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