



Clinical trial results:

A Phase 4 study to evaluate the safety and immunogenicity of trivalent oral polio vaccine in adults previously vaccinated with oral polio vaccine

Summary

EudraCT number	2015-003324-32
Trial protocol	BE
Global end of trial date	01 June 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	UAT1
-----------------------	------

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
Scientific contact	Prof. Dr. PhD. Pierre Van Damme, University of Antwerp, +32 (0)3265 26 58, pierre.vandamme@uantwerpen.be

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	01 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 June 2016
Global end of trial reached?	Yes
Global end of trial date	01 June 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 tOPV in healthy OPV-vaccinated adults.

Protection of trial subjects:

In this study only healthy adults are enrolled who received at least 3 doses of OPV in the past (more than 12 months before the start of the study)

Exclusion criteria (among 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: 128
Worldwide total number of subjects	128
EEA total number of subjects	128

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)	128
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study has been conducted in 2 centres in Belgium (Centre for the Evaluation of vaccination, Vaccine & Infectious Disease Institute, University of Antwerp and Military Hospital Koningin Astrid) between December 2015 and June 2016.

Pre-assignment

Screening details:

In this study a total of 144 subjects were screened of whom 128 were enrolled in Group 1 (79 subjects) or Group 2 (49 subjects).

Only subjects who had received at least 3 vaccinations with OPV in the past were enrolled. No contact with unimmunized or unvaccinated persons (including children <6 months old)

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 tOPV

Arm description:

participants previously vaccinated with oral poliovaccine (OPV) received one dose of trivalent oral polio vaccine (tOPV) on Day 0, administered orally as two drops (0.1 ml)

Arm type	Experimental
Investigational medicinal product name	Polio Sabin™ (oral)
Investigational medicinal product code	tOPV
Other name	
Pharmaceutical forms	Oral drops
Routes of administration	Oral use

Dosage and administration details:

One dose of vaccine (0.1 ml) is contained in two drops which are delivered from the dropper supplied with the multidose container.

Arm title	Group 2: three doses of tOPV
------------------	------------------------------

Arm description:

Participants received three doses of tOPV 28 days apart (Day0, Day 28 and Day 56), administered orally as 2 drops (0.1 ml)

Arm type	Experimental
Investigational medicinal product name	Polio Sabin™ (oral)
Investigational medicinal product code	tOPV
Other name	
Pharmaceutical forms	Oral drops
Routes of administration	Oral use

Dosage and administration details:

. One dose of vaccine (0.1 ml) is contained in two drops which are delivered from the dropper supplied with the multidose container. Subjects in Group 2 received 3 doses of the vaccine, 28 days apart.

Number of subjects in period 1	Group 1: One dose of tOPV	Group 2: three doses of tOPV
Started	79	49
Completed	79	49

Baseline characteristics

Reporting groups

Reporting group title	Group 1: One dose of tOPV
Reporting group description: participants previously vaccinated with oral poliovaccine (OPV) received one dose of trivalent oral polio vaccine (tOPV) on Day 0, administered orally as two drops (0.1 ml)	
Reporting group title	Group 2: three doses of tOPV
Reporting group description: Participants received three doses of tOPV 28 days apart (Day0, Day 28 and Day 56), administered orally as 2 drops (0.1 ml)	

Reporting group values	Group 1: One dose of tOPV	Group 2: three doses of tOPV	Total
Number of subjects	79	49	128
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	35.1	35.1	
standard deviation	± 10.37	± 10.72	-
Gender categorical Units: Subjects			
Female	48	20	68
Male	31	29	60
Ethnicity Units: Subjects			
Caucasian/White	79	47	126
Asian	0	1	1
Black/African American	0	1	1
Other	0	0	0
Number of prior tOPV vaccinations Units: Subjects			
Three	8	6	14
Four	69	43	112
Five or more	2	0	2
Number of prior IPV vaccinations Units: Subjects			
none	49	30	79
one	30	18	48

three	0	1	1
-------	---	---	---

End points

End points reporting groups

Reporting group title	Group 1: One dose of tOPV
Reporting group description: participants previously vaccinated with oral poliovaccine (OPV) received one dose of trivalent oral polio vaccine (tOPV) on Day 0, administered orally as two drops (0.1 ml)	
Reporting group title	Group 2: three doses of tOPV
Reporting group description: Participants received three doses of tOPV 28 days apart (Day0, Day 28 and Day 56), administered orally as 2 drops (0.1 ml)	
Subject analysis set title	Group 2 Pre-Dose 2
Subject analysis set type	Sub-group analysis
Subject analysis set description: participants in Group 2 received 1 dose of tOPV on study Day 0	
Subject analysis set title	Group 2 Post-Dose 2
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants in Group 2 received 2 doses of tOPV 28 days apart (Day 0 and Day 28)	
Subject analysis set title	Group 2 Post-Dose 3
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants in Group 2 received 3 doses of tOPV, 28 days apart (Day 0, D28 and Day 56)	
Subject analysis set title	Groups 1+2: tOPV
Subject analysis set type	Sub-group analysis
Subject analysis set description: participants received one dose of tOPV on study Day 0	
Subject analysis set title	Group 1+ Group 2 Pre-dose 2
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received one dose of tOPV on study Day 0	
Subject analysis set title	Group 1+2: tOPV Post-Dose1
Subject analysis set type	Sub-group analysis
Subject analysis set description: participants received one dose of tOPV on Study Day 0	

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:

- 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 last 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 to establish a historical control for future testing of new tOPV all analyses were descriptive.

End point values	Group 1: One dose of tOPV	Group 2: three doses of tOPV	Group 2 Pre-Dose 2	Group 2 Post-Dose 2
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	79	49	49	49
Units: participants				
>= 1 SAE or Severe AE	14	11	4	4
>= 1 SAE	0	1	0	0
>= 1 SAE Probable/Possible/Unlikely	0	0	0	0
>= 1 Severe AE	14	11	4	4
>= 1 Severe AE Probable/Possible/Unlikely	7	8	3	3

End point values	Group 2 Post-Dose 3			
Subject group type	Subject analysis set			
Number of subjects analysed	48			
Units: participants				
>= 1 SAE or Severe AE	8			
>= 1 SAE	1			
>= 1 SAE Probable/Possible/Unlikely	0			
>= 1 Severe AE	8			
>= 1 Severe AE Probable/Possible/Unlikely	5			

Statistical analyses

No statistical analyses for this end point

Primary: Seroprotection Rate after a single dose of tOPV

End point title	Seroprotection Rate after a single dose of tOPV ^[2]
-----------------	--

End point 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 nOPV hence Groups 1 and 2 are combined for analysis, as specified in the study protocol.

End point type	Primary
----------------	---------

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 to establish a historical control for future testing of new tOPV all analyses were descriptive. Therefore no statistical analyses are reported.

End point values	Groups 1+2: tOPV			
Subject group type	Subject analysis set			
Number of subjects analysed	126			
Units: percentage of participants				
number (confidence interval 95%)				
Day 0 (pre-vaccination) type 1	89.7 (83.0 to 94.4)			
Day 0 (pre-vaccination) type 2	93.7 (87.9 to 97.2)			
Day 0 (pre-vaccination) type 3	79.4 (71.2 to 86.1)			
Day 28 type 1	98.4 (94.4 to 99.8)			
Day 28 type 2	99.2 (95.7 to 100)			
Day 28 type 3	93.7 (87.9 to 97.2)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Solicited Adverse Events Within 7 Days of Vaccination with mOPV2
-----------------	--

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 as probable, possible, unlikely or unrelated.

Analysis Population Description

Participants in the total vaccinated population

End point type	Secondary
----------------	-----------

End point timeframe:

Up to 7 days after each dose (Day 0-7 post-dose 1, Day 28-35 post-dose 2 and Day 56-63 post-dose 3)

End point values	Group 2 Post-Dose 2	Group 2 Post-Dose 3	Group 1+ Group 2 Pre-dose 2	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	49	48	128	
Units: solicited adverse events				
Any solicited adverse event	27	22	86	
Mild	24	21	80	
Moderate	8	8	31	
Severe	1	2	3	
Probably/Possibly/Unlikely related to vaccination	26	22	83	

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
End point 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
End point timeframe:	
Upt to 42 days after last vaccination	

End point values	Group 1: One dose of tOPV	Group 2: three doses of tOPV	Group 2 Pre-Dose 2	Group 2 Post-Dose 2
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	79	49	49	49
Units: participants				
>=1 Unsolicited adverse event	59	40	32	25
Mild	37	36	25	20
Moderate	27	18	9	9
Severe	13	10	4	3
Probable/Possible/Unlikely related to vaccination	39	28	19	18

End point values	Group 2 Post-Dose 3			
------------------	---------------------	--	--	--

Subject group type	Subject analysis set			
Number of subjects analysed	48			
Units: participants				
>=1 Unsolicited adverse event	23			
Mild	11			
Moderate	10			
Severe	6			
Probable/Possible/Unlikely related to vaccination	12			

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 ^[3]
End point description:	
Measure Description:	
Laboratory assessments were collected at Day 0 , Day 7, Day 28 after first vaccination and at Days 35, 56, 63 and 84 for participants in Group 2 who received a 2nd and 3thdose.	
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 84) after the third 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, Day 28 for Groups 1 and 2 and day 35, 56, 63 and 84 for participants in Group 2	

Notes:

[3] - 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: For this endpoint data after first vaccination are combined for both groups

End point values	Group 2: three doses of tOPV	Group 1+2: tOPV Post-Dose1		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	47	128		
Units: participants				
any clinically relevant hematology deviation	4	8		
any causally related hematology deviation	0	0		
clinical relevant chemistry/coagulation deviation	8	13		
causally related chemistry/coagulation deviation	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Poliovirus Neutralizing Antibody titers after a single dose of tOPV2

End point title	Anti-Poliovirus Neutralizing Antibody titers after a single dose of tOPV2
-----------------	---

End point description:

Measure Description:

Neutralizing antibodies against poliovirus types 1, 2, 3 were determined using the World Health Organization (WHO) standard microneutralization assay (WHO EPI GEN 93.9). .

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 nOPV 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	Groups 1+2: tOPV			
Subject group type	Subject analysis set			
Number of subjects analysed	126			
Units: titer				
geometric mean (confidence interval 95%)				
Day 0 (prevaccination) Type 1	197.4 (140.6 to 276.1)			
Day 0 (pre-vaccination) Type 2	187.9 (138.4 to 255.2)			
Day 0 (pre-vaccination) Type 3	107.5 (72.6 to 159.0)			
Day 28 Type 1	657.1 (522.5 to 814.5)			
Day 28 Type 2	471.5 (368.0 to 594.5)			
Day 28 Type 3	234.9 (169.4 to 324.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Seroprotection Rate 28 Days After Two Doses and After Three Doses of tOPV

End point title	Seroprotection Rate 28 Days After Two Doses and After Three Doses of tOPV ^[4]
-----------------	--

End point description:

Measure Description:

Seroprotection rate was defined as the percentage of participants with anti-type 1, 2, 3-specific poliovirus neutralizing antibodies titers $\geq 1:8$.

End point type	Secondary
----------------	-----------

End point timeframe:

Day 56 and Day 84

Notes:

[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 involves only 1 arm as this is the only arm with 3 doses

End point values	Group 2: three doses of tOPV			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: percentage of participants				
number (confidence interval 95%)				
Day 56 Type1	95.7 (85.5 to 99.5)			
Day 56 Type 2	100 (92.5 to 100)			
Day 56 Type 3	93.6 (82.5 to 98.7)			
Day 84 Type 1	97.9 (88.7 to 99.9)			
Day 84 Type 2	100 (92.5 to 100)			
Day 84 Type 3	97.9 (88.7 to 99.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Seroconversion Rate After a Single Dose of tOPV

End point title	Seroconversion Rate After a Single Dose of tOPV ^[5]
-----------------	--

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

End point type	Secondary
----------------	-----------

End point timeframe:

Day 28

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: for this endpoint Day 28 data have been reported combined for both Groups and for Group 2

End point values	Group 2: three doses of tOPV	Groups 1+2: tOPV		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	47	126		
Units: percentage of participants				
number (confidence interval 95%)				
Day 28 Type 1	36.2 (22.7 to 51.5)	34.1 (25.9 to 43.1)		
Day 28 Type 2	29.8 (17.3 to 44.9)	27.0 (19.5 to 35.6)		
Day 28 Type 3	25.5 (13.9 to 40.3)	25.4 (18.1 to 33.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Seroconversion Rate After Two Doses and After Three doses of tOPV

End point title	Seroconversion Rate After Two Doses and After Three doses of tOPV ^[6]
-----------------	--

End point description:

Measure description:

Seroconversion is defined as a change from seronegative to seropositive (poliovirus type-1,2,3-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 and who received 2 and 3 doses of tOPV (Group 2). The seroconversion subset included participants with Baseline titer sufficiently low to enable observation of a four-fold increase.

End point type	Secondary
----------------	-----------

End point timeframe:

Day 56 and Day 84

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: For this endpoint only Group 2 is applicable as this is the only Group with 3 doses

End point values	Group 2: three doses of tOPV			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: percentage of subjects				
number (confidence interval 95%)				
Day 56 Type 1	38.3 (24.5 to 53.6)			
Day 56 Type 2	38.3 (24.5 to 53.6)			
Day 56 Type 3	23.4 (12.3 to 38.0)			
Day 84 Type 1	44.7 (30.2 to 59.9)			
Day 84 Type 2	40.4 (26.4 to 55.7)			
Day 84 Type 3	27.7 (15.6 to 42.6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited adverse events up to 7 days after each vaccination. Unsolicited events up to 42 Days after last vaccination (42 days in Group 1 and 84 days in Group 2). SAEs during the whole study period (42 days in Group 1 and 84 days in Group 2)

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Group 1 one dose of tOPV
-----------------------	--------------------------

Reporting group description:

participants received one dose of trivalent oral polio vaccine (tOPV) on study Day 0.

Reporting group title	Group 2: Three doses of tOPV
-----------------------	------------------------------

Reporting group description: -

Serious adverse events	Group 1 one dose of tOPV	Group 2: Three doses of tOPV	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 79 (0.00%)	1 / 49 (2.04%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 79 (0.00%)	1 / 49 (2.04%)	
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: 0 %

Non-serious adverse events	Group 1 one dose of tOPV	Group 2: Three doses of tOPV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 79 (87.34%)	46 / 49 (93.88%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Schwannoma			
subjects affected / exposed	1 / 79 (1.27%)	0 / 49 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			

Deep vein thrombosis subjects affected / exposed occurrences (all)	0 / 79 (0.00%) 0	1 / 49 (2.04%) 1	
Vasodilatation subjects affected / exposed occurrences (all)	0 / 79 (0.00%) 0	1 / 49 (2.04%) 1	
Haematoma subjects affected / exposed occurrences (all)	1 / 79 (1.27%) 1	0 / 49 (0.00%) 0	
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	29 / 79 (36.71%) 35	32 / 49 (65.31%) 65	
Pyrexia subjects affected / exposed occurrences (all)	4 / 79 (5.06%) 4	4 / 49 (8.16%) 6	
Influenza like illness subjects affected / exposed occurrences (all)	0 / 79 (0.00%) 0	4 / 49 (8.16%) 4	
Chills subjects affected / exposed occurrences (all)	0 / 79 (0.00%) 0	1 / 49 (2.04%) 1	
Peripheral swelling subjects affected / exposed occurrences (all)	1 / 79 (1.27%) 1	0 / 49 (0.00%) 0	
Thirst subjects affected / exposed occurrences (all)	1 / 79 (1.27%) 1	0 / 49 (0.00%) 0	
Reproductive system and breast disorders			
Dysmenorrhoea subjects affected / exposed occurrences (all)	3 / 79 (3.80%) 3	1 / 49 (2.04%) 1	
menorrhagia subjects affected / exposed occurrences (all)	0 / 79 (0.00%) 0	1 / 49 (2.04%) 1	
Respiratory, thoracic and mediastinal			

disorders			
Oropharyngeal pain			
subjects affected / exposed	9 / 79 (11.39%)	10 / 49 (20.41%)	
occurrences (all)	11	10	
Cough			
subjects affected / exposed	1 / 79 (1.27%)	7 / 49 (14.29%)	
occurrences (all)	1	7	
Rhinorrhoea			
subjects affected / exposed	1 / 79 (1.27%)	2 / 49 (4.08%)	
occurrences (all)	1	2	
Nasal congestion			
subjects affected / exposed	2 / 79 (2.53%)	1 / 49 (2.04%)	
occurrences (all)	4	1	
Asthma exercise induced			
subjects affected / exposed	0 / 79 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	2 / 79 (2.53%)	0 / 49 (0.00%)	
occurrences (all)	2	0	
Throat irritation			
subjects affected / exposed	0 / 79 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Nasal dryness			
subjects affected / exposed	1 / 79 (1.27%)	0 / 49 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 79 (0.00%)	3 / 49 (6.12%)	
occurrences (all)	0	3	
Insomnia			
subjects affected / exposed	0 / 79 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Sleep disorder			
subjects affected / exposed	0 / 79 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Mood swings			

subjects affected / exposed occurrences (all)	1 / 79 (1.27%) 1	0 / 49 (0.00%) 0	
Investigations			
C-reactive protein increased subjects affected / exposed occurrences (all)	1 / 79 (1.27%) 1	0 / 49 (0.00%) 0	
White blood cell count decreased subjects affected / exposed occurrences (all)	1 / 79 (1.27%) 1	0 / 49 (0.00%) 0	
White blood cell count increased subjects affected / exposed occurrences (all)	1 / 79 (1.27%) 1	0 / 49 (0.00%) 0	
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	1 / 79 (1.27%) 1	2 / 49 (4.08%) 2	
Ligament sprain subjects affected / exposed occurrences (all)	1 / 79 (1.27%) 1	2 / 49 (4.08%) 2	
Ligament rupture subjects affected / exposed occurrences (all)	0 / 79 (0.00%) 0	1 / 49 (2.04%) 1	
Wound subjects affected / exposed occurrences (all)	0 / 79 (0.00%) 0	1 / 49 (2.04%) 1	
Facial bones fracture subjects affected / exposed occurrences (all)	1 / 79 (1.27%) 1	0 / 49 (0.00%) 0	
Limb injury subjects affected / exposed occurrences (all)	1 / 79 (1.27%) 1	0 / 49 (0.00%) 0	
Skin abrasion subjects affected / exposed occurrences (all)	1 / 79 (1.27%) 2	0 / 49 (0.00%) 0	
Tooth fracture			

subjects affected / exposed occurrences (all)	1 / 79 (1.27%) 1	0 / 49 (0.00%) 0	
Nervous system disorders			
Headache			
subjects affected / exposed	41 / 79 (51.90%)	28 / 49 (57.14%)	
occurrences (all)	57	87	
Paraesthesia			
subjects affected / exposed	3 / 79 (3.80%)	7 / 49 (14.29%)	
occurrences (all)	3	8	
Anaesthesia			
subjects affected / exposed	1 / 79 (1.27%)	2 / 49 (4.08%)	
occurrences (all)	1	2	
Dizziness			
subjects affected / exposed	2 / 79 (2.53%)	0 / 49 (0.00%)	
occurrences (all)	2	0	
Migraine			
subjects affected / exposed	2 / 79 (2.53%)	0 / 49 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 49 (0.00%)	
occurrences (all)	1	0	
Leukopenia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 49 (0.00%)	
occurrences (all)	1	0	
Microcytic anaemia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 49 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 79 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Motion sickness			
subjects affected / exposed	0 / 79 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Vertigo			

subjects affected / exposed occurrences (all)	1 / 79 (1.27%) 1	0 / 49 (0.00%) 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	18 / 79 (22.78%)	20 / 49 (40.82%)	
occurrences (all)	21	28	
Abdominal pain			
subjects affected / exposed	11 / 79 (13.92%)	19 / 49 (38.78%)	
occurrences (all)	13	30	
Nausea			
subjects affected / exposed	8 / 79 (10.13%)	12 / 49 (24.49%)	
occurrences (all)	8	15	
Vomiting			
subjects affected / exposed	5 / 79 (6.33%)	2 / 49 (4.08%)	
occurrences (all)	5	2	
Constipation			
subjects affected / exposed	0 / 79 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Flatulence			
subjects affected / exposed	0 / 79 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Dyspepsia			
subjects affected / exposed	1 / 79 (1.27%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Gastritis			
subjects affected / exposed	1 / 79 (1.27%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Gingival pain			
subjects affected / exposed	0 / 79 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Abdominal distension			
subjects affected / exposed	1 / 79 (1.27%)	0 / 49 (0.00%)	
occurrences (all)	1	0	
Bowel movement irregularity			
subjects affected / exposed	1 / 79 (1.27%)	0 / 49 (0.00%)	
occurrences (all)	1	0	

Skin and subcutaneous tissue disorders	Ecchymosis			
	subjects affected / exposed	1 / 79 (1.27%)	1 / 49 (2.04%)	
	occurrences (all)	1	1	
	Hyperhidrosis			
	subjects affected / exposed	0 / 79 (0.00%)	1 / 49 (2.04%)	
	occurrences (all)	0	1	
Rash	subjects affected / exposed	0 / 79 (0.00%)	1 / 49 (2.04%)	
	occurrences (all)	0	1	
Endocrine disorders				
Hypothyroidism				
subjects affected / exposed				
occurrences (all)				
Musculoskeletal and connective tissue disorders				
Myalgia				
subjects affected / exposed				
occurrences (all)				
Arthralgia				
subjects affected / exposed				
occurrences (all)				
Back pain				
subjects affected / exposed				
occurrences (all)				
Muscle spasms				
subjects affected / exposed				
occurrences (all)				
Tendonitis				
subjects affected / exposed				
occurrences (all)				
Torticollis				
subjects affected / exposed				
occurrences (all)				
Musculoskeletal chest pain				
subjects affected / exposed				
occurrences (all)				

Neck pain			
subjects affected / exposed	1 / 79 (1.27%)	0 / 49 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 79 (1.27%)	0 / 49 (0.00%)	
occurrences (all)	1	0	
Osteoarthritis			
subjects affected / exposed	1 / 79 (1.27%)	0 / 49 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	8 / 79 (10.13%)	13 / 49 (26.53%)	
occurrences (all)	8	18	
Upper respiratory tract infection			
subjects affected / exposed	3 / 79 (3.80%)	4 / 49 (8.16%)	
occurrences (all)	3	4	
Pharyngitis			
subjects affected / exposed	1 / 79 (1.27%)	3 / 49 (6.12%)	
occurrences (all)	1	4	
Rhinitis			
subjects affected / exposed	2 / 79 (2.53%)	3 / 49 (6.12%)	
occurrences (all)	4	3	
Bronchitis			
subjects affected / exposed	2 / 79 (2.53%)	2 / 49 (4.08%)	
occurrences (all)	2	2	
Cystitis			
subjects affected / exposed	1 / 79 (1.27%)	2 / 49 (4.08%)	
occurrences (all)	1	2	
Gastroenteritis			
subjects affected / exposed	3 / 79 (3.80%)	1 / 49 (2.04%)	
occurrences (all)	3	1	
Influenza			
subjects affected / exposed	3 / 79 (3.80%)	1 / 49 (2.04%)	
occurrences (all)	3	1	
Viral infection			

subjects affected / exposed	1 / 79 (1.27%)	2 / 49 (4.08%)
occurrences (all)	1	2
Folliculitis		
subjects affected / exposed	0 / 79 (0.00%)	2 / 49 (4.08%)
occurrences (all)	0	2
Angular cheilitis		
subjects affected / exposed	0 / 79 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	1
Ear infection		
subjects affected / exposed	0 / 79 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	1
Gastroenteritis viral		
subjects affected / exposed	0 / 79 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	1
Wound infection		
subjects affected / exposed	0 / 79 (0.00%)	1 / 49 (2.04%)
occurrences (all)	0	1
Sinusitis		
subjects affected / exposed	1 / 79 (1.27%)	0 / 49 (0.00%)
occurrences (all)	1	0
Tonsillitis		
subjects affected / exposed	1 / 79 (1.27%)	0 / 49 (0.00%)
occurrences (all)	1	0
Tracheitis		
subjects affected / exposed	1 / 79 (1.27%)	0 / 49 (0.00%)
occurrences (all)	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 October 2015	. Change of Sponsor representative . Coordinating investigator's name added . Change to multicenter study by adding 1 additional centre . Important medical events (IMEs) will be considered serious and be processed like SAEs, definition has been added. . Secondary endpoints of immunogenicity: Median titers and seroconversion rate of type-specific polio antibodies at day 28 will be described for both groups combined and D 56 is added for seroconversion rate of type-specific polio antibodies in Group 2. . Exploratory objectives and endpoints: 'in a subset of stool samples' has been added and assessment of the genetic sequence heterogeneity and potential for neurovirulence. . Statistical methods: 'Cumulative rates of seroconversion and sero-protection will be tabulated' has been deleted in synopsis and section 10.2 . Information about the Data Safety Monitoring board has been added . Time and events schedule : Blood samples for polio antibodies on D63 and 70 have been removed Remote daily contact during 14 days after each vaccination has been changed to 10 days after each vaccination . criteria for elimination from per-protocol population adapted . exclusion criterion 12 corrected to prevent administration of a vaccine other than the study vaccine during the entire study period . randomization and blinding: use of randomization envelopes - HCG testing at Day 0 and at Days 28 and 56 for Group 2 has been added . grading of fever added - recovering/resolving and not recovered added as possible outcome - description of solicited adverse events added - section 13.14 Confidentiality adapted: data of subjects will only be forwarded in a coded way - section 10.2: term 'independently' has been deleted as both groups will be assessed combined until Day 28
30 December 2015	. Synopsis + page 32: Inclusion criterion 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 24. . Section 11.2, grading of fever: a typo has been corrected

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported