Clinical trial results:
A PILOT PHASE IV STUDY TO EVALUATE VARIATION IN BONE MINERAL DENSITY, LEAN AND FAT BODY MASS MEASURED BY DUAL-ENERGY X-RAY ABSORPTIOMETRY IN PATIENTS WITH PROSTATE CANCER WITHOUT BONE METASTASIS TREATED WITH DEGARELIX

Summary

EudraCT number	2016-004210-10
Trial protocol	IT
Global end of trial date	12 March 2021

Results information

Result version number	v1 (current)
This version publication date	02 December 2021
First version publication date	02 December 2021

Trial information

Trial identification

Sponsor protocol code	ASSTBS-BLADE-2540-2016

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03202381
WHO universal trial number (UTN)	-
Other trial identifiers	BLADE: ASSTBS-BLADE-2540-2016

Notes:

Sponsors

Sponsor organisation name	ASST spedalicivili di brescia
Sponsor organisation address	p.le spedali civili 1, brescia, Italy, 25123
Public contact	coordinamento ricerca, Azienda Ospedaliera Spedali Civili di Brescia, 0039 0303996851, coordinamento.ricerca@ASST-spedalicivili.it
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Sponsor organisation address	P.LE SPEDALI CIVILI 1, BRESCIA, Italy, 25123
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric	No

investigation plan (PIP)	
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	12 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 March 2020
Global end of trial reached?	Yes
Global end of trial date	12 March 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary endpoints was to assess changes in fat body mass (FBM) after 12 months of Degarelix administration.
Secondary endpoints were to assess changes in lean body mass (LBM), body mass index (BMI), serum lipid profile, serum glucose profile and serum FSH

Protection of trial subjects:	
not applicable	
Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	01 December 2016
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: 35
Worldwide total number of subjects	35
EEA total number of subjects	35

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	8
From 65 to 84 years	25
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Male patients willing and able to provide written informed consent. with histologically confirmed PCa without bone metastasis
at bone scintigraphy, judged eligible to ADT according to current guidelines recommendations after a multisciplinary
discussion were considered eligible for the study

Pre-assignment

Screening details:

screening: patients were assessed for criteria. Exclusion crit. consisted of absolute or relative contraindication to Degarelix, prior ADT treatment,prior/concomitant treatment with bisphosphonates or other drugs known to affect bone metabolism, concom. bone metabolic dis., such as Paget’s disease, primary hyperparathyroid/chronic hypercortisolism

Pre-assignment period milestones

Number of subjects started	35
Number of subjects completed	35

Period 1

Period 1 title	BASELINE
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	degarelix

Arm description:

administered as a subcutaneous injection in the abdominal
region every 28 days, in according to the following schedule:
- Starting dose: 240 mg administered as two consecutive subcutaneous injections of 120 mg each (2 x 3 mL injections).
- Maintenance dose: 80 mg administered as one subcutaneous injection of 80 mg (1 x 4 mL injection).
Treatment will be continued till clinically indicated or till disease progression

Arm type	Experimental
Investigational medicinal product name	degarelix
Investigational medicinal product code	imp 1
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

administered as a subcutaneous injection in the abdominal
region every 28 days, in according to the following schedule:
- Starting dose: 240 mg administered as two consecutive subcutaneous injections of 120 mg each (2 x 3 mL injections).
- Maintenance dose: 80 mg administered as one subcutaneous injection of 80 mg (1 x 4 mL injection).
Treatment will be continued till clinically indicated or till disease progression

Number of subjects in period 1	degarelix
Started	35
Completed	35

Period 2

Period 2 title	treatment period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	degarelix

Arm description:

administered as a subcutaneous injection in the abdominal region every 28 days, in according to the following schedule:
- Starting dose: 240 mg administered as two consecutive subcutaneous injections of 120 mg each (2 x 3 mL injections).
- Maintenance dose: 80 mg administered as one subcutaneous injection of 80 mg (1 x 4 mL injection).
Treatment will be continued till clinically indicated or till disease progression

Arm type	Experimental
Investigational medicinal product name	degarelix
Investigational medicinal product code	imp 1
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
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administered as a subcutaneous injection in the abdominal region every 28 days, in according to the following schedule:
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Number of subjects in period 2	degarelix
Started	35
Completed	29
Not completed	6
Adverse event, serious fatal	1
Consent withdrawn by subject	1
Physician decision	2

Lost to follow-up	2

Period 3

Period 3 title	end of tratment
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	degarelix

Arm description:

administered as a subcutaneous injection in the abdominal region every 28 days, in according to the following schedule:
- Starting dose: 240 mg administered as two consecutive subcutaneous injections of 120 mg each (2 x 3 mL injections).
- Maintenance dose: 80 mg administered as one subcutaneous injection of 80 mg (1 x 4 mL injection).
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Treatment will be continued till clinically indicated or till disease progression

Number of subjects in period 3	degarelix
Started	29
Completed	29

Baseline characteristics

Reporting groups	
Reporting group title	BASELINE

Reporting group description: -

Reporting group values	BASELINE	Total	
Number of subjects	35	35	
Age categorical			
adults (18-64 years) From 65-84 years 85 years and over			
Units: Subjects			
Adults (18-64 years)	8	8	
From 65-84 years	25	25	
85 years and over	2	2	
Gender categorical Units: Subjects			
Female	0	0	
Male	35	35	

End points

End points reporting groups

Reporting group title	degarelix

Reporting group description:

administered as a subcutaneous injection in the abdominal
region every 28 days, in according to the following schedule:
- Starting dose: 240 mg administered as two consecutive subcutaneous injections of 120 mg each (2 x 3 mL injections).
- Maintenance dose: 80 mg administered as one subcutaneous injection of 80 mg (1 x 4 mL injection).

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Treatment will be continued till clinically indicated or till disease progression

Reporting group title	degarelix

Reporting group description:

administered as a subcutaneous injection in the abdominal
region every 28 days, in according to the following schedule:
- Starting dose: 240 mg administered as two consecutive subcutaneous injections of 120 mg each (2 x 3 mL injections).
- Maintenance dose: 80 mg administered as one subcutaneous injection of 80 mg (1 x 4 mL injection).

Treatment will be continued till clinically indicated or till disease progression

Primary: To compare the mean values (adjusted for baseline T0 values) of changes in fat body mass (after 12 months of therapy, T1) as measured by DXA scan (g/cm2).

End point title	To compare the mean values (adjusted for baseline T0 values) of changes in fat body mass (after 12 months of therapy, T1) as measured by DXA scan (g/cm2).

End point description:

changes in fat body mass (after 12 months of therapy, T1) as measured by DXA scan

End point type	Primary

End point timeframe:

12 months

End point values	degarelix	degarelix	degarelix	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	34	29[1]	
Units: g/cm2				
number (not applicable)				
na	35	34	29	

Notes:
[1] - NA

Statistical analyses

Statistical analysis title	final

Statistical analysis description:

To calculate sample size, we relied on a previous prospective cohort study, where body composition was prospectively
assessed in non-metastatic PCa patients treated with LHRH agonists [16]. In order to detect an increase of FBM from 18 kg at baseline to a maximum of 21 kg at 12 months (with a SD of 4.5), with an alpha error of 0.05 and a beta error of 0.10 (which allows for 90% power), a sample size of 35 patients was estimated. This accounted for an anticipated dropout of 10%

Comparison groups	degarelix v degarelix
Number of subjects included in analysis	64
Analysis specification	Post-hoc
Analysis type	other[2]
P-value	< 0.05 [3]
Method	ANOVA
Parameter estimate	Mean difference (final values)

Notes:

[2] - Repeated measures paired t-test and ANOVA test tested for mean differences between bl vs. 12 m for DXA scan results and between bl vs. 6 m. vs. 12 m. for BMI and blood test parameters. Then, linear mixed models with random intercept to account for multiple measurements within each patient were used to estimate differences. Percent changes were calculated as well. P

[3] - All statistical tests were two-sided with a level of significance set at $p < 0.05$. Analyses were performed using the R software environment for statistical computing and graphics
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Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

unexpected serious adverse reactions, occurring from the starting time of trial (screening) treatment until 28 days post cessation of trial treatment

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	degarelix group

Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: the disease progression is not considered an Adverse Events

Serious adverse events	degarelix group		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
General disorders and administration site conditions			
Death	Additional description: na		
subjects affected / exposed	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	degarelix group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)		

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.

First, since the study power was calculated on FBM changes, many of the non-significant findings among secondary endpoints may be due to the low statistical power rather than evidence of these variables not being predictive of the clinical outcom

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33723362