# Clinical trial results:
# Clinical trial - phase II - to test safety and efficay of Etravirine's treatment in Friedreich Ataxia's patients

## Summary

| | |
|---|---|
| EudraCT number | 2019-002618-38 |
| Trial protocol | IT |
| Global end of trial date | 17 January 2023 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 20 June 2024 |
| First version publication date | 20 June 2024 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 721 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04273165 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Associazione La Nostra Famiglia |
| Sponsor organisation address | Via Don Luigi Monza, 1, Ponte Lambro, Italy, 22037 |
| Public contact | Segreteria Scientifica, Associazione La Nostra Famiglia, +39 031877330, medea@lanostrafamiglia.it |
| Scientific contact | Segreteria Scientifica, Associazione La Nostra Famiglia, +39 031877330, medea@lanostrafamiglia.it |

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 | 28 May 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 17 January 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 January 2023 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Test the safety of ETR treatment in patients with FRDA (two groups of patients treated with 2 different doses: 200 mg / day and 400 mg / day). The goal is to monitor all EAs that will occur during 4 months of treatment with ETR compared to EAs recorded during 4 months of observation before and 4 months after treatment.

Protection of trial subjects:

Presence among trial documentation of a patient report form for any adverse event experienced. Presence of a dedicated phone number for safety issues available 24/7. Physical exmination during visits, including vital signs, whole body skin inspection, blood testing, urine testing.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 17 September 2020 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Scientific research |
| Long term follow-up duration | 4 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Italy: 35 |
| Worldwide total number of subjects | 35 |
| EEA total number of subjects | 35 |

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) | 1 |
| Adolescents (12-17 years) | 4 |
| Adults (18-64 years) | 30 |

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

## Subject disposition

### Recruitment

Recruitment details:

Recruitment was promoted by advertising the study through patients' associations and among patients currently followed at the clinical site. Recruitment was done at the clinical site.

### Pre-assignment

Screening details:

38 patients were screened for inclusion. Of these, 35 were enrolled and 3 excluded. Of the excluded, 2 were not capable of completing the exercise test, 1 withdrew consent immediately after the screening visit.

### Period 1

| | |
|---|---|
| Period 1 title | Etravirine treatment months 0 to 2 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Blinding implementation details:

No blinding was done

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Etravirine 200 mg/day |

Arm description:

2 months treatment with etravirine 200 mg/day

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Intelence |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Intelence tablets strength 200mg ; 1 tablet per day in the morning, for 2 months

| | |
|---|---|
| **Arm title** | Etravirine 400 mg/day |

Arm description:

2 months treatment with etravirine 400 mg/day

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Intelence |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Intelence tablets strength 200mg ; 2 tablets per day in the morning, for 2 months

| Number of subjects in period 1 | Etravirine 200 mg/day | Etravirine 400 mg/day |
|---|---|---|
| Started | 17 | 18 |
| Completed | 17 | 17 |
| Not completed | 0 | 1 |
| Adverse event, non-fatal | - | 1 |

| Period 2 | |
|---|---|
| Period 2 title | Continuation of etravirine months 3 to 4 |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

| Arms | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Etravirine 200 mg/day |

Arm description:

2 months treatment with etravirine 200 mg/day

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Intelence |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Intelence tablets strength 200mg ; 1 tablet per day in the morning, for 2 months

| | |
|---|---|
| **Arm title** | Etravirine 400 mg/day |

Arm description:

2 months treatment with etravirine 400 mg/day

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Intelence |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Intelence tablets strength 200mg ; 2 tablets per day in the morning, for 2 months

| Number of subjects in period 2 | Etravirine 200 mg/day | Etravirine 400 mg/day |
|---|---|---|
| Started | 17 | 17 |
| Completed | 17 | 17 |

| Period 3 | |
|---|---|
| Period 3 title | Follow-up without treatment mo. 5 to 8 |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |
| **Arms** | |
| Are arms mutually exclusive? | Yes |
| **Arm title** | Etravirine 200 mg/day |
| Arm description:<br>4 months without treatment | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |
| **Arm title** | Etravirine 400 mg/day |
| Arm description:<br>4 months without treatment | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 3 | Etravirine 200 mg/day | Etravirine 400 mg/day |
|---|---|---|
| Started | 17 | 17 |
| Completed | 17 | 17 |

## Baseline characteristics

### Reporting groups

| Reporting group title | Etravirine treatment months 0 to 2 |
|---|---|

Reporting group description: -

| Reporting group values | Etravirine treatment months 0 to 2 | Total | |
|---|---|---|---|
| Number of subjects | 35 | 35 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 1 | 1 | |
| Adolescents (12-17 years) | 4 | 4 | |
| Adults (18-64 years) | 30 | 30 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 11.83 | | |
| standard deviation | ± 5.7 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 19 | 19 | |
| Male | 16 | 16 | |

## End points

| End points reporting groups | |
|---|---|
| Reporting group title | Etravirine 200 mg/day |
| Reporting group description:<br>2 months treatment with etravirine 200 mg/day | |
| Reporting group title | Etravirine 400 mg/day |
| Reporting group description:<br>2 months treatment with etravirine 400 mg/day | |
| Reporting group title | Etravirine 200 mg/day |
| Reporting group description:<br>2 months treatment with etravirine 200 mg/day | |
| Reporting group title | Etravirine 400 mg/day |
| Reporting group description:<br>2 months treatment with etravirine 400 mg/day | |
| Reporting group title | Etravirine 200 mg/day |
| Reporting group description:<br>4 months without treatment | |
| Reporting group title | Etravirine 400 mg/day |
| Reporting group description:<br>4 months without treatment | |

| Primary: Number of adverse drug reactions | |
|---|---|
| End point title | Number of adverse drug reactions |
| End point description:<br>see adverse events | |
| End point type | Primary |
| End point timeframe:<br>2 months treatment<br>4 months treatment<br>4 months treatment then 4 months no treatment | |

| End point values | Etravirine 200 mg/day | Etravirine 400 mg/day | Etravirine 200 mg/day | Etravirine 400 mg/day |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 17 | 17[1] | 17 | 17 |
| Units: number | 17 | 18 | 17 | 17 |

Notes:

[1] - 1 drop out due to non severe ADR

| End point values | Etravirine 200 mg/day | Etravirine 400 mg/day | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 17 | | |
| Units: number | 17 | 17 | | |

## Statistical analyses

| **Statistical analysis title** | Chi-squared of adverse events |
|---|---|
| Comparison groups | Etravirine 200 mg/day v Etravirine 400 mg/day v Etravirine 200 mg/day v Etravirine 400 mg/day v Etravirine 200 mg/day v Etravirine 400 mg/day |
| Number of subjects included in analysis | 102 |
| Analysis specification | Post-hoc |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | Chi-squared |
| Parameter estimate | no estimation |

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events:<br>Period 1: Etravirine treatment months 0 to 2<br>Period 2: Continuation of etravirine months 3 to 4<br>Period 3: Follow-up without treatment months 5 to 8 | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 17 |

| Reporting groups | |
|---|---|
| Reporting group title | Etravirine 200 months 0-2 |
| Reporting group description:<br>Etravirine 200 months 0-2 | |
| Reporting group title | Etravirine 400 months 0-2 |
| Reporting group description:<br>Etravirine 400 months 0-2 | |
| Reporting group title | Etravirine 200 months 3-4 |
| Reporting group description:<br>Etravirine 200 months 3-4 | |
| Reporting group title | Etravirine 400 months 3-4 |
| Reporting group description:<br>Etravirine 400 months 3-4 | |
| Reporting group title | Etravirine 200 months 5-8 |
| Reporting group description:<br>Etravirine 200 months 5-8 follow up without treatment | |
| Reporting group title | Etravirine 400 months 5-8 |
| Reporting group description:<br>Etravirine 200 months 5-8 follow up without treatment | |

| Serious adverse events | Etravirine 200 months 0-2 | Etravirine 400 months 0-2 | Etravirine 200 months 3-4 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Tachycardia | Additional description: Supraventricular tachycardic arrhythmia | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Etravirine 400 months 3-4 | Etravirine 200 months 5-8 | Etravirine 400 months 5-8 |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 0 / 17 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Tachycardia | Additional description: Supraventricular tachycardic arrhythmia | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 0 / 17 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| **Non-serious adverse events** | Etravirine 200 months 0-2 | Etravirine 400 months 0-2 | Etravirine 200 months 3-4 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 17 / 17 (100.00%) | 18 / 18 (100.00%) | 2 / 17 (11.76%) |
| Investigations | | | |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 2 / 18 (11.11%) | 2 / 17 (11.76%) |
| occurrences (all) | 2 | 2 | 2 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 3 / 17 (17.65%) | 0 / 18 (0.00%) | 2 / 17 (11.76%) |
| occurrences (all) | 3 | 0 | 3 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 18 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 18 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| Amylase increased | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 1 | 0 | 1 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vascular disorders | | | |

| | | | |
|---|---|---|---|
| Hypotension | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 2 / 18 (11.11%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 2 | 0 | 1 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 6 / 17 (35.29%) | 10 / 18 (55.56%) | 1 / 17 (5.88%) |
| occurrences (all) | 7 | 18 | 1 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 2 / 18 (11.11%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Oedema peripheral | Additional description: Feeling of swollen feet | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Diarrhea | | | |
| subjects affected / exposed | 3 / 17 (17.65%) | 4 / 18 (22.22%) | 0 / 17 (0.00%) |
| occurrences (all) | 5 | 7 | 0 |
| Nausea | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 3 / 18 (16.67%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 18 (5.56%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|---|---|---|
| Rash | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 2 / 18 (11.11%) | 0 / 17 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal and urinary disorders | | | |
| Urinary incontinence | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Psychiatric disorders | | | |
| Anger | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 18 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| **Non-serious adverse events** | Etravirine 400 months 3-4 | Etravirine 200 months 5-8 | Etravirine 400 months 5-8 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 5 / 17 (29.41%) | 0 / 17 (0.00%) | 11 / 17 (64.71%) |
| Investigations | | | |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 17 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 2 | 1 | 1 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Amylase increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 17 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 1 | 0 | 1 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 17 (0.00%) | 2 / 17 (11.76%) |
| occurrences (all) | 3 | 0 | 4 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 2 / 17 (11.76%) |
| occurrences (all) | 0 | 0 | 2 |
| Oedema peripheral | Additional description: Feeling of swollen feet | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Diarrhea | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 17 (0.00%) | 3 / 17 (17.65%) |
| occurrences (all) | 1 | 0 | 3 |
| Nausea | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 17 (0.00%) | 2 / 17 (11.76%) |
| occurrences (all) | 2 | 0 | 5 |
| Vomiting | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 17 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 1 | 0 | 4 |
| Constipation | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Anger | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 1 / 17 (5.88%) |
| occurrences (all) | 0 | 0 | 2 |
| Musculoskeletal and connective tissue disorders | | | |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 0 / 17 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 03 March 2022 | Extended recruitment and overall trial duration |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported