



Clinical trial results:

A Phase 2b Open-label Extension Study to Evaluate the Long-term Safety and Efficacy of NEOD001 in Subjects with Light Chain (AL) Amyloidosis who were previously enrolled in Study NEOD001-201 (PRONTO)

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2016-004664-18 |
| Trial protocol | GB DE ES GR AT IT |
| Global end of trial date | 30 May 2018 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 12 December 2018 |
| First version publication date | 12 December 2018 |

Trial information

Trial identification

| | |
|-----------------------|---|
| Sponsor protocol code | 0 |
|-----------------------|---|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03154047 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Prothena Therapeutics Limited, now merged into Prothena Biosciences Limited |
| Sponsor organisation address | Adelphi Plaza, Upper George's Street, Co. Dublin, Dun Laoghaire, Ireland, A96 T927 |
| Public contact | Clinical Trials Office, Prothena Biosciences Inc, info@prothena.com |
| Scientific contact | Communications Office, Prothena Biosciences Inc, info@prothena.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 | 05 October 2018 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 30 May 2018 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to evaluate the long-term safety and efficacy of NEOD001 in subjects with AL amyloidosis who completed Study NEOD001-201.

Protection of trial subjects:

This study was conducted in compliance with International Conference on Harmonisation (ICH) Good Clinical Practice, the principles of the Declaration of Helsinki, and with the laws of the countries in which the study was conducted.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 01 August 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Spain: 5 |
| Country: Number of subjects enrolled | United Kingdom: 7 |
| Country: Number of subjects enrolled | Germany: 6 |
| Country: Number of subjects enrolled | Greece: 7 |
| Country: Number of subjects enrolled | Australia: 8 |
| Country: Number of subjects enrolled | Israel: 8 |
| Country: Number of subjects enrolled | United States: 39 |
| Worldwide total number of subjects | 80 |
| EEA total number of subjects | 25 |

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) | 36 |
| From 65 to 84 years | 44 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

A total of 80 subjects were enrolled in this study and were included in the OLE Safety Population.

Pre-assignment

Screening details:

Subject screening occurred 28 days prior to the first administration of study drug (i.e., Month 1-Day 1 Visit), which may have overlapped with the last visit in Study NEOD001-201. If all eligibility requirements were met, the subject was enrolled and screening assessments were completed.

Period 1

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

Arms

| | |
|------------------|------------------|
| Arm title | NEOD001 24 mg/kg |
|------------------|------------------|

Arm description:

NEOD001, 24 mg/kg IV every 4 weeks for 38 months

| | |
|--|----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | NEOD001 24 mg/kg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

The NEOD001 dose was 24 mg/kg up to a maximum total dose of 2500 mg. NEOD001 was prepared in a 250 mL IV bag of 0.9% saline. NEOD001 was administered once every 28 days (a ± 5 -day window was allowed for visits starting after Month 1) over 60 (± 10) minutes unless a longer infusion duration was established for the individual subject in Study NEOD001-201. The length of the infusion may have been extended over a longer period of time as clinically indicated. A minimum of 21 days between doses was required.

| | |
|---------------------------------------|------------------|
| Number of subjects in period 1 | NEOD001 24 mg/kg |
| Started | 80 |
| Completed | 0 |
| Not completed | 80 |
| Consent withdrawn by subject | 3 |
| Death | 1 |
| Study Terminated by Sponsor | 76 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Overall trial |
| Reporting group description: - | |

| Reporting group values | Overall trial | Total | |
|---------------------------|---------------|-------|--|
| Number of subjects | 80 | 80 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 36 | 36 | |
| From 65-84 years | 44 | 44 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 64.5 | | |
| standard deviation | ± 8.62 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 30 | 30 | |
| Male | 50 | 50 | |
| Race | | | |
| Units: Subjects | | | |
| Asian | 1 | 1 | |
| Black or African American | 2 | 2 | |
| White | 74 | 74 | |
| Other | 3 | 3 | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Not Hispanic or Latino | 79 | 79 | |
| Not Reported | 1 | 1 | |

Subject analysis sets

| | |
|----------------------------|-----------------------|
| Subject analysis set title | OLE Safety Population |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

OLE Safety Population includes all randomized subjects who received any amount of study drug

| Reporting group values | OLE Safety Population | | |
|------------------------|-----------------------|--|--|
| Number of subjects | 80 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 36 | | |
| From 65-84 years | 44 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 64.5 | | |
| standard deviation | ± 8.62 | | |

| | | | |
|---------------------------|----|--|--|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 30 | | |
| Male | 50 | | |
| Race | | | |
| Units: Subjects | | | |
| Asian | 1 | | |
| Black or African American | 2 | | |
| White | 74 | | |
| Other | 3 | | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Not Hispanic or Latino | 79 | | |
| Not Reported | 1 | | |

End points

End points reporting groups

| | |
|---|-----------------------|
| Reporting group title | NEOD001 24 mg/kg |
| Reporting group description: NEOD001, 24 mg/kg IV every 4 weeks for 38 months | |
| Subject analysis set title | OLE Safety Population |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: OLE Safety Population includes all randomized subjects who received any amount of study drug | |

Primary: Long-term safety and tolerability

| | |
|---|--|
| End point title | Long-term safety and tolerability ^[1] |
| End point description: AEs are defined as any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease which either occurs during study, having been absent at baseline, or, if present at baseline, appears to worsen. Serious adverse events are any untoward medical occurrences that result in death, are life threatening, require (or prolong) hospitalization, cause persistent or significant disability/incapacity, result in congenital anomalies or birth defects, or are other conditions which in judgment of investigators represent significant hazards. | |
| End point type | Primary |
| End point timeframe: Each subjects study participation may have been up to 38 months or until the study was terminated. | |
| 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: Only descriptive summary statistics was planned for this outcome measure. | |

| End point values | OLE Safety Population | | | |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | | | | |
| Units: Adverse events | | | | |
| Serious Adverse Events | 13 | | | |
| Non-serious Adverse Events | 57 | | | |
| Deaths (all causes) | 1 | | | |
| Deaths Resulting from Adverse Events | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Initiation of study drug through the last study visit or up to 30 days after date of last dose, whichever is later.

Adverse event reporting additional description:

AE that newly appears, increases in frequency, or worsens in severity following initiation of study drug and through the last study visit or up to 30 days after date of last dose, whichever is later.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | NEOD001 24 mg/kg |
|-----------------------|------------------|

Reporting group description:

NEOD001 24 mg/kg IV every 4 weeks for 38 months

| Serious adverse events | NEOD001 24 mg/kg | | |
|---|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 13 / 80 (16.25%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | 1 | | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 1 / 80 (1.25%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 80 (1.25%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 80 (1.25%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |

| | | | |
|---|----------------------------------|--|--|
| Cerebrovascular accident subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 80 (2.50%) 0 / 2 0 / 0 | | |
| Gastrointestinal disorders Gastrointestinal angiodysplasia haemorrhagic subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 80 (1.25%) 0 / 1 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders Pneumothorax subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 80 (1.25%) 0 / 1 0 / 0 | | |
| Infections and infestations Device related infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 80 (1.25%) 0 / 1 0 / 0 | | |
| Endocarditis bacterial subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 80 (1.25%) 0 / 2 0 / 1 | | |
| Influenza subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 80 (1.25%) 0 / 1 0 / 0 | | |
| Lung infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 80 (1.25%) 0 / 1 0 / 0 | | |
| Pneumonia | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 80 (1.25%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 80 (1.25%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Septic embolus | | | |
| subjects affected / exposed | 1 / 80 (1.25%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Fluid overload | | | |
| subjects affected / exposed | 1 / 80 (1.25%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 80 (1.25%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| | | | |
|---|------------------|--|--|
| Non-serious adverse events | NEOD001 24 mg/kg | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 28 / 80 (35.00%) | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 5 / 80 (6.25%) | | |
| occurrences (all) | 5 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 11 / 80 (13.75%) | | |
| occurrences (all) | 11 | | |
| Oedema peripheral | | | |

| | | | |
|--|------------------------|--|--|
| subjects affected / exposed occurrences (all) | 4 / 80 (5.00%) 4 | | |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 7 / 80 (8.75%) 7 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 4 / 80 (5.00%) 4 | | |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) | 10 / 80 (12.50%) 13 | | |

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