



Clinical trial results:

A Clinical Trial Of The Intra-Tumoural Concentration And Activity Of Nilotinib In Intra-Cutaneous Schwannomas (PHNT NilotinibNF2)

Summary

EudraCT number	2010-023508-28
Trial protocol	GB
Global end of trial date	01 March 2016

Results information

Result version number	v1 (current)
This version publication date	17 April 2019
First version publication date	17 April 2019

Trial information

Trial identification

Sponsor protocol code	CAMN107GB05T
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	R&D (sponsor) ref.: 10/P/148, PenCTU ref.: 2011/CTIMP-007, REC ref. : 11/SC/0035119

Notes:

Sponsors

Sponsor organisation name	University Hospitals Plymouth NHS Trust (formerly Plymouth Hospitals NHS Trust)
Sponsor organisation address	Research Office, L2 MSCP, Bircham Park Offices, 1 Roscoff Rise, Derriford, Plymouth, United Kingdom, PL6 5FP
Public contact	Dr Chris Rollinson, Research Governance Manager, University Hospitals Plymouth NHS Trust, Research Development and Innovation, 01752 432842, c.rollinson@nhs.net
Scientific contact	Prof Oliver Hanemann, Consultant Neurologist, University of Plymouth, Faculty of Medicine and Dentistry, 01752 437418, oliver.hanemann@plymouth.ac.uk

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	Interim
Date of interim/final analysis	01 March 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 March 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To ensure molecular target inhibition occurs with oral nilotinib in NF2 patients with CS, and to determine whether target inhibition in serum with oral nilotinib in NF2 patients with ICS can act as a biomarker.

Protection of trial subjects:

The study is approved by the MHRA and the South Central - Berkshire Research Ethics Committee (NRES). Study monitoring is conducted by UHPNT and an Independent Trial Management Team (TMT) is set up for the study oversight.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 May 2011
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 Kingdom: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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

Subject disposition

Recruitment

Recruitment details:

Patients from the NF2 clinic patient databases in Plymouth and Manchester will be identified by the Investigator at the relevant site, who will contact the patients by letter to ask them if they are interested in participating in the study.

Pre-assignment

Screening details:

Patients who are interested in taking part will be invited to attend for a screening visit lasting last approximately four hours in order to check their eligibility to participate. Written informed consent will be obtained at the screening visit.

Pre-assignment period milestones

Number of subjects started	5
Number of subjects completed	5

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	Nilotinib
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Nilotinib
Investigational medicinal product code	
Other name	Tasigna
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A prescription for 14 days' supply of nilotinib 400mg will be issued at the baseline visit. The participant should commence dosing the day after the baseline visit, starting with the morning dose. To avoid Day 15 occurring on a Saturday, baseline visits will take place on Monday to Thursday. Participants will take 2 x 200mg capsules (400mg) twice daily by mouth each morning and evening approximately 12 hours.

Number of subjects in period 1	Nilotinib
Started	5
Completed	1
Not completed	4
Consent withdrawn by subject	3
Screening failure	1

Baseline characteristics

Reporting groups

Reporting group title	Nilotinib
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Reporting group description: -

Reporting group values	Nilotinib	Total	
Number of subjects	5	5	
Age categorical			
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)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	5	5	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	2	2	
Male	3	3	

End points

End points reporting groups

Reporting group title	Nilotinib
Reporting group description: -	

Primary: Target inhibition by nilotinib in CS biopsies

End point title	Target inhibition by nilotinib in CS biopsies ^[1]
End point description:	

End point type	Primary
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End point timeframe:

Steady state nilotinib serum concentrations at Study Day 15.

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: This study was terminated early due to funding withdrawal. Recruitment in this patient group proved difficult. Five patients were screened, four were enrolled and only 1 successfully completed the study (total needed was 15). Therefore there is no result-related data to report.

End point values	Nilotinib			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: steady state plasma concentrations	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All SAEs, SARs including SUSARs are reported to the RD Office (sponsor) within 24 hours. RD Office to report to MHRA and REC within 7 days if fatal or life-threatening and all other SUSARs within 15 days.

Adverse event reporting additional description:

AEs should be recorded from the time a participant gives written consent for the study until the end of study follow up visit (Study Day 28). Where possible, multiple symptoms should be recorded as separate events. For the purposes of this study, an exacerbation of NF2 symptoms should be recorded as an adverse event.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	19

Reporting groups

Reporting group title	Nilotinib
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Reporting group description:

Patients dosed with the study IMP (Nilotinib).

Serious adverse events	Nilotinib		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Nilotinib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
General disorders and administration site conditions			
Malaise	Additional description: Tiredness		
subjects affected / exposed	3 / 3 (100.00%)		
occurrences (all)	4		
Pain	Additional description: Pain at biopsy site		

subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Feeling abnormal	Additional description: feeling faint		
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 3 (100.00%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Renal and urinary disorders			
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Urine abnormality	Additional description: Dark urine		
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Headache			
subjects affected / exposed	3 / 3 (100.00%)		
occurrences (all)	4		
Pain			
subjects affected / exposed	3 / 3 (100.00%)		
occurrences (all)	10		
Muscular weakness			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hunger	Additional description: Loss of appetite		
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 April 2012	Substantial amendment to temporarily halt recruitment as a result of notification of urgent safety measure .
16 May 2012	Substantial amendment to reduce the dose from 800mg to 600mg.
06 March 2013	Substantial amendment primarily to the statistical section reducing the sample size.
14 August 2013	Substantial amendment to reflect an update to the SmPC and the addition of a PIC recruitment process.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Study was terminated early due to a failure to recruit sufficient participants.

Notes: