in the study. 7 subjects did not receive any vaccine. 1 subject who was randomised to 13vPnC group received 20vPnC vaccination at Dose 1 which was not as per randomisation. Hence, data of these subjects were excluded from analysis.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	20vPnC

Arm description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 20-valent Pneumococcal Conjugate Vaccine (20vPnC) intramuscularly (IM). The first dose was given at Day 1, with the second and third doses given at 42-63 day intervals. Dose 4 was administered between 12 to 15 months of age. Subjects were followed up to 6 months after last dose.

Arm type	Experimental
Investigational medicinal product name	20-Valent Pneumococcal Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL dose of 20vPnC intramuscularly on Visits 1, 2, 3, and 5 with Dose 1, 2, 3, and 4, respectively.

Arm title	13vPnC

Arm description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 mL 13-valent Pneumococcal Conjugate Vaccine (13vPnC) intramuscularly. The first dose was given at Day 1, with the second and third doses given at 42-63 day intervals. Dose 4 was administered between 12 to 15 months of age. Subjects were followed up to 6 months after last dose.

Arm type	Active comparator
Investigational medicinal product name	13-Valent Pneumococcal Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL dose of 13vPnC intramuscularly on Visits 1, 2, 3, and 5 with Dose 1, 2, 3, and 4, respectively.

Number of subjects in period 1	20vPnC	13vPnC
Started	1000	503
Dose 1 (Vaccination 1)	1000	503
Dose 2	972	491
Dose 3	964	482
Dose 4	923	461
Completed	910	450
Not completed	90	53
Physician decision	1	-
Adverse Event	2	-
No longer meets eligibility criteria	14	11
Lost to follow-up	31	21
Withdrawal by parent/guardian	31	15
Protocol deviation	11	6

Baseline characteristics

Reporting groups	
Reporting group title	20vPnC
Reporting group description:	
Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 20-valent Pneumococcal Conjugate Vaccine (20vPnC) intramuscularly (IM). The first dose was given at Day 1, with the second and third doses given at 42-63 day intervals. Dose 4 was administered between 12 to 15 months of age. Subjects were followed up to 6 months after last dose.	
Reporting group title	13vPnC
Reporting group description:	
Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 mL 13-valent Pneumococcal Conjugate Vaccine (13vPnC) intramuscularly. The first dose was given at Day 1, with the second and third doses given at 42-63 day intervals. Dose 4 was administered between 12 to 15 months of age. Subjects were followed up to 6 months after last dose.	

Reporting group values	20vPnC	13vPnC	Total
Number of subjects	1000	503	1503
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)	1000	503	1503
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: days			
arithmetic mean	64.6	65.0	
standard deviation	± 8.51	± 8.95	-
Gender Categorical Units: Subjects			
Female	483	259	742
Male	517	244	761
Race Units: Subjects			
White	868	445	1313
Black or African American	55	15	70
Asian	21	10	31
American Indian or Alaskan native	4	1	5
Native Hawaiian or other Pacific Islander	2	2	4
Multiracial	35	21	56
Not reported	15	9	24
Ethnicity Units: Subjects			

Hispanic/Latino	367	193	560
Non-Hispanic/non-Latino	621	303	924
Not reported	12	7	19

End points

End points reporting groups

Reporting group title	20vPnC

Reporting group description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 20-valent Pneumococcal Conjugate Vaccine (20vPnC) intramuscularly (IM). The first dose was given at Day 1, with the second and third doses given at 42-63 day intervals. Dose 4 was administered between 12 to 15 months of age. Subjects were followed up to 6 months after last dose.

Reporting group title	13vPnC

Reporting group description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 mL 13-valent Pneumococcal Conjugate Vaccine (13vPnC) intramuscularly. The first dose was given at Day 1, with the second and third doses given at 42-63 day intervals. Dose 4 was administered between 12 to 15 months of age. Subjects were followed up to 6 months after last dose.

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 1

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 1[1]

End point description:

Local reactions included pain at injection site, redness and swelling. Redness and swelling were measured and recorded in measuring device (caliper) units. 1 measuring device unit =0.5 centimeter (cm). Pain at injection site was graded as mild: hurts if gently touched; moderate: hurts if gently touched with crying; severe: limited limb movement. Redness and swelling were graded as mild: greater than (>) 0.0 to 2.0 cm; moderate >2.0 to 7.0 cm; and severe: >7.0 cm. Safety population included all the subjects who received at least 1 dose of the investigational product (IP) with safety follow up after any dose. Here, 'Number of Subjects Analysed' = number of subjects with any electronic diary (e-diary) data reported after Dose 1.

End point type	Primary

End point timeframe:

Within 7 Days after Dose 1

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	992	498		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness: Mild	18.0 (15.7 to 20.6)	16.5 (13.3 to 20.0)		
Redness: Moderate	3.7 (2.6 to 5.1)	3.0 (1.7 to 4.9)		
Redness: Severe	0 (0.0 to 0.4)	0 (0.0 to 0.7)		
Swelling: Mild	13.8 (11.7 to 16.1)	11.2 (8.6 to 14.4)		
Swelling: Moderate	6.1 (4.7 to 7.8)	5.4 (3.6 to 7.8)		
Swelling: Severe	0 (0.0 to 0.4)	0 (0.0 to 0.7)		
Pain at injection site: Mild	24.8 (22.1 to 27.6)	25.3 (21.5 to 29.4)		
Pain at injection site: Moderate	15.5 (13.3 to 17.9)	16.7 (13.5 to 20.2)		
Pain at injection site: Severe	0.2 (0.0 to 0.7)	0 (0.0 to 0.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 2

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 2[2]

End point description:

Local reactions included pain at injection site, redness and swelling. Redness and swelling were measured and recorded in measuring device (caliper) units. 1 measuring device unit =0.5 cm. Pain at injection site was graded as mild: hurts if gently touched; moderate: hurts if gently touched with crying; severe: limited limb movement. Redness and swelling were graded as mild: >0.0 to 2.0 cm; moderate >2.0 to 7.0 cm; and severe: >7.0 cm. Safety population included all the subjects who received at least 1 dose of the investigational product with safety follow up after any dose. Here, 'Number of Subjects Analysed' = number of subjects with any e-diary data reported after Dose 2.

End point type	Primary

End point timeframe:

Within 7 Days after Dose 2

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	952	485		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness: Mild	20.4 (17.9 to 23.1)	19.4 (16.0 to 23.2)		
Redness: Moderate	3.2 (2.1 to 4.5)	3.9 (2.4 to 6.1)		
Redness: Severe	0 (0.0 to 0.4)	0 (0.0 to 0.8)		
Swelling: Mild	13.4 (11.3 to 15.8)	13.4 (10.5 to 16.8)		
Swelling: Moderate	4.4 (3.2 to 5.9)	5.6 (3.7 to 8.0)		
Swelling: Severe	0 (0.0 to 0.4)	0 (0.0 to 0.8)		
Pain at the injection site: Mild	20.8 (18.3 to 23.5)	20.2 (16.7 to 24.1)		
Pain at the injection site: Moderate	10.7 (8.8 to 12.9)	11.8 (9.0 to 15.0)		
Pain at the injection site: Severe	0.7 (0.3 to 1.5)	0.8 (0.2 to 2.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 3

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 3[3]

End point description:

Local reactions included pain at injection site, redness and swelling. Redness and swelling were measured and recorded in measuring device (caliper) units. 1 measuring device unit =0.5 cm. Pain at injection site was graded as mild: hurts if gently touched; moderate: hurts if gently touched with crying; severe: limited limb movement. Redness and swelling were graded as mild: >0.0 to 2.0 cm; moderate >2.0 to 7.0 cm; and severe: >7.0 cm. Safety population included all the subjects who received at least 1 dose of the investigational product with safety follow up after any dose. Here, 'Number of Subjects Analysed' = number of subjects with any e-diary data reported after Dose 3.

End point type	Primary

End point timeframe:

Within 7 Days after Dose 3

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	940	477		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness: Mild	19.4 (16.9 to 22.0)	17.0 (13.7 to 20.7)		
Redness: Moderate	3.8 (2.7 to 5.3)	3.1 (1.8 to 5.1)		
Redness: Severe	0 (0.0 to 0.4)	0.2 (0.0 to 1.2)		
Swelling: Mild	12.2 (10.2 to 14.5)	13.0 (10.1 to 16.4)		
Swelling: Moderate	4.1 (3.0 to 5.6)	3.1 (1.8 to 5.1)		
Swelling: Severe	0 (0.0 to 0.4)	0.2 (0.0 to 1.2)		
Pain at the injection site: Mild	16.3 (14.0 to 18.8)	16.6 (13.3 to 20.2)		
Pain at the injection site: Moderate	8.3 (6.6 to 10.2)	10.3 (7.7 to 13.4)		
Pain at the injection site: Severe	0.1 (0.0 to 0.6)	0 (0.0 to 0.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 4

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 4[4]

End point description:

Local reactions included pain at injection site, redness and swelling. Redness and swelling were measured and recorded in measuring device (caliper) units. 1 measuring device unit =0.5 cm. Pain at injection site was graded as mild: hurts if gently touched; moderate: hurts if gently touched with crying; severe: limited limb movement. Redness and swelling were graded as mild: >0.0 to 2.0 cm; moderate >2.0 to 7.0 cm; and severe: >7.0 cm. Safety population included all the subjects who received at least 1 dose of the investigational product with safety follow up after any dose. Here, 'Number of Subjects Analysed' = number of subjects with any e-diary data reported after Dose 4.

End point type	Primary

End point timeframe:

Within 7 Days after Dose 4

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	892	454		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness: Mild	15.1 (12.8 to 17.7)	19.4 (15.8 to 23.3)		
Redness: Moderate	5.9 (4.5 to 7.7)	2.4 (1.2 to 4.3)		
Redness: Severe	0.1 (0.0 to 0.6)	0 (0.0 to 0.8)		
Swelling: Mild	10.1 (8.2 to 12.3)	11.5 (8.7 to 14.7)		
Swelling: Moderate	4.7 (3.4 to 6.3)	2.9 (1.5 to 4.8)		
Swelling: Severe	0 (0.0 to 0.4)	0 (0.0 to 0.8)		
Pain at the injection site: Mild	19.8 (17.3 to 22.6)	21.8 (18.1 to 25.9)		
Pain at the injection site: Moderate	10.2 (8.3 to 12.4)	10.1 (7.5 to 13.3)		
Pain at the injection site: Severe	0.8 (0.3 to 1.6)	0 (0.0 to 0.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 1

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 1[5]

End point description:

Systemic events included fever, decreased appetite, drowsiness, and irritability. Fever was defined as an axillary temperature greater than or equal to (>=)38.0 degree Celsius (C), and categorised as >=38.0 to 38.4 degree C, >38.4 to 38.9 degree C,>38.9 to 40.0 degree C and >40.0 degree C; decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed); drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabling, not interested in usual daily activity); Irritability: graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable, crying could not be comforted). Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. 'Number of Subjects Analysed' = number of subjects with any e-diary data reported after Dose 1.

End point type	Primary

End point timeframe:

Within 7 Days after Dose 1

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	992	498		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0 degree C	9.3 (7.5 to 11.3)	9.8 (7.4 to 12.8)		
Fever: >=38.0 degree C to 38.4 degree C	6.3 (4.8 to 7.9)	7.8 (5.6 to 10.6)		
Fever: >38.4 degree C to 38.9 degree C	2.3 (1.5 to 3.5)	1.8 (0.8 to 3.4)		
Fever: >38.9 degree C to 40.0 degree C	0.7 (0.3 to 1.4)	0.2 (0.0 to 1.1)		
Fever: >40.0 degree C	0 (0.0 to 0.4)	0 (0.0 to 0.7)		
Decreased appetite: Mild	14.2 (12.1 to 16.5)	14.7 (11.7 to 18.1)		
Decreased appetite: Moderate	10.3 (8.5 to 12.3)	8.6 (6.3 to 11.5)		
Decreased appetite: Severe	0.5 (0.2 to 1.2)	0.4 (0.0 to 1.4)		
Drowsiness: Mild	48.5 (45.3 to 51.6)	47.4 (42.9 to 51.9)		
Drowsiness: Moderate	15.8 (13.6 to 18.2)	14.5 (11.5 to 17.9)		
Drowsiness: Severe	0.5 (0.2 to 1.2)	0.4 (0.0 to 1.4)		
Irritability: Mild	22.7 (20.1 to 25.4)	22.9 (19.3 to 26.8)		
Irritability: Moderate	41.2 (38.1 to 44.4)	41.4 (37.0 to 45.8)		
Irritability: Severe	4.3 (3.2 to 5.8)	4.2 (2.6 to 6.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 2

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 2[6]

End point description:

Systemic events included fever, decreased appetite, drowsiness and irritability. Fever was defined as an axillary temperature >=38.0 degree C, and categorised as >=38.0 to 38.4 degree C, >38.4 to 38.9 degree C,>38.9 to 40.0 degree C and >40.0 degree C; decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed); drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabling, not interested in usual daily activity); Irritability: graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable, crying could not be comforted). Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. 'Number of Subjects Analysed' = number of subjects with any e-diary data reported after Dose 2.

End point type	Primary

End point timeframe:

Within 7 Days after Dose 2

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	952	485		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0 degree C	15.5 (13.3 to 18.0)	11.3 (8.7 to 14.5)		
Fever: >=38.0 degree C to 38.4 degree C	10.6 (8.7 to 12.7)	8.5 (6.1 to 11.3)		
Fever: >38.4 degree C to 38.9 degree C	3.6 (2.5 to 5.0)	2.7 (1.4 to 4.5)		
Fever: >38.9 degree C to 40.0 degree C	1.4 (0.7 to 2.3)	0.2 (0.0 to 1.1)		
Fever: >40.0 degree C	0 (0.0 to 0.4)	0 (0.0 to 0.8)		
Decreased appetite: Mild	13.4 (11.3 to 15.8)	12.0 (9.2 to 15.2)		
Decreased appetite: Moderate	9.6 (7.8 to 11.6)	8.2 (6.0 to 11.1)		
Decreased appetite: Severe	0.7 (0.3 to 1.5)	0.4 (0.0 to 1.5)		
Drowsiness: Mild	35.3 (32.3 to 38.4)	35.3 (31.0 to 39.7)		
Drowsiness: Moderate	13.4 (11.3 to 15.8)	13.8 (10.9 to 17.2)		
Drowsiness: Severe	0.4 (0.1 to 1.1)	1.2 (0.5 to 2.7)		
Irritability: Mild	23.2 (20.6 to 26.0)	19.8 (16.3 to 23.6)		
Irritability: Moderate	37.3 (34.2 to 40.4)	42.7 (38.2 to 47.2)		
Irritability: Severe	4.2 (3.0 to 5.7)	5.2 (3.4 to 7.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 3

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 3[7]

End point description:

Systemic events included fever, decreased appetite, drowsiness and irritability. Fever was defined as an axillary temperature >=38.0 degree C, and categorised as >=38.0 to 38.4 degree C, >38.4 to 38.9 degree C,>38.9 to 40.0 degree C and >40.0 degree C; decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed); drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabling, not interested in usual daily activity); Irritability: graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable, crying could not be comforted). Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. 'Number of Subjects Analysed' = number of subjects with any e-diary data reported after Dose 3.

End point type	Primary

End point timeframe:

Within 7 Days after Dose 3

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	940	477		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0 degree C	11.6 (9.6 to 13.8)	9.9 (7.3 to 12.9)		
Fever: >=38.0 degree C to 38.4 degree C	7.4 (5.9 to 9.3)	8.2 (5.9 to 11.0)		
Fever: >38.4 degree C to 38.9 degree C	2.9 (1.9 to 4.2)	0.6 (0.1 to 1.8)		
Fever: >38.9 degree C to 40.0 degree C	1.3 (0.7 to 2.2)	1.0 (0.3 to 2.4)		
Fever: >40.0 degree C	0 (0.0 to 0.4)	0 (0.0 to 0.8)		
Decreased appetite: Mild	15.0 (12.8 to 17.4)	10.5 (7.9 to 13.6)		
Decreased appetite: Moderate	8.2 (6.5 to 10.1)	6.3 (4.3 to 8.9)		
Decreased appetite: Severe	0.4 (0.1 to 1.1)	0.4 (0.1 to 1.5)		
Drowsiness: Mild	26.6 (23.8 to 29.5)	27.3 (23.3 to 31.5)		
Drowsiness: Moderate	8.5 (6.8 to 10.5)	9.0 (6.6 to 12.0)		
Drowsiness: Severe	0.2 (0.0 to 0.8)	0 (0.0 to 0.8)		
Irritability: Mild	22.3 (19.7 to 25.1)	22.2 (18.6 to 26.2)		
Irritability: Moderate	30.1 (27.2 to 33.2)	29.8 (25.7 to 34.1)		
Irritability: Severe	2.3 (1.5 to 3.5)	2.7 (1.5 to 4.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 4

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 4[8]

End point description:

Systemic events included fever, decreased appetite, drowsiness and irritability. Fever was defined as an axillary temperature >=38.0 degree C, and categorised as >=38.0 to 38.4 degree C, >38.4 to 38.9 degree C, >38.9 to 40.0 degree C and >40.0 degree C; decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed); drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabling, not interested in usual daily activity); Irritability: graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable, crying could not be comforted). Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. 'Number of Subjects Analysed' = number of subjects with any e-diary data reported after Dose 4.

End point type	Primary

End point timeframe:

Within 7 Days after Dose 4

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	892	454		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0 degree C	18.0 (15.6 to 20.7)	17.0 (13.6 to 20.7)		
Fever: >=38.0 degree C to 38.4 degree C	9.8 (7.9 to 11.9)	9.5 (6.9 to 12.5)		
Fever: >38.4 degree C to 38.9 degree C	4.5 (3.2 to 6.1)	4.2 (2.5 to 6.5)		
Fever: >38.9 degree C to 40.0 degree C	3.7 (2.6 to 5.2)	3.1 (1.7 to 5.1)		
Fever: >40.0 degree C	0.1 (0.0 to 0.6)	0.2 (0.0 to 1.2)		
Decreased appetite: Mild	16.1 (13.8 to 18.7)	12.3 (9.5 to 15.7)		
Decreased appetite: Moderate	10.5 (8.6 to 12.7)	11.7 (8.9 to 15.0)		
Decreased appetite: Severe	1.7 (0.9 to 2.8)	1.8 (0.8 to 3.4)		
Drowsiness: Mild	24.2 (21.4 to 27.2)	25.1 (21.2 to 29.4)		
Drowsiness: Moderate	12.2 (10.1 to 14.6)	10.6 (7.9 to 13.8)		
Drowsiness: Severe	0.7 (0.2 to 1.5)	0.2 (0.0 to 1.2)		
Irritability: Mild	21.4 (18.8 to 24.3)	22.0 (18.3 to 26.1)		
Irritability: Moderate	31.4 (28.4 to 34.5)	29.7 (25.6 to 34.2)		
Irritability: Severe	2.5 (1.6 to 3.7)	3.3 (1.9 to 5.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Adverse Events (AEs) From Dose 1 to 1 Month After Dose 3

End point title	Percentage of Subjects With Adverse Events (AEs) From Dose 1 to 1 Month After Dose 3[9]

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject, temporally associated with the use of study vaccine, whether or not considered related to the study vaccine. Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose.

End point type	Primary

End point timeframe:

From Day 1 of Dose 1 to 1 Month after Dose 3

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1000	503		
Units: Percentage of subjects				
number (confidence interval 95%)	29.6 (26.8 to 32.5)	27.6 (23.8 to 31.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With AEs From Dose 4 to 1 Month After Dose 4

End point title	Percentage of Subjects With AEs From Dose 4 to 1 Month After Dose 4[10]

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study vaccine, whether or not considered related to the study vaccine. Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. Here, 'Number of Subjects Analysed' = number of subjects who received Dose 4.

End point type	Primary

End point timeframe:

From Dose 4 to 1 Month after Dose 4

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	923	461		
Units: Percentage of subjects				
number (confidence interval 95%)	15.1 (12.8 to 17.5)	15.8 (12.6 to 19.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Serious Adverse Events (SAEs) From Dose 1 to 6 Months After Dose 4

End point title	Percentage of Subjects With Serious Adverse Events (SAEs) From Dose 1 to 6 Months After Dose 4[11]

End point description:

A SAE was any untoward medical occurrence that, at any dose: resulted in death; required inpatient hospitalisation or prolongation of existing hospitalisation; was life-threatening; resulted in persistent or significant disability/incapacity; congenital anomaly/birth defect and other important medical events. Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose.

End point type	Primary

End point timeframe:

From Day 1 of Dose 1 to 6 Months after Dose 4

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1000	503		
Units: Percentage of subjects				
number (confidence interval 95%)	4.4 (3.2 to 5.9)	5.6 (3.7 to 7.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Newly Diagnosed Chronic Medical Conditions (NDCMCs) From Dose 1 to 6 Months After Dose 4

End point title	Percentage of Subjects With Newly Diagnosed Chronic Medical Conditions (NDCMCs) From Dose 1 to 6 Months After Dose 4[12]

End point description:

An NDCMC was defined as a significant disease or medical condition, not previously identified, that is expected to be persistent or was otherwise long-lasting in its effects. Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose.

End point type	Primary

End point timeframe:

From Day 1 of Dose 1 to 6 Months after Dose 4

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1000	503		
Units: Percentage of subjects				
number (confidence interval 95%)	2.8 (1.9 to 4.0)	2.8 (1.5 to 4.6)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Local reactions/systemic events:[systematic assessment (SA)]: Within 7 days after Dose 1, 2, 3, 4; Non-SA: SAEs: Day 1 up to 6 months after Dose4, other AEs(NSAEs): Day 1 of Dose1 up to 1 month after Dose3 and from Day 1 of Dose4 up to 1 month after Dose4

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another subject, or one subject may have experienced both a serious and non-serious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	13vPnC

Reporting group description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 mL 13vPnC intramuscularly. The first dose was given at Day 1, with the second and third doses given at 42-63 day intervals. Dose 4 was administered between 12 to 15 months of age. Subjects were followed up to 6 months after last dose.

Reporting group title	20vPnC

Reporting group description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 mL 20vPnC intramuscularly. The first dose was given at Day 1, with the second and third doses given at 42-63 day intervals. Dose 4 was administered between 12 to 15 months of age. Subjects were followed up to 6 months after last dose.

Serious adverse events	13vPnC	20vPnC	
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 503 (5.57%)	44 / 1000 (4.40%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Skull fracture			
subjects affected / exposed	1 / 503 (0.20%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body aspiration			

subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile convulsion			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infantile spasms			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 503 (0.20%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 503 (0.20%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Adverse food reaction			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	3 / 503 (0.60%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Allergic colitis			
subjects affected / exposed	1 / 503 (0.20%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			

subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	1 / 503 (0.20%)	0 / 1000 (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			
Bronchospasm			
subjects affected / exposed	1 / 503 (0.20%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 503 (0.20%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Hypersensitivity vasculitis			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Breath holding			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (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			

subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenovirus infection			
subjects affected / exposed	0 / 503 (0.00%)	2 / 1000 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	5 / 503 (0.99%)	5 / 1000 (0.50%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 503 (0.20%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 503 (0.20%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			
subjects affected / exposed	1 / 503 (0.20%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	1 / 503 (0.20%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 503 (0.20%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			

subjects affected / exposed	1 / 503 (0.20%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 503 (0.40%)	3 / 1000 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	2 / 503 (0.40%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			
subjects affected / exposed	1 / 503 (0.20%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			

subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (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 / 503 (0.00%)	2 / 1000 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viraemia			
subjects affected / exposed	1 / 503 (0.20%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	1 / 503 (0.20%)	0 / 1000 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 503 (0.40%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 503 (0.00%)	2 / 1000 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchitis			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			

subjects affected / exposed	1 / 503 (0.20%)	0 / 1000 (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			
Dehydration			
subjects affected / exposed	0 / 503 (0.00%)	1 / 1000 (0.10%)	
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	13vPnC	20vPnC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	481 / 503 (95.63%)	960 / 1000 (96.00%)	
Nervous system disorders			
Hypersomnia (INCREASED SLEEP)			
alternative assessment type: Systematic			
subjects affected / exposed	389 / 503 (77.34%)	809 / 1000 (80.90%)	
occurrences (all)	1069	2104	
General disorders and administration site conditions			
Injection site erythema (REDNESS)			
alternative assessment type: Systematic			
subjects affected / exposed	224 / 503 (44.53%)	455 / 1000 (45.50%)	
occurrences (all)	423	875	
Injection site pain (PAIN)			
alternative assessment type: Systematic			
subjects affected / exposed	309 / 503 (61.43%)	609 / 1000 (60.90%)	
occurrences (all)	663	1253	
Injection site swelling (SWELLING)			
alternative assessment type: Systematic			
subjects affected / exposed	176 / 503 (34.99%)	372 / 1000 (37.20%)	
occurrences (all)	344	704	
Pyrexia (FEVER)			
alternative assessment type:			

Systematic			
subjects affected / exposed	159 / 503 (31.61%)	336 / 1000 (33.60%)	
occurrences (all)	245	550	
Psychiatric disorders			
Irritability (IRRITABILITY)			
alternative assessment type: Systematic			
subjects affected / exposed	432 / 503 (85.88%)	883 / 1000 (88.30%)	
occurrences (all)	1556	3018	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	28 / 503 (5.57%)	59 / 1000 (5.90%)	
occurrences (all)	30	67	
Metabolism and nutrition disorders			
Decreased appetite (DECREASED APPETITE)			
alternative assessment type: Systematic			
subjects affected / exposed	249 / 503 (49.50%)	549 / 1000 (54.90%)	
occurrences (all)	487	1117	

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