



Clinical trial results:

A phase IV, open-label, single-center study to evaluate long term immunogenicity up to 15 years after the first booster immunization with Encepur Adults (Polygeline-free Tick-borne Encephalitis vaccine for adults) in adults who received 1 of 3 different primary vaccination schedules

Summary

EudraCT number	2017-001356-59
Trial protocol	CZ
Global end of trial date	08 March 2022

Results information

Result version number	v1 (current)
This version publication date	06 November 2022
First version publication date	06 November 2022

Trial information

Trial identification

Sponsor protocol code	205847
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03294135
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	GSK Clinical Trials Call Centre, GlaxoSmithKline Biologicals, +44 20 8990 4466, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Clinical Trials Call Centre, GlaxoSmithKline Biologicals, +44 20 8990 4466, 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	03 May 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 October 2021
Global end of trial reached?	Yes
Global end of trial date	08 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study was to investigate the persistence of antibody response in adults up to 15 years after one Encepur Adults booster dose.

Protection of trial subjects:

The subjects were observed closely for at least 30 minutes following the administration of the vaccine, with appropriate medical treatment readily available in case of anaphylaxis.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 October 2017
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	Czechia: 194
Worldwide total number of subjects	194
EEA total number of subjects	194

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)	159
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

194 subjects, who participated in study V48P7E2(NCT01562444), received in a parent V48P7 study one of the following primary schedules: rapid(R), conventional(C), or accelerated conventional(AC), who received a booster dose in study V48P7E1(NCT00387634) or before study V48P7E1(only R-schedule), and agreed to participate in this study, were enrolled.

Pre-assignment

Screening details:

No participant received vaccination in study V48P7E2 (NCT01562444).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Conventional Group

Arm description:

Participants who received primary vaccination in study V48P7 on Days 0, 28 (+10) and 300 (+21) (55 participants) and who received a booster vaccination in study V48P7E1 (NCT00387634) (55 participants). For these participants a second booster vaccination within six months after the annual blood draw was to be administered within the present study only in case their Neutralization Test (NT) titer resulted below 10.

Arm type	Experimental
Investigational medicinal product name	Encepur Adults
Investigational medicinal product code	
Other name	Polygeline-free Tick-borne Encephalitis vaccine for adults
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

One dose of study vaccine (0.5 mL) will be administered intramuscularly (IM) in the deltoid of the non-dominant arm.

Arm title	Accelerated/Rapid Group
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Arm description:

Participants who received primary vaccination in study V48P7 on Days 0, 7 (+3) and 21 (+7) (66 participants) and who received a booster vaccination either in study V48P7E1 (NCT00387634) (9 participants) or before enrolment in study V48P7E1 (NCT00387634) (40 participants). For these participants a second booster vaccination within six months after the annual blood draw was to be administered within the present study only in case their NT titer resulted below 10.

Arm type	Experimental
Investigational medicinal product name	Encepur Adults
Investigational medicinal product code	
Other name	Polygeline-free Tick-borne Encephalitis vaccine for adults
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

One dose of study vaccine (0.5 mL) will be administered intramuscularly (IM) in the deltoid of the non-dominant arm.

Arm title	Accelerated Conventional Group
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Arm description:

Participants who received primary vaccination in study V48P7 on Days 0, 14 (+3) and 300 (+21) (133 participants) and who received a booster vaccination in study V48P7E1 (NCT00387634) (109 participants). For these participants a second booster vaccination within six months after the annual blood draw was to be administered within the present study only in case their NT titer resulted below 10.

Arm type	Experimental
Investigational medicinal product name	Encepur Adults
Investigational medicinal product code	
Other name	Polygeline-free Tick-borne Encephalitis vaccine for adults
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

One dose of study vaccine (0.5 mL) will be administered intramuscularly (IM) in the deltoid of the non-dominant arm.

Number of subjects in period 1	Conventional Group	Accelerated/Rapid Group	Accelerated Conventional Group
Started	50	43	101
Completed	46	43	99
Not completed	4	0	2
Consent withdrawn by subject	-	-	1
Not specified	2	-	-
Lost to follow-up	1	-	1
Serious Adverse Event	1	-	-

Baseline characteristics

Reporting groups

Reporting group title	Conventional Group
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Reporting group description:

Participants who received primary vaccination in study V48P7 on Days 0, 28 (+10) and 300 (+21) (55 participants) and who received a booster vaccination in study V48P7E1 (NCT00387634) (55 participants). For these participants a second booster vaccination within six months after the annual blood draw was to be administered within the present study only in case their Neutralization Test (NT) titer resulted below 10.

Reporting group title	Accelerated/Rapid Group
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Reporting group description:

Participants who received primary vaccination in study V48P7 on Days 0, 7 (+3) and 21 (+7) (66 participants) and who received a booster vaccination either in study V48P7E1 (NCT00387634) (9 participants) or before enrolment in study V48P7E1 (NCT00387634) (40 participants). For these participants a second booster vaccination within six months after the annual blood draw was to be administered within the present study only in case their NT titer resulted below 10.

Reporting group title	Accelerated Conventional Group
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Reporting group description:

Participants who received primary vaccination in study V48P7 on Days 0, 14 (+3) and 300 (+21) (133 participants) and who received a booster vaccination in study V48P7E1 (NCT00387634) (109 participants). For these participants a second booster vaccination within six months after the annual blood draw was to be administered within the present study only in case their NT titer resulted below 10.

Reporting group values	Conventional Group	Accelerated/Rapid Group	Accelerated Conventional Group
Number of subjects	50	43	101
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	42	34	83
From 65-84 years	8	9	18
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	47.0	48.8	48.1
standard deviation	± 14.1	± 15.3	± 14.5
Sex: Female, Male Units: Participants			
Female	31	22	52
Male	19	21	49
Race/Ethnicity, Customized Units: Subjects			
WHITE	50	43	101

Reporting group values	Total		
Number of subjects	194		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	159		
From 65-84 years	35		
85 years and over	0		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Participants			
Female	105		
Male	89		
Race/Ethnicity, Customized			
Units: Subjects			
WHITE	194		

End points

End points reporting groups

Reporting group title	Conventional Group
Reporting group description: Participants who received primary vaccination in study V48P7 on Days 0, 28 (+10) and 300 (+21) (55 participants) and who received a booster vaccination in study V48P7E1 (NCT00387634) (55 participants). For these participants a second booster vaccination within six months after the annual blood draw was to be administered within the present study only in case their Neutralization Test (NT) titer resulted below 10.	
Reporting group title	Accelerated/Rapid Group
Reporting group description: Participants who received primary vaccination in study V48P7 on Days 0, 7 (+3) and 21 (+7) (66 participants) and who received a booster vaccination either in study V48P7E1 (NCT00387634) (9 participants) or before enrolment in study V48P7E1 (NCT00387634) (40 participants). For these participants a second booster vaccination within six months after the annual blood draw was to be administered within the present study only in case their NT titer resulted below 10.	
Reporting group title	Accelerated Conventional Group
Reporting group description: Participants who received primary vaccination in study V48P7 on Days 0, 14 (+3) and 300 (+21) (133 participants) and who received a booster vaccination in study V48P7E1 (NCT00387634) (109 participants). For these participants a second booster vaccination within six months after the annual blood draw was to be administered within the present study only in case their NT titer resulted below 10.	

Primary: Percentage of participants with detectable TBE Neutralizing Antibody Titers equal to or above 10 at Year 11

End point title	Percentage of participants with detectable TBE Neutralizing Antibody Titers equal to or above 10 at Year 11 ^[1]
End point description: Antibody titers were measured by GSK Biologicals' Neutralization test. Analysis of the percentages of participants with antibody titers ≥ 2 was not performed as planned in the protocol, as only 3 participants had antibody titers between 2 and 10 during the whole study period. The analysis was performed on the Per Protocol set-1 (PPS-1) which consisted of all participants who provided evaluable serum samples at the relevant time points and have no major protocol violation.	
End point type	Primary
End point timeframe: At Year 11	

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Conventional Group	Accelerated/Rapid Group	Accelerated Conventional Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	43	101	
Units: Percentage of participants				
number (confidence interval 95%)	100 (92.6 to 100)	100 (91.8 to 100)	99.0 (94.6 to 100)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with detectable TBE Neutralizing Antibody Titers equal to or above 10 at Year 12

End point title	Percentage of participants with detectable TBE Neutralizing Antibody Titers equal to or above 10 at Year 12 ^[2]
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End point description:

Antibody titers were measured by GSK Biologicals' Neutralization test. Analysis of the percentages of participants with antibody titers ≥ 2 was not performed as planned in the protocol, as only 3 participants had antibody titers between 2 and 10 during the whole study period. The analysis was performed on the PPS-1 which consisted of all participants who provided evaluable serum samples at the relevant time points and have no major protocol violation.

End point type	Primary
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End point timeframe:

At Year 12

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Conventional Group	Accelerated/Rapid Group	Accelerated Conventional Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	43	101	
Units: Percentage of participants				
number (confidence interval 95%)	98.0 (89.4 to 99.9)	100 (91.8 to 100)	99.0 (94.6 to 100)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with detectable TBE Neutralizing Antibody Titers equal to or above 10 at Year 13

End point title	Percentage of participants with detectable TBE Neutralizing Antibody Titers equal to or above 10 at Year 13 ^[3]
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End point description:

Antibody titers were measured by GSK Biologicals' Neutralization test. Analysis of the percentages of participants with antibody titers ≥ 2 was not performed as planned in the protocol, as only 3 participants had antibody titers between 2 and 10 during the whole study period. The analysis was performed on the PPS-1 which consisted of all participants who provided evaluable serum samples at the relevant time points and have no major protocol violation.

End point type	Primary
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End point timeframe:

At Year 13

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Conventional Group	Accelerated/Rapid Group	Accelerated Conventional Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	43	101	
Units: Percentage of participants				
number (confidence interval 95%)	95.9 (86.0 to 99.5)	100 (91.8 to 100)	99.0 (94.6 to 100)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with detectable TBE Neutralizing Antibody Titers equal to or above 10 at Year 14

End point title	Percentage of participants with detectable TBE Neutralizing Antibody Titers equal to or above 10 at Year 14 ^[4]
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End point description:

Antibody titers were measured by GSK Biologicals' Neutralization test. Analysis of the percentages of participants with antibody titers ≥ 2 was not performed as planned in the protocol, as only 3 participants had antibody titers between 2 and 10 during the whole study period.

The analysis was performed on the PPS-1 which consisted of all participants who provided evaluable serum samples at the relevant time points and have no major protocol violation.

End point type	Primary
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End point timeframe:

At Year 14

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Conventional Group	Accelerated/Rapid Group	Accelerated Conventional Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	43	101	
Units: Percentage of participants				
number (confidence interval 95%)	95.9 (86.0 to 99.5)	100 (91.8 to 100)	99.0 (94.6 to 100)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with detectable TBE Neutralizing Antibody Titers equal to or above 10 at Year 15

End point title	Percentage of participants with detectable TBE Neutralizing Antibody Titers equal to or above 10 at Year 15 ^[5]
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End point description:

Antibody titers were measured by GSK Biologicals' Neutralization test. Analysis of the percentages of participants with antibody titers ≥ 2 was not performed as planned in the protocol, as only 3 participants had antibody titers between 2 and 10 during the whole study period.

The analysis was performed on the PPS-1 which consisted of all participants who provided evaluable serum samples at the relevant time points and have no major protocol violation.

End point type	Primary
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End point timeframe:

At Year 15

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Conventional Group	Accelerated/Rapid Group	Accelerated Conventional Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	43	100	
Units: Percentage of participants				
number (confidence interval 95%)	95.8 (85.7 to 99.5)	100 (91.8 to 100)	99.0 (94.6 to 100)	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Antibody Titers (GMTs) by age categories at Year 11

End point title	Geometric Mean Antibody Titers (GMTs) by age categories at Year 11 ^[6]
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End point description:

Immunogenicity was measured in terms of GMTs of serum TBE Neutralizing Antibody Titers at Year 11. GMTs were assessed for following age subgroups: 25 to 49 years, equal to or above (\geq) 50 years and ≥ 60 years.

The analysis was performed on the PPS-1 which consisted of all participants who provided evaluable serum samples at the relevant time points and have no major protocol violation.

End point type	Primary
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End point timeframe:

At Year 11

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Conventional Group	Accelerated/Rapid Group	Accelerated Conventional Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	43	101	
Units: Titers				
geometric mean (confidence interval 95%)				
25 to 49 Years of Age (N=24,23,55)	368.8 (208.9 to 651.1)	301.5 (168.7 to 538.7)	235.2 (161.6 to 342.3)	
>=50 Years of Age (N=24,20,46)	129.6 (76.7 to 218.8)	177.4 (100.0 to 314.9)	128.1 (87.7 to 187.0)	
>=60 Years of Age (N=12,13,26)	127.5 (61.3 to 265.4)	160.2 (79.2 to 324.0)	103.0 (62.6 to 169.5)	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Antibody Titers (GMTs) by age categories at Year 12

End point title	Geometric Mean Antibody Titers (GMTs) by age categories at Year 12 ^[7]
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End point description:

Immunogenicity was measured in terms of GMTs of serum TBE Neutralizing Antibody Titers at Year 12. GMTs were assessed for following age subgroups: 25 to 49 years, >= 50 years and >= 60 years. The analysis was performed on the PPS-1 which consisted of all participants who provided evaluable serum samples at the relevant time points and have no major protocol violation.

End point type	Primary
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End point timeframe:

At Year 12

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Conventional Group	Accelerated/Rapid Group	Accelerated Conventional Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	43	101	
Units: Titers				
geometric mean (confidence interval 95%)				
25 to 49 Years of Age (N=26,23,55)	323.7 (185.0 to 566.3)	334.6 (184.6 to 606.4)	264.3 (179.9 to 388.3)	
>=50 Years of Age (N=24,20,46)	154.5 (87.6 to 272.4)	205.8 (110.6 to 383.0)	158.2 (105.0 to 238.3)	
>=60 Years of Age (N=12,13,26)	133.6 (62.5 to 285.6)	190.8 (92.0 to 395.9)	141.0 (84.2 to 236.3)	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Antibody Titers (GMTs) by age categories at Year 13

End point title	Geometric Mean Antibody Titers (GMTs) by age categories at Year 13 ^[8]
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End point description:

Immunogenicity was measured in terms of GMTs of serum TBE Neutralizing Antibody Titers at Year 13. GMTs were assessed for following age subgroups: 25 to 49 years, ≥ 50 years and ≥ 60 years. The analysis was performed on the PPS-1 which consisted of all participants who provided evaluable serum samples at the relevant time points and have no major protocol violation.

End point type	Primary
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End point timeframe:

At Year 13

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Conventional Group	Accelerated/Rapid Group	Accelerated Conventional Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	43	101	
Units: Titers				
geometric mean (confidence interval 95%)				
25 to 49 Years of Age (N=26,23,55)	196.9 (112.2 to 345.6)	238.4 (131.1 to 433.6)	172.8 (117.3 to 254.3)	
≥ 50 Years of Age (N=23,20,46)	98.3 (56.6 to 170.9)	132.1 (73.0 to 238.9)	110.9 (75.0 to 164.0)	
≥ 60 Years of Age (N=12,13,26)	93.5 (44.7 to 195.6)	114.8 (56.5 to 233.4)	96.9 (58.7 to 160.0)	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Antibody Titers (GMTs) by age categories at Year 14

End point title	Geometric Mean Antibody Titers (GMTs) by age categories at Year 14 ^[9]
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End point description:

Immunogenicity was measured in terms of GMTs of serum TBE Neutralizing Antibody Titers at Year 14. GMTs were assessed for following age subgroups: 25 to 49 years, ≥ 50 years and ≥ 60 years. The analysis was performed on the PPS-1 which consisted of all participants who provided evaluable serum samples at the relevant time points and have no major protocol violation.

End point type	Primary
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End point timeframe:

At Year 14

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Conventional Group	Accelerated/Rapid Group	Accelerated Conventional Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	43	101	
Units: Titers				
geometric mean (confidence interval 95%)				
25 to 49 Years of Age (N=26,23,55)	299.7 (164.2 to 547.0)	299.1 (157.8 to 567.1)	248.2 (164.1 to 375.4)	
>=50 Years of Age (N=23,20,46)	147.5 (81.2 to 268.0)	169.7 (89.5 to 321.8)	131.1 (86.0 to 200.0)	
>=60 Years of Age (N=12,13,26)	139.4 (67.2 to 289.3)	149.9 (74.3 to 302.4)	117.9 (71.8 to 193.7)	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Antibody Titers (GMTs) by age categories at Year 15

End point title	Geometric Mean Antibody Titers (GMTs) by age categories at Year 15 ^[10]
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End point description:

Immunogenicity was measured in terms of GMTs of serum TBE Neutralizing Antibody Titers at Year 15. GMTs were assessed for following age subgroups: 25 to 49 years, >= 50 years and >= 60 years. The analysis was performed on the PPS-1 which consisted of all participants who provided evaluable serum samples at the relevant time points and have no major protocol violation.

End point type	Primary
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End point timeframe:

At Year 15

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Conventional Group	Accelerated/Rapid Group	Accelerated Conventional Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	43	101	
Units: Titers				
geometric mean (confidence interval 95%)				
25 to 49 Years of Age (N=26,23,55)	217.6 (125.2 to 378.2)	281.6 (156.5 to 506.9)	183.9 (125.7 to 268.9)	
>=50 Years of Age (N=22,20,45)	98.9 (54.4 to 180.0)	157.0 (83.8 to 294.1)	103.3 (67.9 to 156.9)	
>=60 Years of Age (N=11,13,25)	114.1 (52.5 to 247.8)	158.1 (77.5 to 322.7)	90.7 (54.2 to 151.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with detectable TBE Neutralizing Antibody Titers equal to or above 2 and equal to or above 10 as measured by GSK Biologicals' NT, overall and by study group

End point title	Percentage of participants with detectable TBE Neutralizing Antibody Titers equal to or above 2 and equal to or above 10 as measured by GSK Biologicals' NT, overall and by study group
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End point description:

Immunogenicity was planned to be measured in terms of percentage of participants with TBE Neutralizing Antibody Titers ≥ 2 and ≥ 10 at 21 days after the booster vaccination. The analysis was planned to be performed on the PPS-2 which consisted of all participants who provided evaluable serum samples after booster dose and have no major protocol violation. However only 1 participant received the booster dose, therefore the analysis was not performed.

End point type	Secondary
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End point timeframe:

At 21 days after the booster vaccination

End point values	Conventional Group	Accelerated/Rapid Group	Accelerated Conventional Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[11]	0 ^[12]	0 ^[13]	
Units: Percentage of participants				
number (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[11] - As there was only 1 subject in this category, lower and upper limits were not calculated.

[12] - As there was only 1 subject in this category, lower and upper limits were not calculated.

[13] - As there was only 1 subject in this category, lower and upper limits were not calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Antibody Titers (GMTs) as measured by GSK Biologicals' NT, overall and by study group

End point title	Geometric Mean Antibody Titers (GMTs) as measured by GSK Biologicals' NT, overall and by study group
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End point description:

Immunogenicity was planned to be measured in terms of GMTs of serum TBE Neutralizing Antibody Titers at 21 days after the booster vaccination. The analysis was planned to be performed on the PPS-2 which consisted of all participants who provided evaluable serum samples after booster dose and have no major protocol violation. However only 1 participant received the booster dose, therefore the analysis was not performed.

End point type	Secondary
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End point timeframe:

At 21 days after the booster vaccination

End point values	Conventional Group	Accelerated/Rapid Group	Accelerated Conventional Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[14]	0 ^[15]	0 ^[16]	
Units: Titers				
geometric mean (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[14] - As there was only 1 subject in this category, lower and upper limits were not calculated.

[15] - As there was only 1 subject in this category, lower and upper limits were not calculated.

[16] - As there was only 1 subject in this category, lower and upper limits were not calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Ratios (GMRs) blood draw after/before booster as measured by GSK Biologicals' NT, overall and by study group

End point title	Geometric Mean Ratios (GMRs) blood draw after/before booster as measured by GSK Biologicals' NT, overall and by study group
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End point description:

Immunogenicity was planned to be measured in terms of GMRs of serum TBE Neutralizing Antibody Titers at 21 days after the booster vaccination.

The analysis was planned to be performed on the PPS-2 which consisted of all participants who provided evaluable serum samples after booster dose and have no major protocol violation. However only 1 participant received the booster dose, therefore the analysis was not performed.

End point type	Secondary
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End point timeframe:

At 21 days after the booster vaccination

End point values	Conventional Group	Accelerated/Rapid Group	Accelerated Conventional Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[17]	0 ^[18]	0 ^[19]	
Units: Titers				
geometric mean (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[17] - As there was only 1 subject in this category, lower and upper limits were not calculated.

[18] - As there was only 1 subject in this category, lower and upper limits were not calculated.

[19] - As there was only 1 subject in this category, lower and upper limits were not calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with detectable TBE Neutralizing Antibody Titers equal to and above 10 as measured by GSK Biologicals' NT, overall and by study group

End point title	Percentage of participants with detectable TBE Neutralizing Antibody Titers equal to and above 10 as measured by GSK
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End point description:

Immunogenicity was measured in terms of percentage of participants with TBE Neutralizing Antibody Titers ≥ 10 from Year 1 to Year 15.

The analysis was performed on the set of subjects who completed the entire 15-year follow-up with no protocol deviations related to the persistence analysis.

End point type

Secondary

End point timeframe:

From Year 1 up to Year 15

End point values	Conventional Group	Accelerated/Rapid Group	Accelerated Conventional Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	43	101	
Units: Percentage of participants				
number (confidence interval 95%)				
Year 1 (N=47,42,100)	100 (92.5 to 100)	100 (91.6 to 100)	100 (96.4 to 100)	
Year 2 (N=48,42,100)	100 (92.6 to 100)	100 (91.6 to 100)	100 (96.3 to 100)	
Year 3 (N=48,42,100)	100 (92.6 to 100)	100 (91.6 to 100)	100 (96.4 to 100)	
Year 4 (N=46,41,100)	100 (92.3 to 100)	97.6 (87.1 to 99.9)	100 (96.4 to 100)	
Year 5 (N=48,43,100)	100 (92.6 to 100)	100 (91.8 to 100)	100 (96.4 to 100)	
Year 6 (N=48,43,100)	100 (92.6 to 100)	100 (91.8 to 100)	100 (96.4 to 100)	
Year 7(N=48,43,98)	100 (92.6 to 100)	100 (91.8 to 100)	100 (96.3 to 100)	
Year 8 (N=47,42,97)	100 (92.5 to 100)	100 (91.6 to 100)	100 (96.3 to 100)	
Year 9 (N=45,42,97)	100 (92.1 to 100)	100 (91.6 to 100)	100 (96.3 to 100)	
Year 10 (N=46,42,98)	100 (92.3 to 100)	100 (91.6 to 100)	100 (96.3 to 100)	
Year 11 (N=46,43,100)	100 (92.3 to 100)	100 (91.8 to 100)	99.0 (94.6 to 100)	
Year 12 (N=48,43,100)	97.9 (88.9 to 99.9)	100 (91.8 to 100)	99.0 (94.6 to 100)	
Year 13 (N=48,43,100)	95.8 (85.7 to 99.5)	100 (91.8 to 100)	99.0 (94.6 to 100)	
Year 14 (N=48,43,100)	95.8 (85.7 to 99.5)	100 (91.8 to 100)	99.0 (94.6 to 100)	
Year 15 (N=48,43,100)	95.8 (85.7 to 99.5)	100 (91.8 to 100)	99.0 (94.6 to 100)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with serious adverse events (SAEs)

End point title	Number of participants with serious adverse events (SAEs) ^[20]
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End point description:

SAEs are defined as any untoward medical occurrence that results in death, is life- threatening, requires hospitalisation or prolongation of existing hospitalisation, results in disability/incapacity or is a congenital anomaly/birth defect in the offspring of a study subject.

The analysis was performed on the Safety population which included all subjects who received a booster vaccination in this study. Only one participant (from the Accelerated/Rapid Group) received a booster dose.

End point type	Secondary
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End point timeframe:

From Day 0 to Day 21 after booster vaccination

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only one participant (from the Conventional Group) received a booster dose during this study.

End point values	Conventional Group			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

SAEs that led to withdrawal or were related to study vaccination were collected throughout the study period (Year 11 to Year 15). Other SAEs were collected only after the booster vaccination administration (Day 0-Day 21).

Adverse event reporting additional description:

Other adverse events were not collected as per protocol.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

Reporting group title	Conventional Group
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Reporting group description:

Participants received a second booster vaccination six months after the blood draw only in case their results were with an NT titer below 10 and who belonged to the following vaccination schedule in the primary studies: primary vaccination of 66 participants in study V48P7 on Days 0, 28 (+10) and 300 (+21), booster vaccination of 55 participants in study V48P7E1 (NCT00387634).

Reporting group title	Accelerated Conventional Group
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Reporting group description:

Participants received a second booster vaccination six months after the blood draw only in case their results were with an NT titer below 10 and who belonged to the following vaccination schedule in the primary studies: primary vaccination of 133 participants in study V48P7 on Days 0, 14 (+3) and 300 (+21), booster vaccination of 109 participants in study V48P7E1 (NCT00387634).

Reporting group title	Accelerated/Rapid Group
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Reporting group description:

Participants received a second booster vaccination six months after the blood draw only in case their results were with an NT titer below 10 and who belonged to the following vaccination schedule in the primary studies: primary vaccination of 66 participants in study V48P7 on Days 0, 7 (+3) and 21 (+7), booster vaccination of 9 participants in study V48P7E1 (NCT00387634) 40 participants received their booster vaccination before enrolment in study V48P7E1 (NCT00387634).

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: Non-serious adverse events were not collected as per protocol.

Serious adverse events	Conventional Group	Accelerated Conventional Group	Accelerated/Rapid Group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 50 (2.00%)	1 / 101 (0.99%)	0 / 43 (0.00%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Death due to glioblastoma			
subjects affected / exposed	1 / 50 (2.00%)	0 / 101 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Infections and infestations			

Death due to primary COVID-19 pneumonia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 101 (0.99%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

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

Non-serious adverse events	Conventional Group	Accelerated Conventional Group	Accelerated/Rapid Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)	0 / 101 (0.00%)	0 / 43 (0.00%)

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