

**Clinical trial results:**

A Phase 2a Randomized, Double-blind, Placebo-controlled Trial to Evaluate the Safety, Immunogenicity, and Efficacy of Bris10 M2SR (H3N2 A/Brisbane/10/2007) Vaccine Administered as a Single Intranasal Dose (Versus Placebo) in Healthy Adult Volunteers who are Subsequently Challenged with a Live, Antigenically Different Wild-type Influenza Type A Virus (A/Belgium/4217/2015 H3N2)

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2017-004971-30 |
| Trial protocol | BE |
| Global end of trial date | 06 March 2019 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 19 March 2020 |
| First version publication date | 19 March 2020 |

Trial information**Trial identification**

| | |
|-----------------------|------------------|
| Sponsor protocol code | FLUGEN-H3N2-V002 |
|-----------------------|------------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | FluGen Inc. |
| Sponsor organisation address | 597 Science Drive, Madison, United States, WI USA 53711 |
| Public contact | Pamuk Bilsel, FluGen, Inc, 001 608-442-6562, pbilsel@flugen.com |
| Scientific contact | Pamuk Bilsel, FluGen, Inc, 001 608-442-6562, pbilsel@flugen.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 | 06 March 2019 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 March 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

- Assess the effect of vaccination with Bris10/2007 M2SR (H3N2) vaccine on influenza viral shedding after intranasal challenge with a drifted H3N2 virus, A/Belgium/4217/2015.
- Assess the safety of the Bris10 M2SR (H3N2) vaccine during the period from study vaccine administration until influenza virus challenge.

Protection of trial subjects:

This study was conducted in compliance with the protocol, the ICH Note for Guidance on Good Clinical Practice (CMPM/ICH/135/95) and with the applicable regulatory requirement(s)

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 15 May 2018 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 6 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Belgium: 108 |
| Worldwide total number of subjects | 108 |
| EEA total number of subjects | 108 |

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) | 108 |

| | |
|---------------------|---|
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted in the SGS clinical pharmacology phase 1 unit in Antwerp, Belgium.

Pre-assignment

Screening details:

Screening for eligible, healthy male and non-pregnant female subjects who were 18 to 55 years old was performed within approximately 7 weeks prior to randomization/vaccine administration. A total of 108 subjects were randomized into the study and were vaccinated (56 placebo, 52 Bris10 M2SR), according to randomization.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Blinding implementation details:

All subjects underwent the same procedures. The unblinded pharmacy staff or delegate prepared doses (active and placebo), filled delivery devices, and applied an opaque label to the device barrel to obscure any coloration of the contents. The unblinded site staff and unblinded monitor agreed in writing to maintain the blind by not providing details of the dose (active or placebo) to any blinded clinic staff including the investigator or any study subjects.

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

Subjects randomized to and receiving placebo

| | |
|--|----------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Nasal spray |
| Routes of administration | Intranasal use |

Dosage and administration details:

The reference product (placebo) used in this study was a physiological saline suitable for intranasal delivery. Commercially available supplies of placebo (0.9% NaCl 10 mL) were used and supplied by the site following approval from the Sponsor. The placebo was drawn into a nasal sprayer for intranasal delivery. Doses of placebo were administered according to the same procedures as Bris10 M2SR vaccine.

| | |
|------------------|-------------|
| Arm title | BRIS10 M2SR |
|------------------|-------------|

Arm description:

Subjects randomized to and receiving BRIS10 M2SR

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | FluGen's H3N2 (A/Brisbane/10/2007) M2SR Vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Nasal spray |
| Routes of administration | Intranasal use |

Dosage and administration details:

The vaccine was provided frozen and in single-use cryovials. An unblinded pharmacist thawed the vial contents to room temperature just prior to dose administration. The contents were diluted to the dosing

concentration with provided diluent for each subject. The final diluted product was drawn into a nasal sprayer for intranasal delivery.

| Number of subjects in period 1 | Placebo | BRIS10 M2SR |
|---------------------------------------|---------|-------------|
| Started | 56 | 52 |
| Completed | 51 | 48 |
| Not completed | 5 | 4 |
| Consent withdrawn by subject | 1 | - |
| due to excl criteria 1 in part B | 4 | 3 |
| Due to bed capacity | - | 1 |

Baseline characteristics

Reporting groups

| | |
|--|-------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects randomized to and receiving placebo | |
| Reporting group title | BRIS10 M2SR |
| Reporting group description: | |
| Subjects randomized to and receiving BRIS10 M2SR | |

| Reporting group values | Placebo | BRIS10 M2SR | Total |
|---------------------------|--------------|--------------|-------|
| Number of subjects | 56 | 52 | 108 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-55 years) | 56 | 52 | 108 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 38.9 | 39.6 | |
| standard deviation | ± 11.84 | ± 9.68 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 21 | 21 | 42 |
| Male | 35 | 31 | 66 |
| Race | | | |
| Units: Subjects | | | |
| Asian | 0 | 1 | 1 |
| Black or African American | 1 | 1 | 2 |
| White | 55 | 50 | 105 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Not Hispanic or Latino | 56 | 52 | 108 |
| Age categorical | | | |
| Units: Subjects | | | |
| Age ≤ 50 yrs | 44 | 44 | 88 |
| Age > 50 yrs | 12 | 8 | 20 |
| Smoking status | | | |
| Units: Subjects | | | |
| Ex-Smoker | 13 | 16 | 29 |
| Non-Smoker | 42 | 34 | 76 |
| Smoker | 1 | 2 | 3 |
| Age continuous | | | |
| Units: years | | | |
| median | 40.0 | 40.5 | |
| full range (min-max) | 18.0 to 55.0 | 22.0 to 55.0 | - |
| Weight - 1 | | | |
| Units: kg | | | |
| arithmetic mean | 75.0 | 73.8 | |
| standard deviation | ± 12.20 | ± 12.83 | - |

| | | | |
|--|-------------------------|-------------------------|---|
| Weight - 2 Units: kg median full range (min-max) | 73.4 52.3 to 106.8 | 72.1 49.7 to 122.0 | - |
| BMI - 1 Units: kg/m2 arithmetic mean standard deviation | 24.29 ± 2.919 | 24.37 ± 3.218 | - |
| BMI - 2 Units: kg/m2 median full range (min-max) | 24.61 19.07 to 30.54 | 23.81 18.66 to 30.96 | - |

End points

End points reporting groups

| | |
|--|-------------|
| Reporting group title | Placebo |
| Reporting group description: Subjects randomized to and receiving placebo | |
| Reporting group title | BRIS10 M2SR |
| Reporting group description: Subjects randomized to and receiving BRIS10 M2SR | |

Primary: Summary of qRT-PCR Viral Load Following Challenge (FAS) - AUC - 1

| | |
|--|--|
| End point title | Summary of qRT-PCR Viral Load Following Challenge (FAS) - AUC - 1 ^[1] |
| End point description: Primary endpoint 1: Area under the curve (AUC) of the influenza RNA log ₁₀ viral load by qRT-PCR from nasopharyngeal swabs of study subjects in the vaccine and placebo groups. | |
| End point type | Primary |
| End point timeframe: From the time of challenge inoculation with A/Belgium/4217/2015 until discharge (10 days after inoculation). | |
| 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: There were no pre-specified tests of hypotheses. Analyses were descriptive summaries of results. | |

| End point values | Placebo | BRIS10 M2SR | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 48 | | |
| Units: n, n Missing | | | | |
| AUC (n) | 51 | 48 | | |
| AUC (n Missing) | 0 | 0 | | |
| ln(AUC) (n) | 51 | 48 | | |
| ln(AUC) (n Missing) | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Summary of qRT-PCR Viral Load Following Challenge (FAS) - AUC - 2

| | |
|--|--|
| End point title | Summary of qRT-PCR Viral Load Following Challenge (FAS) - AUC - 2 ^[2] |
| End point description: Primary endpoint 1: Area under the curve (AUC) of the influenza RNA log ₁₀ viral load by qRT-PCR from nasopharyngeal swabs of study subjects in the vaccine and placebo groups. | |
| End point type | Primary |
| End point timeframe: From the time of challenge inoculation with A/Belgium/4217/2015 until discharge (10 days after | |

inoculation).

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: There were no pre-specified tests of hypotheses. Analyses were descriptive summaries of results.

| End point values | Placebo | BRIS10 M2SR | | |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 48 | | |
| Units: Viral load | | | | |
| arithmetic mean (standard deviation) | | | | |
| AUC | 513.85 (± 444.798) | 423.99 (± 420.644) | | |
| ln(AUC) | 5.11 (± 2.348) | 4.78 (± 2.296) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Summary of qRT-PCR Viral Load Following Challenge (FAS) - AUC - 3

| | |
|-----------------|--|
| End point title | Summary of qRT-PCR Viral Load Following Challenge (FAS) - AUC - 3 ^[3] |
|-----------------|--|

End point description:

Primary endpoint 1: Area under the curve (AUC) of the influenza RNA log10 viral load by qRT-PCR from nasopharyngeal swabs of study subjects in the vaccine and placebo groups.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From the time of challenge inoculation with A/Belgium/4217/2015 until discharge (10 days after inoculation).

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: There were no pre-specified tests of hypotheses. Analyses were descriptive summaries of results.

| End point values | Placebo | BRIS10 M2SR | | |
|-------------------------------|--------------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 48 | | |
| Units: Viral load | | | | |
| median (full range (min-max)) | | | | |
| AUC | 501.33 (0.00 to 1404.25) | 303.23 (0.00 to 1216.12) | | |
| ln(AUC) | 6.22 (0.00 to 7.25) | 5.71 (0.00 to 7.10) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Overall Summary of Adverse Events – Vaccine Period (Safety Set) - 1

| | |
|-----------------|--|
| End point title | Overall Summary of Adverse Events – Vaccine Period (Safety Set) - 1 ^[4] |
|-----------------|--|

End point description:

Primary endpoint 2: Number of study subjects reporting solicited and unsolicited adverse events (AEs) and serious adverse events (SAEs)

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From the time of administration of the vaccine or placebo until administration of challenge virus.

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: There were no pre-specified tests of hypotheses. Analyses were descriptive summaries of results.

| End point values | Placebo | BRIS10 M2SR | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 52 | | |
| Units: Number of subjects | | | | |
| # Subjects with at least 1 TEAE | 34 | 32 | | |
| # Subjects with at least 1 TEAE related to vaccine | 28 | 21 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Overall Summary of Adverse Events – Vaccine Period (Safety Set) - 2

| | |
|-----------------|--|
| End point title | Overall Summary of Adverse Events – Vaccine Period (Safety Set) - 2 ^[5] |
|-----------------|--|

End point description:

Primary endpoint 2: Proportions of study subjects reporting solicited and unsolicited adverse events (AEs) and serious adverse events (SAEs).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From the time of administration of the vaccine or placebo until administration of challenge virus.

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: There were no pre-specified tests of hypotheses. Analyses were descriptive summaries of results.

| End point values | Placebo | BRIS10 M2SR | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 52 | | |
| Units: % of Subjects | | | | |
| % Subjects with at least 1 TEAE | 61 | 62 | | |
| % Subjects with at least 1 TEAE related to vaccine | 50 | 40 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Overall Infection and Influenza Illness (Full Analysis Set)

| | |
|--|--|
| End point title | Summary of Overall Infection and Influenza Illness (Full Analysis Set) |
| End point description: | |
| Secondary endpoint: the proportion of study subjects in vaccine and placebo groups with infection following challenge with A/Belgium/4217/2015 as determined by qRT-PCR.2 and the proportion of study subjects in vaccine and placebo groups with infection AND influenza illness following intranasal challenge with A/Belgium/4217/2015. | |
| - Infection is defined as at least two consecutive qRT-PCR positive swabs starting on the second day after challenge (Day 3). | |
| - Influenza illness is defined as either at least one respiratory symptom on two consecutive days OR at least one respiratory and at least one systemic symptom on two consecutive days. | |
| End point type | Secondary |
| End point timeframe: | |
| During the trial | |

| End point values | Placebo | BRIS10 M2SR | | |
|--------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 48 | | |
| Units: Number of Subjects | | | | |
| Infected | 36 | 26 | | |
| Influenza illness | 29 | 23 | | |
| Infected and Influenza illness | 25 | 16 | | |

Statistical analyses

| | |
|---|---------------------------------|
| Statistical analysis title | Proportion of subjects infected |
| Comparison groups | Placebo v BRIS10 M2SR |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[6] |
| P-value | = 0.10133 |
| Method | Fisher exact |

Notes:

[6] - Descriptive

| | |
|----------------------------|---|
| Statistical analysis title | Proportion of subjects with Influenza illness |
|----------------------------|---|

| | |
|---|-----------------------|
| Comparison groups | Placebo v BRIS10 M2SR |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[7] |
| P-value | = 0.42383 |
| Method | Fisher exact |

Notes:

[7] - Descriptive

| | |
|---|---|
| Statistical analysis title | Proportion of subjects infected & Influenza illness |
| Comparison groups | Placebo v BRIS10 M2SR |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[8] |
| P-value | = 0.15316 |
| Method | Fisher exact |

Notes:

[8] - Descriptive

Secondary: Treatment-Emergent Adverse Events (TEAE)

| | |
|-----------------|--|
| End point title | Treatment-Emergent Adverse Events (TEAE) |
|-----------------|--|

End point description:

Secondary endpoint: Number (+%) of study subjects reporting treatment-emergent solicited and unsolicited AEs and SAEs.

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

End point timeframe:

During the study

| End point values | Placebo | BRIS10 M2SR | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 52 | | |
| Units: Number (+%) of subjects | | | | |
| Nbr of subjects with any TEAE | 34 | 32 | | |
| % of subjects with any TEAE | 61 | 62 | | |
| Nbr of subjects with any vaccine related TEAE | 28 | 21 | | |
| % of subjects with any vaccine related TEAE | 50 | 40 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Challenge-Emergent Adverse Events (CEAE)

| | |
|-----------------|--|
| End point title | Challenge-Emergent Adverse Events (CEAE) |
|-----------------|--|

End point description:

Secondary endpoint: Number (+%) of study subjects reporting challenge -emergent solicited and unsolicited AEs and SAEs.

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

End point timeframe:

During the study

| End point values | Placebo | BRIS10 M2SR | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 52 | | |
| Units: Number and % of subjects | | | | |
| Nbr of subjects with any CEAE | 39 | 36 | | |
| % of subjects with any CEAE | 76 | 75 | | |
| Nbr of subjects with any inoculation related CEAE | 37 | 34 | | |
| % of subjects with any inoculation related CEAE | 73 | 71 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are monitored continuously from day of IP treatment until the last study-related activity (typically Day 28)

Adverse event reporting additional description:

At regular intervals during the study, subjects will be asked non-leading questions to determine the occurrence of any AEs. All AEs reported spontaneously during the course of the study will be recorded as well. Solicited and unsolicited signs and symptoms will be reported as AEs after review by the Investigator or designee.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 20.0 |

Reporting groups

| | |
|-----------------------|----------------|
| Reporting group title | Placebo - TEAE |
|-----------------------|----------------|

Reporting group description:

Subjects randomized to and receiving placebo

| | |
|-----------------------|--------------------|
| Reporting group title | BRIS10 M2SR - TEAE |
|-----------------------|--------------------|

Reporting group description:

Subjects randomized to and receiving BRIS10 M2SR

| | |
|-----------------------|----------------|
| Reporting group title | Placebo - CEAE |
|-----------------------|----------------|

Reporting group description: -

| | |
|-----------------------|--------------------|
| Reporting group title | BRIS10 M2SR - CEAE |
|-----------------------|--------------------|

Reporting group description: -

| Serious adverse events | Placebo - TEAE | BRIS10 M2SR - TEAE | Placebo - CEAE |
|---|----------------|--------------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 52 (0.00%) | 0 / 51 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |

| Serious adverse events | BRIS10 M2SR - CEAE | | |
|---|--------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

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

| Non-serious adverse events | Placebo - TEAE | BRIS10 M2SR - TEAE | Placebo - CEAE |
|---|------------------|--------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 34 / 56 (60.71%) | 32 / 52 (61.54%) | 39 / 51 (76.47%) |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 6 / 56 (10.71%) | 4 / 52 (7.69%) | 0 / 51 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Malaise | | | |
| subjects affected / exposed | 2 / 56 (3.57%) | 0 / 52 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 52 (1.92%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 52 (0.00%) | 34 / 51 (66.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Vessel puncture site haematoma | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 52 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 1 |
| Feeling hot | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 52 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 52 (1.92%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Reproductive system and breast disorders | | | |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 52 (0.00%) | 4 / 51 (7.84%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Nasal congestion | | | |
| subjects affected / exposed | 9 / 56 (16.07%) | 7 / 52 (13.46%) | 1 / 51 (1.96%) |
| occurrences (all) | 1 | 1 | 1 |
| Rhinorrhoea | | | |

| | | | |
|--|-----------------|-----------------|----------------|
| subjects affected / exposed | 9 / 56 (16.07%) | 8 / 52 (15.38%) | 0 / 51 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Cough | | | |
| subjects affected / exposed | 4 / 56 (7.14%) | 2 / 52 (3.85%) | 0 / 51 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Throat irritation | | | |
| subjects affected / exposed | 4 / 56 (7.14%) | 6 / 52 (11.54%) | 0 / 51 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Respiratory tract irritation | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 52 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sneezing | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 52 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 1 | 0 | 1 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 2 / 52 (3.85%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 52 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 52 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Fracture | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 52 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Arthropod bite | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 52 (1.92%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 52 (1.92%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin wound | | | |

| | | | |
|---|-----------------------|-----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 0 / 52 (0.00%) 0 | 1 / 51 (1.96%) 1 |
| Injury subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 0 / 52 (0.00%) 0 | 0 / 51 (0.00%) 0 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 16 / 56 (28.57%) 1 | 11 / 52 (21.15%) 1 | 1 / 51 (1.96%) 1 |
| Dysgeusia subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 1 / 52 (1.92%) 1 | 0 / 51 (0.00%) 0 |
| Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 1 / 52 (1.92%) 1 | 0 / 51 (0.00%) 0 |
| Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 0 / 52 (0.00%) 0 | 0 / 51 (0.00%) 0 |
| Vertigo subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 0 / 52 (0.00%) 0 | 0 / 51 (0.00%) 0 |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 1 / 56 (1.79%) 1 | 1 / 52 (1.92%) 1 | 0 / 51 (0.00%) 0 |
| Constipation subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 1 / 52 (1.92%) 1 | 0 / 51 (0.00%) 0 |
| Tooth disorder subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 1 / 52 (1.92%) 1 | 0 / 51 (0.00%) 0 |
| Toothache subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 1 / 52 (1.92%) 1 | 0 / 51 (0.00%) 0 |
| Vomiting | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 52 (1.92%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 52 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 52 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 52 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 52 (1.92%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 52 (1.92%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 52 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |
| subjects affected / exposed | 3 / 56 (5.36%) | 0 / 52 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 2 / 56 (3.57%) | 0 / 52 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 52 (1.92%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 52 (1.92%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infections and infestations | | | |

| | | | |
|-----------------------------------|----------------|----------------|----------------|
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 56 (3.57%) | 1 / 52 (1.92%) | 1 / 51 (1.96%) |
| occurrences (all) | 1 | 1 | 1 |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 56 (1.79%) | 0 / 52 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Herpes simplex | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 1 / 52 (1.92%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 52 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 0 | 0 | 1 |
| Fungal skin infection | | | |
| subjects affected / exposed | 0 / 56 (0.00%) | 0 / 52 (0.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|-----------------------|--|--|
| Non-serious adverse events | BRIS10 M2SR - CEAE | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 36 / 48 (75.00%) | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Malaise | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Chills | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Influenza like illness | | | |
| subjects affected / exposed | 30 / 48 (62.50%) | | |
| occurrences (all) | 1 | | |
| Vessel puncture site haematoma | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | | |
| occurrences (all) | 1 | | |
| Feeling hot | | | |

| | | | |
|---|--|--|--|
| subjects affected / exposed occurrences (all) | 1 / 48 (2.08%) 1 | | |
| Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Respiratory, thoracic and mediastinal disorders Nasal congestion subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Throat irritation subjects affected / exposed occurrences (all) Respiratory tract irritation subjects affected / exposed occurrences (all) Sneezing subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 0 / 48 (0.00%) 0 0 / 48 (0.00%) 0 0 / 48 (0.00%) 0 0 / 48 (0.00%) 0 1 / 48 (2.08%) 1 0 / 48 (0.00%) 0 1 / 48 (2.08%) 1 | | |
| Investigations | | | |

| | | | |
|--|---------------------|--|--|
| Hepatic enzyme increased subjects affected / exposed occurrences (all) | 1 / 48 (2.08%) 1 | | |
| Injury, poisoning and procedural complications | | | |
| Fracture subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Arthropod bite subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Ligament sprain subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Skin wound subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Injury subjects affected / exposed occurrences (all) | 1 / 48 (2.08%) 1 | | |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Dysgeusia subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Blood and lymphatic system disorders | | | |
| Lymphadenopathy subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Ear and labyrinth disorders | | | |
| Ear pain subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | | |
| Vertigo | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tooth disorder | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Toothache | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | | |
| occurrences (all) | 1 | | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | | |
| occurrences (all) | 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pruritus | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 48 (2.08%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | | |
| occurrences (all) | 1 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Herpes simplex | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 48 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fungal skin infection | | | |
| subjects affected / exposed | 1 / 48 (2.08%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported