Clinical trial results:
Randomised, phase III multicenter, open study of lanreotide in non metastatic castration-resistant prostate cancer patients presenting elevated Chromogranin A levels

Summary

EudraCT number	2010-019862-10
Trial protocol	IT
Global end of trial date	25 June 2013

Results information

Result version number	v2 (current)
This version publication date	27 February 2016
First version publication date	12 August 2015
Version creation reason	• Correction of full data set Review and correction

Trial information

Trial identification

Sponsor protocol code	A 93-52030-738

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01313273
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ipsen
Sponsor organisation address	Via Del Bosco Rinnovato, 6, Assago - Milano, Italy, 20090
Public contact	Medical Director, Oncology, Ipsen, clinical.trials@ipsen.com
Scientific contact	Medical Director, Oncology, Ipsen, clinical.trials@ipsen.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	01 September 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 September 2012
Global end of trial reached?	Yes
Global end of trial date	25 June 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy in terms of Progression-free survival (PFS) of the administration of non steroidal anti androgens and LHRH-a (Arm A) versus lanreotide in addition to non steroidal anti androgens and LHRH-a (Arm B) as second line approach in non metastatic prostate cancer patients with castrate resistant disease and elevated CgA circulating levels. According to the updated guidelines of the PCWG2 Progression-free survival (PFS) will be considered a composite end point defined as the time from random assignment to disease progression in bone or soft-tissue, symptoms, or death.A rising PSA alone will not be considered an indicator of disease progression since radiographic or symptomatic progression better reflect changes in clinical status.Subjects stopping the study for any reason, including isolated PSA increase, will be censored at their last date of evaluation.Patients without tumor progression or death at the time of analysis will be censored at their last date of evaluation

Protection of trial subjects:

The Sponsor is responsible for monitoring this data to verify that the rights and well being of subjects are protected and that the trial is conducted in compliance with the protocol, GCP and regulatory requirements.
Lanreotide has been proven to be effective in reducing plasma CgA levels. All those evidence, support exploring the antineoplastic activity and efficacy of lanreotide in patients with progressive disease to first line hormonal treatment and eligible for second line hormone therapy (castration resistant patients) .

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 June 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: 3
Worldwide total number of subjects	3
EEA total number of subjects	3

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)	2
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects ≥18 years meeting inclusion criteria were recruited for this study.

Pre-assignment

Screening details:

Investigators screened 8 subjects. Randomized 3 subjects and 5 were not randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A : Non-steroidal Anti Androgens + LHRH-a

Arm description:

Non-steroidal anti androgens (e.g. bicalutamide 50 mg/day) plus Luteinizing Hormone-Releasing Hormone Analogues (LHRH-a) (e.g. triptorelin 3.75 mg/month) till progression.

Arm type	Experimental
Investigational medicinal product name	Second line hormonal treatment
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Submucosal use

Dosage and administration details:

Luteinizing hormone-releasing hormone analogues (LHRH-a) ± Anti androgen were administered until the date of disease progression

Arm title	Arm B : Lanreotide + Non Steroidal Anti Androgens and LHRH-a

Arm description:

Lanreotide 120 mg injection every 28 days till progression or for a maximum of 24 months plus non steroidal anti androgens (e.g. bicalutamide 50 mg/day) and LHRH-a (e.g. triptorelin 3.75 mg/month) till progression.

Arm type	Experimental
Investigational medicinal product name	Second line hormonal treatment + lanreotide 120 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Lanreotide, non steroidal anti androgens and LHRH-a to be administered till progression or for a maximum of 24 months.

Number of subjects in period 1	Arm A : Non-steroidal Anti Androgens + LHRH-a	Arm B : Lanreotide + Non Steroidal Anti Androgens and LHRH-a
Started	2	1
Completed	0	0
Not completed	2	1
Screening Chromogranin A-in normal range	-	1
INCLUSION CRITERIA 4 NOT RESPECTED	1	-
Withdrawal by Subject	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Arm A : Non-steroidal Anti Androgens + LHRH-a
Reporting group description:	
Non-steroidal anti androgens (e.g. bicalutamide 50 mg/day) plus Luteinizing Hormone-Releasing Hormone Analogues (LHRH-a) (e.g. triptorelin 3.75 mg/month) till progression.	
Reporting group title	Arm B : Lanreotide + Non Steroidal Anti Androgens and LHRH-a
Reporting group description:	
Lanreotide 120 mg injection every 28 days till progression or for a maximum of 24 months plus non steroidal anti androgens (e.g. bicalutamide 50 mg/day) and LHRH-a (e.g. triptorelin 3.75 mg/month) till progression.	

Reporting group values	Arm A : Non-steroidal Anti Androgens + LHRH-a	Arm B : Lanreotide + Non Steroidal Anti Androgens and LHRH-a	Total
Number of subjects	2	1	3
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1	1	2
From 65-84 years	1	0	1
85 years and over	0	0	0
Age continuous			
Value of age continuous, for total participants is 61.00 (57.00 to 84.00).			
Units: years			
median	72.5	57	
full range (min-max)	61 to 84	57 to 57	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	2	1	3
Region of Enrollment Units: Subjects			
Italy	2	1	3

End points

End points reporting groups

Reporting group title	Arm A : Non-steroidal Anti Androgens + LHRH-a
Reporting group description:	
Non-steroidal anti androgens (e.g. bicalutamide 50 mg/day) plus Luteinizing Hormone-Releasing Hormone Analogues (LHRH-a) (e.g. triptorelin 3.75 mg/month) till progression.	
Reporting group title	Arm B : Lanreotide + Non Steroidal Anti Androgens and LHRH-a
Reporting group description:	
Lanreotide 120 mg injection every 28 days till progression or for a maximum of 24 months plus non steroidal anti androgens (e.g. bicalutamide 50 mg/day) and LHRH-a (e.g. triptorelin 3.75 mg/month) till progression.	

Primary: Progression-free Survival

End point title	Progression-free Survival[1]
End point description:	
Study early terminated due to poor enrollment.	
End point type	Primary
End point timeframe:	
Week 96	

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 details provided.

End point values	Arm A : Non-steroidal Anti Androgens + LHRH-a	Arm B : Lanreotide + Non Steroidal Anti Androgens and LHRH-a		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: Participants				
Number of Participants Analyzed	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Prostate Specific Antigen (PSA) Response

End point title	Prostate Specific Antigen (PSA) Response
End point description:	
Study early terminated due to poor enrollment.	
End point type	Secondary
End point timeframe:	
Week 96	

End point values	Arm A : Non-steroidal Anti Androgens + LHRH-a	Arm B : Lanreotide + Non Steroidal Anti Androgens and LHRH-a		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Participants				

Notes:

[2] - Study early terminated due to poor enrollment

[3] - Study early terminated due to poor enrollment

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time to PSA Response

End point title	Median Time to PSA Response

End point description:

Study early terminated due to poor enrollment.

End point type	Secondary

End point timeframe:

Week 96

End point values	Arm A : Non-steroidal Anti Androgens + LHRH-a	Arm B : Lanreotide + Non Steroidal Anti Androgens and LHRH-a		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: Participants				

Notes:

[4] - Study early terminated due to poor enrollment

[5] - Study early terminated due to poor enrollment

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in Chromogranin A Serum Levels

End point title	Reduction in Chromogranin A Serum Levels

End point description:

Study early terminated due to poor enrollment

End point type	Secondary

End point timeframe:

Baseline, Week 96

End point values	Arm A : Non-steroidal Anti Androgens + LHRH-a	Arm B : Lanreotide + Non Steroidal Anti Androgens and LHRH-a		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: Participants				

Notes:

[6] - Study early terminated due to poor enrollment

[7] - Study early terminated due to poor enrollment

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were reported from Baseline (visit 2) to visit 10 (Week 96 - End of study)

Adverse event reporting additional description:

All AEs documented for this study were treatment emergent. Overall, for 1 patient (100.0%) of Arm B at least one AE, at least one AE related to study treatment and at least one severe AE were reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Arm A : Non-steroidal Anti Androgens + LHRH-a
Reporting group description: -	
Reporting group title	Arm B : Lanreotide + Non-steroidal Antiandrogens and LHRH-a
Reporting group description: -	

Serious adverse events	Arm A : Non-steroidal Anti Androgens + LHRH-a	Arm B : Lanreotide + Non-steroidal Antiandrogens and LHRH-a	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Arm A : Non-steroidal Anti Androgens + LHRH-a	Arm B : Lanreotide + Non-steroidal Antiandrogens and LHRH-a	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	1 / 1 (100.00%)	
Investigations			
Transaminases increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 1 (100.00%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 October 2011	- Inclusion of patients with stable metastatic disease and exclusion of the non metastatic patients (this required the change in study title) - Inclusion of patients already treated with maximal androgen blockade (MAB) i.e. LHRHa + antiandrogen. This modified also the study design: to evaluate the efficacy in terms of PFS of the administration of second – line hormonal treatment (Arm A) versus second - line hormonal treatment + lanreotide (Arm B) (based on the definition of "second-line hormonal therapy" according to Italian guidelines - AIOM / Prostate Cancer 11-2009) - The inclusion criterion relative to the serum creatinine was modified (new cutoff <1.5xULN) - In order to avoid possible bias due to different type of treatment of patient at inclusion (MAB or LHRHa alone), a new randomization list has been generated to account for stratification by type of treatment at inclusion - Inclusion of patients with stable metastatic disease besides the non metastatic patients already required in the main protocol (this required the change in study title) - Exclusion of patients with visceral metastasis and patients taking narcotic for analgesia for bone pain. This was introduced to avoid the enrolment of patients with an high stage disease which could require anticancer therapy

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
12 November 2012	Study terminated due to poor enrollment.	-

Notes:

Limitations and caveats

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

Study terminated due to poor enrollment

Notes: