



Clinical trial results:

A Phase 4 study to evaluate the safety and immunogenicity of monovalent oral polio vaccine type 2 in healthy OPV-vaccinated adults

Summary

EudraCT number	2015-003325-33
Trial protocol	BE
Global end of trial date	30 May 2016

Results information

Result version number	v1 (current)
This version publication date	26 June 2022
First version publication date	26 June 2022

Trial information

Trial identification

Sponsor protocol code	UAM1
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University of Antwerp
Sponsor organisation address	Universiteitsplein 1, Wilrijk, Belgium, 2610
Public contact	Ilse De Coster, MD, University of Antwerp , +32 (0)3265 26 52, ilse.decoster@uantwerpen.be
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 May 2016
Global end of trial reached?	Yes
Global end of trial date	30 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the study are to assess the safety (serious adverse events [SAEs] and severe adverse events [AEs]) and immunogenicity (seroprotection rate) of SABIN mOPV2 in healthy OPV-vaccinated adults.

Protection of trial subjects:

In this study only adults who have received at least 3 doses of OPV in the past will be enrolled.

exclusion criteria (amongst others):

- . Having Crohn's disease or ulcerative colitis or having had major surgery of the gastrointestinal tract involving significant loss or resection of the bowel;
- . A known allergy, hypersensitivity, or intolerance to the study vaccine, or to any of its components, or to any antibiotics;
- . Any confirmed or suspected immunosuppressive or immunodeficiency condition (including human immunodeficiency virus [HIV] infection);
- . Will have household or professional contact with known immunosuppressed people or people without full polio vaccination (i.e. complete priming) within 28 days after vaccination;
- . Neonatal nurses or others having professional contact with children under 6 months old within 28 days after vaccination;
- . Chronic administration (i.e., longer than 14 days) of immunosuppressant drugs or other immune-modifying drugs within 6 months prior to the first vaccine dose or planned use during the study. For instance, for corticosteroids, this means prednisone, or equivalent, ≥ 0.5 mg/kg/day (inhaled and topical steroids are allowed, whereas intra-articular and epidural injection/administration of steroids are not allowed);
- . Presence of contraindications to administration of the study vaccine on Day 0: acute severe febrile illness deemed by the Investigator to be a contraindication for vaccination or persistent diarrhea or vomiting;

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2015
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	Belgium: 100
Worldwide total number of subjects	100
EEA total number of subjects	100

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	100
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a single center, open, randomized study, conducted at the Centre for the Evaluation of Vaccination, Vaccine & Infectious Disease Institute, University of Antwerp, Belgium between 25 January 2016 and 30 May 2016.

Pre-assignment

Screening details:

One hundred and twelve volunteers were screened and 100 participants were enrolled. Eligible participants were healthy adults aged 18-50 years who had received at least 3 vaccinations with oral polio vaccine (OPV) in the past.

No contact with immunosuppressed people or people (incl. children <6 m) without full polio vaccination 28d after dosing

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: One dose of mOPV2

Arm description:

Participants received one dose of monovalent oral polio vaccine type 2 (mOPV2) on study day 0, administered orally as 2 drops (0.1 mL total; approximately 10⁶ 50% cell culture infectious dose units (CCID50)).

Arm type	Experimental
Investigational medicinal product name	Polio Sabin™ Mono Two
Investigational medicinal product code	mOPV2
Other name	
Pharmaceutical forms	Oral drops
Routes of administration	Oral use

Dosage and administration details:

participants in Group 1 received one dose of vaccine (0.1 ml) contained in two drops which are delivered from the polyethylene dropper supplied with the multidose container.

Arm title	Group 2: Two doses of mOPV2
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Arm description:

Participants received two doses of mOPV2 28 days apart (Day0 and Day 28), administered orally as 2 drops (0.1 mL total; approximately 10⁶ CCID50)

Arm type	Experimental
Investigational medicinal product name	Polio Sabin™ Mono Two
Investigational medicinal product code	mOPV2
Other name	
Pharmaceutical forms	Oral drops
Routes of administration	Oral use

Dosage and administration details:

Participants received two doses of mOPV2 28 days apart (Day0 and Day 28), administered orally as 2 drops (0.1 mL total) which are delivered from the polyethylene dropper supplied with the multidose container.

Number of subjects in period 1	Group 1: One dose of mOPV2	Group 2: Two doses of mOPV2
Started	50	50
Completed	50	50

Baseline characteristics

Reporting groups

Reporting group title	Group 1: One dose of mOPV2
Reporting group description: Participants received one dose of monovalent oral polio vaccine type 2 (mOPV2) on study day 0, administered orally as 2 drops (0.1 mL total; approximately 10# 50% cell culture infectious dose units (CCID50)).	
Reporting group title	Group 2: Two doses of mOPV2
Reporting group description: Participants received two doses of mOPV2 28 days apart (Day0 and Day 28), administered orally as 2 drops (0.1 mL total; approximately 10# CCID50)	

Reporting group values	Group 1: One dose of mOPV2	Group 2: Two doses of mOPV2	Total
Number of subjects	50	50	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)			0
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: years			
arithmetic mean	26	28	
standard deviation	± 8	± 9	-
Gender categorical Units: Subjects			
Female	31	25	56
Male	19	25	44
Race Units: Subjects			
White	48	49	97
Asian	2	0	2
Black or African American	0	1	1
Other	0	0	0
Number of Prior OPV vaccinations Units: Subjects			
None	0	0	0
Three	6	6	12
Four	44	44	88
Five	0	0	0
Number of Prior IPV vaccinations Units: Subjects			

None	46	47	93
One	4	3	7
Four	0	0	0
Five	0	0	0
Six or more	0	0	0

End points

End points reporting groups

Reporting group title	Group 1: One dose of mOPV2
Reporting group description: Participants received one dose of monovalent oral polio vaccine type 2 (mOPV2) on study day 0, administered orally as 2 drops (0.1 mL total; approximately 10 ⁸ 50% cell culture infectious dose units (CCID50)).	
Reporting group title	Group 2: Two doses of mOPV2
Reporting group description: Participants received two doses of mOPV2 28 days apart (Day0 and Day 28), administered orally as 2 drops (0.1 mL total; approximately 10 ⁸ CCID50)	
Subject analysis set title	Group 1+2: mOPV2
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received one dose of mOPV2 on study Day 0	
Subject analysis set title	Group 1+2: mOPV2 Post-dose 1
Subject analysis set type	Sub-group analysis
Subject analysis set description: participants received vaccination with mOPV2 on study Day 0	
Subject analysis set title	Group 2: mOPV2 Post-dose 2
Subject analysis set type	Sub-group analysis
Subject analysis set description: participants received a second vaccination with mOPV2 on Day 28	
Subject analysis set title	Group 2: Two doses of mOPV2
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received two doses of mOPV2 28 days apart (Day 0 and Day 28)	

Primary: Number of participants with Serious Adverse Events and Severe Adverse Events

End point title	Number of participants with Serious Adverse Events and Severe Adverse Events ^[1]
End point description: An SAE is any untoward medical occurrence that at any dose met any of the following conditions: <ul style="list-style-type: none">• Resulted in death;• Was life-threatening;• Required inpatient hospitalization or prolongation of existing inpatient hospitalization;• Resulted in persistent or significant disability/incapacity;• Was a congenital anomaly/birth defect;• Was medically important. A solicited AE is a pre-selected sign or symptom that occurred within 7 days after each dose, whereas unsolicited AEs were collected throughout the study. Solicited AEs included headache, fatigue, myalgia, arthralgia, paresthesia, anesthesia, paralysis, nausea, vomiting, diarrhea, abdominal pain, and fever. A severe AE is an AE that prevented normal everyday activities and which was not classified as an SAE. A related AE is an AE the investigator considered probably or possibly caused by the study vaccine, meaning that there was a reasonable temporal association or the AE was not attributable to other conditions.	
End point type	Primary
End point timeframe: Up to 42 days after each vaccination	

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: In this study all analyses are descriptive, therefore no statistical analyses have been specified.

End point values	Group 1: One dose of mOPV2	Group 2: Two doses of mOPV2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: participants				
Serious or Severe adverse event	9	13		
Serious adverse event	0	0		
Serious solicited adverse events	0	0		
Serious unsolicited adverse events	0	0		
Serious adverse events related to study vaccine	0	0		
Severe adverse events	9	13		
Severe solicited adverse events	2	3		
Severe unsolicited adverse events	7	10		
Severe adverse events related to study vaccine	4	3		

Statistical analyses

No statistical analyses for this end point

Primary: Seroprotection Rate after a single dose of mOPV2

End point title	Seroprotection Rate after a single dose of mOPV2 ^[2]
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End point description:

Measure Description:

Seroprotection rate was defined as the percentage of participants with anti-type 2-specific poliovirus neutralizing antibody titers \geq 1:8.

Neutralizing antibodies against poliovirus type 2 were determined using the World Health Organization (WHO) standard microneutralization assay (WHO EPI GEN 93.9). The lower limit of quantitation (LLOQ) was 5.7 and the upper limit of quantitation (ULOQ) was 1448.

Analysis Population Description:

Participants in the per-protocol population. The per-protocol population excluded participants with missed doses or major protocol deviations considered to have a potential impact on immunogenicity from the time of the deviation and at all time points thereafter.

This endpoint was analyzed after one dose of mOPV hence Groups 1 and 2 are combined for analysis, as specified in the study protocol.

End point type	Primary
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End point timeframe:

Baseline (Day 0 prior to vaccination) and Day 28

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: In this study all analyses are descriptive, therefore no statistical analyses have been specified

End point values	Group 1+2: mOPV2			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: percentage of participants				
number (confidence interval 95%)				
Day 0 (pre-vaccination)	97 (92 to 99)			
Day 28	98 (93 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants With Solicited Adverse Events Within 7 Days of Vaccination with mOPV2

End point title	Number of participants With Solicited Adverse Events Within 7 Days of Vaccination with mOPV2
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End point description:

Participants completed 7-day diary cards soliciting systemic adverse events and daily oral temperature. Solicited events comprised selected signs and symptoms including headache, fatigue, myalgia, arthralgia, paresthesia, anesthesia, paralysis, nausea, vomiting, diarrhea and abdominal pain, or fever defined as a temperature $\geq 37.0^{\circ}\text{C}$. AEs were graded as mild (easily tolerated with minimal discomfort or temp. 37.5°C to 38.0°C), moderate (sufficiently discomforting to interfere with normal everyday activities, or temp. 38.1°C to 39.0°C), or severe (preventing normal everyday activities, or temperatures $> 39.0^{\circ}\text{C}$). AEs were assessed by the investigator for causality. Probably related suggests that a reasonable temporal sequence of the AE with vaccine administration exists and, in the Investigator's clinical judgment, it is likely that a causal relationship exists between the vaccine administration and the AE.

Analysis Population Description

Participants in the total vaccinated population

End point type	Secondary
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End point timeframe:

Up to 7 days after each dose (Day 0-7 post-dose 1 and Day 28-35 post-dose 2)

End point values	Group 1+2: mOPV2 Post- dose 1	Group 2: mOPV2 Post- dose 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	100	50		
Units: participants				
Any solicited adverse event	62	18		
Mild	47	10		
Moderate	11	7		
Severe	4	1		
Probably related to vaccination	12	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Unsolicited adverse events

End point title	Number of Participants with Unsolicited adverse events
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End point description:

Measure Description:

Unsolicited events comprised other signs and symptoms that participants reported through the end of the study. Each

unsolicited AE was rated on a 3-point scale of increasing intensity:

- Grade 1: Mild; an AE that was easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.
- Grade 2: Moderate; an AE that was sufficiently discomforting to interfere with normal everyday activities.
- Grade 3: Severe; an AE that prevented normal everyday activities. Each adverse event was assessed by the investigator for causality as unrelated, unlikely, possibly, or probably related to the vaccination.

Analysis Population Description:

Total vaccinated population

End point type	Secondary
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End point timeframe:

Up to 42 days after each vaccination

End point values	Group 1: One dose of mOPV2	Group 2: Two doses of mOPV2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: participants				
Any unsolicited adverse event	34	38		
Mild	11	16		
Moderate	16	12		
Severe	7	10		
Probably related to vaccination	3	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Clinically Relevant Laboratory Abnormalities Up to 28 days after Each Vaccination

End point title	Number of participants with Clinically Relevant Laboratory Abnormalities Up to 28 days after Each Vaccination
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End point description:

Measure Description:

Laboratory assessments were collected at one-week intervals from Day 0 , 7 and 28 for Groups 1 and 2 and at Days

35 and 56 for participants in Group 2 who received a 2nd dose.

The Investigator reviewed laboratory values outside the normal range and assessed their clinical relevance.

Any clinically relevant abnormal lab values that occurred at any visit up to 28 days after the first vaccination (in

combined Groups 1 and 2) and up to 28 days (Day 56) after the second dose (Group 2) are reported.

Analysis Population Description

Participants in the total vaccinated population

End point type	Secondary
End point timeframe:	
Day 0, Day 7, and Day 28 for Groups 1 and 2 and at Day 35 and Day 56 for participants in Group 2	

End point values	Group 1+2: mOPV2 Post-dose 1	Group 2: Two doses of mOPV2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	100	50		
Units: participants	21	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Poliovirus Type-2 Neutralizing Antibody Titers After A Single Dose of mOPV2

End point title	Anti-Poliovirus Type-2 Neutralizing Antibody Titers After A Single Dose of mOPV2
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End point description:

Measure Description:

Neutralizing antibodies against poliovirus type 2 were determined using the World Health Organization (WHO) standard microneutralization assay (WHO EPI GEN 93.9). Data were calculated on log₂-transformed type 2 neutralizing titers and back transformed for the presentation below.

Analysis Population Description

Per-protocol population. The per-protocol population excluded participants with missed doses or major protocol deviations considered to have a potential impact on immunogenicity from the time of the deviation and at all time points thereafter. This endpoint was analyzed after one dose of mOPV hence Groups 1 and 2 are combined for analysis, as specified in the study protocol.

End point type	Secondary
End point timeframe:	
Day 0 and Day 28	

End point values	Group 1+2: mOPV2			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: titer				
median (inter-quartile range (Q1-Q3))				
Day 0 (pre-vaccination)	228 (144 to 362)			
Day 28	815 (324 to 1152)			

Statistical analyses

No statistical analyses for this end point

Secondary: Seroprotection Rate 28 Days After Two Doses of mOPV2

End point title | Seroprotection Rate 28 Days After Two Doses of mOPV2

End point description:

Measure Description:

Seroprotection rate was defined as the percentage of participants with anti-type 2-specific poliovirus neutralizing antibodies titers $\geq 1:8$.

Analysis Population Description

Participants in the per-protocol population who received 2 doses of mOPV2 (Group 2).

End point type | Secondary

End point timeframe:

Day 56

End point values	Group 2: Two doses of mOPV2			
Subject group type	Subject analysis set			
Number of subjects analysed	50			
Units: percentage of participants				
number (confidence interval 95%)	98 (89 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Seroconversion Rate After a Single Dose of mOPV2

End point title | Seroconversion Rate After a Single Dose of mOPV2

End point description:

Measure Description:

Seroconversion is defined as a change from seronegative to seropositive (poliovirus type-2-specific neutralizing antibody titers $\geq 1:8$), or for participants seropositive at Baseline, an antibody titer increase of ≥ 4 -fold over Baseline titer.

Analysis Population Description

Participants in the seroconversion subset of the per-protocol population. The seroconversion subset included participants with Baseline titer sufficiently low to enable observation of a four-fold increase without breaching the ULOQ.

Since this endpoint was analyzed after 1 dose of mOPV, Groups 1 and 2 are combined for analysis.

End point type | Secondary

End point timeframe:

Day 28

End point values	Group 1+2: mOPV2			
Subject group type	Subject analysis set			
Number of subjects analysed	62			
Units: percentage of participants				
number (confidence interval 95%)	29 (18 to 42)			

Statistical analyses

No statistical analyses for this end point

Secondary: Seroconversion Rate After Two Doses of mOPV2

End point title	Seroconversion Rate After Two Doses of mOPV2
End point description:	
Measure description:	Seroconversion is defined as a change from seronegative to seropositive (poliovirus type-2-specific neutralizing antibody titers $\geq 1:8$), or for participants seropositive at Baseline, an antibody titer increase of ≥ 4 -fold over Baseline titer.
Analysis Population Description:	Participants in the seroconversion subset of the per-protocol population previously vaccinated with OPV and who received 2 doses of mOPV2 (Group 2). The seroconversion subset included participants with Baseline titer sufficiently low to enable observation of a four-fold increase without breaching the ULOQ.
End point type	Secondary
End point timeframe:	
Day 56	

End point values	Group 2: Two doses of mOPV2			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: percentage of participants				
number (confidence interval 95%)	38 (21 to 58)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 42 days after each vaccination (42 days in Group 1 and 70 days for Group 2).

Adverse event reporting additional description:

unsolicited adverse events

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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Reporting groups

Reporting group title	Group 1: One dose of mOPV2
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Reporting group description:

Participants received one dose of monovalent oral polio vaccine type 2 (mOPV2) on study day 0, administered orally as 2 drops (0.1 mL total; approximately 10# 50% cell culture infectious dose units (CCID50)).

Reporting group title	Group 2: Two doses of mOPV2
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Reporting group description:

Participants received two doses of mOPV2 28 days apart (Day0 and Day 28), administered orally as 2 drops (0.1 mL total; approximately 10# CCID50)

Serious adverse events	Group 1: One dose of mOPV2	Group 2: Two doses of mOPV2	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Group 1: One dose of mOPV2	Group 2: Two doses of mOPV2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 50 (84.00%)	44 / 50 (88.00%)	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	2	
Fatigue			
subjects affected / exposed	2 / 50 (4.00%)	2 / 50 (4.00%)	
occurrences (all)	2	2	
Hangover			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	3 / 50 (6.00%)	0 / 50 (0.00%)	
occurrences (all)	3	0	
Facial pain			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 50 (2.00%)	2 / 50 (4.00%)	
occurrences (all)	2	2	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	4 / 50 (8.00%)	5 / 50 (10.00%)	
occurrences (all)	5	5	
Cough			
subjects affected / exposed	0 / 50 (0.00%)	3 / 50 (6.00%)	
occurrences (all)	0	3	
Dyspnoea			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Increased upper airway secretion			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Emotional distress			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	

Insomnia subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	0 / 50 (0.00%) 0	
Panic attack subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	0 / 50 (0.00%) 0	
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	1 / 50 (2.00%) 1	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	2 / 50 (4.00%) 2	
C-reactive protein increased subjects affected / exposed occurrences (all)	2 / 50 (4.00%) 2	2 / 50 (4.00%) 2	
Injury, poisoning and procedural complications Skin abrasion subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	1 / 50 (2.00%) 1	
Jaw fracture subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 50 (2.00%) 1	
Tooth fracture subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 2	0 / 50 (0.00%) 0	
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	0 / 50 (0.00%) 0	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	8 / 50 (16.00%) 9	12 / 50 (24.00%) 25	
Dizziness			

subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	0 / 50 (0.00%) 0	
Tremor subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	0 / 50 (0.00%) 0	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	1 / 50 (2.00%) 1	
Eye disorders Blepharitis subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	0 / 50 (0.00%) 0	
Conjunctival irritation subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 50 (2.00%) 1	
Gastrointestinal disorders Abdominal Pain subjects affected / exposed occurrences (all)	2 / 50 (4.00%) 2	1 / 50 (2.00%) 5	
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	0 / 50 (0.00%) 0	
Aphthous ulcer subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	0 / 50 (0.00%) 0	
Constipation subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	3 / 50 (6.00%) 4	
Dental caries subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 50 (2.00%) 1	
Diarrhoea subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 8	4 / 50 (8.00%) 4	
Gastrointestinal sounds abnormal			

subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 50 (2.00%) 2	
Nausea subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3	1 / 50 (2.00%) 1	
Toothache subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 50 (2.00%) 1	
Gastrointestinal hypermotility subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 50 (2.00%) 1	
Oral pain subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 50 (2.00%) 1	
paresthesia oral subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 50 (2.00%) 1	
Salivary gland pain subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 50 (2.00%) 1	
Skin and subcutaneous tissue disorders			
Acne subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 50 (2.00%) 1	
Ecchymosis subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 50 (2.00%) 1	
Skin irritation subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 50 (2.00%) 2	
Skin lesion subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 50 (2.00%) 2	
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	1 / 50 (2.00%)	3 / 50 (6.00%)	
occurrences (all)	1	3	
Myalgia			
subjects affected / exposed	2 / 50 (4.00%)	1 / 50 (2.00%)	
occurrences (all)	2	1	
Arthralgia			
subjects affected / exposed	0 / 50 (0.00%)	2 / 50 (4.00%)	
occurrences (all)	0	2	
Neck pain			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Infections and infestations			
Ear infection			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	2 / 50 (4.00%)	3 / 50 (6.00%)	
occurrences (all)	2	3	
Influenza			
subjects affected / exposed	1 / 50 (2.00%)	2 / 50 (4.00%)	
occurrences (all)	1	2	
Nasopharyngitis			
subjects affected / exposed	8 / 50 (16.00%)	13 / 50 (26.00%)	
occurrences (all)	9	17	
Oral herpes			
subjects affected / exposed	0 / 50 (0.00%)	2 / 50 (4.00%)	
occurrences (all)	0	2	
Pharyngitis			

subjects affected / exposed	2 / 50 (4.00%)	0 / 50 (0.00%)
occurrences (all)	2	0
Rhinitis		
subjects affected / exposed	0 / 50 (0.00%)	3 / 50 (6.00%)
occurrences (all)	0	3
Upper respiratory tract infection		
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)
occurrences (all)	1	0
Laryngitis		
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	1
Tonsillitis		
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	1
Tooth abscess		
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	1
Viral diarrhoea		
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)
occurrences (all)	1	0
Chlamydial infection		
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)
occurrences (all)	1	0
Folliculitis		
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	1
Thermal burn		
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 October 2015	<ul style="list-style-type: none">• Sponsor representative has been changed: name and address has been replaced on Signature page, Synopsis and Study administrative structure• Coordinating investigator and clinical lab has been added to the Study administrative structure.• Important medical events (IMEs) although not fulfilling the regulatory definition of a serious adverse event (SAE), will be considered serious and be processed like SAEs. Accordingly the determinations of safety objectives and endpoints have been adapted in synopsis and section 2 and 3.• Secondary endpoints of immunogenicity: Median titers and seroconversion rate of type-specific polio antibodies at day 28 will be described for both groups combined.• Exploratory objectives and endpoints: 'in a subset of stool samples' has been added to the descriptive analysis of viral shedding and assessment of the genetic sequence heterogeneity and potential for neurovirulence. Synopsis and section 2• Statistical methods: 'Cumulative rates of seroconversion and seroprotection will be tabulated' has been deleted in synopsis and section 10.2• Information about the Data Safety Monitoring board has been added in Synopsis, section 4.1 and 11.10.• Time and events schedule : Remote daily contact during 14 days after each vaccination has been changed to 10 days after each vaccination . Phone call has been deleted and whatsapp and email has been added. Group 2: an additional stool sampling has been added at days V4 -1 or 2 days and V7 - 1 or 2 days to ensure stool sampling close before next vaccine dose. Group 1: stool sample day 28 replaced by stool sample on V4 -1 or 2 day and for Group 2: time points for stool sampling have been reformulated to make it more clear. Section 6.5: adapted to use of randomization envelopes Grading of fever, possible outcomes 'recovering' and 'not recovered', description of solicited AEs and hCG testing on Day 0 and Day 28 have been added definition of intention to treat population added
01 January 2016	<ul style="list-style-type: none">• Synopsis + page 36: Inclusion criterium 2 has been changed because in Belgium it is difficult to objectify 4 OPV doses for this age category (18-50y) and to be in accordance with the similar studies for children and infants in Lithuania and Latin-America.• Study Administrative Structure: As the project manager has been changed, the name of the new project manager has been added on page 28.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported