Clinical trial results:
Safety and Immunogenicity of Sanofi Pasteur's Diphtheria, Tetanus, and Acellular Pertussis (DTaP)-Inactivated Poliovirus (IPV)-Hepatitis B (HB)-polyribosyl ribitol phosphate conjugated to tetanus protein (PRP-T) combined vaccine (DTaP-IPV-HB-PRP-T) Given as a Primary Series of Vaccination in Infants

Summary

EudraCT number	2013-003267-55
Trial protocol	PL
Global end of trial date	29 August 2016

Results information

Result version number	v1 (current)
This version publication date	16 September 2017
First version publication date	16 September 2017

Trial information

Trial identification

Sponsor protocol code	A3L45

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1143-8252

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	2 avenue Pont Pasteur, Lyon cedex 07, France, F-69367
Public contact	Global Medical Affairs, Sanofi Pasteur SA, 33 (0)4 37 37 7464, olga.lyabis@sanofi.com
Scientific contact	Global Medical Affairs, Sanofi Pasteur SA, 33 (0)4 37 37 74 64, olga.lyabis@sanofi.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	31 January 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Russian Federation: To describe the safety and reactogenicity of the study vaccine after a single dose in infants 6 months of age who had previously received 2 vaccinations of Pentaxim and 2 doses of HB vaccine and to evaluate the immunogenicity of the study vaccine 1 month after vaccination
Poland: To describe the safety and reactogenicity after each and all doses of the study vaccine administered as a 3-dose primary series

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were enrolled and vaccinated in the study. Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment was also available on site in case of any immediate allergic reactions.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	27 August 2015
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	Poland: 50
Country: Number of subjects enrolled	Russian Federation: 100
Worldwide total number of subjects	150
EEA total number of subjects	50

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	150

months)	
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:

Study subjects were enrolled from 27 August 2015 to 09 February 2016 (Russia) and 12 January 2016 to 13 April 2016 (Poland) at 5 clinic centers in the Russian Federation and 2 clinic centers in Poland.

Pre-assignment

Screening details:

A total of 150 subjects who met all inclusion criteria and no exclusion criteria were enrolled and vaccinated.

Period 1

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

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	DTaP-IPV-HB-PRP~T combined vaccine (Russian Federation)

Arm description:

Infants received a single dose of DTaP-IPV-HB-PRP~T combined vaccine (Russian Federation).

Arm type	Experimental
Investigational medicinal product name	DTaP-IPV-HB-PRP~T combined vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular into the upper outer surface in the middle of the thigh, single dose (Russian Federation).

Arm title	DTaP-IPV-HB-PRP~T combined vaccine (Poland)

Arm description:

Infants received a 3-dose primary vaccination series of DTaP-IPV-HB-PRP~T (Poland) at Day 0, Day 45, and Day 90.

Arm type	Experimental
Investigational medicinal product name	DTaP-IPV-HB-PRP~T combined vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular into the upper outer surface in the middle of the thigh, 1 dose each at Day 0, Day 45, and Day 90 (Poland)

Number of subjects in period 1	DTaP-IPV-HB-PRP~T combined vaccine (Russian Federation)	DTaP-IPV-HB-PRP~T combined vaccine (Poland)
Started	100	50
Completed	100	50

Baseline characteristics

Reporting groups	
Reporting group title	DTaP-IPV-HB-PRP~T combined vaccine (Russian Federation)
Reporting group description:	
Infants received a single dose of DTaP-IPV-HB-PRP~T combined vaccine (Russian Federation).	
Reporting group title	DTaP-IPV-HB-PRP~T combined vaccine (Poland)
Reporting group description:	
Infants received a 3-dose primary vaccination series of DTaP-IPV-HB-PRP~T (Poland) at Day 0, Day 45, and Day 90.	

Reporting group values	DTaP-IPV-HB-PRP~T combined vaccine (Russian Federation)	DTaP-IPV-HB-PRP~T combined vaccine (Poland)	Total
Number of subjects	100	50	150
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)	100	50	150
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			
Age is reported in months for infants in the Russian Federation group and in weeks for infants in the Poland group.			
Units: months			
arithmetic mean	6.6	7	
standard deviation	± 0.3	± 0.6	-
Gender categorical Units: Subjects			
Female	50	26	76
Male	50	24	74

End points

End points reporting groups

Reporting group title	DTaP-IPV-HB-PRP~T combined vaccine (Russian Federation)
Reporting group description:	
Infants received a single dose of DTaP-IPV-HB-PRP~T combined vaccine (Russian Federation).	
Reporting group title	DTaP-IPV-HB-PRP~T combined vaccine (Poland)
Reporting group description:	
Infants received a 3-dose primary vaccination series of DTaP-IPV-HB-PRP~T (Poland) at Day 0, Day 45, and Day 90.	

Primary: Percentage of Subjects Reporting Solicited Injection-site or Systemic Reactions After Vaccination with a Single Dose of Hexavalent DTaP-IPV-HB-PRP-T Combined Vaccine in Russian Federation

End point title	Percentage of Subjects Reporting Solicited Injection-site or Systemic Reactions After Vaccination with a Single Dose of Hexavalent DTaP-IPV-HB-PRP-T Combined Vaccine in Russian Federation[1][2]
End point description:	
Solicited injection site reactions: Pain, Erythema, and Swelling. Solicited systemic reactions: Pyrexia, Vomiting, Crying, Somnolence, Decreased appetite, Irritability. Grade 3 Injection site reactions: Pain, Cries when injected limb is moved, or the movement of the limb is reduced; Erythema and Swelling, ≥50 mm. Grade 3 Systemic reactions: Pyrexia, >39.5°C; Vomiting, ≥6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal, >3 hours; Somnolence, Sleeping most of the time or difficult to wake up; Decreased appetite, Refuses ≥3 feeds/meals or refuses most feeds/meals; Irritability, Inconsolable.	
End point type	Primary
End point timeframe:	
Day 0 up to Day 7 post-vaccination (Russian Federation)	

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: Descriptive analyses were performed based on the study group and study vaccine administered for this outcome.
[2] - 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: Only solicited injection-site and systemic reactions that occurred after a single dose of the combined vaccine (Russian Federation) are reported for this outcome.

End point values	DTaP-IPV-HB-PRP~T combined vaccine (Russian Federation)			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Percentage of subjects				
number (not applicable)				
Any Injection site Pain	26			
Grade 3 Injection site Pain	4			
Any Injection site Erythema	25			
Grade 3 Injection site Erythema	0			
Any Injection site Swelling	17			
Grade 3 Injection site Swelling	2			

Any Pyrexia	11			
Grade 3 Pyrexia	0			
Any Vomiting	4			
Grade 3 Vomiting	0			
Any Crying abnormal	23			
Grade 3 Crying abnormal	4			
Any Somnolence	27			
Grade 3 Somnolence	0			
Any Decreased appetite	19			
Grade 3 Decreased appetite	0			
Any Irritability	38			
Grade 3 Irritability	5			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Solicited Injection-site or Systemic Reactions After Any and Each Dose of a Three-Dose Primary Series of Hexavalent DTaP-IPV-HB-PRP-T Combined Vaccine in Poland

End point title	Percentage of Subjects Reporting Solicited Injection-site or Systemic Reactions After Any and Each Dose of a Three-Dose Primary Series of Hexavalent DTaP-IPV-HB-PRP-T Combined Vaccine in Poland[3][4]

End point description:

Solicited injection site reactions: Pain, Erythema, and Swelling. Solicited systemic reactions: Pyrexia, Vomiting, Crying, Somnolence, Decreased appetite, Irritability. Grade 3 Injection site reactions: Pain, Cries when injected limb is moved, or the movement of the limb is reduced; Erythema and Swelling, ≥50 mm. Grade 3 Systemic reactions: Pyrexia, >39.5°C; Vomiting, ≥6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal, >3 hours; Somnolence, Sleeping most of the time or difficult to wake up; Decreased appetite, Refuses ≥3 feeds/meals or refuses most feeds/meals; Irritability, Inconsolable.

End point type	Primary

End point timeframe:

Day 0 up to Day 7 post-any and each vaccination

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: Descriptive analyses were performed based on the study group and study vaccine administered for this outcome.
[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: Only solicited injection-site and systemic reactions that occurred after a three-dose primary series of the combined vaccine (Poland) are reported for this outcome.

End point values	DTaP-IPV-HB-PRP~T combined vaccine (Poland)			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: Percentage of subjects				
number (not applicable)				
Any Injection site Pain	78			

Grade 3 Injection site Pain	8			
Any Injection site Pain; Post Injection 1	60			
Grade 3 Injection site Pain; Post Injection 1	6			
Any Injection site Pain; Post Injection 2	52			
Grade 3 Injection site Pain; Post Injection 2	2			
Any Injection site Pain; Post Injection 3	54			
Grade 3 Injection site Pain; Post Injection 3	2			
Any Injection site Erythema	72			
Grade 3 Injection site Erythema	8			
Any Injection site Erythema; Post Injection 1	42			
Grade 3 Injection site Erythema; Post Injection 1	6			
Any Injection site Erythema; Post Injection 2	46			
Grade 3 Injection site Erythema; Post Injection 2	4			
Any Injection site Erythema; Post Injection 3	56			
Grade 3 Injection site Erythema; Post Injection 3	0			
Any Injection site Swelling	58			
Grade 3 Injection site Swelling	8			
Any Injection site Swelling; Post Injection 1	32			
Grade 3 Injection site Swelling; Post Injection 1	6			
Any Injection site Swelling; Post Injection 2	28			
Grade 3 Injection site Swelling; Post Injection 2	2			
Any Injection site Swelling; Post Injection 3	40			
Grade 3 Injection site Swelling; Post Injection 3	2			
Any Pyrexia	28			
Grade 3 Pyrexia	2			
Any Pyrexia; Post Injection 1	10			
Grade 3 Pyrexia; Post Injection 1	0			
Any Pyrexia; Post Injection 2	12			
Grade 3 Pyrexia; Post Injection 2	0			
Any Pyrexia; Post Injection 3	14			
Grade 3 Pyrexia; Post Injection 3	2			
Any Vomiting	30			
Grade 3 Vomiting	0			
Any Vomiting; Post Injection 1	16			
Grade 3 Vomiting; Post Injection 1	0			
Any Vomiting; Post Injection 2	14			
Grade 3 Vomiting; Post Injection 2	0			
Any Vomiting; Post Injection 3	8			
Grade 3 Vomiting; Post Injection 3	0			
Any Crying abnormal	92			
Grade 3 Crying abnormal	8			
Any Crying abnormal; Post Injection 1	84			

Grade 3 Crying abnormal; Post Injection 1	2			
Any Crying abnormal; Post Injection 2	62			
Grade 3 Crying abnormal; Post Injection 2	6			
Any Crying abnormal; Post Injection 3	54			
Grade 3 Crying abnormal; Post Injection 3	0			
Any Somnolence	76			
Grade 3 Somnolence	4			
Any Somnolence; Post Injection 1	62			
Grade 3 Somnolence; Post Injection 1	4			
Any Somnolence; Post Injection 2	50			
Grade 3 Somnolence; Post Injection 2	0			
Any Somnolence; Post Injection 3	38			
Grade 3 Somnolence; Post Injection 3	0			
Any Decreased appetite	48			
Grade 3 Decreased appetite	2			
Any Decreased appetite; Post Injection 1	24			
Grade 3 Decreased appetite; Post Injection 1	0			
Any Decreased appetite; Post Injection 2	26			
Grade 3 Decreased appetite; Post Injection 2	0			
Any Decreased appetite; Post Injection 3	22			
Grade 3 Decreased appetite; Post Injection 3	2			
Any Irritability	90			
Grade 3 Irritability	10			
Any Irritability; Post Injection 1	74			
Grade 3 Irritability; Post Injection 1	2			
Any Irritability; Post Injection 2	66			
Grade 3 Irritability; Post Injection 2	6			
Any Irritability; Post Injection 3	56			
Grade 3 Irritability; Post Injection 3	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Seroprotection After Vaccination with a Single Dose of Hexavalent DTaP-IPV-HB-PRP-T Combined Vaccine in Russian Federation

End point title	Percentage of Subjects with Seroprotection After Vaccination with a Single Dose of Hexavalent DTaP-IPV-HB-PRP-T Combined Vaccine in Russian Federation[5]

End point description:

Anti-Diphtheria antibodies were assessed by a toxin neutralization test. Anti-Tetanus was assessed using an enzyme-linked immunosorbent assay. Anti-Haemophilus influenza type b (Hib) capsular PRP antibodies were assessed by a Farr-type radioimmunoassay. Anti-Hepatitis B was measured using the commercially available VITROS ECi/ECIQ Immunodiagnostic System using chemiluminescence. Anti-

Poliovirus (Polio) types 1, 2, and 3 antibodies were assessed by a neutralization assay. Seroprotection was defined as the following: Anti-Diphtheria ≥0.01 International Units (IU)/mL, ≥0.1 IU/mL, and ≥1.0 IU/mL; Anti-Tetanus ≥0.01 IU/mL, ≥0.1 IU/mL, ≥1.0 IU/mL; Anti-PRP ≥0.15 µg/mL and ≥1.0 µg/mL; Anti-Polio types 1, 2, and 3 ≥8 (1/dilution), Anti-Hepatitis B ≥10 mIU/mL and ≥100 mIU/mL.

End point type	Secondary

End point timeframe:

1 month post-dose 1

Notes:

[5] - 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: Immunogenicity data are only available in infants who received a single dose of the combined vaccine (Russian Federation).

End point values	DTaP-IPV-HB-PRP~T combined vaccine (Russian Federation)			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: Percentage of subjects				
number (not applicable)				
Anti-Diphtheria; ≥0.01 IU/mL	100			
Anti-Diphtheria; ≥0.1 IU/mL	68.8			
Anti-Diphtheria; ≥1.0 IU/mL	20.4			
Anti-Tetanus; ≥0.01 IU/mL	100			
Anti-Tetanus; ≥0.1 IU/mL	100			
Anti-Tetanus; ≥1.0 IU/mL	82			
Anti-Polio 1; ≥8 (1/dilution)	100			
Anti-Polio 2; ≥8 (1/dilution)	100			
Anti-Polio 3; ≥8 (1/dilution)	100			
Anti-Hepatitis B; ≥10 mIU/mL	100			
Anti-Hepatitis B; ≥100 mIU/mL	96.9			
Anti-PRP; ≥0.15 µg/mL	97.9			
Anti-PRP; ≥1.0 µg/mL	92.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentrations (GMCs) of Antibodies Against Vaccine Antigens After Vaccination with a Single Dose of Hexavalent DTaP-IPV-HB-PRP-T Combined Vaccine in Russian Federation

End point title	Geometric Mean Concentrations (GMCs) of Antibodies Against Vaccine Antigens After Vaccination with a Single Dose of Hexavalent DTaP-IPV-HB-PRP-T Combined Vaccine in Russian Federation[6]

End point description:

Anti-Diphtheria antibodies were assessed by a toxin neutralization test. Anti-Tetanus, Anti-Pertussis toxoid, and Anti-Filamentous hemagglutinin (FHA) antibodies were assessed using an enzyme-linked immunosorbent assay. Anti-Hib capsular PRP antibodies were assessed by a Farr-type radioimmunoassay. Anti-Hepatitis B was measured using the commercially available VITROS ECi/ECIQ Immunodiagnostic System using chemiluminescence. Anti-Polio types 1, 2, and 3 antibodies were assessed by a neutralization assay.

End point type	Secondary

End point timeframe:

1 month post-dose 1

Notes:

[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: Immunogenicity data are only available in infants who received a single dose of the combined vaccine (Russian Federation).

End point values	DTaP-IPV-HB-PRP~T combined vaccine (Russian Federation)			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: Concentration (1/dilution)				
geometric mean (confidence interval 95%)				
Anti-Diphtheria	0.278 (0.205 to 0.377)			
Anti-Tetanus	2.08 (1.76 to 2.46)			
Anti-Pertussis toxoid	123 (104 to 145)			
Anti-FHA	154 (135 to 177)			
Anti-Polio 1	1358 (1035 to 1782)			
Anti-Polio 2	2597 (2010 to 3355)			
Anti-Polio 3	2749 (1904 to 3969)			
Anti-Hepatitis B	1679 (1254 to 2248)			
Anti-PRP	6.25 (4.58 to 8.53)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from Day 0 up to Day 30 post-dose 3.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	DTaP-IPV-HB-PRP~T combined vaccine (Russian Federation)

Reporting group description:

Infants received a single dose of DTaP-IPV-HB-PRP~T combined vaccine (Russian Federation).

Reporting group title	DTaP-IPV-HB-PRP~T combined vaccine (Poland)

Reporting group description:

Infants received a 3-dose primary vaccination series of DTaP-IPV-HB-PRP~T (Poland) at Day 0, Day 45, and Day 90.

Serious adverse events	DTaP-IPV-HB-PRP~T combined vaccine (Russian Federation)	DTaP-IPV-HB-PRP~T combined vaccine (Poland)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 100 (0.00%)	5 / 50 (10.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	0 / 100 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 100 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 100 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonellosis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 100 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			
subjects affected / exposed	0 / 100 (0.00%)	1 / 50 (2.00%)	
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	DTaP-IPV-HB-PRP~T combined vaccine (Russian Federation)	DTaP-IPV-HB-PRP~T combined vaccine (Poland)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 100 (38.00%)	46 / 50 (92.00%)	
Nervous system disorders			
Somnolence			
alternative assessment type: Systematic			
subjects affected / exposed	27 / 100 (27.00%)	38 / 50 (76.00%)	
occurrences (all)	27	38	
General disorders and administration site conditions			

Injection site Pain			
alternative assessment type: Systematic			
subjects affected / exposed	26 / 100 (26.00%)	39 / 50 (78.00%)	
occurrences (all)	26	39	
Injection site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	25 / 100 (25.00%)	36 / 50 (72.00%)	
occurrences (all)	25	36	
Injection site Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	17 / 100 (17.00%)	29 / 50 (58.00%)	
occurrences (all)	17	29	
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 100 (11.00%)	14 / 50 (28.00%)	
occurrences (all)	11	14	
Gastrointestinal disorders			
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 100 (4.00%)	15 / 50 (30.00%)	
occurrences (all)	4	15	
Psychiatric disorders			
Crying abnormal			
alternative assessment type: Systematic			
subjects affected / exposed	23 / 100 (23.00%)	46 / 50 (92.00%)	
occurrences (all)	23	46	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	38 / 100 (38.00%)	45 / 50 (90.00%)	
occurrences (all)	38	45	
Infections and infestations			
Rhinitis			
subjects affected / exposed	1 / 100 (1.00%)	6 / 50 (12.00%)	
occurrences (all)	1	8	
Metabolism and nutrition disorders			

Decreased appetite alternative assessment type: Systematic subjects affected / exposed occurrences (all)	19 / 100 (19.00%) 19	24 / 50 (48.00%) 24	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 March 2015	Clarified the age of infants to be included in the study from 6 months to 6 months and 29 days, excluded infants under 6 months of age, included a recommendation to start the study in a limited group of subjects; if satisfactory results were observed (absence of SAEs), then the study would continue, and revised the wording describing the site of injection from "anterolateral thigh" to "upper outer part of the middle thigh" to be consistent with local Russian guidelines.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported