Clinical trial results:
A Phase IV, Uncontrolled, Open-Label, Single-Center Study in Adolescents and Adults: Evaluation of Immunogenicity and Safety of the First Booster Vaccination With Novartis Vaccines and Diagnostics (Ex Chiron's) TBE Vaccine for Adults in Participants of Study V48P7 and Long-Term Evaluation of Immunogenicity up to 5 Years After First Booster Vaccination.

Summary

EudraCT number	2006-001676-21
Trial protocol	CZ
Global end of trial date	07 October 2011

Results information

Result version number	v1 (current)
This version publication date	12 December 2016
First version publication date	01 August 2015

Trial information

Trial identification

Sponsor protocol code	V48P7E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00387634
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics GmbH & Co. KG
Sponsor organisation address	Postfach 1630, Marburg, Germany, 35006
Public contact	Posting Director, Novartis Vaccines , RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines , RegistryContactVaccinesUS@novartis.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 August 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 October 2011
Global end of trial reached?	Yes
Global end of trial date	07 October 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Descriptive evaluation of subjects with respect to antibody titers and percentage of subjects with neutralizing antibodies on day 0 in study V48P7E1 (ie, day of first booster vaccination after primary vaccination in study V48P7 for subjects who did not get a booster vaccination, or first blood draw for those who did receive a booster dose), on day 21 in study V48P7E1 (7 days) and year 1, 2, 3, 4, and 5 (±30 days each) after booster vaccination with Novartis Vaccines and Diagnostics (ex Chiron's) tick borne encephalitis (TBE) vaccine for adults as measured by neutralization test ([NT]; in-house, Novartis Vaccines and Diagnostics).

Protection of trial subjects:

This study was performed with the ethical principles that have their origin in the Declaration of Helsinki, that are consistent with GCP according to International Conference on Harmonisation (ICH) guidelines, the applicable regulatory requirements(s) for the country in which the study was conducted, and applicable standard operating procedures (SOPs).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 September 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 323
Worldwide total number of subjects	323
EEA total number of subjects	323

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)	20
Adults (18-64 years)	293
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled in 1 site in Czech Republic.

Pre-assignment

Screening details:

All the enrolled subjects were included in the trial.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	TBE_R

Arm description:

Subjects received First booster vaccine at 3 years after the completion of the primary vaccination series of study V48P7. Primary vaccination: Rapid (R) schedule group- all 3 vaccinations were given within 3 weeks, with an interval of 1 week between the first and second vaccination and an interval of 2 weeks between the second and third vaccination (ie, on day 0, day 7, day 21 of study V48P7).

Arm type	Experimental
Investigational medicinal product name	TBE vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml

Arm title	TBE_R_B

Arm description:

Subjects received the first booster between study V48P7 and V48P7E1 at 12 to 18 months after the completion of the primary vaccination series of study V48P7. Primary vaccination: Rapid (R) schedule group- all 3 vaccinations were given within 3 weeks, with an interval of 1 week between the first and second vaccination and an interval of 2 weeks between the second and third vaccination (ie, on day 0, day 7, day 21 of study V48P7). Subjects in the arm did not receive any intervention (only blood draw).

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	TBE_C

Arm description:

Subjects received First booster vaccine at 3 years after the completion of the primary vaccination series of study V48P7. Primary vaccination Conventional schedule group-consisted of 3 vaccinations with an interval of 1 month between the first and second vaccination and an interval of 10 months to 12 months between the second and third vaccination (ie, on day 0, day 28, day 300 of study V48P7).

Arm type	Experimental

Investigational medicinal product name	TBE vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml

Arm title	TBE_MC

Arm description:

Subjects received First booster vaccine at 3 years after the completion of the primary vaccination series of study V48P7. Primary vaccination Modified conventional (MC) schedule group-TBE vaccine was given with a reduced interval between first and second vaccination; ie, from 28 days to 21 days (ie, vaccinations on day 0, day 21, day 300 of study V48P7).

Arm type	Experimental
Investigational medicinal product name	TBE vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml

Arm title	TBE_AC

Arm description:

Subjects received First booster vaccine at 3 years after the completion of the primary vaccination series of study V48P7. Primary vaccination Accelerated conventional (AC) schedule group-TBE vaccine was given by means of an even more reduced interval between the first and second vaccination; ie, from 28 days to 14 days (ie, vaccinations on day 0, day 14, and day 300 of study V48P7).

Arm type	Experimental
Investigational medicinal product name	TBE vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml

Number of subjects in period 1	TBE_R	TBE_R_B	TBE_C
Started	9	40	55
Completed	9	39	52
Not completed	0	1	3
Death	-	1	1
Lost to follow-up	-	-	1
Protocol deviation	-	-	1

Number of subjects in period 1	TBE_MC	TBE_AC
Started	110	109

Completed	107	106
Not completed	3	3
Death	-	2
Lost to follow-up	1	-
Protocol deviation	2	1

Baseline characteristics

Reporting groups

Reporting group title	TBE_R

Reporting group description:

Subjects received First booster vaccine at 3 years after the completion of the primary vaccination series of study V48P7. Primary vaccination: Rapid (R) schedule group- all 3 vaccinations were given within 3 weeks, with an interval of 1 week between the first and second vaccination and an interval of 2 weeks between the second and third vaccination (ie, on day 0, day 7, day 21 of study V48P7).

Reporting group title	TBE_R_B

Reporting group description:

Subjects received the first booster between study V48P7 and V48P7E1 at 12 to 18 months after the completion of the primary vaccination series of study V48P7. Primary vaccination: Rapid (R) schedule group- all 3 vaccinations were given within 3 weeks, with an interval of 1 week between the first and second vaccination and an interval of 2 weeks between the second and third vaccination (ie, on day 0, day 7, day 21 of study V48P7). Subjects in the arm did not receive any intervention (only blood draw).

Reporting group title	TBE_C

Reporting group description:

Subjects received First booster vaccine at 3 years after the completion of the primary vaccination series of study V48P7. Primary vaccination Conventional schedule group-consisted of 3 vaccinations with an interval of 1 month between the first and second vaccination and an interval of 10 months to 12 months between the second and third vaccination (ie, on day 0, day 28, day 300 of study V48P7).

Reporting group title	TBE_MC

Reporting group description:

Subjects received First booster vaccine at 3 years after the completion of the primary vaccination series of study V48P7. Primary vaccination Modified conventional (MC) schedule group-TBE vaccine was given with a reduced interval between first and second vaccination; ie, from 28 days to 21 days (ie, vaccinations on day 0, day 21, day 300 of study V48P7).

Reporting group title	TBE_AC

Reporting group description:

Subjects received First booster vaccine at 3 years after the completion of the primary vaccination series of study V48P7. Primary vaccination Accelerated conventional (AC) schedule group-TBE vaccine was given by means of an even more reduced interval between the first and second vaccination; ie, from 28 days to 14 days (ie, vaccinations on day 0, day 14, and day 300 of study V48P7).

Reporting group values	TBE_R	TBE_R_B	TBE_C
Number of subjects	9	40	55
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			

Age continuous			
Units: years			
arithmetic mean	31.6	38.1	36.3
standard deviation	± 9.2	± 16.4	± 14.5
Gender categorical			
Units: Subjects			
Female	5	19	35
Male	4	21	20

Reporting group values	TBE_MC	TBE_AC	Total
Number of subjects	110	109	323
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	37.5	37.1	
standard deviation	± 14.3	± 14.4	-
Gender categorical			
Units: Subjects			
Female	63	58	180
Male	47	51	143

Subject analysis sets

Subject analysis set title	All enrolled set
Subject analysis set type	Per protocol

Subject analysis set description:

The enrolled population contained all subjects enrolled in the study, ie, with a record in DEMOG panel. This population was used for the analysis of demographics, concomitant medications, medical history and all subject listings.

Subject analysis set title	Full Analysis Set (FAS) Immunogenecity
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects who:
▫ were admitted to the study, irrespective whether they received study vaccination or not;
▫ provided at least one evaluable serum sample

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population included all subjects who received a booster vaccination on day 0 (V48P7E1) excluding TBE_R_B group and provided postvaccination safety data.

Subject analysis set title	Per-Protocol (PP) Population, Immunogenicity
Subject analysis set type	Per protocol

Subject analysis set description:

The PPS comprised all subjects who:
▫ received the relevant booster vaccination correctly or had completed the rapid schedule and had already received a booster vaccination prior to admission into the present study;
▫ provided evaluable serum samples at the relevant time points;
▫ presented no major violations regarding concomitant medication/concomitant disease;
▫ had no major violations of inclusion/exclusion criteria.
Specifically, subjects meeting the following criteria were excluded from the PPS:
▫ subjects who received another vaccine within 4 weeks after the administration of the study vaccine*;
▫ subjects treated with immunoglobulins, whole blood or plasma derivates up to 4 weeks after administration of study vaccine subjects treated with immunosuppressants or systemic corticosteroids during the study period, except short term use of topic corticosteroids or low-dose systemic use (e.g.,up to 10 mg of prednisolone for up to 14 days).
Subjects meeting the following crite

Reporting group values	All enrolled set	Full Analysis Set (FAS) Immunogenecity	Safety Population
Number of subjects	323	323	278
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	37.1		
standard deviation	± 14.5	±	±
Gender categorical Units: Subjects			
Female	180		
Male	143		

Reporting group values	Per-Protocol (PP) Population, Immunogenicity		
Number of subjects	289		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			

From 65-84 years 85 years and over			

Age continuous Units: years arithmetic mean standard deviation	±		
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	TBE_R

Reporting group description:

Subjects received First booster vaccine at 3 years after the completion of the primary vaccination series of study V48P7. Primary vaccination: Rapid (R) schedule group- all 3 vaccinations were given within 3 weeks, with an interval of 1 week between the first and second vaccination and an interval of 2 weeks between the second and third vaccination (ie, on day 0, day 7, day 21 of study V48P7).

Reporting group title	TBE_R_B

Reporting group description:

Subjects received the first booster between study V48P7 and V48P7E1 at 12 to 18 months after the completion of the primary vaccination series of study V48P7. Primary vaccination: Rapid (R) schedule group- all 3 vaccinations were given within 3 weeks, with an interval of 1 week between the first and second vaccination and an interval of 2 weeks between the second and third vaccination (ie, on day 0, day 7, day 21 of study V48P7). Subjects in the arm did not receive any intervention (only blood draw).

Reporting group title	TBE_C

Reporting group description:

Subjects received First booster vaccine at 3 years after the completion of the primary vaccination series of study V48P7. Primary vaccination Conventional schedule group-consisted of 3 vaccinations with an interval of 1 month between the first and second vaccination and an interval of 10 months to 12 months between the second and third vaccination (ie, on day 0, day 28, day 300 of study V48P7).

Reporting group title	TBE_MC

Reporting group description:

Subjects received First booster vaccine at 3 years after the completion of the primary vaccination series of study V48P7. Primary vaccination Modified conventional (MC) schedule group-TBE vaccine was given with a reduced interval between first and second vaccination; ie, from 28 days to 21 days (ie, vaccinations on day 0, day 21, day 300 of study V48P7).

Reporting group title	TBE_AC

Reporting group description:

Subjects received First booster vaccine at 3 years after the completion of the primary vaccination series of study V48P7. Primary vaccination Accelerated conventional (AC) schedule group-TBE vaccine was given by means of an even more reduced interval between the first and second vaccination; ie, from 28 days to 14 days (ie, vaccinations on day 0, day 14, and day 300 of study V48P7).

Subject analysis set title	All enrolled set
Subject analysis set type	Per protocol

Subject analysis set description:

The enrolled population contained all subjects enrolled in the study, ie, with a record in DEMOG panel. This population was used for the analysis of demographics, concomitant medications, medical history and all subject listings.

Subject analysis set title	Full Analysis Set (FAS) Immunogenecity
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects who:
- were admitted to the study, irrespective whether they received study vaccination or not;
- provided at least one evaluable serum sample

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population included all subjects who received a booster vaccination on day 0 (V48P7E1) excluding TBE_R_B group and provided postvaccination safety data.

Subject analysis set title	Per-Protocol (PP) Population, Immunogenicity
Subject analysis set type	Per protocol

Subject analysis set description:

The PPS comprised all subjects who:
▫ received the relevant booster vaccination correctly or had completed the rapid schedule and had already received a booster vaccination prior to admission into the present study;
▫ provided evaluable serum samples at the relevant time points;
▫ presented no major violations regarding concomitant medication/concomitant disease;
▫ had no major violations of inclusion/exclusion criteria.
Specifically, subjects meeting the following criteria were excluded from the PPS:
▫ subjects who received another vaccine within 4 weeks after the administration of the study vaccine*;
▫ subjects treated with immunoglobulins, whole blood or plasma derivates up to 4 weeks after administration of study vaccine subjects treated with immunosuppressants or systemic corticosteroids during the study period, except short term use of topic corticosteroids or low-dose systemic use (e.g.,up to 10 mg of prednisolone for up to 14 days).
Subjects meeting the following crite

Primary: 1. Percentage of Subjects With Antibody Titers ≥2 as Measured by NT.

End point title	1. Percentage of Subjects With Antibody Titers ≥2 as Measured by NT.[1]

End point description:

Immunogenicity was measured in terms of the Percentage of Subjects With Antibody Titers ≥2 as Measured by Neutralization-test (NT). Data are reported based on the Per Protocol Set (PPS).

End point type	Primary

End point timeframe:

Year 5

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: No statistical analysis is associated to this endpoint. The analyses were run descriptively.

End point values	TBE_R	TBE_R_B	TBE_C	TBE_MC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	37	51	101
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 0	88 (47 to 100)	100 (91 to 100)	100 (93 to 100)	99 (95 to 100)
Day 21 (N=8,0,51,101,100)	100 (63 to 100)	0 (0 to 0)	100 (93 to 100)	100 (96 to 100)
Year 1 (N=8,35,50,100,101)	100 (63 to 100)	100 (90 to 100)	100 (93 to 100)	100 (96 to 100)
Year 2 (N=8,35,51,99,100)	100 (63 to 100)	100 (90 to 100)	100 (93 to 100)	100 (96 to 100)
Year 3 (N=8,35,49,100,100)	100 (63 to 100)	97 (85 to 100)	100 (93 to 100)	100 (96 to 100)
Year 4 (N=7,34,48,99,100)	100 (59 to 100)	100 (90 to 100)	100 (93 to 100)	100 (96 to 100)
Year 5 (N=8,36,48,98,99)	100 (63 to 100)	100 (90 to 100)	100 (93 to 100)	100 (96 to 100)

End point values	TBE_AC			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Percentage of subjects				

number (confidence interval 95%)				
Day 0	100 (96 to 100)			
Day 21 (N=8,0,51,101,100)	100 (96 to 100)			
Year 1 (N=8,35,50,100,101)	100 (96 to 100)			
Year 2 (N=8,35,51,99,100)	100 (96 to 100)			
Year 3 (N=8,35,49,100,100)	100 (96 to 100)			
Year 4 (N=7,34,48,99,100)	100 (96 to 100)			
Year 5 (N=8,36,48,98,99)	100 (96 to 100)			

Statistical analyses

No statistical analyses for this end point

Primary: 2. Percentage of Subjects With Antibody Titers ≥10 as Measured by NT.

End point title	2. Percentage of Subjects With Antibody Titers ≥10 as Measured by NT.[2]

End point description:

Immunogenicity was measured in terms of the Percentage of Subjects With Antibody Titers ≥10 as Measured by NT. Data are reported based on the PPS.

End point type	Primary

End point timeframe:

Year 5

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: No statistical analysis is associated to this endpoint. The analyses were run descriptively.

End point values	TBE_R	TBE_R_B	TBE_C	TBE_MC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	37	51	101
Units: Percentage of Subjects				
number (confidence interval 95%)				
Day 0	75 (35 to 97)	97 (86 to 100)	98 (90 to 100)	97 (92 to 99)
Day 21 (N=8,0,51,101,100)	100 (63 to 100)	0 (0 to 0)	100 (93 to 100)	100 (96 to 100)
Year 1 (N=8,35,50,100,101)	100 (63 to 100)	97 (85 to 100)	100 (93 to 100)	100 (96 to 100)
Year 2 (N=8,35,51,99,100)	100 (63 to 100)	97 (85 to 100)	100 (93 to 100)	99 (95 to 100)
Year 3 (N=8,35,49,100,100)	100 (63 to 100)	97 (85 to 100)	100 (93 to 100)	95 (89 to 98)
Year 4 (N=7,34,48,99,100)	100 (59 to 100)	94 (80 to 99)	100 (93 to 100)	97 (91 to 99)
Year 5 (N=8,36,48,98,99)	100 (63 to 100)	97 (85 to 100)	100 (93 to 100)	98 (93 to 100)

End point values	TBE_AC			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Percentage of Subjects				
number (confidence interval 95%)				
Day 0	99 (95 to 100)			
Day 21 (N=8,0,51,101,100)	100 (96 to 100)			
Year 1 (N=8,35,50,100,101)	100 (96 to 100)			
Year 2 (N=8,35,51,99,100)	100 (96 to 100)			
Year 3 (N=8,35,49,100,100)	100 (96 to 100)			
Year 4 (N=7,34,48,99,100)	100 (96 to 100)			
Year 5 (N=8,36,48,98,99)	100 (96 to 100)			

Statistical analyses

No statistical analyses for this end point

Primary: 3. Geometric Mean Antibody Titers (GMT) as Measured by NT.

End point title	3. Geometric Mean Antibody Titers (GMT) as Measured by

End point description:

Immunogenicity was measured in terms of the Geometric Mean Antibody Titers (GMT) as Measured by NT. Data are reported based on the PPS.

End point type	Primary

End point timeframe:

Year 5

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: No statistical analysis is associated to this endpoint. The analyses were run descriptively.

End point values	TBE_R	TBE_R_B	TBE_C	TBE_MC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	37	51	101
Units: Titers				
geometric mean (confidence interval 95%)				
Day 0	67 (22 to 201)	395 (236 to 658)	232 (150 to 359)	206 (151 to 281)
Day 21 (N=8,0,51,101,100)	1476 (646 to 3373)	0 (0 to 0)	1182 (852 to 1640)	1024 (812 to 1293)
Year 1 (N=8,35,50,100,101)	378 (152 to 936)	234 (152 to 362)	240 (167 to 345)	249 (193 to 322)

Year 2 (N=8,35,51,99,100)	370 (150 to 913)	235 (152 to 362)	229 (160 to 237)	211 (163 to 272)
Year 3 (N=8,35,49,100,100)	331 (121 to 910)	235 (145 to 380)	230 (153 to 346)	211 (159 to 281)
Year 4 (N=7,34,48,99,100)	137 (50 to 379)	192 (121 to 304)	250 (169 to 368)	208 (159 to 273)
Year 5 (N=8,36,48,98,99)	429 (151 to 1217)	358 (219 to 586)	300 (196 to 460)	281 (208 to 378)

End point values	TBE_AC			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Titers				
geometric mean (confidence interval 95%)				
Day 0	237 (174 to 323)			
Day 21 (N=8,0,51,101,100)	1059 (838 to 1338)			
Year 1 (N=8,35,50,100,101)	246 (190 to 317)			
Year 2 (N=8,35,51,99,100)	232 (180 to 300)			
Year 3 (N=8,35,49,100,100)	228 (171 to 303)			
Year 4 (N=7,34,48,99,100)	253 (193 to 331)			
Year 5 (N=8,36,48,98,99)	305 (227 to 410)			

Statistical analyses

No statistical analyses for this end point

Primary: 4. Ratios of Geometric Mean Antibody Titers (GMT) as Measured by NT.

End point title	4. Ratios of Geometric Mean Antibody Titers (GMT) as Measured by NT.[4]

End point description:

Immunogenicity was measured in terms of the Ratios of Geometric Mean Antibody Titers (GMT) as Measured by NT. Data are reported based on the PPS.

End point type	Primary

End point timeframe:

Year 5

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is associated to this endpoint. The analyses were run descriptively.

End point values	TBE_R	TBE_R_B	TBE_C	TBE_MC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	37	51	101
Units: Ratio of GMTs				
number (confidence interval 95%)				
Day 21/Day 0 (N=8,0,51,101,100)	22 (11 to 45)	0 (0 to 0)	5.1 (3.85 to 6.75)	4.97 (4.07 to 6.07)
year 1/day 0 (N=8,35,50,100,101)	5.66 (2.83 to 11)	0.57 (0.41 to 0.79)	1.04 (0.79 to 1.37)	1.21 (1 to 1.48)
Year2/day 0 (N=8,35,51,99,100)	5.55 (3.09 to 9.96)	0.57 (0.43 to 0.75)	0.99 (0.78 to 1.24)	1.03 (0.87 to 1.21)
Year 3/day 0 (N=8,35,49,100,100)	4.97 (2.8 to 8.8)	0.57 (0.43 to 0.75)	1.04 (0.82 to 1.31)	1.05 (0.89 to 1.23)
Year 4/day 0 (N=7,34,48,99,100)	2.15 (0.92 to 5)	0.47 (0.32 to 0.69)	1.06 (0.77 to 1.46)	1.04 (0.83 to 1.31)
Year 5/day 0 (N=8,36,48,98,99)	6.44 (3.56 to 12)	0.88 (0.67 to 1.16)	1.28 (1 to 1.63)	1.38 (1.16 to 1.63)

End point values	TBE_AC			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Ratio of GMTs				
number (confidence interval 95%)				
Day 21/Day 0 (N=8,0,51,101,100)	4.5 (3.68 to 5.49)			
year 1/day 0 (N=8,35,50,100,101)	1.04 (0.85 to 1.26)			
Year2/day 0 (N=8,35,51,99,100)	0.96 (0.82 to 1.14)			
Year 3/day 0 (N=8,35,49,100,100)	0.95 (0.81 to 1.12)			
Year 4/day 0 (N=7,34,48,99,100)	1.05 (0.84 to 1.32)			
Year 5/day 0 (N=8,36,48,98,99)	1.28 (1.08 to 1.51)			

Statistical analyses

No statistical analyses for this end point

Primary: 5. Geometric Mean Antibody Titers as Measured by NT for Rapid Schedule Only.

End point title	5. Geometric Mean Antibody Titers as Measured by NT for Rapid Schedule Only.[5][6]

End point description:

Immunogenicity was measured in terms of the Geometric Mean Antibody Titers as Measured by NT for Rapid Schedule Only. Data are reported based on the PPS.

End point type	Primary

End point timeframe:

Visit 6 up to visit 10 (Day 0)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is associated to this endpoint. The analyses were run descriptively.

[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: No statistical analysis is associated to this endpoint. The analyses were run descriptively.

End point values	TBE_R	TBE_R_B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	37		
Units: Titers				
geometric mean (confidence interval 95%)				
Visit 6	64 (27 to 152)	42 (28 to 63)		
Visit 7	19 (7.76 to 45)	33 (22 to 49)		
Visit 8	14 (6.29 to 30)	24 (17 to 34)		
Visit 10	67 (21 to 208)	395 (232 to 670)		

Statistical analyses

No statistical analyses for this end point

Primary: 6. Ratios of Geometric Mean Antibody Titers as Measured by NT for Rapid Schedule Only.

End point title	6. Ratios of Geometric Mean Antibody Titers as Measured by NT for Rapid Schedule Only.[7][8]

End point description:

Immunogenicity was measured in terms of the ratios of the Geometric Mean Antibody Titers as Measured by NT for Rapid Schedule Only. Data are reported based on the PPS.

End point type	Primary

End point timeframe:

up to Visit 10 (Day 0)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is associated to this endpoint. The analyses were run descriptively.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint. The analyses were run descriptively.

End point values	TBE_R	TBE_R_B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	37		
Units: Ratio of GMTs				
number (confidence interval 95%)				
Visit 10: Visit 6	1.04 (0.3 to 3.57)	9.4 (5.3 to 17)		
Visit 10: Visit 7	3.56 (1.26 to 10)	12 (7.46 to 20)		
Visit 10: Visit 8	4.87 (1.82 to 13)	16 (10 to 26)		

Statistical analyses

No statistical analyses for this end point

Primary: 7. Geometric Mean Antibody Titers as Measured by NT for Conventional Schedules.

End point title	7. Geometric Mean Antibody Titers as Measured by NT for Conventional Schedules.[9][10]

End point description:

Immunogenicity was measured in terms of the Geometric Mean Antibody Titers as Measured by NT for Conventional Schedules. Data are reported based on the PPS.

End point type	Primary

End point timeframe:

up to visit 10 (Day 0)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is associated to this endpoint. The analyses were run descriptively.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint. The analyses were run descriptively.

End point values	TBE_C	TBE_MC	TBE_AC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	101	101	
Units: Titers				
geometric mean (confidence interval 95%)				
Visit 9	1131 (770 to 1660)	1133 (862 to 1489)	1143 (870 to 1501)	
Visit 10	232 (150 to 359)	206 (151 to 281)	237 (174 to 323)	

Statistical analyses

No statistical analyses for this end point

Primary: 8. Ratios of the Geometric Mean Antibody Titers as Measured by NT for Conventional Schedules.

End point title	8. Ratios of the Geometric Mean Antibody Titers as Measured by NT for Conventional Schedules.[11][12]

End point description:

Immunogenicity was measured in terms of the ratios of the Geometric Mean Antibody Titers as Measured by NT for Conventional Schedules. Data are reported based on the PPS.

End point type	Primary

End point timeframe:

up to Visit 10 (Day 0)

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is associated to this endpoint. The analyses were run descriptively.

[12] - 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: No statistical analysis is associated to this endpoint. The analyses were run descriptively.

End point values	TBE_C	TBE_MC	TBE_AC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	101	101	
Units: Ratio of GMTs				
number (confidence interval 95%)				
Visit 10/visit 9	0.21 (0.16 to 0.26)	0.18 (0.15 to 0.21)	0.21 (0.18 to 0.24)	

Statistical analyses

No statistical analyses for this end point

Secondary: 9. Number of subjects with solicited local and solicited systemic AEs

End point title	9. Number of subjects with solicited local and solicited systemic AEs[13]

End point description:

Safety was assessed in terms of the Number of subjects with solicited local and solicited systemic AEs up to 3 days after booster vaccination.

End point type	Secondary

End point timeframe:

4 days (up to day 3)

Notes:

[13] - 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: No statistical analysis is associated to this endpoint. The analyses were run descriptively.

End point values	TBE_R	TBE_C	TBE_MC	TBE_AC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	55	108	106
Units: Subjects				
Pain_Classification A	7	35	59	52
Erythema (mm)_Classification A	1	3	9	9
Swelling (mm)_Classification A	0	4	7	6
Pain_Classification B	7	35	59	52
Erythema (mm)_Classification B	0	1	4	1
Swelling (mm)_Classification B	0	3	6	1
Nausea	1	2	3	4
Malaise	1	3	8	7
Myalgia	3	12	18	13

Arthralgia	1	3	7	3
Headache	2	8	12	17

Statistical analyses

No statistical analyses for this end point

Secondary: 10. Number of Subjects with unsolicited AEs.

End point title	10. Number of Subjects with unsolicited AEs.[14]

End point description:

Safety was assessed in terms of the number of subjects with unsolicited Adverse Events from Day 0 up to Day 21.

End point type	Secondary

End point timeframe:

Day 0 up to day 21.

Notes:

[14] - 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: No statistical analysis is associated to this endpoint. The analyses were run descriptively.

End point values	TBE_R	TBE_C	TBE_MC	TBE_AC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	55	108	106
Units: Partecipants				
Any Adverse Events	1	9	12	14
At least possibly related AEs	1	3	5	3
Serious AEs	0	3	5	7
At least possibly related SAEs	0	0	0	0
Deaths	0	1	0	2

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 0 through year 5.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	TBE_R

Reporting group description:

Subjects received First booster vaccine at 3 years after the completion of the primary vaccination series of study V48P7. Primary vaccination: Rapid (R) schedule group- all 3 vaccinations were given within 3 weeks, with an interval of 1 week between the first and second vaccination and an interval of 2 weeks between the second and third vaccination (ie, on day 0, day 7, day 21 of study V48P7).

Reporting group title	TBE_C

Reporting group description:

Subjects received First booster vaccine at 3 years after the completion of the primary vaccination series of study V48P7. Primary vaccination Conventional schedule group-consisted of 3 vaccinations with an interval of 1 month between the first and second vaccination and an interval of 10 months to 12 months between the second and third vaccination (ie, on day 0, day 28, day 300 of study V48P7).

Reporting group title	TBE_MC

Reporting group description:

Subjects received First booster vaccine at 3 years after the completion of the primary vaccination series of study V48P7. Primary vaccination Modified conventional (MC) schedule group-TBE vaccine was given with a reduced interval between first and second vaccination; ie, from 28 days to 21 days (ie, vaccinations on day 0, day 21, day 300 of study V48P7).

Reporting group title	TBE_AC

Reporting group description:

Subjects received First booster vaccine at 3 years after the completion of the primary vaccination series of study V48P7. Primary vaccination Accelerated conventional (AC) schedule group-TBE vaccine was given by means of an even more reduced interval between the first and second vaccination; ie, from 28 days to 14 days (ie, vaccinations on day 0, day 14, and day 300 of study V48P7).

Serious adverse events	TBE_R	TBE_C	TBE_MC
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	3 / 55 (5.45%)	5 / 108 (4.63%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0		0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 9 (0.00%)	1 / 55 (1.82%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma			

subjects affected / exposed	0 / 9 (0.00%)	1 / 55 (1.82%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Malignant melanoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 55 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle Fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 55 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 55 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patella Fracture			
subjects affected / exposed	0 / 9 (0.00%)	1 / 55 (1.82%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 55 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 55 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Trisomy 21			
subjects affected / exposed	0 / 9 (0.00%)	0 / 55 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	0 / 9 (0.00%)	0 / 55 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial Infarction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 55 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular Tachycardia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 55 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 9 (0.00%)	0 / 55 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Peroneal Nerve Palsy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 55 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 55 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 55 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			

subjects affected / exposed	0 / 9 (0.00%)	0 / 55 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	TBE_AC		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 106 (6.60%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Glioblastoma			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	1 / 1		
Malignant melanoma			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ankle Fracture			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Patella Fracture			

subjects affected / exposed	0 / 106 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal Fracture				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thoracic vertebral fracture				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Trisomy 21				
subjects affected / exposed	0 / 106 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Angina Pectoris				
subjects affected / exposed	0 / 106 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial Infarction				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	1 / 1			
Supraventricular Tachycardia				
subjects affected / exposed	0 / 106 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Abortion induced				
subjects affected / exposed	0 / 106 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Nervous system disorders			
Peroneal Nerve Palsy			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 106 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	TBE_R	TBE_C	TBE_MC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 9 (77.78%)	40 / 55 (72.73%)	69 / 108 (63.89%)
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 9 (22.22%)	8 / 55 (14.55%)	12 / 108 (11.11%)
occurrences (all)	3	10	14
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	1 / 9 (11.11%)	3 / 55 (5.45%)	9 / 108 (8.33%)
occurrences (all)	1	3	9
Injectino site pain			

subjects affected / exposed	7 / 9 (77.78%)	35 / 55 (63.64%)	59 / 108 (54.63%)
occurrences (all)	7	35	60
Injection site swelling			
subjects affected / exposed	0 / 9 (0.00%)	4 / 55 (7.27%)	7 / 108 (6.48%)
occurrences (all)	0	4	7
Malaise			
subjects affected / exposed	1 / 9 (11.11%)	3 / 55 (5.45%)	8 / 108 (7.41%)
occurrences (all)	1	4	8
Pyrexia			
subjects affected / exposed	1 / 9 (11.11%)	2 / 55 (3.64%)	3 / 108 (2.78%)
occurrences (all)	1	2	3
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 9 (11.11%)	2 / 55 (3.64%)	3 / 108 (2.78%)
occurrences (all)	1	3	3
Musculoskeletal and connective tissue disorders			
Athralgia			
subjects affected / exposed	1 / 9 (11.11%)	3 / 55 (5.45%)	7 / 108 (6.48%)
occurrences (all)	1	3	9
Myalgia			
subjects affected / exposed	3 / 9 (33.33%)	12 / 55 (21.82%)	18 / 108 (16.67%)
occurrences (all)	3	14	19

Non-serious adverse events	TBE_AC		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	62 / 106 (58.49%)		
Nervous system disorders			
Headache			
subjects affected / exposed	17 / 106 (16.04%)		
occurrences (all)	19		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	9 / 106 (8.49%)		
occurrences (all)	9		
Injectino site pain			

subjects affected / exposed	52 / 106 (49.06%)		
occurrences (all)	53		
Injection site swelling			
subjects affected / exposed	6 / 106 (5.66%)		
occurrences (all)	6		
Malaise			
subjects affected / exposed	7 / 106 (6.60%)		
occurrences (all)	8		
Pyrexia			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 106 (3.77%)		
occurrences (all)	5		
Musculoskeletal and connective tissue disorders			
Athralgia			
subjects affected / exposed	3 / 106 (2.83%)		
occurrences (all)	3		
Myalgia			
subjects affected / exposed	13 / 106 (12.26%)		
occurrences (all)	13		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 February 2008	slight revision of wording regarding points of time of blood withdrawal; adjustment related to ELISA tests (ie, TBE antibody titers were to be determined by Neutralization Test only).Specification of SAE reporting procedure

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24950352