Clinical trial results:
A phase IV, open-label, single-center study to evaluate long term immunogenicity up to 10 years after the first booster immunization with Tick Borne Encephalitis vaccine in adults who received 1 of 3 different primary vaccination schedules

Summary

EudraCT number	2011-003255-19
Trial protocol	CZ
Global end of trial date	30 September 2016

Results information

Result version number	v3
This version publication date	14 October 2017
First version publication date	22 February 2015
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	205335

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01562444
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium,
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, (44)2089 904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, (44)2089 904466, GSKClinicalSupportHD@gsk.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	30 September 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 September 2016
Global end of trial reached?	Yes
Global end of trial date	30 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Immunogenicity Objectives:
To evaluate the persistence of antibody response to a booster vaccine starting 6 years after the booster administration and following subjects up to 10 years after first booster administration.

Protection of trial subjects:

The clinical study was designed, implemented and reported in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations (including European Directive 2001/20/EC, US Code of Federal Regulations Title 21, and Japanese Ministry of Health, Labor, and Welfare), and with the ethical principles laid down in the Declaration of Helsinki. Eligible subjects were included in the study after providing written (witnessed, where required by law or regulation), Independent Ethics Committee (IEC)-approved informed consent, or, if incapable of doing so, after such consent was provided by a legally acceptable representative of the subject.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 March 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 205
Worldwide total number of subjects	205
EEA total number of subjects	205

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)	189
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects who completed V48P7E1 study having received primary vaccination according to rapid (R), conventional (C) or accelerated conventional (AC) schedule were included in the study. Since modified conventional (MC) had not been accepted by health authorities as primary vaccination schedule, this group from V48P7 was not enrolled in this study.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	205
Number of subjects completed	205

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 Group

Arm description:

Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to rapid (R) schedule i.e., on days 0, 7 (+3) and 21 (+7) in the parent study (V48P7) and who were administered 1 booster dose of Encepur adults either 12-18 months after R schedule completion or in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination (for those subjects boostered before V48P7E1 study start, the blood draw occurred annually starting from >6 years up to >10 years after booster vaccination).

Arm type	Blood draw
Investigational medicinal product name	Blood draw
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Anticoagulant and preservative solution for blood
Routes of administration	Route of administration not applicable

Dosage and administration details:

Annual blood draw at years 6 (Visit 18), 7 (Visit 19), 8 (Visit 20), 9 (Visit 21) and 10 (Visit 22)

Arm title	TBE_C Group

Arm description:

Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to conventional (C) schedule i.e., on days 0, 28 (+10) and 300 (+21) in the parent study (V48P7) and were administered 1 booster dose of Encepur adults in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination.

Arm type	Blood draw

Investigational medicinal product name	Blood draw
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Anticoagulant and preservative solution for blood
Routes of administration	Route of administration not applicable

Dosage and administration details:

Annual blood draw at years 6 (Visit 18), 7 (Visit 19), 8 (Visit 20), 9 (Visit 21) and 10 (Visit 22)

Arm title	TBE_AC Group

Arm description:

Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to accelerated conventional (AC) schedule i.e., on days 0, 14 (+3) and 300 (+21) in the parent study (V48P7) and were administered 1 booster dose of Encepur adults in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination.

Arm type	Blood draw
Investigational medicinal product name	Blood draw
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Anticoagulant and preservative solution for blood
Routes of administration	Route of administration not applicable

Dosage and administration details:

Annual blood draw at years 6 (Visit 18), 7 (Visit 19), 8 (Visit 20), 9 (Visit 21) and 10 (Visit 22)

Number of subjects in period 1	TBE_R Group	TBE_C Group	TBE_AC Group
Started	48	51	106
Completed	43	49	99
Not completed	5	2	7
Protocol forbidden medication	1	-	-
Did not meet entry criteria	2	-	3
Unavailable serological results	-	2	2
Protocol forbidden concomitant vaccine	1	-	1
Did not comply with blood draw schedule	1	-	1

Baseline characteristics

Reporting groups	
Reporting group title	TBE_R Group
Reporting group description:	
Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to rapid (R) schedule i.e., on days 0, 7 (+3) and 21 (+7) in the parent study (V48P7) and who were administered 1 booster dose of Encepur adults either 12-18 months after R schedule completion or in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination (for those subjects boostered before V48P7E1 study start, the blood draw occurred annually starting from >6 years up to >10 years after booster vaccination).	
Reporting group title	TBE_C Group
Reporting group description:	
Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to conventional (C) schedule i.e., on days 0, 28 (+10) and 300 (+21) in the parent study (V48P7) and were administered 1 booster dose of Encepur adults in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination.	
Reporting group title	TBE_AC Group
Reporting group description:	
Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to accelerated conventional (AC) schedule i.e., on days 0, 14 (+3) and 300 (+21) in the parent study (V48P7) and were administered 1 booster dose of Encepur adults in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination.	

Reporting group values	TBE_R Group	TBE_C Group	TBE_AC Group
Number of subjects	48	51	106
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 42.7 ± 15.25	 41.8 ± 14.34	 42.4 ± 14.35
Gender categorical Units: Subjects			
Female	24	32	55
Male	24	19	51
Race/Ethnicity, Customized Units: Subjects			
White	48	51	106

Reporting group values	Total		
Number of subjects	205		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- 		
Gender categorical Units: Subjects			
Female	111		
Male	94		
Race/Ethnicity, Customized Units: Subjects			
White	205		

End points

End points reporting groups

Reporting group title	TBE_R Group
Reporting group description:	
Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to rapid (R) schedule i.e., on days 0, 7 (+3) and 21 (+7) in the parent study (V48P7) and who were administered 1 booster dose of Encepur adults either 12-18 months after R schedule completion or in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination (for those subjects boostered before V48P7E1 study start, the blood draw occurred annually starting from >6 years up to >10 years after booster vaccination).	
Reporting group title	TBE_C Group
Reporting group description:	
Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to conventional (C) schedule i.e., on days 0, 28 (+10) and 300 (+21) in the parent study (V48P7) and were administered 1 booster dose of Encepur adults in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination.	
Reporting group title	TBE_AC Group
Reporting group description:	
Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to accelerated conventional (AC) schedule i.e., on days 0, 14 (+3) and 300 (+21) in the parent study (V48P7) and were administered 1 booster dose of Encepur adults in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination.	

Primary: Percentage of subjects with detectable TBE antibody titers greater than or equal to (≥) 2

End point title	Percentage of subjects with detectable TBE antibody titers greater than or equal to (≥) 2[1]
End point description:	
Antibody titers were measured by GlaxoSmithKline (GSK) neutralizing antibody (NT) assay.	
End point type	Primary
End point timeframe:	
At Year 6	

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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	106	
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of subjects	95.83 (85.75 to 99.49)	100 (93.02 to 100)	97.17 (91.95 to 99.41)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 2

End point title	Percentage of subjects with detectable TBE antibody titers ≥

End point description:

Antibody titers were measured by GSK NT assay.

End point type	Primary

End point timeframe:

At Year 7

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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	106	
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of subjects	93.75 (82.8 to 98.69)	100 (93.02 to 100)	95.28 (89.33 to 98.45)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 2

End point title	Percentage of subjects with detectable TBE antibody titers ≥

End point description:

Antibody titers were measured by GSK NT assay.

End point type	Primary

End point timeframe:

At Year 8

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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	106	
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of subjects	89.58 (77.34 to 96.53)	98.04 (89.55 to 99.95)	93.4 (86.87 to 97.3)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 2

End point title	Percentage of subjects with detectable TBE antibody titers ≥

End point description:

Antibody titers were measured by GSK NT assay.

End point type	Primary

End point timeframe:

At Year 9

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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	106	
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of subjects	89.58 (77.34 to 96.53)	94.12 (83.76 to 98.77)	92.45 (85.67 to 96.69)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 2

End point title	Percentage of subjects with detectable TBE antibody titers ≥

End point description:

Antibody titers were measured by GSK NT assay.

End point type	Primary

End point timeframe:

At Year 10

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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	106	
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of subjects	89.58 (77.34 to 96.53)	96.08 (86.54 to 99.52)	93.4 (86.87 to 97.3)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 10

End point title	Percentage of subjects with detectable TBE antibody titers ≥

End point description:

Antibody titers were measured by GSK NT assay.

End point type	Primary

End point timeframe:

At Year 6

Notes:

[6] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	106	
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of subjects	95.83 (85.75 to 99.49)	100 (93.02 to 100)	97.17 (91.95 to 99.41)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 10

End point title	Percentage of subjects with detectable TBE antibody titers ≥

End point description:

Antibody titers were measured by GSK NT assay.

End point type	Primary

End point timeframe:

At Year 7

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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	106	
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of subjects	93.75 (82.8 to 98.69)	100 (93.02 to 100)	95.28 (89.33 to 98.45)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 10

End point title	Percentage of subjects with detectable TBE antibody titers ≥

End point description:

Antibody titers were measured by GSK NT assay.

End point type	Primary

End point timeframe:

At Year 8

Notes:

[8] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	106	
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of subjects	89.58 (77.34 to 96.53)	98.04 (89.55 to 99.95)	92.45 (85.67 to 96.69)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 10

End point title	Percentage of subjects with detectable TBE antibody titers ≥

End point description:

Antibody titers were measured by GSK NT assay.

End point type	Primary

End point timeframe:

At Year 9

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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	106	
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of subjects	89.58 (77.34 to 96.53)	94.12 (83.76 to 98.77)	92.45 (85.67 to 96.69)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 10

End point title	Percentage of subjects with detectable TBE antibody titers ≥

End point description:

Antibody titers were measured by GSK NT assay.

End point type	Primary

End point timeframe:

At Year 10

Notes:

[10] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	106	
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of subjects	89.58 (77.34 to 96.53)	94.12 (83.76 to 98.77)	93.4 (86.87 to 97.3)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of Geometric Mean Antibody Titers (GMTs)

End point title	Evaluation of Geometric Mean Antibody Titers (GMTs)[11]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate Geometric Mean Ratios (GMRs). Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of

V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 6

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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	106	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=9;51;104)	76 (28 to 208)	228 (149 to 348)	228 (170 to 307)	
Baseline GMT post booster (N=48;51;105)	467 (325 to 670)	1135 (799 to 1611)	985 (771 to 1257)	
GMT Year 6	292 (184 to 463)	293 (187 to 458)	221 (162 to 302)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs

End point title	Evaluation of GMTs[12]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 7

Notes:

[12] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	106	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=9;51;104)	76 (28 to 208)	228 (149 to 348)	228 (170 to 307)	
Baseline GMT post booster (N=48;51;105)	467 (325 to 670)	1135 (799 to 1611)	985 (771 to 1257)	

GMT Year 7	295 (180 to 484)	343 (212 to 555)	254 (182 to 355)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs

End point title	Evaluation of GMTs[13]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At year 8

Notes:

[13] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	106	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=9;51;104)	76 (28 to 208)	228 (149 to 348)	228 (170 to 307)	
Baseline GMT post booster (N=48;51;105)	467 (325 to 670)	1135 (799 to 1611)	985 (771 to 1257)	
GMT Year 8	134 (79 to 227)	211 (127 to 352)	155 (109 to 221)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs

End point title	Evaluation of GMTs[14]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 9

Notes:

[14] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	106	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=9;51;104)	76 (28 to 208)	228 (149 to 348)	228 (170 to 307)	
Baseline GMT post booster (N=48;51;105)	467 (325 to 670)	1135 (799 to 1611)	985 (771 to 1257)	
GMT Year 9	211 (119 to 375)	214 (122 to 374)	194 (131 to 285)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs

End point title	Evaluation of GMTs[15]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 10

Notes:

[15] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	106	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=9;51;104)	76 (28 to 208)	228 (149 to 348)	228 (170 to 307)	
Baseline GMT post booster (N=48;51;105)	467 (325 to 670)	1135 (799 to 1611)	985 (771 to 1257)	
GMT Year 10	166 (94 to 295)	245 (140 to 428)	180 (122 to 265)	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Ratios (GMRs) calculated to pre booster baselines

End point title	Geometric Mean Ratios (GMRs) calculated to pre booster baselines[16]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 6

Notes:

[16] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	51	104	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	6.73 (3.23 to 14.02)	1.28 (0.94 to 1.75)	0.99 (0.8 to 1.23)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines

End point title	GMRs calculated to pre booster baselines[17]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 7

Notes:

[17] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	51	104	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	3.85 (1.48 to 10)	1.51 (1.01 to 2.25)	1.13 (0.85 to 1.5)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines

End point title	GMRs calculated to pre booster baselines[18]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 8

Notes:

[18] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	51	104	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.67 (0.23 to 1.91)	0.93 (0.6 to 1.44)	0.69 (0.51 to 0.95)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines

End point title	GMRs calculated to pre booster baselines[19]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 9

Notes:

[19] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	51	104	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	1.08 (0.33 to 3.53)	0.94 (0.57 to 1.54)	0.85 (0.6 to 1.21)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines

End point title	GMRs calculated to pre booster baselines[20]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 10

Notes:

[20] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	51	104	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.76 (0.26 to 2.24)	1.08 (0.68 to 1.69)	0.8 (0.59 to 1.1)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines

End point title	GMRs calculated to post booster baselines[21]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post

booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 6

Notes:

[21] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	105	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.63 (0.46 to 0.86)	0.26 (0.19 to 0.35)	0.22 (0.18 to 0.28)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines

End point title	GMRs calculated to post booster baselines[22]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 7

Notes:

[22] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	105	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.63 (0.41 to 0.96)	0.3 (0.2 to 0.46)	0.25 (0.19 to 0.34)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines

End point title	GMRs calculated to post booster baselines[23]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 8

Notes:

[23] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	105	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.29 (0.18 to 0.47)	0.19 (0.12 to 0.3)	0.16 (0.11 to 0.22)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines

End point title	GMRs calculated to post booster baselines[24]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 9

Notes:

[24] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	105	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.45 (0.27 to 0.77)	0.19 (0.11 to 0.32)	0.2 (0.14 to 0.28)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines

End point title	GMRs calculated to post booster baselines[25]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 10

Notes:

[25] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	51	105	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.36 (0.21 to 0.6)	0.22 (0.13 to 0.36)	0.18 (0.13 to 0.26)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 2 by age groups

End point title	Percentage of subjects with detectable TBE antibody titers ≥ 2 by age groups[26]

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years, ≥ 50 years, and ≥ 60 years.

End point type	Primary

End point timeframe:

At Year 6

Notes:

[26] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	81	
Units: Percentage of subjects				
number (confidence interval 95%)				
15-49 years: Antibody Titers ≥ 2	94.29 (80.84 to 99.3)	100 (90.97 to 100)	96.3 (89.56 to 99.23)	
≥ 50 years: Antibody Titers ≥ 2 (N=13;12;25)	100 (75.29 to 100)	100 (73.54 to 100)	100 (86.28 to 100)	
≥ 60 years: Antibody Titers ≥ 2 (N=4;3;7)	100 (39.76 to 100)	100 (29.24 to 100)	100 (59.04 to 100)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 2 by age groups

End point title	Percentage of subjects with detectable TBE antibody titers ≥ 2 by age groups[27]

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years, ≥ 50 years, and ≥ 60 years.

End point type	Primary

End point timeframe:

At Year 7

Notes:

[27] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	81	
Units: Percentage of subjects				
number (confidence interval 95%)				
15-49 years: Antibody Titers ≥ 2	91.43 (76.94 to 98.2)	100 (90.97 to 100)	93.83 (86.18 to 97.97)	
≥ 50 years: Antibody Titers ≥ 2 (N=13;12;25)	100 (75.29 to 100)	100 (73.54 to 100)	100 (86.28 to 100)	
≥ 60 years: Antibody Titers ≥ 2 (N=4;3;7)	100 (39.76 to 100)	100 (29.24 to 100)	100 (59.04 to 100)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 2 by age groups

End point title	Percentage of subjects with detectable TBE antibody titers ≥ 2 by age groups[28]

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years, ≥ 50 years, and ≥ 60 years.

End point type	Primary

End point timeframe:

At Year 8

Notes:

[28] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	81	
Units: Percentage of subjects				
number (confidence interval 95%)				
15-49 years: Antibody Titers ≥ 2	88.57 (73.26 to 96.8)	97.44 (86.52 to 99.94)	92.59 (84.57 to 97.23)	
≥ 50 years: Antibody Titers ≥ 2 (N=13;12;25)	92.31 (63.97 to 99.81)	100 (73.54 to 100)	96 (79.65 to 99.9)	
≥ 60 years: Antibody Titers ≥ 2 (N=4;3;7)	100 (39.76 to 100)	100 (29.24 to 100)	100 (59.04 to 100)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 2 by age groups

End point title	Percentage of subjects with detectable TBE antibody titers ≥ 2 by age groups[29]

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years, ≥ 50 years, and ≥ 60 years.

End point type	Primary

End point timeframe:

At Year 9

Notes:

[29] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	81	
Units: Percentage of subjects				
number (confidence interval 95%)				
15-49 years: Antibody Titers ≥ 2	88.57 (73.26 to 96.8)	92.31 (79.13 to 98.38)	91.36 (83 to 96.45)	

≥ 50 years: Antibody Titers ≥ 2 (N=13;12;25)	92.31 (63.97 to 99.81)	100 (73.54 to 100)	96 (79.65 to 99.9)	
≥ 60 years: Antibody Titers ≥ 2 (N=4;3;7)	100 (39.76 to 100)	100 (29.24 to 100)	100 (59.04 to 100)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 2 by age groups

End point title	Percentage of subjects with detectable TBE antibody titers ≥ 2 by age groups[30]

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years, ≥ 50 years, and ≥ 60 years.

End point type	Primary

End point timeframe:

At Year 10

Notes:

[30] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	81	
Units: Percentage of subjects				
number (confidence interval 95%)				
15-49 years: Antibody Titers ≥ 2	88.57 (73.26 to 96.8)	94.87 (82.68 to 99.37)	92.59 (84.57 to 97.23)	
≥ 50 years: Antibody Titers ≥ 2 (N=13;12;25)	92.31 (63.97 to 99.81)	100 (73.54 to 100)	96 (79.65 to 99.9)	
≥ 60 years: Antibody Titers ≥ 2 (N=4;3;7)	100 (39.76 to 100)	100 (29.24 to 100)	100 (59.04 to 100)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 10 by age groups

End point title	Percentage of subjects with detectable TBE antibody titers ≥ 10 by age groups[31]

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years, ≥ 50 years, and ≥ 60 years.

End point type	Primary

End point timeframe:

At Year 6

Notes:

[31] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	81	
Units: Percentage of subjects				
number (confidence interval 95%)				
15-49 years: Antibody Titers ≥ 10	94.29 (80.84 to 99.3)	100 (90.97 to 100)	96.3 (89.56 to 99.23)	
≥ 50 years: Antibody Titers ≥ 10 (N=13;12;25)	100 (75.29 to 100)	100 (73.54 to 100)	100 (86.28 to 100)	
≥ 60 years: Antibody Titers ≥ 10 (N=4;3;7)	100 (39.76 to 100)	100 (29.24 to 100)	100 (59.04 to 100)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 10 by age groups

End point title	Percentage of subjects with detectable TBE antibody titers ≥ 10 by age groups[32]

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years, ≥ 50 years, and ≥ 60 years.

End point type	Primary

End point timeframe:

At Year 7

Notes:

[32] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	81	
Units: Number of subjects				
number (confidence interval 95%)				
15-49 years: Antibody Titers ≥ 10	91.43 (76.94 to 98.2)	100 (90.97 to 100)	93.83 (86.18 to 97.97)	
≥ 50 years: Antibody Titers ≥ 10 (N=13;12;25)	100 (75.29 to 100)	100 (73.54 to 100)	100 (86.28 to 100)	
≥ 60 years: Antibody Titers ≥ 10 (N=4;3;7)	100 (39.76 to 100)	100 (29.24 to 100)	100 (59.04 to 100)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 10 by age groups

End point title	Percentage of subjects with detectable TBE antibody titers ≥ 10 by age groups[33]

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years, ≥ 50 years, and ≥ 60 years.

End point type	Primary

End point timeframe:

At Year 8

Notes:

[33] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	81	
Units: Percentage of subjects				
number (confidence interval 95%)				
15-49 years: Antibody Titers ≥ 10	88.57 (73.26 to 96.8)	97.44 (86.52 to 99.94)	91.36 (83 to 96.45)	
≥ 50 years: Antibody Titers ≥ 10 (N=13;12;25)	92.31 (63.97 to 99.81)	100 (73.54 to 100)	96 (79.65 to 99.9)	
≥ 60 years: Antibody Titers ≥ 10 (N=4;3;7)	100 (39.76 to 100)	100 (29.24 to 100)	100 (59.04 to 100)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 10 by age groups

End point title	Percentage of subjects with detectable TBE antibody titers ≥ 10 by age groups[34]

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years, ≥ 50 years, and ≥ 60 years.

End point type	Primary

End point timeframe:

At Year 9

Notes:

[34] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	81	
Units: Percentage of subjects				
number (confidence interval 95%)				
15-49 years: Antibody Titers ≥ 10	88.57 (73.26 to 96.8)	92.31 (79.13 to 98.38)	91.36 (83 to 96.45)	
≥ 50 years: Antibody Titers ≥ 10 (N=13;12;25)	92.31 (63.97 to 99.81)	100 (73.54 to 100)	96 (79.65 to 99.9)	
≥ 60 years: Antibody Titers ≥ 10 (N=4;3;7)	100 (39.76 to 100)	100 (29.24 to 100)	100 (59.04 to 100)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with detectable TBE antibody titers ≥ 10 by age groups

End point title	Percentage of subjects with detectable TBE antibody titers ≥ 10 by age groups[35]

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years, ≥ 50 years, and ≥ 60 years.

End point type	Primary

End point timeframe:

At Year 10

Notes:

[35] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	81	
Units: Percentage of subjects				
number (confidence interval 95%)				
15-49 years: Antibody Titers ≥ 10	88.57 (73.26 to 96.8)	94.87 (82.68 to 99.37)	92.59 (84.57 to 97.23)	
≥ 50 years: Antibody Titers ≥ 10 (N=13;12;25)	92.31 (63.97 to 99.81)	91.67 (61.52 to 99.79)	96 (79.65 to 99.9)	
≥ 60 years: Antibody Titers ≥ 10 (N=4;3;7)	100 (39.76 to 100)	66.67 (9.43 to 99.16)	100 (59.04 to 100)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs in the age group of 15-49 years

End point title	Evaluation of GMTs in the age group of 15-49 years[36]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 6

Notes:

[36] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	81	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=9;39;79)	76 (27 to 215)	253 (153 to 417)	263 (185 to 375)	
Baseline GMT post booster (N=35;39;80)	638 (413 to 984)	1299 (861 to 1959)	1008 (757 to 1343)	
GMT Year 6	332 (186 to 593)	341 (197 to 590)	235 (160 to 344)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs in the age group of 15-49 years

End point title	Evaluation of GMTs in the age group of 15-49 years[37]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 7

Notes:

[37] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	81	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=9;39;79)	76 (27 to 215)	253 (153 to 417)	263 (185 to 375)	
Baseline GMT post booster (N=35;39;80)	638 (413 to 984)	1299 (861 to 1959)	1008 (757 to 1343)	
GMT Year 7	304 (164 to 564)	384 (214 to 691)	250 (166 to 375)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs in the age group of 15-49 years

End point title	Evaluation of GMTs in the age group of 15-49 years[38]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 8

Notes:

[38] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	81	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=9;39;79)	76 (27 to 215)	253 (153 to 417)	263 (185 to 375)	
Baseline GMT post booster (N=35;39;80)	638 (413 to 984)	1299 (861 to 1959)	1008 (757 to 1343)	
GMT Year 8	151 (80 to 287)	219 (119 to 402)	160 (105 to 243)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs in the age group of 15-49 years

End point title	Evaluation of GMTs in the age group of 15-49 years[39]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 9

Notes:

[39] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	81	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=9;39;79)	76 (27 to 215)	253 (153 to 417)	263 (185 to 375)	
Baseline GMT post booster (N=35;39;80)	638 (413 to 984)	1299 (861 to 1959)	1008 (757 to 1343)	
GMT Year 9	218 (107 to 443)	211 (108 to 413)	191 (120 to 305)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs in the age group of 15-49 years

End point title	Evaluation of GMTs in the age group of 15-49 years[40]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 10

Notes:

[40] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	81	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=9;39;79)	76 (27 to 215)	253 (153 to 417)	263 (185 to 375)	
Baseline GMT post booster (N=35;39;80)	638 (413 to 984)	1299 (861 to 1959)	1008 (757 to 1343)	
GMT Year 10	188 (92 to 382)	266 (136 to 520)	200 (126 to 319)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs in the age group of ≥ 50 years

End point title	Evaluation of GMTs in the age group of ≥ 50 years[41]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 6

Notes:

[41] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	12	25	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=0;12;25)	0 (0 to 0)	163 (77 to 348)	145 (86 to 244)	
Baseline GMT post booster	201 (111 to 364)	733 (395 to 1361)	914 (595 to 1403)	
GMT Year 6	207 (107 to 401)	178 (89 to 355)	183 (114 to 295)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs in the age group of ≥ 50 years

End point title	Evaluation of GMTs in the age group of ≥ 50 years[42]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 7

Notes:

[42] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	12	25	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=0;12;25)	0 (0 to 0)	163 (77 to 348)	145 (86 to 244)	
Baseline GMT post booster	201 (111 to 364)	733 (395 to 1361)	914 (595 to 1403)	
GMT Year 7	272 (126 to 588)	237 (107 to 528)	270 (155 to 470)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs in the age group of ≥ 50 years

End point title	Evaluation of GMTs in the age group of ≥ 50 years[43]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 8

Notes:

[43] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	12	25	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=0;12;25)	0 (0 to 0)	163 (77 to 348)	145 (86 to 244)	
Baseline GMT post booster	201 (111 to 364)	733 (395 to 1361)	914 (595 to 1403)	
GMT Year 8	98 (39 to 245)	189 (73 to 492)	142 (73 to 275)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs in the age group of ≥ 50 years

End point title	Evaluation of GMTs in the age group of ≥ 50 years[44]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 9

Notes:

[44] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	12	25	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=0;12;25)	0 (0 to 0)	163 (77 to 348)	145 (86 to 244)	
Baseline GMT post booster	201 (111 to 364)	733 (395 to 1361)	914 (595 to 1403)	
GMT Year 9	193 (74 to 505)	224 (82 to 609)	202 (101 to 403)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs in the age group of ≥ 50 years

End point title	Evaluation of GMTs in the age group of ≥ 50 years[45]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 10

Notes:

[45] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	12	25	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=0;12;25)	0 (0 to 0)	163 (77 to 348)	145 (86 to 244)	
Baseline GMT post booster	201 (111 to 364)	733 (395 to 1361)	914 (595 to 1403)	
GMT Year 10	119 (47 to 302)	189 (72 to 496)	129 (66 to 251)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs in the age group of ≥ 60 years

End point title	Evaluation of GMTs in the age group of ≥ 60 years[46]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 6

Notes:

[46] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	3	7	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=0;3;7)	0 (0 to 0)	64 (13 to 316)	69 (24 to 197)	
Baseline GMT post booster	173 (71 to 425)	573 (203 to 1616)	498 (253 to 982)	
GMT Year 6	189 (52 to 688)	96 (22 to 427)	76 (29 to 202)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs in the age group of ≥ 60 years

End point title	Evaluation of GMTs in the age group of ≥ 60 years[47]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 7

Notes:

[47] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	3	7	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=0;3;7)	0 (0 to 0)	64 (31 to 316)	69 (24 to 197)	
Baseline GMT post booster	173 (71 to 425)	573 (203 to 1616)	498 (253 to 982)	
GMT Year 7	133 (26 to 677)	120 (18 to 789)	105 (31 to 360)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs in the age group of ≥ 60 years

End point title	Evaluation of GMTs in the age group of ≥ 60 years[48]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 8

Notes:

[48] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	3	7	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=0;3;7)	0 (0 to 0)	64 (13 to 316)	69 (24 to 197)	
Baseline GMT post booster	173 (71 to 425)	573 (203 to 1616)	498 (253 to 982)	
GMT Year 8	128 (26 to 620)	81 (13 to 504)	71 (21 to 234)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs in the age group of ≥ 60 years

End point title	Evaluation of GMTs in the age group of ≥ 60 years[49]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 9

Notes:

[49] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	3	7	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=0;3;7)	0 (0 to 0)	64 (13 to 316)	69 (24 to 197)	
Baseline GMT post booster	173 (71 to 425)	573 (203 to 1616)	498 (253 to 982)	
GMT Year 9	224 (52 to 965)	67 (12 to 362)	128 (42 to 385)	

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of GMTs in the age group of ≥ 60 years

End point title	Evaluation of GMTs in the age group of ≥ 60 years[50]

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 10

Notes:

[50] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	3	7	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline GMT pre booster (N=0;3;7)	0 (0 to 0)	64 (13 to 316)	69 (24 to 197)	
Baseline GMT post booster	173 (71 to 425)	573 (203 to 1616)	498 (253 to 982)	
GMT Year 10	181 (35 to 928)	57 (9 to 377)	72 (21 to 248)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines in the age group of 15-49 years

End point title	GMRs calculated to pre booster baselines in the age group of 15-49 years[51]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 6

Notes:

[51] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	39	79	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	6.73 (3.02 to 15.01)	1.35 (0.92 to 1.98)	0.92 (0.7 to 1.2)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines in the age group of 15-49 years

End point title	GMRs calculated to pre booster baselines in the age group of 15-49 years[52]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 7

Notes:

[52] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	39	79	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	3.85 (1.34 to 11.04)	1.52 (0.92 to 2.52)	0.96 (0.68 to 1.38)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines in the age group of 15-49 years

End point title	GMRs calculated to pre booster baselines in the age group of 15-49 years[53]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 8

Notes:

[53] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	39	79	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.67 (0.22 to 2.08)	0.87 (0.5 to 1.49)	0.62 (0.42 to 0.91)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines in the age group of 15-49 years

End point title	GMRs calculated to pre booster baselines in the age group of 15-49 years[54]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 9

Notes:

[54] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	39	79	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	1.08 (0.3 to 3.88)	0.84 (0.45 to 1.54)	0.73 (0.47 to 1.12)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines in the age group of 15-49 years

End point title	GMRs calculated to pre booster baselines in the age group of 15-49 years[55]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 10

Notes:

[55] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	39	79	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.76 (0.24 to 2.48)	1.05 (0.6 to 1.85)	0.78 (0.52 to 1.16)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines in the age group of ≥ 50 years

End point title	GMRs calculated to pre booster baselines in the age group of ≥ 50 years[56]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 6

Notes:

[56] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[57]	12	25	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	(to)	1.09 (0.75 to 1.59)	1.27 (0.98 to 1.64)	

Notes:

[57] - There were no subjects in the TBE_R group with baselines calculated using pre booster values

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines in the age group of ≥ 50 years

End point title	GMRs calculated to pre booster baselines in the age group of ≥ 50 years[58]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 7

Notes:

[58] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[59]	12	25	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	(to)	1.45 (1.01 to 2.1)	1.87 (1.45 to 2.41)	

Notes:

[59] - There were no subjects in the TBE_R group with baselines calculated using pre booster values

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines in the age group of ≥ 50 years

End point title	GMRs calculated to pre booster baselines in the age group of ≥ 50 years[60]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 8

Notes:

[60] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[61]	12	25	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	(to)	1.16 (0.62 to 2.17)	0.98 (0.63 to 1.52)	

Notes:

[61] - There were no subjects in the TBE_R group with baselines calculated using pre booster values

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines in the age group of ≥ 50 years

End point title	GMRs calculated to pre booster baselines in the age group of ≥ 50 years[62]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 9

Notes:

[62] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[63]	12	25	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	(to)	1.37 (0.71 to 2.65)	1.39 (0.88 to 2.21)	

Notes:

[63] - There were no subjects in the TBE_R group with baselines calculated using pre booster values

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines in the age group of ≥ 50 years

End point title	GMRs calculated to pre booster baselines in the age group of ≥ 50 years[64]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 10

Notes:

[64] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[65]	12	25	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	(to)	1.16 (0.63 to 2.12)	0.89 (0.58 to 1.35)	

Notes:

[65] - There were no subjects in the TBE_R group with baselines calculated using pre booster values

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines in the age group of ≥ 60 years

End point title	GMRs calculated to pre booster baselines in the age group of ≥ 60 years[66]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 6

Notes:

[66] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[67]	3	7	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	(to)	1.5 (0.76 to 2.97)	1.1 (0.7 to 1.72)	

Notes:

[67] - There were no subjects in the TBE_R group with baselines calculated using pre booster values

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines in the age group of ≥ 60 years

End point title	GMRs calculated to pre booster baselines in the age group of ≥ 60 years[68]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 7

Notes:

[68] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[69]	3	7	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	(to)	1.88 (0.97 to 3.64)	1.52 (0.99 to 2.35)	

Notes:

[69] - There were no subjects in the TBE_R group with baselines calculated using pre booster values

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines in the age group of ≥ 60 years

End point title	GMRs calculated to pre booster baselines in the age group of ≥ 60 years[70]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 8

Notes:

[70] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[71]	3	7	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	(to)	1.27 (0.44 to 3.66)	1.03 (0.51 to 2.05)	

Notes:

[71] - There were no subjects in the TBE_R group with baselines calculated using pre booster values

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines in the age group of ≥ 60 years

End point title	GMRs calculated to pre booster baselines in the age group of ≥ 60 years[72]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 9

Notes:

[72] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[73]	3	7	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	(to)	1.05 (0.37 to 2.94)	1.85 (0.94 to 3.64)	

Notes:

[73] - There were no subjects in the TBE_R group with baselines calculated using pre booster values

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to pre booster baselines in the age group of ≥ 60 years

End point title	GMRs calculated to pre booster baselines in the age group of ≥ 60 years[74]

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

End point type	Primary

End point timeframe:

At Year 10

Notes:

[74] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[75]	3	7	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	(to)	0.89 (0.39 to 2.06)	1.04 (0.6 to 1.81)	

Notes:

[75] - There were no subjects in the TBE_R group with baselines calculated using pre booster values

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines in the age group of 15-49 years

End point title	GMRs calculated to post booster baselines in the age group of 15-49 years[76]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 6

Notes:

[76] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	80	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.52 (0.35 to 0.78)	0.26 (0.18 to 0.38)	0.23 (0.18 to 0.3)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines in the age group of 15-49 years

End point title	GMRs calculated to post booster baselines in the age group of 15-49 years[77]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 7

Notes:

[77] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	80	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.48 (0.28 to 0.81)	0.3 (0.18 to 0.49)	0.24 (0.17 to 0.35)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines in the age group of 15-49 years

End point title	GMRs calculated to post booster baselines in the age group of 15-49 years[78]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 8

Notes:

[78] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	80	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.24 (0.13 to 0.43)	0.17 (0.1 to 0.3)	0.16 (0.11 to 0.23)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines in the age group of 15-49 years

End point title	GMRs calculated to post booster baselines in the age group of 15-49 years[79]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 9

Notes:

[79] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	80	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.34 (0.18 to 0.66)	0.16 (0.09 to 0.3)	0.19 (0.12 to 0.3)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines in the age group of 15-49 years

End point title	GMRs calculated to post booster baselines in the age group of 15-49 years[80]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 10

Notes:

[80] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	39	80	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.29 (0.15 to 0.56)	0.2 (0.11 to 0.38)	0.2 (0.13 to 0.3)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines in the age group of ≥ 50 years

End point title	GMRs calculated to post booster baselines in the age group of ≥ 50 years[81]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 6

Notes:

[81] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	12	25	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	1.03 (0.7 to 1.52)	0.24 (0.16 to 0.37)	0.2 (0.15 to 0.27)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines in the age group of ≥ 50 years

End point title	GMRs calculated to post booster baselines in the age group of ≥ 50 years[82]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 7

Notes:

[82] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	12	25	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	1.36 (0.79 to 2.33)	0.32 (0.18 to 0.57)	0.3 (0.2 to 0.44)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines in the age group of ≥ 50 years

End point title	GMRs calculated to post booster baselines in the age group of ≥ 50 years[83]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 8

Notes:

[83] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	12	25	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.49 (0.23 to 1.04)	0.26 (0.12 to 0.57)	0.16 (0.09 to 0.27)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines in the age group of ≥ 50 years

End point title	GMRs calculated to post booster baselines in the age group of ≥ 50 years[84]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 9

Notes:

[84] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	12	25	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.96 (0.44 to 2.08)	0.31 (0.14 to 0.68)	0.22 (0.13 to 0.39)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines in the age group of ≥ 50 years

End point title	GMRs calculated to post booster baselines in the age group of ≥ 50 years[85]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 10

Notes:

[85] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	12	25	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.59 (0.28 to 1.24)	0.26 (0.12 to 0.55)	0.14 (0.08 to 0.24)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines in the age group of ≥ 60 years

End point title	GMRs calculated to post booster baselines in the age group of ≥ 60 years[86]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 6

Notes:

[86] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	3	7	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	1.09 (0.47 to 2.55)	0.17 (0.06 to 0.45)	0.15 (0.08 to 0.29)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines in the age group of ≥ 60 years

End point title	GMRs calculated to post booster baselines in the age group of ≥ 60 years[87]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 7

Notes:

[87] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	3	7	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.77 (0.21 to 2.86)	0.21 (0.05 to 0.96)	0.21 (0.08 to 0.57)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines in the age group of ≥ 60 years

End point title	GMRs calculated to post booster baselines in the age group of ≥ 60 years[88]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 8

Notes:

[88] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	3	7	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	0.74 (0.2 to 2.72)	0.14 (0.03 to 0.64)	0.14 (0.05 to 0.38)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines in the age group of ≥ 60 years

End point title	GMRs calculated to post booster baselines in the age group of ≥ 60 years[89]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 9

Notes:

[89] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	3	7	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	1.29 (0.43 to 3.84)	0.12 (0.03 to 0.41)	0.26 (0.11 to 0.58)	

Statistical analyses

No statistical analyses for this end point

Primary: GMRs calculated to post booster baselines in the age group of ≥ 60 years

End point title	GMRs calculated to post booster baselines in the age group of ≥ 60 years[90]

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type	Primary

End point timeframe:

At Year 10

Notes:

[90] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

End point values	TBE_R Group	TBE_C Group	TBE_AC Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	3	7	
Units: Ratios				
geometric mean (confidence interval 95%)				
Ratios	1.05 (0.31 to 3.49)	0.1 (0.02 to 0.4)	0.14 (0.06 to 0.36)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Not applicable (NA)	
Adverse event reporting additional description:	
The study was intended to evaluate the persistence of antibody response up to 10 years after booster vaccine administration. Safety profile of the vaccine was not evaluated as per study protocol. Hence, there are no safety results as per planned analysis.	
Assessment type	Systematic

Dictionary used	
Dictionary name	NA
Dictionary version	NA

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: The study was intended to evaluate the persistence of antibody response up to 10 years after booster vaccine administration. Safety profile of the vaccine was not evaluated as per study protocol. Hence, there are no safety results as per planned analysis.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported