



Clinical trial results:

Proof-of-Concept Multicentre, Prospective, Randomised, Open-Label-Parallel-Group Clinical Trial to Assess the Efficacy of Brachytherapy With or Without Hormone Therapy Using Triptorelin 22.5 mg 6-Month Formulation in Patients With Recurrence of Prostate Cancer Previously Treated With Radiotherapy

Summary

EudraCT number	2010-019158-41
Trial protocol	ES
Global end of trial date	10 December 2014

Results information

Result version number	v1 (current)
This version publication date	21 July 2019
First version publication date	21 July 2019

Trial information

Trial identification

Sponsor protocol code	A-92-52014-177
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01374087
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ipsen Pharma, S.A.
Sponsor organisation address	Torre Realia, Plaza Europa 41-43, Planta 7, Barcelona, Spain, 08908
Public contact	Medical Director, Ipsen Pharma, S.A., clinical.trials@ipsen.com
Scientific contact	Medical Director, Ipsen Pharma, S.A., 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	10 December 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 December 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of brachytherapy versus brachytherapy plus triptorelin 22.5 milligrams (mg) (single injection) in subjects with recurrence of prostate cancer previously treated with radiotherapy. ≥

Protection of trial subjects:

This study was carried out in full accordance of an Independent Ethics Committee, the standards on informed consent, the Declaration of Helsinki and the Good Clinical Practice directives issued by the International Conference on Harmonisation, as well as by all local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 November 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	Spain: 32
Worldwide total number of subjects	32
EEA total number of subjects	32

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)	7
From 65 to 84 years	25
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects with recurrence of prostate cancer previously treated with radiotherapy were recruited in 11 sites in Spain from November 2011 until December 2014 when the study was prematurely discontinued.

Pre-assignment

Screening details:

35 subjects were screened and 3 did not meet inclusion criteria. Of those who met the inclusion criteria and none of the exclusion criteria, 32 were randomised to treatment and 31 received treatment after 1 subject (in the Brachytherapy + Triptorelin arm) withdrew consent.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Brachytherapy

Arm description:

Subjects were randomised to receive brachytherapy alone, as either a low dose rate ([125]I) or high dose rate ([192]I).

Arm type	Brachytherapy
No investigational medicinal product assigned in this arm	
Arm title	Brachytherapy + Triptorelin 22.5 mg

Arm description:

Subjects received brachytherapy as either a low dose rate ([125]I) or high dose rate ([192]I). Subjects also received a single intramuscular injection of 22.5 mg triptorelin at Visit 2 (Day 1).

Arm type	Experimental
Investigational medicinal product name	Triptorelin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Triptorelin was dispensed as a freeze-dried white to off-white powder and reconstituted using 2 millilitres of water for injections, and immediately administered by intramuscular injection.

Number of subjects in period 1^[1]	Brachytherapy	Brachytherapy + Triptorelin 22.5 mg
Started	16	15
Completed	0	0
Not completed	16	15
Disease progression	2	2
Adverse event, non-fatal	1	-
Study discontinued	13	13

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 32 subjects were randomised to treatment but only 31 subjects received treatment.

Baseline characteristics

Reporting groups

Reporting group title	Brachytherapy
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Reporting group description:

Subjects were randomised to receive brachytherapy alone, as either a low dose rate ([125]I) or high dose rate ([192]I).

Reporting group title	Brachytherapy + Triptorelin 22.5 mg
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Reporting group description:

Subjects received brachytherapy as either a low dose rate ([125]I) or high dose rate ([192]I). Subjects also received a single intramuscular injection of 22.5 mg triptorelin at Visit 2 (Day 1).

Reporting group values	Brachytherapy	Brachytherapy + Triptorelin 22.5 mg	Total
Number of subjects	16	15	31
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)	3	4	7
From 65-84 years	13	11	24
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	67.75	67.93	
standard deviation	± 4.23	± 5.28	-
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	16	15	31

End points

End points reporting groups

Reporting group title	Brachytherapy
Reporting group description: Subjects were randomised to receive brachytherapy alone, as either a low dose rate ([125]I) or high dose rate ([192]I).	
Reporting group title	Brachytherapy + Triptorelin 22.5 mg
Reporting group description: Subjects received brachytherapy as either a low dose rate ([125]I) or high dose rate ([192]I). Subjects also received a single intramuscular injection of 22.5 mg triptorelin at Visit 2 (Day 1).	

Primary: Biochemical Failure-free Survival (BFFS)

End point title	Biochemical Failure-free Survival (BFFS) ^[1]
End point description: BFFS was determined by a prostate-specific antigen (PSA) increase of 2 nanograms per millilitre (ng/mL) or more in comparison with the pre-study nadir PSA and confirmed in the course of follow-up by a second value 3 weeks later or longer over the 5 year follow-up. Time to BFFS was defined from treatment initiation to the first time when PSA increase of 2 ng/mL was observed.	
End point type	Primary
End point timeframe: From Day 1 (treatment administration) up to 5 years.	

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 efficacy analysis was performed and therefore no statistical analysis is specified.

End point values	Brachytherapy	Brachytherapy + Triptorelin 22.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[2]	0 ^[3]		
Units: Months				

Notes:

[2] - No efficacy analysis was performed.

[3] - No efficacy analysis was performed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events were collected from treatment initiation (Day 1) to end of the study.

Adverse event reporting additional description:

The Safety population consisted of all randomised subjects who received at least 1 dose of study medication.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Brachytherapy
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Reporting group description:

Subjects were randomised to receive brachytherapy alone, as either a low dose rate ([125]I) or high dose rate ([192]I).

Reporting group title	Brachytherapy + Triptorelin 22.5 mg
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Reporting group description:

Subjects received brachytherapy as either a low dose rate ([125]I) or high dose rate ([192]I). Subjects also received a single intramuscular injection of 22.5 mg triptorelin at Visit 2 (Day 1).

Serious adverse events	Brachytherapy	Brachytherapy + Triptorelin 22.5 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 16 (18.75%)	2 / 15 (13.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Liver abscess			

subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal abscess			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Brachytherapy	Brachytherapy + Triptorelin 22.5 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 16 (68.75%)	10 / 15 (66.67%)	
Injury, poisoning and procedural complications			
Radiation skin injury			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Blood pressure inadequately controlled			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Flushing			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Hypertensive crisis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Hypotension subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0	
General disorders and administration site conditions			
Catheter site haemorrhage subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0	
Implant site pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Puncture site pain subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0	
Gastrointestinal disorders			
Anal pruritus subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Anorectal disorder subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0	
Constipation subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 2	
Dyspepsia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0	
Nausea subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Proctitis			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Vomiting subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0	
Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Nipple pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Perineal pain subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0	
Pruritus genital subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Respiratory, thoracic and mediastinal disorders Suffocation feeling subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 4	4 / 15 (26.67%) 5	
Haematuria subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	3 / 15 (20.00%) 3	
Hypertonic bladder subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 3	1 / 15 (6.67%) 1	
Incontinence subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0	
Micturition urgency			

subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Nephropathy toxic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Nocturia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Pollakiuria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Urinary incontinence			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	2	2	
Urinary retention			
subjects affected / exposed	3 / 16 (18.75%)	0 / 15 (0.00%)	
occurrences (all)	3	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Erythrasma			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Orchitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Pilonidal cyst			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	

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

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

The study was prematurely stopped due to slow enrolment and all subjects were withdrawn following study termination in December 2014. Due to the small number of participating subjects no inferential analyses were performed for the efficacy endpoints.
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Notes: