Clinical trial results:
An exploratory, open label, single-arm study to evaluate the effect of Eligard® 6-month on biomarkers of disease in patients with metastatic prostate cancer

EudraCT number	2012-000101-69
Trial protocol	NL
Global end of trial date	05 August 2015

Result version number	v1 (current)
This version publication date	13 August 2016
First version publication date	13 August 2016

Sponsor protocol code	EGD-EC-005

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01933022
WHO universal trial number (UTN)	-
Other trial identifiers	Acronym: EFFECT

Notes:

Sponsor organisation name	Astellas Pharma Europe Ltd.
Sponsor organisation address	2000 Hillswood Drive, Chertsey, Surrey, United Kingdom, KT16 0RS
Public contact	Clinical Trial Disclosure, Astellas Pharma Europe Ltd., Astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Trial Disclosure, Astellas Pharma Europe Ltd., Astellas.resultsdisclosure@astellas.com

Notes:

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:

Analysis stage	Final
Date of interim/final analysis	05 August 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 August 2015
Was the trial ended prematurely?	Yes

Notes:

Main objective of the trial:

To explore the effect of Eligard® on the following prostate cancer biomarkers:
1. Testosterone in serum
2. Prostate Specific Antigen (PSA) in serum
3. Prostate Cancer Antigen 3 (PCA3) in urine
4. PSA Messenger Ribonucleic Acid (mRNA) in blood/Peripheral Blood Mononuclear Cell
5. PCA3 mRNA in blood/PBMC
6. Transmembrane Protease, Serine 2 Erythroblast Transformation- Specific (ETS)-related gene (TMPRSS2-ERG) mRNA in blood/PBMC

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki. Astellas ensures that the use and disclosure of protected health information (PHI) obtained during a research study complies with the federal, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 August 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Country: Number of subjects enrolled	Netherlands: 2
Worldwide total number of subjects	2
EEA total number of subjects	2

Notes:

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	1
From 65 to 84 years	1
85 years and over	0

Recruitment details:

This multicenter study was conducted at 5 sites in the Netherlands.

Screening details:

Participants screened were aged 18 years or older with confirmed metastatic prostate cancer for whom androgen deprivation therapy (ADT) was indicated. 16 participants signed informed consents for entry into the study, of which 14 participants were screen failures.

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

Blinding implementation details:

This was an open label study.

	leuprorelin 45 mg

Arm description:

Participants received 1 subcutaneous injection of leuprorelin 45 mg 6-months extended release.

Arm type	Experimental
Investigational medicinal product name	leuprorelin
Investigational medicinal product code	EGD
Other name	Eligard®, leuprorelin acetate
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Leuprorelin 45 mg (6-month formulation of Leuprorelin acetate) powder and solvent for solution was administered subcutaneously (single dose).

	leuprorelin 45 mg
Started	2
Completed	1
Not completed	1
Enrolled but did not receive study drug	1

Reporting group title	leuprorelin 45 mg

Reporting group description:

Participants received 1 subcutaneous injection of leuprorelin 45 mg 6-months extended release.

	leuprorelin 45 mg	Total	
Number of subjects	2	2	
Age categorical			
The safety analysis set (SAF) was the planned analysis population for baseline characteristics. The SAF would have consisted of all participants who received study drug.			
Units: Subjects			
Adults (18-64 years)	1	1	
From 65-84 years	1	1	
Gender categorical			
The SAF was the planned analysis population for baseline characteristics.			
Units:			
Male	2	2	
Female	0	0	

Reporting group title	leuprorelin 45 mg

Reporting group description:

Participants received 1 subcutaneous injection of leuprorelin 45 mg 6-months extended release.

End point title	Changes from Baseline of Testosterone Levels in Serum[1]

End point description:

The serum testosterone levels were to be determined using Radio Immuno Assay (RIA). Planned analysis of changes from baseline of clinical evaluation variables was not possible due to small sample size (one study participant) and variations in assay results. Therefore there were no clinical evaluation conclusions made.

End point type	Primary

End point timeframe:

Baseline to week 1, 6, 12 and 24

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, planned analysis not possible, only one participant completed the study.

	leuprorelin 45 mg			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: nmol/L				
arithmetic mean (standard deviation)	()			

Notes:

[2] - Planned analysis not possible due to small sample size (1 participant).

No statistical analyses for this end point

End point title	Changes from Baseline of PSA Level in Serum[3]

End point description:

The serum PSA levels were to be determined using immunoassay. Planned analysis of changes from baseline of clinical evaluation variables was not possible due to small sample size (one study participant) and variations in assay results. Therefore there were no clinical evaluation conclusions made.

End point type	Primary

End point timeframe:

Baseline to week 1, 6, 12 and 24

Notes:

[3] - 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, planned analysis not possible, only one participant completed the study.

	leuprorelin 45 mg			
Subject group type				

Notes:

[7] - 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, planned analysis not possible, only one participant completed the study.

	leuprorelin 45 mg			
Subject group type	Reporting group			
Number of subjects analysed	0[8]			
Units: copies/PCR				
arithmetic mean (standard deviation)	()			

Notes:

[8] - Planned analysis not possible due to small sample size (1 participant).

No statistical analyses for this end point

End point title	Changes from Baseline of Number of PCA3 mRNA Copies in Blood/PBMC[9]

End point description:

The number of PBMC PCA3 mRNA copies were to be determined by using real time RT-PCR. Planned analysis of changes from baseline of clinical evaluation variables was not possible due to small sample size (one study participant) and variations in assay results. Therefore there were no clinical evaluation conclusions made.

End point type	Primary

End point timeframe:

Baseline to week 1, 6, 12 and 24

Notes:

[9] - 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, planned analysis not possible, only one participant completed the study.

	leuprorelin 45 mg			
Subject group type	Reporting group			
Number of subjects analysed	0[10]			
Units: copies/PCR				
arithmetic mean (standard deviation)	()			

Notes:

[10] - Planned analysis not possible due to small sample size (1 participant).

No statistical analyses for this end point

End point title	Changes from Baseline of Number of TMPRSS2-ERG mRNA Copies in Blood/PBMC[11]

End point description:

The number of PBMC TMPRSS2-ERG mRNA copies were to be determined by using real time RT-PCR. Planned analysis of changes from baseline of clinical evaluation variables was not possible due to small

sample size (one study participant) and variations in assay results. Therefore there were no clinical evaluation conclusions made.

End point type	Primary

End point timeframe:

Baseline to week 1, 6, 12 and 24

Notes:

[11] - 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, planned analysis not possible, only one participant completed the study.

	leuprorelin 45 mg			
Subject group type	Reporting group			
Number of subjects analysed	0[12]			
Units: copies/PCR				
arithmetic mean (standard deviation)	()			

Notes:

[12] - Planned analysis not possible due to small sample size (1 participant).

No statistical analyses for this end point

End point title	Number of Participants with Adverse Events (AEs)

End point description:

The SAF was the planned analysis population for AEs. An Adverse Event (AE) is defined as any untoward medical occurrence in a participant who was administered study drug & which does not necessarily have a causal relationship with the treatment. An AE starting or worsening after first study drug intake will be considered as treatment emergent (TEAE).

End point type	Secondary

End point timeframe:

From first dose of study drug up to end of study (up to 24 weeks)

	leuprorelin 45 mg			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Participants				
AEs	1			
Serious Adverse Events (SAEs)	0			
Drug-related AEs	0			
Deaths	0			
AEs leading to permanent discontinuation of drug	0			

No statistical analyses for this end point

Timeframe for reporting adverse events:
From first dose of study drug up to end of study (up to 24 weeks)
Adverse event reporting additional description:
The SAF was the planned analysis population for AEs.

Assessment type	Systematic

Dictionary name	MedDRA
Dictionary version	17.0

Reporting group title	Eligard 45 mg
Reporting group description:	
Participants received received 1 subcutaneous injection of Eligard® 45 mg 6-months extended release.	

	Eligard 45 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

	Eligard 45 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		
Groin pain			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		
Joint swelling			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		

Were there any global substantial amendments to the protocol? Yes

11 April 2014	1. Inclusion criterion changed from Positive blood PCA3 mRNA at screening to: Positive blood PSA mRNA at screening 2. Exclusion criterion 3, exclusion criterion 9, Previous Drugs and Therapies, and Concomitant Medication wording were updated to allow use of anti-androgens when used to prevent testosterone flare up, starting from up to 2 weeks prior to Eligard® injection and continuing for up to 3 weeks, according to local treatment guidelines. 3. There were 3 other substantial changes, which were administrative changes such as clarification of terminology and contact detail changes.

Notes:

Were there any global interruptions to the trial? No

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

This study was discontinued/terminated early by the Sponsor due to the lack of feasibility of finding patients meeting all inclusion criteria.

Notes: