Clinical trial results:
A Phase II Study of PNT2258 in Patients With Richter's Transformation (RT)

Summary

EudraCT number	2015-001814-85
Trial protocol	GB BE HU
Global end of trial date	07 June 2016

Results information

Result version number	v1 (current)
This version publication date	13 March 2020
First version publication date	13 March 2020

Trial information

Trial identification

Sponsor protocol code	PNT2258-04-Richter's

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02378038
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ProNAi Therapeutics, Inc. (now known as Sierra Oncology)
Sponsor organisation address	46701 Commerce Center Drive, Plymouth Michigan, United States, 48170
Public contact	Corporate Affairs, Sierra Oncology, info@sierraoncology.com
Scientific contact	Corporate Affairs, Sierra Oncology, info@sierraoncology.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	22 August 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 June 2016
Global end of trial reached?	Yes
Global end of trial date	07 June 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess overall response rate (ORR) defined as the proportion of patients with complete response (CR) or partial response (PR) according to the revised 2014 International Working Group (IWG) criteria for lymphomas based upon blinded independent review.

Protection of trial subjects:

An Independent Data Monitoring Committee was established in order to monitor the ongoing safety of subjects enrolled in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 October 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 5
Worldwide total number of subjects	5
EEA total number of subjects	0

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)	0
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was initiated in August 2015 and the first subject was enrolled on 27 October 2015. Enrollment was closed as of 07 June 2016. Subjects were enrolled at oncology clinics in the USA.

Pre-assignment

Screening details:

7 subjects entered screening. 2 subjects did not meet the eligibility criteria, and thus 5 subjects were enrolled to the study.

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	PNT2258

Arm description:

PNT2258 administered at 120 mg/m2 on days 1-5 of a 21-day cycle for 8 induction cycles followed by continuation phase therapy at a dose of 100 mg/m2 on days 1-4 of a 28-day cycle.

Arm type	Experimental
Investigational medicinal product name	PNT2258
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

PNT2258 administered at 120 mg/m2 on days 1-5 of a 21-day cycle for 8 induction cycles followed by continuation phase therapy at a dose of 100 mg/m2 on days 1-4 of a 28-day cycle.

Number of subjects in period 1	PNT2258
Started	5
Completed	0
Not completed	5
Disease progression	4
Death	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	5	5	
Age categorical Units: Subjects			
Age continuous Units: years median full range (min-max)	 73 65 to 76	 -	
Gender categorical Units: Subjects			
Female	2	2	
Male	3	3	

End points

End points reporting groups

Reporting group title	PNT2258

Reporting group description:

PNT2258 administered at 120 mg/m2 on days 1-5 of a 21-day cycle for 8 induction cycles followed by continuation phase therapy at a dose of 100 mg/m2 on days 1-4 of a 28-day cycle.

Primary: Overall Response Rate

End point title	Overall Response Rate[1]

End point description:

Proportion of subjects with complete response (CR/CMR) or partial response (PR/PMR)

End point type	Primary

End point timeframe:

2 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: Not applicable due to the small number of subjects analyzed.

End point values	PNT2258			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: subjects	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate

End point title	Disease Control Rate

End point description:

Proportion of subjects with stable disease or better (CR/CMR, PR/PMR or SD/NMR)

End point type	Secondary

End point timeframe:

2 months

End point values	PNT2258			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: subjects	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Overall Response

End point title	Duration of Overall Response

End point description:

End point type	Secondary

End point timeframe:

2 months

End point values	PNT2258			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: months				
median (full range (min-max))	(to)			

Notes:

[2] - No data displayed because endpoint has zero total participants analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response

End point title	Time to Response

End point description:

End point type	Secondary

End point timeframe:

2 months

End point values	PNT2258			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: months				
median (full range (min-max))	(to)			

Notes:

[3] - No data displayed because endpoint has zero total participants analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

End point type	Secondary

End point timeframe:

2 months

End point values	PNT2258			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: months				
median (full range (min-max))	(to)			

Notes:

[4] - No data displayed because endpoint has zero total participants analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of PNT2258 until 30 days after the last dose of PNT2258

Adverse event reporting additional description:

Events assessed as at least possibly related to PNT2258 are considered to be causally related to treatment.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 5 (80.00%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Cardiac disorders			
Atrial fibrillation			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiomyopathy			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Haemorrhage intracranial			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

General disorders and administration site conditions			
Disease progression			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Listeriosis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypercalcaemia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Vascular disorders			
Embolism			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Hypertension			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 5 (40.00%)		
occurrences (all)	2		
Hypotension			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest discomfort			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Chest pain			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 5 (40.00%)		
occurrences (all)	2		
Chills			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Early satiety			

alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 5 (60.00%)		
occurrences (all)	3		
Oedema peripheral			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 5 (40.00%)		
occurrences (all)	2		
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Dyspnoea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Haemoptysis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Pleural effusion			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Pulmonary hypertension			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Pulmonary oedema			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Psychiatric disorders			
Confusional state			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Insomnia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	2		
Blood alkaline phosphatase increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Blood bilirubin increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Blood creatinine increased			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Blood phosphorus decreased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Neutrophil count decreased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Platelet count decreased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 5 (40.00%)		
occurrences (all)	3		
White blood cell count decreased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Infusion related reaction			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Dysgeusia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Peripheral sensory neuropathy			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 5 (40.00%)		
occurrences (all)	2		
Ear and labyrinth disorders			
Hearing impaired			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 5 (40.00%)		
occurrences (all)	2		
Faecal incontinence			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Toothache			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			

Decubitis ulcer alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Pruritis alternative assessment type: Systematic subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2		
Urticaria alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Renal and urinary disorders Urinary incontinence alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Musculoskeletal and connective tissue disorders Arthralgia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Joint stiffness alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Muscular weakness alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Infections and infestations Cytomegalovirus viraemia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		

Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Decreased appetite			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Dehydration			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Fluid overload			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Hyperglycaemia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	2		
Hypermagnesaemia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Hypokalaemia			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 5 (40.00%)		
occurrences (all)	2		
Hypomagnesaemia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Hypophosphataemia			
alternative assessment type: Systematic			

subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 March 2016	This protocol amendment: - allowed for the enrollment of first line Richter's transformation patients - updated the definition for response evaluable population and per protocol analysis populations - added additional organ function requirements (bone marrow function and coagulation profile) - added exclusion criteria of ongoing risk of bleeding and CNS or leptomeningeal involvement of lymphoma - increased the minimum period to use acceptable methods of contraception after treatment cessation

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
07 June 2016	On the basis of interim data assessments, the study was closed to further enrollment.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Early termination of enrollment, and thus very few subjects were analyzed..

Notes: