Clinical trial results:
Prevenar Post-Licensure Safety Study in Russia: Frequency Of Fever Post Vaccination

Summary

EudraCT number	2017-001529-41
Trial protocol	Outside EU/EEA
Global end of trial date	01 August 2011

Results information

Result version number	v1 (current)
This version publication date	17 August 2017
First version publication date	17 August 2017

Trial information

Trial identification

Sponsor protocol code	0887X1-4596

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01207583
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 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 December 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 August 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to estimate the incidence of febrile reactions of greater than or equal to (>=) 38 degrees Celsius (C) to less than or equal to (<=) 39 degrees C; greater than (>) 39 degrees C to <=40 degrees C; > 40 degrees C occurring within 2 days following vaccination with Prevenar (7-valent pneumococcal conjugate vaccine [PCV7]) co-administered with other routine childhood vaccines under the conditions of routine daily use in the Russian Federation within the licensed indication

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 Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 January 2010
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	Russian Federation: 100
Worldwide total number of subjects	100
EEA total number of subjects	0

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)	100
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:

This study was conducted at 4 sites in Russia. Study was started on 28 January 2010 and completed on 01 August 2011.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Primary Cohort (3-6 Months)

Arm description:

Subjects in the age group 3-6 months received 4 doses (Dose 1, Dose 2, Dose 3 and Dose 4) of PCV7 as standard care as per the summary of product characteristics (SmPC).

Arm type	Experimental
Investigational medicinal product name	PCV7
Investigational medicinal product code	
Other name	Prevenar
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

PCV7 was administered intramuscularly as standard care as per the SmPC.

Arm title	Catch-up Cohort (7-11 Months)

Arm description:

Subjects in the age group 7-11 months received 3 doses (Dose 1, Dose 2 and Dose 3) of PCV7 as standard care as per the SmPC.

Arm type	Experimental
Investigational medicinal product name	PCV7
Investigational medicinal product code	
Other name	Prevenar
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

PCV7 was administered intramuscularly as standard care as per the SmPC.

Arm title	Catch-up Cohort (12-23 Months)

Arm description:

Subjects in the age group 12-23 months received 2 doses (Dose 1 and Dose 2) of PCV7 as standard care as per the SmPC.

Arm type	Experimental
Investigational medicinal product name	PCV7
Investigational medicinal product code	
Other name	Prevenar
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

PCV7 was administered intramuscularly as standard care as per the SmPC.

Number of subjects in period 1	Primary Cohort (3-6 Months)	Catch-up Cohort (7-11 Months)	Catch-up Cohort (12-23 Months)
Started	14	31	55
Dose 1	14	31	55
Dose 2	13	29	54
Dose 3	13	27	0 [1]
Dose 4	7 [2]	0 [3]	0 [4]
Completed	13	26	54
Not completed	1	5	1
Withdrawal by Subject	-	3	1
Lost to follow-up	-	2	-
Subject failed to return	1	-	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Out of 54 subjects who received Dose 2, none of the subjects received Dose 3 and 4 as Dose 2 was last dose for those subjects in Catch-up Cohort (12-23 Months). However, all 54 subjects completed the study till follow-up visit.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Out of 13 subjects who received Dose 3, only 7 subjects received Dose 4. However, all 13 subjects completed the study till follow-up visit.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Out of 27 subjects who received Dose 3, none of the subjects received Dose 4 as Dose 3 was last dose for those subjects in Catch-up Cohort (7-11 Months). However, 26 subjects completed the study till follow-up visit.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Out of 54 subjects who received Dose 2, none of the subjects received Dose 3 and 4 as Dose 2 was last dose for those subjects in Catch-up Cohort (12-23 Months). However, all 54 subjects completed the study till follow-up visit.

Baseline characteristics

Reporting groups	
Reporting group title	Primary Cohort (3-6 Months)
Reporting group description:	
Subjects in the age group 3-6 months received 4 doses (Dose 1, Dose 2, Dose 3 and Dose 4) of PCV7 as standard care as per the summary of product characteristics (SmPC).	
Reporting group title	Catch-up Cohort (7-11 Months)
Reporting group description:	
Subjects in the age group 7-11 months received 3 doses (Dose 1, Dose 2 and Dose 3) of PCV7 as standard care as per the SmPC.	
Reporting group title	Catch-up Cohort (12-23 Months)
Reporting group description:	
Subjects in the age group 12-23 months received 2 doses (Dose 1 and Dose 2) of PCV7 as standard care as per the SmPC.	

Reporting group values	Primary Cohort (3-6 Months)	Catch-up Cohort (7-11 Months)	Catch-up Cohort (12-23 Months)
Number of subjects	14	31	55
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)	14	31	55
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: months			
arithmetic mean	5.42	9.33	17.37
standard deviation	± 1.27	± 1.26	± 3.03
Gender Categorical Units: Subjects			
Female	5	13	19
Male	9	18	36

Reporting group values	Total		
Number of subjects	100		
Age Categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	100		
Children (2-11 years)	0		

Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: months			
arithmetic mean			
standard deviation	-		
Gender Categorical Units: Subjects			
Female	37		
Male	63		

End points

End points reporting groups

Reporting group title	Primary Cohort (3-6 Months)
Reporting group description:	
Subjects in the age group 3-6 months received 4 doses (Dose 1, Dose 2, Dose 3 and Dose 4) of PCV7 as standard care as per the summary of product characteristics (SmPC).	
Reporting group title	Catch-up Cohort (7-11 Months)
Reporting group description:	
Subjects in the age group 7-11 months received 3 doses (Dose 1, Dose 2 and Dose 3) of PCV7 as standard care as per the SmPC.	
Reporting group title	Catch-up Cohort (12-23 Months)
Reporting group description:	
Subjects in the age group 12-23 months received 2 doses (Dose 1 and Dose 2) of PCV7 as standard care as per the SmPC.	

Primary: Percentage of Subjects With Febrile Reactions Post-dose 1

End point title	Percentage of Subjects With Febrile Reactions Post-dose 1[1]
End point description:	
Febrile reactions were defined as reactions which caused a rise in body temperature following vaccination in children. Fever was defined as a temperature of >=38 degrees C. Percentage of subjects with febrile reaction of >=38 degrees C to <=39 degrees C, >39 degrees C to <=40 degrees C and >40 degrees C were observed. Safety set (post-dose 1) population included all subjects who received Dose 1 and who had safety follow-up data following Dose 1.	
End point type	Primary
End point timeframe:	
Day 1 to Day 3 post-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 analyzed for this endpoint

End point values	Primary Cohort (3-6 Months)	Catch-up Cohort (7-11 Months)	Catch-up Cohort (12-23 Months)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	31	55	
Units: percentage of subjects				
number (confidence interval 95%)				
38 to 39 degrees C	14.3 (4 to 39.9)	16.1 (7.1 to 32.6)	1.8 (0.3 to 9.6)	
>39 to 40 degrees C	0 (0 to 21.5)	3.2 (0.6 to 16.2)	3.6 (1 to 12.3)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Febrile Reactions Post-dose 2

End point title	Percentage of Subjects With Febrile Reactions Post-dose 2[2]

End point description:

Febrile reactions were defined as reactions which caused a rise in body temperature following vaccination in children. Fever was defined as a temperature of >=38 degrees C. Percentage of subjects with febrile reaction of >=38 degrees C to <=39 degrees C was observed. Safety set (post-dose 2) population included all subjects who received Dose 2 and who had safety follow-up data following Dose 2.

End point type	Primary

End point timeframe:

Day 1 to Day 3 post-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 analyzed for this endpoint

End point values	Primary Cohort (3-6 Months)	Catch-up Cohort (7-11 Months)	Catch-up Cohort (12-23 Months)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	29	54	
Units: percentage of subjects				
number (confidence interval 95%)	23.1 (8.2 to 50.3)	10.3 (3.6 to 26.4)	0 (0 to 6.6)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Febrile Reactions Post-dose 3

End point title	Percentage of Subjects With Febrile Reactions Post-dose 3[3][4]

End point description:

Febrile reactions were defined as reactions which caused a rise in body temperature following vaccination in children. Fever was defined as a temperature of >=38 degrees C. Percentage of subjects with febrile reaction of >=38 degrees C to <=39 degrees C was observed. Safety set (post-dose 3) population included all subjects who received Dose 3 and who had safety follow-up data following Dose 3.

End point type	Primary

End point timeframe:

Day 1 to Day 3 post-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 analyzed for this endpoint

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned not to be analyzed for reporting arm Catch-up Cohort (12-23 Months).

End point values	Primary Cohort (3-6 Months)	Catch-up Cohort (7-11 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	26		
Units: percentage of subjects				
number (confidence interval 95%)	15.4 (4.3 to 42.2)	0 (0 to 12.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Febrile Reactions Post-dose 4

End point title	Percentage of Subjects With Febrile Reactions Post-dose 4[5][6]

End point description:

Febrile reactions were defined as reactions which caused a rise in body temperature following vaccination in children. Fever was defined as a temperature of >=38 degrees C. Percentage of subjects with febrile reaction of >=38 degrees C was observed. Safety set (post-dose 4) population included all subjects who received Dose 4 and who had safety follow-up data following Dose 4.

End point type	Primary

End point timeframe:

Day 1 to Day 3 post-dose 4

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 analyzed for this endpoint

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned not to be analyzed for reporting arms Catch-up Cohort (7-11 Months) and Catch-up Cohort (12-23 Months).

End point values	Primary Cohort (3-6 Months)			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: percentage of subjects				
number (confidence interval 95%)	0 (0 to 35.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Pre-Specified Local Reactions Post-dose 1

End point title	Percentage of Subjects With Pre-Specified Local Reactions Post-dose 1

End point description:

Local reactions were reported using an electronic diary. Tenderness was scaled as Any (tenderness present); Significant (present and interfered with limb movement). Induration and redness were scaled as Any (induration or redness present); Mild (<2.5 centimeters [cm]); Moderate (>=2.5 cm to <5.0 cm); Severe (>=5.0 cm). Subjects may be represented in more than 1 category. Solicited local

reactions included redness, swelling and tenderness while unsolicited local reactions included injection site hematoma, injection site hemorrhage, injection site induration and injection site warmth. Safety set (post-dose 1) population included all subjects who received Dose 1 and who had safety follow-up data following Dose 1.

End point type	Secondary

End point timeframe:

Day 1 to Day 3 post-dose 1

End point values	Primary Cohort (3-6 Months)	Catch-up Cohort (7-11 Months)	Catch-up Cohort (12-23 Months)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	31	55	
Units: percentage of subjects				
number (not applicable)				
Redness	7.1	19.4	27.3	
Swelling	0	6.5	25.5	
Tenderness	7.1	29	23.6	
Injection site hematoma	0	0	1.8	
Injection site hemorrhage	0	3.2	1.8	
Injection site induration	7.1	0	0	
Injection site warmth	0	0	1.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Pre-Specified Local Reactions Post-dose 2

End point title	Percentage of Subjects With Pre-Specified Local Reactions Post-dose 2

End point description:

Local reactions were reported using an electronic diary. Tenderness was scaled as Any (tenderness present); Significant (present and interfered with limb movement). Induration and redness were scaled as Any (induration or redness present); Mild (<2.5 cm); Moderate (>=2.5 cm to <5.0 cm); Severe (>=5.0 cm). Subjects may be represented in more than 1 category. Solicited local reactions included redness, swelling and tenderness while unsolicited local reactions included injection site hematoma, injection site hemorrhage, injection site induration and injection site warmth. Safety set (post-dose 2) population included all subjects who received Dose 2 and who had safety follow-up data following Dose 2.

End point type	Secondary

End point timeframe:

Day 1 to Day 3 post-dose 2

End point values	Primary Cohort (3-6 Months)	Catch-up Cohort (7-11 Months)	Catch-up Cohort (12-23 Months)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	29	54	
Units: percentage of subjects				
number (not applicable)				
Redness	23.1	13.8	20.4	
Swelling	0	0	11.1	
Tenderness	0	6.9	16.7	
Injection site hemorrhage	0	0	3.7	
Injection site induration	0	0	1.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Pre-Specified Local Reactions Post-dose 3

End point title	Percentage of Subjects With Pre-Specified Local Reactions Post-dose 3[7]

End point description:

Local reactions were reported using an electronic diary. Tenderness was scaled as Any (tenderness present); Significant (present and interfered with limb movement). Induration and redness were scaled as Any (induration or redness present); Mild (<2.5 cm); Moderate (>=2.5 cm to <5.0 cm); Severe (>=5.0 cm). Subjects may be represented in more than 1 category. Solicited local reactions included redness, swelling and tenderness while unsolicited local reactions included injection site hematoma, injection site hemorrhage, injection site induration and injection site warmth. Safety set (post-dose 3) population included all subjects who received Dose 3 and who had safety follow-up data following Dose 3.

End point type	Secondary

End point timeframe:

Day 1 to Day 3 post-dose 3

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned not to be analyzed for reporting arm Catch-up Cohort (12-23 Months).

End point values	Primary Cohort (3-6 Months)	Catch-up Cohort (7-11 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	26		
Units: percentage of subjects				
number (not applicable)				
Redness	15.4	3.8		
Swelling	7.7	3.8		
Tenderness	7.7	7.7		
Injection site induration	7.7	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Pre-Specified Local Reactions Post-dose 4

End point title	Percentage of Subjects With Pre-Specified Local Reactions Post-dose 4[8]

End point description:

Local reactions were reported using an electronic diary. Tenderness was scaled as Any (tenderness present); Significant (present and interfered with limb movement). Induration and redness were scaled as Any (induration or redness present); Mild (<2.5 cm); Moderate (>=2.5 cm to <5.0 cm); Severe (>=5.0 cm). Subjects may be represented in more than 1 category. Solicited local reactions included redness, swelling and tenderness while unsolicited local reactions included injection site hematoma, injection site hemorrhage, injection site induration and injection site warmth. Safety set (post-dose 4) population included all subjects who received Dose 4 and who had safety follow-up data following Dose 4.

End point type	Secondary

End point timeframe:

Day 1 to Day 3 post-dose 4

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was planned not to be analyzed for reporting arms Catch-up Cohort (7-11 Months) and Catch-up Cohort (12-23 Months).

End point values	Primary Cohort (3-6 Months)			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: percentage of subjects				
number (not applicable)				
Redness	14.3			
Swelling	14.3			
Injection site induration	14.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Pre-Specified Systemic Events Post-dose 1

End point title	Percentage of Subjects With Pre-Specified Systemic Events Post-dose 1

End point description:

Systemic events (any fever >=38 degrees C, decreased appetite, diarrhea, restless sleep, unusual crying, unusual fussiness, unusual irritability, and vomiting) were reported using an electronic diary. Subjects may be represented in more than 1 categories. Safety set (post-dose 1) population included all subjects who received Dose 1 and who had safety follow-up data following Dose 1.

End point type	Secondary

End point timeframe:

Day 1 to Day 3 post-dose 1

End point values	Primary Cohort (3-6 Months)	Catch-up Cohort (7-11 Months)	Catch-up Cohort (12-23 Months)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	31	55	
Units: percentage of subjects				
number (not applicable)				
Decreased appetite	7.1	19.4	23.6	
Diarrhea	7.1	3.2	9.1	
Fever	14.3	19.4	5.5	
Restless sleep	7.1	32.3	27.3	
Unusual crying	14.3	25.8	30.9	
Unusual fussiness	7.1	6.5	12.7	
Unusual irritability	21.4	19.4	25.5	
Vomiting	0	6.5	3.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Pre-Specified Systemic Events Post-dose 2

End point title	Percentage of Subjects With Pre-Specified Systemic Events Post-dose 2

End point description:

Systemic events (any fever >=38 degrees C, decreased appetite, diarrhea, restless sleep, unusual crying, unusual fussiness, unusual irritability, and vomiting) were reported using an electronic diary. Subjects may be represented in more than 1 category. Safety set (post-dose 2) population included all subjects who received Dose 2 and who had safety follow-up data following Dose 2.

End point type	Secondary

End point timeframe:

Day 1 to Day 3 post-dose 2

End point values	Primary Cohort (3-6 Months)	Catch-up Cohort (7-11 Months)	Catch-up Cohort (12-23 Months)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	29	54	
Units: percentage of subjects				
number (not applicable)				
Decreased appetite	15.4	10.3	9.3	
Diarrhea	15.4	3.4	0	
Fever	23.1	10.3	0	
Restless sleep	23.1	24.1	16.7	
Unusual crying	23.1	20.7	13	
Unusual fussiness	15.4	6.9	7.4	
Unusual irritability	23.1	6.9	9.3	
Vomiting	7.7	0	1.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Pre-Specified Systemic Events Post-dose 3

End point title	Percentage of Subjects With Pre-Specified Systemic Events Post-dose 3[9]

End point description:

Systemic events (any fever >=38 degrees C, decreased appetite, diarrhea, restless sleep, unusual crying, unusual fussiness, unusual irritability, and vomiting) were reported using an electronic diary. Subjects may be represented in more than 1 category. Safety set (post-dose 3) population included all subjects who received Dose 3 and who had safety follow-up data following Dose 3.

End point type	Secondary

End point timeframe:

Day 1 to Day 3 post-dose 3

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Justification for warning: This endpoint was planned not to be analyzed for reporting arm Catch-up Cohort (12-23 Months).

End point values	Primary Cohort (3-6 Months)	Catch-up Cohort (7-11 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	26		
Units: percentage of subjects				
number (not applicable)				
Decreased appetite	7.7	0		
Diarrhea	15.4	3.8		
Fever	15.4	0		
Restless sleep	46.2	11.5		
Unusual crying	15.4	11.5		
Unusual fussiness	15.4	0		
Unusual irritability	7.7	7.7		
Vomiting	15.4	3.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Pre-Specified Systemic Events Post-dose 4

End point title	Percentage of Subjects With Pre-Specified Systemic Events Post-dose 4[10]

End point description:

Systemic events (any fever >=38 degrees C, decreased appetite, diarrhea, restless sleep, unusual crying, unusual fussiness, unusual irritability, and vomiting) were reported using an electronic diary. Subjects may be represented in more than 1 category. Safety set (post-dose 4) population included all subjects who received Dose 4 and who had safety follow-up data following Dose 4.

End point type	Secondary

End point timeframe:

Day 1 to Day 3 post-dose 4

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned not to be analyzed for reporting arms Catch-up Cohort (7-11 Months) and Catch-up Cohort (12-23 Months).

End point values	Primary Cohort (3-6 Months)			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: percentage of subjects				
number (not applicable)				
Restless sleep	28.6			
Unusual crying	14.3			
Unusual irritability	14.3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious AEs were collected within 30 days after each dose and non-serious AEs were collected within 7 days after each dose.

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 nonserious 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	14.0

Reporting groups

Reporting group title	Dose 1 (Primary Cohort [3-6 Months])

Reporting group description:

Subjects in the age group 3-6 months received Dose 1 of PCV7 vaccine as standard care as per the SmPC.

Reporting group title	Dose 2 (Primary Cohort [3-6 Months])

Reporting group description:

Subjects in the age group 3-6 months received Dose 2 of PCV7 vaccine as standard care as per the SmPC.

Reporting group title	Dose 3 (Primary Cohort [3-6 Months])

Reporting group description:

Subjects in the age group 3-6 months received Dose 3 of PCV7 vaccine as standard care as per the SmPC.

Reporting group title	Dose 4 (Primary Cohort [3-6 Months])

Reporting group description:

Subjects in the age group 3-6 months received Dose 4 of PCV7 vaccine as standard care as per the SmPC.

Reporting group title	Dose 1 (Catch-up Cohort [7-11 Months])

Reporting group description:

Subjects in the age group 7-11 months received Dose 1 of PCV7 vaccine as standard care as per the SmPC.

Reporting group title	Dose 2 (Catch-up Cohort [7-11 Months])

Reporting group description:

Subjects in the age group 7-11 months received Dose 2 of PCV7 vaccine as standard care as per the SmPC.

Reporting group title	Dose 3 (Catch-up Cohort [7-11 Months])

Reporting group description:

Subjects in the age group 7-11 months received Dose 3 of PCV7 vaccine as standard care as per the SmPC.

Reporting group title	Dose 1 (Catch-up Cohort [12-23 Months])

Reporting group description:

Subjects in the age group 12-23 months received Dose 1 of PCV7 vaccine as standard care as per the SmPC.

Reporting group title	Dose 2 (Catch-up Cohort [12-23 Months])

Reporting group description:

Subjects in the age group 12-23 months received Dose 2 of PCV7 vaccine as standard care as per the SmPC.

Serious adverse events	Dose 1 (Primary Cohort [3-6 Months])	Dose 2 (Primary Cohort [3-6 Months])	Dose 3 (Primary Cohort [3-6 Months])
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Dose 4 (Primary Cohort [3-6 Months])	Dose 1 (Catch-up Cohort [7-11 Months])	Dose 2 (Catch-up Cohort [7-11 Months])
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Dose 3 (Catch-up Cohort [7-11 Months])	Dose 1 (Catch-up Cohort [12-23 Months])	Dose 2 (Catch-up Cohort [12-23 Months])
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)	1 / 55 (1.82%)	0 / 54 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 55 (1.82%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 55 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Dose 1 (Primary Cohort [3-6 Months])	Dose 2 (Primary Cohort [3-6 Months])	Dose 3 (Primary Cohort [3-6 Months])
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 14 (42.86%)	6 / 13 (46.15%)	6 / 13 (46.15%)
Investigations			
Body temperature increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Crying			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	1 / 13 (7.69%)
occurrences (all)	1	1	1
Injection site induration			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Gait disturbance			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			

subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Disbacteriosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	1 / 13 (7.69%)
occurrences (all)	1	1	1
Erythema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Enterovirus infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rotavirus infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			

subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Dose 4 (Primary Cohort [3-6 Months])	Dose 1 (Catch-up Cohort [7-11 Months])	Dose 2 (Catch-up Cohort [7-11 Months])
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)	17 / 31 (54.84%)	8 / 29 (27.59%)
Investigations			
Body temperature increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Crying			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Injection site induration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Disbacteriosis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Enterovirus infection			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	0 / 29 (0.00%)
occurrences (all)	0	2	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	2 / 29 (6.90%)
occurrences (all)	0	2	2
Rotavirus infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Dose 3 (Catch-up Cohort [7-11 Months])	Dose 1 (Catch-up Cohort [12-23 Months])	Dose 2 (Catch-up Cohort [12-23 Months])

Total subjects affected by non-serious adverse events subjects affected / exposed	5 / 26 (19.23%)	27 / 55 (49.09%)	16 / 54 (29.63%)
Investigations Body temperature increased subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	0 / 55 (0.00%) 0	1 / 54 (1.85%) 1
Nervous system disorders Crying subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 55 (0.00%) 0	0 / 54 (0.00%) 0
General disorders and administration site conditions Injection site erythema subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 55 (0.00%) 0	0 / 54 (0.00%) 0
Injection site induration subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	1 / 55 (1.82%) 1	0 / 54 (0.00%) 0
Gait disturbance subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	0 / 55 (0.00%) 0	0 / 54 (0.00%) 0
Injection site reaction subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	0 / 55 (0.00%) 0	0 / 54 (0.00%) 0
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	1 / 55 (1.82%) 1	0 / 54 (0.00%) 0
Disbacteriosis subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 55 (0.00%) 0	0 / 54 (0.00%) 0
Skin and subcutaneous tissue disorders Dermatitis atopic subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 55 (0.00%) 0	0 / 54 (0.00%) 0
Erythema subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	2 / 55 (3.64%) 2	0 / 54 (0.00%) 0

Rash			
subjects affected / exposed	0 / 26 (0.00%)	1 / 55 (1.82%)	2 / 54 (3.70%)
occurrences (all)	0	1	2
Skin irritation			
subjects affected / exposed	0 / 26 (0.00%)	1 / 55 (1.82%)	0 / 54 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 26 (0.00%)	1 / 55 (1.82%)	0 / 54 (0.00%)
occurrences (all)	0	1	0
Enterovirus infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 55 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 26 (0.00%)	0 / 55 (0.00%)	3 / 54 (5.56%)
occurrences (all)	0	0	3
Rotavirus infection			
subjects affected / exposed	0 / 26 (0.00%)	1 / 55 (1.82%)	0 / 54 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 26 (0.00%)	1 / 55 (1.82%)	0 / 54 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 55 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0

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