# Clinical trial results:
# An open-label, multi-center, expanded access program of ranibizumab in patients with visual impairment due to diabetic macular edema for whom no suitable therapeutic alternatives exist.

## Summary

| | |
|---|---|
| EudraCT number | 2011-002731-26 |
| Trial protocol | IT |
| Global end of trial date | 08 October 2013 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 17 December 2020 |
| First version publication date | 17 December 2020 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | CRFB002DIT01 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, +41 +39 02 96541, |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, +41 +39 02 96541, |

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 | 08 October 2013 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 08 October 2013 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To provide early access to ranibizumab in patients with macular edema and visual impairment secondary to diabetes mellitus for whom no suitable therapeutic alternatives exist (i.e. existing therapies, e.g. laser photocoagulation, have failed or are not indicated).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

| | |
|---|---|
| Background therapy: - | |
| Evidence for comparator: - | |
| Actual start date of recruitment | 07 November 2011 |
| 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 | Italy: 617 |
| Worldwide total number of subjects | 617 |
| EEA total number of subjects | 617 |

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) | 275 |
| From 65 to 84 years | 338 |

| | |
|---|---|
| 85 years and over | 4 |

## Subject disposition

### Recruitment

Recruitment details:

A total of 620 subjects were screened and 617 subjects were enrolled in the study.

### Pre-assignment

Screening details:

Subjects were enrolled at 33 sites in Italy. The first subject was screened on 7 November 2011. The last study visit occurred on 8 October 2013

### Period 1

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

### Arms

| | |
|---|---|
| **Arm title** | Overall Study |

Arm description:

Subjects received 0.5 mg ranibizumab intravitreal injection according to the approved label: the treatment was given monthly until maximum visual acuity (VA) was achieved (the subjects VA was stable for three consecutive monthly assessments).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Ranibizumab |
| Investigational medicinal product code | |
| Other name | Lucentis® |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravitreal use |

Dosage and administration details:

Subjects received 0.5 mg ranibizumab as intravitreal injection monthly until maximum VA was achieved.

| **Number of subjects in period 1** | Overall Study |
|---|---|
| Started | 617 |
| Completed | 515 |
| Not completed | 102 |
| Adverse event, serious fatal | 3 |
| Consent withdrawn by subject | 32 |
| Subject's condition not required program drug | 4 |
| Adverse event, non-fatal | 19 |
| Protocol violation | 8 |
| Unsatisfactory therapeutic effect | 8 |
| Lost to follow-up | 27 |
| Abnormal test procedure result(s) | 1 |

## Baseline characteristics

### Reporting groups

| Reporting group title | Overall Study |
|---|---|

Reporting group description: -

| Reporting group values | Overall Study | Total | |
|---|---|---|---|
| Number of subjects | 617 | 617 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 0 | |
| Newborns (0-27 days) | | 0 | |
| Infants and toddlers (28 days-23 months) | | 0 | |
| Children (2-11 years) | | 0 | |
| Adolescents (12-17 years) | | 0 | |
| Adults (18-64 years) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 65.525 | | |
| standard deviation | ± 9.145 | - | |
| Gender categorical | | | |
| Please note, the data in the CSR that was provided for the gender was for the Full Analysis Set (FAS), 612. All other Baseline categories were supplied for the Enrolled patient (617). Data was provided for the actual number of subjects enrolled in the study by gender for consistency. | | | |
| Units: Subjects | | | |
| Female | 228 | 228 | |
| Male | 389 | 389 | |

## End points

### End points reporting groups

| Reporting group title | Overall Study |
|---|---|

Reporting group description:

Subjects received 0.5 mg ranibizumab intravitreal injection according to the approved label: the treatment was given monthly until maximum visual acuity (VA) was achieved (the subjects VA was stable for three consecutive monthly assessments).

### Primary: Percentage of Subjects Experiencing any Serious Adverse Events (SAEs)

| End point title | Percentage of Subjects Experiencing any Serious Adverse Events (SAEs)[1] |
|---|---|

End point description:

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

End point timeframe:

Baseline up to end of program (Up to approximately 23 months)

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: No statistical analysis was planned or performed.

| End point values | Overall Study | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 612[2] | | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 29 | | | |

Notes:

[2] - All subjects who received at least one dose of ranibizumab and had at least one post-baseline safety

### Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: Baseline up to end of program (Up to approximately 23 months) | |
| Assessment type | Systematic |
| **Dictionary used** | |
| Dictionary name | MedDRA |
| Dictionary version | 14.0 |
| **Reporting groups** | |
| Reporting group title | Unilateral DME |
| Reporting group description: Unilateral DME | |
| Reporting group title | Bilateral DME |
| Reporting group description: Bilateral DME | |

| Serious adverse events | Unilateral DME | Bilateral DME | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 157 (4.46%) | 22 / 455 (4.84%) | |
| number of deaths (all causes) | 1 | 2 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Bladder papilloma | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal neoplasm | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 455 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic neoplasm | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 455 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung neoplasm malignant | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Non-Hodgkin's lymphoma | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Arterial disorder | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 455 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Cataract operation | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Inflammation | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleurisy | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 455 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial flutter | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 455 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 3 / 455 (0.66%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Congestive cardiomyopathy | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 455 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic cardiomyopathy | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 455 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 455 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhagic stroke | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic cerebral infarction | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 455 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Ocular hypertension | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vitreous haemorrhage | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Renal failure acute | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 455 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Urethral obstruction | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abscess | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Unilateral DME | Bilateral DME | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 5 / 157 (3.18%) | 30 / 455 (6.59%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 2 / 455 (0.44%) | |
| occurrences (all) | 0 | 2 | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Surgical and medical procedures | | | |
| Cataract operation | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 2 / 455 (0.44%) | |
| occurrences (all) | 0 | 2 | |
| Cholecystectomy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Investigations | | | |
| Intraocular pressure increased | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Injury, poisoning and procedural complications | | | |
| Toxicity to various agents | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Nervous system disorders | | | |
| Diabetic neuropathy | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Presyncope | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Blood and lymphatic system disorders | | | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 2 / 157 (1.27%) | 4 / 455 (0.88%) | |
| occurrences (all) | 3 | 4 | |
| Conjunctival haemorrhage | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Conjunctivitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 157 (1.27%) | 0 / 455 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Diabetic retinal oedema | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 6 / 455 (1.32%) | |
| occurrences (all) | 0 | 6 | |
| Diabetic retinopathy | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Lacrimation increased | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Macular ischaemia | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Macular oedema | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Ocular hypertension | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 455 (0.22%) | |
| occurrences (all) | 1 | 1 | |
| Retinal exudates | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Uveitis | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Vitreous haemorrhage | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 455 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Renal and urinary disorders | | | |
| Microalbuminuria | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 455 (0.22%) | |
| occurrences (all) | 0 | 1 | |
| Infections and infestations | | | |
| Influenza | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 3 / 455 (0.66%) | |
| occurrences (all) | 0 | 3 | |
| Labyrinthitis | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 2 / 455 (0.44%) | |
| occurrences (all) | 0 | 2 | |

## 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