



## 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 |
|-----------------------|--------|

#### 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                |
| <b>Arm title</b>             | 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.

|                  |                         |
|------------------|-------------------------|
| <b>Arm title</b> | Accelerated/Rapid Group |
|------------------|-------------------------|

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.

|                  |                                |
|------------------|--------------------------------|
| <b>Arm title</b> | 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.

| <b>Number of subjects in period 1</b> | 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 |
|-----------------------|--------------------|

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.

| Reporting group values                             | Conventional Group | Accelerated/Rapid Group | Accelerated Conventional Group |
|----------------------------------------------------|--------------------|-------------------------|--------------------------------|
| Number of subjects                                 | 50                 | 43                      | 101                            |
| Age categorical<br>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<br>Units: Years                     |                    |                         |                                |
| arithmetic mean                                    | 47.0               | 48.8                    | 48.1                           |
| standard deviation                                 | ± 14.1             | ± 15.3                  | ± 14.5                         |
| Sex: Female, Male<br>Units: Participants           |                    |                         |                                |
| Female                                             | 31                 | 22                      | 52                             |
| Male                                               | 19                 | 21                      | 49                             |
| Race/Ethnicity, Customized<br>Units: Subjects      |                    |                         |                                |
| WHITE                                              | 50                 | 43                      | 101                            |

|                                                       |       |  |  |
|-------------------------------------------------------|-------|--|--|
| <b>Reporting group values</b>                         | Total |  |  |
| Number of subjects                                    | 194   |  |  |
| Age categorical                                       |       |  |  |
| Units: Subjects                                       |       |  |  |
| In utero                                              | 0     |  |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0     |  |  |
| Newborns (0-27 days)                                  | 0     |  |  |
| Infants and toddlers (28 days-23<br>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:<br>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:<br>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:<br>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 <sup>[1]</sup> |
| End point description:<br>Antibody titers were measured by GSK Biologicals' Neutralization test. Analysis of the percentages of participants with antibody titers $\geq 2$ was not performed as planned in the protocol, as only 3 participants had antibody titers between 2 and 10 during the whole study period.<br>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:<br>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 <sup>[2]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------------------------------|

End point description:

Antibody titers were measured by GSK Biologicals' Neutralization test. Analysis of the percentages of participants with antibody titers  $\geq 2$  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 |
|----------------|---------|

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 <sup>[3]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------------------------------|

End point description:

Antibody titers were measured by GSK Biologicals' Neutralization test. Analysis of the percentages of participants with antibody titers  $\geq 2$  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 |
|----------------|---------|

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 <sup>[4]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------------------------------|

End point description:

Antibody titers were measured by GSK Biologicals' Neutralization test. Analysis of the percentages of participants with antibody titers  $\geq 2$  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 |
|----------------|---------|

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

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

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|                 |                                                                                                                            |
|-----------------|----------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of participants with detectable TBE Neutralizing Antibody Titers equal to or above 10 at Year 15 <sup>[5]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------------------------------|

End point description:

Antibody titers were measured by GSK Biologicals' Neutralization test. Analysis of the percentages of participants with antibody titers  $\geq 2$  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 |
|----------------|---------|

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)             |  |

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**Statistical analyses**

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No statistical analyses for this end point

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

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|                 |                                                                                   |
|-----------------|-----------------------------------------------------------------------------------|
| End point title | Geometric Mean Antibody Titers (GMTs) by age categories at Year 11 <sup>[6]</sup> |
|-----------------|-----------------------------------------------------------------------------------|

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  $\geq 60$  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 |
|----------------|---------|

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 <sup>[7]</sup> |
|-----------------|-----------------------------------------------------------------------------------|

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 |
|----------------|---------|

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 <sup>[8]</sup> |
|-----------------|-----------------------------------------------------------------------------------|

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,  $\geq 50$  years and  $\geq 60$  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 |
|----------------|---------|

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)         |  |
| $\geq 50$ 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)          |  |
| $\geq 60$ 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 <sup>[9]</sup> |
|-----------------|-----------------------------------------------------------------------------------|

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,  $\geq 50$  years and  $\geq 60$  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 |
|----------------|---------|

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 <sup>[10]</sup> |
|-----------------|------------------------------------------------------------------------------------|

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 |
|----------------|---------|

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

**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 |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

## End point description:

Immunogenicity was planned to be measured in terms of percentage of participants with TBE Neutralizing Antibody Titers  $\geq 2$  and  $\geq 10$  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 |
|----------------|-----------|

## 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 <sup>[11]</sup>  | 0 <sup>[12]</sup>       | 0 <sup>[13]</sup>              |  |
| 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 |
|-----------------|------------------------------------------------------------------------------------------------------|

## 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 |
|----------------|-----------|

## 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 <sup>[14]</sup>  | 0 <sup>[15]</sup>       | 0 <sup>[16]</sup>              |  |
| 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 |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------|

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 |
|----------------|-----------|

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 <sup>[17]</sup>  | 0 <sup>[18]</sup>       | 0 <sup>[19]</sup>              |  |
| 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 |
|-----------------|----------------------------------------------------------------------------------------------------------------------|

**End point description:**

Immunogenicity was measured in terms of percentage of participants with TBE Neutralizing Antibody Titers  $\geq 10$  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

| <b>End point values</b>           | 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) <sup>[20]</sup> |
|-----------------|---------------------------------------------------------------------------|

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 |
|----------------|-----------|

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.

|                             |                    |  |  |  |
|-----------------------------|--------------------|--|--|--|
| <b>End point values</b>     | 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<sup>[1]</sup>

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 |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Conventional Group |
|-----------------------|--------------------|

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 |
|-----------------------|--------------------------------|

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 |
|-----------------------|-------------------------|

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 %

| <b>Non-serious adverse events</b>                     | 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

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported