



## Clinical trial results: Immunogenicity of Adacel® and BOOSTRIX® Vaccines in Adolescents Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2015-005629-38    |
| Trial protocol           | Outside EU/EEA    |
| Global end of trial date | 10 September 2012 |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 19 February 2016 |
| First version publication date | 19 February 2016 |

### Trial information

#### Trial identification

|                       |       |
|-----------------------|-------|
| Sponsor protocol code | Td551 |
|-----------------------|-------|

#### Additional study identifiers

|                                    |                 |
|------------------------------------|-----------------|
| ISRCTN number                      | -               |
| ClinicalTrials.gov id (NCT number) | NCT01629589     |
| WHO universal trial number (UTN)   | U1111-1127-6774 |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Sanofi Pasteur Inc.  |
| Sponsor organisation address | 1 Discovery Drive, Swiftwater, United States, 18370  |
| Public contact               | Medical Team Leader, Scientific and Medical Affairs Department, Sanofi Pasteur Inc., 1 570-957-5433, vitali.pool@sanofipasteur.com |
| Scientific contact           | Medical Team Leader, Scientific and Medical Affairs Department, Sanofi Pasteur Inc., 1 570-957-5433, vitali.pool@sanofipasteur.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? | Yes |

Notes:

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**Results analysis stage**

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|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 08 May 2013       |
| Is this the analysis of the primary completion data? | No                |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 10 September 2012 |
| Was the trial ended prematurely?                     | No                |

Notes:

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**General information about the trial**

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Main objective of the trial:

Immunogenicity

- To describe seroprotection rates against tetanus and diphtheria in subjects randomized to receive either Adacel or Boostrix vaccine.
- To describe pre- and post-vaccination tetanus, diphtheria, and pertussis geometric mean antibody concentrations (GMCs) in subjects randomized to receive either Adacel or Boostrix vaccine.
- To describe booster response rates against tetanus, diphtheria, and pertussis in subjects randomized to receive either Adacel or Boostrix vaccine.

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Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and vaccinated in the study. Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment was also available on site in case of any immediate allergic reactions.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 20 June 2012 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | No           |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 423 |
| Worldwide total number of subjects   | 423                |
| EEA total number of subjects         | 0                  |

Notes:

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**Subjects enrolled per age group**

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|  |   |
|--|---|
| In utero                               | 0 |
| Preterm newborn - gestational age < 37 | 0 |

|  |     |
|--|-----|
| wk                                       |     |
| Newborns (0-27 days)                     | 0   |
| Infants and toddlers (28 days-23 months) | 0   |
| Children (2-11 years)                    | 0   |
| Adolescents (12-17 years)                | 423 |
| Adults (18-64 years)                     | 0   |
| From 65 to 84 years                      | 0   |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details:

The study subjects were enrolled from 20 June 2012 to 10 September 2012 at 8 centers in the United States.

### Pre-assignment

Screening details:

A total of 423 subjects that met all of the inclusion and none of the exclusion criteria were randomized, 422 were vaccinated in this study.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall trial (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Not blinded                    |

Blinding implementation details:

Not applicable

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | Adacel® Vaccine Group |
|------------------|-----------------------|

Arm description:

Subjects received a single dose of Adacel® vaccine.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Tetanus toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Adacel®) |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Suspension for injection   |
| Routes of administration               | Intramuscular use  |

Dosage and administration details:

0.5 mL, intramuscular, 1 injection on Day 0.

|                  |                         |
|------------------|-------------------------|
| <b>Arm title</b> | BOOSTRIX® Vaccine Group |
|------------------|-------------------------|

Arm description:

Subjects received a single dose of BOOSTRIX® vaccine.

|  |   |
|--|---|
| Arm type                               | Active comparator   |
| Investigational medicinal product name | Tetanus toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine (BOOSTRIX®) |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Suspension for injection  |
| Routes of administration               | Intramuscular use   |

Dosage and administration details:

0.5 mL, intramuscular, 1 injection on Day 0.

| <b>Number of subjects in period 1</b> | <b>Adacel® Vaccine Group</b> | <b>BOOSTRIX® Vaccine Group</b> |
|---------------------------------------|------------------------------|--------------------------------|
| Started                               | 212                          | 211                            |
| Completed                             | 204                          | 204                            |
| Not completed                         | 8                            | 7                              |
| Consent withdrawn by subject          | 2                            | 3                              |
| Did not receive study vaccine         | -                            | 1                              |
| Lost to follow-up                     | 2                            | 1                              |
| Protocol deviation                    | 4                            | 2                              |

## Baseline characteristics

### Reporting groups

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Adacel® Vaccine Group |
|-----------------------|-----------------------|

Reporting group description:

Subjects received a single dose of Adacel® vaccine.

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | BOOSTRIX® Vaccine Group |
|-----------------------|-------------------------|

Reporting group description:

Subjects received a single dose of BOOSTRIX® vaccine.

| Reporting group values                                | Adacel® Vaccine Group | BOOSTRIX® Vaccine Group | Total |
|---|-----------------------|-------------------------|-------|
| Number of subjects                                    | 212                   | 211                     | 423   |
| Age categorical<br>Units: Subjects                    |                       |                         |       |
| In utero  | 0                     | 0                       | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0                     | 0                       | 0     |
| Newborns (0-27 days)                                  | 0                     | 0                       | 0     |
| Infants and toddlers (28 days-23<br>months)           | 0                     | 0                       | 0     |
| Children (2-11 years)                                 | 0                     | 0                       | 0     |
| Adolescents (12-17 years)                             | 212                   | 211                     | 423   |
| Adults (18-64 years)                                  | 0                     | 0                       | 0     |
| From 65-84 years                                      | 0                     | 0                       | 0     |
| 85 years and over                                     | 0                     | 0                       | 0     |
| Age continuous<br>Units: years                        |                       |                         |       |
| arithmetic mean                                       | 11.6                  | 11.6                    |       |
| standard deviation                                    | ± 0.5                 | ± 0.5                   | -     |
| Gender categorical<br>Units: Subjects                 |                       |                         |       |
| Female  | 105                   | 106                     | 211   |
| Male  | 107                   | 105                     | 212   |

## End points

### End points reporting groups

|   |                         |
|---|-------------------------|
| Reporting group title                                 | Adacel® Vaccine Group   |
| Reporting group description:                          |                         |
| Subjects received a single dose of Adacel® vaccine.   |                         |
| Reporting group title                                 | BOOSTRIX® Vaccine Group |
| Reporting group description:                          |                         |
| Subjects received a single dose of BOOSTRIX® vaccine. |                         |

### Primary: Number of Subjects With Antibody Responses to Tetanus and Diphtheria Components Following Vaccination With Either Adacel® or BOOSTRIX®

|   |   |
|---|---|
| End point title   | Number of Subjects With Antibody Responses to Tetanus and Diphtheria Components Following Vaccination With Either Adacel® or BOOSTRIX® <sup>[1]</sup> |
| End point description:  |   |
| Tetanus antibody was assayed by enzyme-linked immunosorbent assay (ELISA) and Diphtheria antibody by a toxin neutralization test. Antibody responses to tetanus and diphtheria components were defined as titers $\geq 0.1$ IU/mL and $\geq 1.0$ IU/mL. |   |
| End point type  | Primary   |
| End point timeframe:  |   |
| Day 0 (pre-vaccination) and Day 28 (post-vaccination)   |   |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

| End point values                                | Adacel® Vaccine Group | BOOSTRIX® Vaccine Group |  |  |
|---|-----------------------|-------------------------|--|--|
| Subject group type                              | Reporting group       | Reporting group         |  |  |
| Number of subjects analysed                     | 196                   | 194                     |  |  |
| Units: Number of subjects                       |                       |                         |  |  |
| number (not applicable)                         |                       |                         |  |  |
| Tetanus (pre-vaccination); $\geq 0.1$ IU/mL     | 172                   | 177                     |  |  |
| Tetanus (post-vaccination); $\geq 0.1$ IU/mL    | 196                   | 194                     |  |  |
| Diphtheria (pre-vaccination); $\geq 0.1$ IU/mL  | 135                   | 139                     |  |  |
| Diphtheria (post-vaccination); $\geq 0.1$ IU/mL | 196                   | 194                     |  |  |
| Tetanus (pre-vaccination); $\geq 1.0$ IU/mL     | 33                    | 48                      |  |  |
| Tetanus (post-vaccination); $\geq 1.0$ IU/mL    | 195                   | 194                     |  |  |
| Diphtheria (pre-vaccination); $\geq 1.0$ IU/mL  | 28                    | 26                      |  |  |
| Diphtheria (post-vaccination); $\geq 1.0$ IU/mL | 183                   | 186                     |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Concentrations of Tetanus and Diphtheria Antibodies Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine

|                        |   |
|------------------------|---|
| End point title        | Geometric Mean Concentrations of Tetanus and Diphtheria Antibodies Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine |
| End point description: | Tetanus antibody was assayed by enzyme-linked immunosorbent assay (ELISA) and Diphtheria antibody by a toxin neutralization test. |
| End point type         | Secondary   |
| End point timeframe:   | Day 0 (pre-vaccination) to Day 28 post-vaccination  |

| End point values                         | Adacel®<br>Vaccine Group | BOOSTRIX®<br>Vaccine Group |  |  |
|--|--------------------------|----------------------------|--|--|
| Subject group type                       | Reporting group          | Reporting group            |  |  |
| Number of subjects analysed              | 196                      | 194                        |  |  |
| Units: Titers (1/dil)                    |                          |                            |  |  |
| geometric mean (confidence interval 95%) |                          |                            |  |  |
| Tetanus (pre-vaccination)                | 0.422 (0.363 to 0.492)   | 0.456 (0.393 to 0.528)     |  |  |
| Tetanus (post-vaccination)               | 18.9 (16.4 to 21.8)      | 9.18 (8.1 to 10.4)         |  |  |
| Diphtheria (pre-vaccination)             | 0.211 (0.171 to 0.26)    | 0.221 (0.181 to 0.269)     |  |  |
| Diphtheria (post-vaccination)            | 8.17 (6.83 to 9.77)      | 5.62 (4.85 to 6.51)        |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Booster Responses Against Tetanus and Diphtheria Antigens Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine

|                        |   |
|------------------------|---|
| End point title        | Number of Subjects With Booster Responses Against Tetanus and Diphtheria Antigens Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine  |
| End point description: | Adacel booster response defined as: a 4-fold increase in pre- to post-vaccination antibody concentrations for subjects with a pre-vaccination concentration $\leq 2.56$ IU/mL for diphtheria and $\leq 2.7$ IU/mL for tetanus, and defined as a 2-fold increase for subjects with a pre-vaccination concentration $> 2.56$ IU/mL for diphtheria and $> 2.7$ IU/mL for tetanus.<br><br>Boostrix booster response defined as: a post-vaccination titer $\geq 4$ times the lower limit of quantitation (LLOQ) for subjects with a pre-vaccination titer $< \text{LLOQ}$ , a post-vaccination titer $\geq 4$ times the pre-vaccination titer for subjects with a pre-vaccination titer between LLOQ and 4X LLOQ, or a post-vaccination titer at least twice the pre-vaccination titer for subjects with a pre-vaccination titer $\geq 4\text{X LLOQ}$ . |
| End point type         | Secondary   |

End point timeframe:  
Day 28 post-vaccination

| End point values            | Adacel®<br>Vaccine Group | BOOSTRIX®<br>Vaccine Group |  |  |
|-----------------------------|--------------------------|----------------------------|--|--|
| Subject group type          | Reporting group          | Reporting group            |  |  |
| Number of subjects analysed | 196                      | 194                        |  |  |
| Units: Number of subjects   |                          |                            |  |  |
| number (not applicable)     |                          |                            |  |  |
| Tetanus                     | 194                      | 191                        |  |  |
| Diphtheria                  | 189                      | 188                        |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Concentrations of Pertussis Antibodies Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine

|                        |   |
|------------------------|---|
| End point title        | Geometric Mean Concentrations of Pertussis Antibodies Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine  |
| End point description: | Pertussis antibodies Pertussis toxoid (PT), Filamentous hemagglutinin (FHA), Pertactin (PRN), and Fimbriae types 2 and 3 (FIM 2&3) were assayed by enzyme-linked immunosorbent assay (ELISA). |
| End point type         | Secondary   |
| End point timeframe:   | Day 0 (pre-vaccination) to Day 28 post-vaccination  |

| End point values                             | Adacel®<br>Vaccine Group | BOOSTRIX®<br>Vaccine Group |  |  |
|--|--------------------------|----------------------------|--|--|
| Subject group type                           | Reporting group          | Reporting group            |  |  |
| Number of subjects analysed                  | 196                      | 194                        |  |  |
| Units: Titers (1/dil)                        |                          |                            |  |  |
| geometric mean (confidence interval 95%)     |                          |                            |  |  |
| Pertussis toxoid (pre-vaccination)           | 5.59 (4.67 to 6.68)      | 5.69 (4.71 to 6.88)        |  |  |
| Pertussis toxoid (post-vaccination)          | 31 (27 to 35.7)          | 44.1 (39 to 49.9)          |  |  |
| Filamentous hemagglutinin (pre-vaccination)  | 22.7 (19 to 27.2)        | 22.7 (19.4 to 26.6)        |  |  |
| Filamentous hemagglutinin (post-vaccination) | 255 (228 to 286)         | 318 (292 to 347)           |  |  |
| Pertactin (pre-vaccination)                  | 12.3 (10.5 to 14.4)      | 10.3 (8.99 to 11.9)        |  |  |
| Pertactin (post-vaccination)                 | 263 (223 to 310)         | 252 (214 to 295)           |  |  |

|   |                     |                     |  |  |
|---|---------------------|---------------------|--|--|
| Fimbriae types 2 and 3 (pre-vaccination)  | 5.95 (4.88 to 7.24) | 6.55 (5.33 to 8.04) |  |  |
| Fimbriae types 2 and 3 (post-vaccination) | 346 (269 to 446)    | 11.1 (8.79 to 14)   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Booster Responses Against Pertussis Antibodies Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine

|                 |   |
|-----------------|---|
| End point title | Number of Subjects With Booster Responses Against Pertussis Antibodies Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine |
|-----------------|---|

End point description:

Adacel booster response defined as: a 4-fold increase in pre- to post-vaccination antibody concentrations for subjects with a pre-vaccination concentration  $\leq$  93 ELISA Unit (EU)/mL for Pertussis toxoid (PT),  $\leq$  170 EU/mL for Filamentous hemagglutinin (FHA),  $\leq$  115 EU/mL for pertactin (PRN), or  $\leq$  285 EU/mL for Fimbriae types 2 and 3 (FIM), and defined as a 2-fold increase for subjects with a pre-vaccination concentration  $>$  93 EU/mL for PT,  $>$  170 EU/mL for FHA,  $>$  115 EU/mL for PRN, or  $>$  285 EU/mL for FIM.

Boostrix booster response defined as: a post-vaccination titer  $\geq$  4 times the LLOQ for subjects with a pre-vaccination titer  $<$  LLOQ, a post-vaccination titer  $\geq$  4 times the pre-vaccination titer for subjects with a pre-vaccination titer between LLOQ and 4X LLOQ, or a post-vaccination titer at least twice the pre-vaccination titer for subjects with a pre-vaccination titer  $\geq$  4X LLOQ.

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

End point timeframe:

Day 28 post-vaccination

| End point values            | Adacel® Vaccine Group | BOOSTRIX® Vaccine Group |  |  |
|-----------------------------|-----------------------|-------------------------|--|--|
| Subject group type          | Reporting group       | Reporting group         |  |  |
| Number of subjects analysed | 196                   | 194                     |  |  |
| Units: Number of subjects   |                       |                         |  |  |
| number (not applicable)     |                       |                         |  |  |
| Pertussis toxoid            | 97                    | 142                     |  |  |
| Filamentous hemagglutinin   | 167                   | 189                     |  |  |
| Pertactin                   | 186                   | 189                     |  |  |
| Fimbriae types 2 and 3      | 181                   | 31                      |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects Reporting Immediate Unsolicited Adverse Events Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine

|                 |  |
|-----------------|--|
| End point title | Number of Subjects Reporting Immediate Unsolicited Adverse Events Following Vaccination With Either Adacel® or |
|-----------------|--|

**End point description:**

The occurrence, nature (Medical Dictionary for Regulatory Activities [MedDRA] preferred term), duration, intensity, and relationship to vaccination of adverse events (AEs) reported in the 15 minutes after vaccination and systemic AEs.

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

**End point timeframe:**

Up to 15 minutes post-vaccination

| <b>End point values</b>     | Adacel®<br>Vaccine Group | BOOSTRIX®<br>Vaccine Group |  |  |
|-----------------------------|--------------------------|----------------------------|--|--|
| Subject group type          | Reporting group          | Reporting group            |  |  |
| Number of subjects analysed | 211                      | 211                        |  |  |
| Units: Number of subjects   |                          |                            |  |  |
| number (not applicable)     |                          |                            |  |  |
| Headache                    | 1                        | 0                          |  |  |
| Nausea                      | 1                        | 0                          |  |  |

**Statistical analyses**

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from Day 0 up to Day 28 post-vaccination.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 14.0 |
|--------------------|------|

### Reporting groups

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Adacel® Vaccine Group |
|-----------------------|-----------------------|

Reporting group description:

Subjects received a single dose of Adacel® vaccine.

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | BOOSTRIX® Vaccine Group |
|-----------------------|-------------------------|

Reporting group description:

Subjects received a single dose of BOOSTRIX® vaccine.

| Serious adverse events                            | Adacel® Vaccine Group | BOOSTRIX® Vaccine Group |  |
|---|-----------------------|-------------------------|--|
| Total subjects affected by serious adverse events |                       |                         |  |
| subjects affected / exposed                       | 0 / 211 (0.00%)       | 0 / 211 (0.00%)         |  |
| number of deaths (all causes)                     | 0                     | 0                       |  |
| number of deaths resulting from adverse events    | 0                     | 0                       |  |

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

| Non-serious adverse events                            | Adacel® Vaccine Group | BOOSTRIX® Vaccine Group |  |
|---|-----------------------|-------------------------|--|
| Total subjects affected by non-serious adverse events |                       |                         |  |
| subjects affected / exposed                           | 58 / 211 (27.49%)     | 70 / 211 (33.18%)       |  |
| Nervous system disorders                              |                       |                         |  |
| Headache  |                       |                         |  |
| alternative assessment type: Systematic               |                       |                         |  |
| subjects affected / exposed                           | 21 / 211 (9.95%)      | 31 / 211 (14.69%)       |  |
| occurrences (all)                                     | 26                    | 39                      |  |
| General disorders and administration site conditions  |                       |                         |  |
| Injection site Pain                                   |                       |                         |  |
| alternative assessment type: Systematic               |                       |                         |  |

|   |                         |                         |  |
|---|-------------------------|-------------------------|--|
| subjects affected / exposed<br>occurrences (all)  | 34 / 211 (16.11%)<br>36 | 43 / 211 (20.38%)<br>46 |  |
| Respiratory, thoracic and mediastinal disorders<br>Oropharyngeal pain<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all) | 11 / 211 (5.21%)<br>11  | 4 / 211 (1.90%)<br>5    |  |

## **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