



## Clinical trial results:

### Toxicity of first-line abiraterone versus enzalutamide in men with metastatic castration-resistant prostate cancer: A randomized clinical trial

#### Summary

EudraCT number	2017-000099-27
Trial protocol	DK
Global end of trial date	06 January 2020

#### Results information

Result version number	v1 (current)
This version publication date	27 October 2022
First version publication date	27 October 2022
Summary attachment (see zip file)	Summary attachment (EudraCT summary attachment.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	HEAT01
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##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	Herlev and Gentofte Hospital
Sponsor organisation address	Borgmester Ib Juulsvej 1, Herlev, Denmark, 2730
Public contact	The Department of Urology, The Department of Urology, 38686349 38689927, klara.kvorning.ternov@regionh.dk
Scientific contact	The Department of Urology, The Department of Urology, 38686349 38689927, klara.kvorning.ternov@regionh.dk

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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	06 January 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 January 2020
Global end of trial reached?	Yes
Global end of trial date	06 January 2020
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

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Main objective of the trial:

The main objective of this project is to investigate if there is a group-difference in treatment related adverse effects between abiraterone and enzalutamide in regards to:

- Fatigue
- Metabolic profile
- Health related quality of life (HQoL)

The aim of performing the above is to generate knowledge in order to enable a more individualized treatment of patients with mCRPC, based on the therapies profile of adverse effects and the patients' individual needs.

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Protection of trial subjects:

Informed consent and measurement of adverse events, HRQoL and fatigue

Background therapy:

Androgen deprivation therapy

Evidence for comparator: -

Actual start date of recruitment	02 June 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Denmark: 169
Worldwide total number of subjects	169
EEA total number of subjects	169

Notes:

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**Subjects enrolled per age group**

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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)	15
From 65 to 84 years	133
85 years and over	21

## Subject disposition

### Recruitment

Recruitment details:

Between 2nd June 2017 and 27th September 2019, 170 patients were randomly assigned to enzalutamide (n Z 84) or AAP (n Z 85)

### Pre-assignment

Screening details:

Eligible patients had metastatic prostate cancer and disease progression on ADT (testosterone 1.7 nmol/L), as per the Prostate Cancer Working Group 3 criteria. Exclusion criteria included diabetes mellitus, visceral metastases, docetaxel in the hormone-naïve setting, other malignancies and heart failure.

### Period 1

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

Blinding implementation details:

None

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	enzalutamide

Arm description:

enzalutamide

Arm type	Active comparator
Investigational medicinal product name	enzalutamide
Investigational medicinal product code	
Other name	Xtandi
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

60 mg/day orally

<b>Arm title</b>	abiraterone
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Arm description:

Abiraterone acetate 1000mg + 10 mg prednisone

Arm type	Active comparator
Investigational medicinal product name	abiraterone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

abiraterone acetate tablets (1000 mg/day orally either 1 h before or 2 h after the intake of food) in the evening combined with prednisone tablets (10 mg/day orally) in the morning.

<b>Number of subjects in period 1</b>	enzalutamide	abiraterone
Started	84	85
Completed	84	85

## Baseline characteristics

### Reporting groups

Reporting group title	Overall
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Reporting group description: -

Reporting group values	Overall	Total	
Number of subjects	169	169	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
median	75		
full range (min-max)	51 to 88	-	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	169	169	

## End points

### End points reporting groups

Reporting group title	enzalutamide
Reporting group description:	enzalutamide
Reporting group title	abiraterone
Reporting group description:	Abiraterone acetate 1000mg + 10 mg prednisone

### Primary: Between-group differences in changed level of fatigue assessed with the questionnaire Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue)

End point title	Between-group differences in changed level of fatigue assessed with the questionnaire Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue)
End point description:	
End point type	Primary
End point timeframe:	mean change from baseline to 12-week follow-up

End point values	enzalutamide	abiraterone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	85		
Units: FACIT-Fatigue points				
arithmetic mean (confidence interval 95%)	-2.3 (-3.9 to -0.7)	0.9 (-0.8 to 2.6)		

### Statistical analyses

Statistical analysis title	mixed effect models
Statistical analysis description:	
The between-group differences in changed outcomes were analysed with linear mixed effect models constrained longitudinal analysis	
Comparison groups	enzalutamide v abiraterone
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	other <sup>[1]</sup>
P-value	> 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	3.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	5.6

Notes:

[1] - The between-group differences in changed outcomes were analysed with linear mixed effect models constrained longitudinal analysis



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Side effects are monitored at the three-month follow-up visit

Assessment type	Systematic
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### Dictionary used

Dictionary name	CTCAE
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Dictionary version	4
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### Reporting groups

Reporting group title	enzalutamide
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Reporting group description:

enzalutamide

Reporting group title	abiraterone
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Reporting group description:

Abiraterone acetate 1000mg + 10 mg prednisone

Serious adverse events	enzalutamide	abiraterone	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 84 (8.33%)	7 / 85 (8.24%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
CPK increased	Additional description: Rhabdomyolysis		
subjects affected / exposed	1 / 84 (1.19%)	0 / 85 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Vascular disorders - Other, specify	Additional description: life-threatening bleeding from a varices		
subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 84 (1.19%)	0 / 85 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Esophagitis			
subjects affected / exposed	1 / 84 (1.19%)	0 / 85 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 84 (0.00%)	1 / 85 (1.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary tract obstruction			
subjects affected / exposed	2 / 84 (2.38%)	2 / 85 (2.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 84 (1.19%)	0 / 85 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 84 (2.38%)	2 / 85 (2.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone infection			
subjects affected / exposed	1 / 84 (1.19%)	0 / 85 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	1 / 84 (1.19%)	1 / 85 (1.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			

subjects affected / exposed	2 / 84 (2.38%)	0 / 85 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalemia			
subjects affected / exposed	1 / 84 (1.19%)	0 / 85 (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: 0.05 %

Non-serious adverse events	enzalutamide	abiraterone	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	77 / 84 (91.67%)	77 / 85 (90.59%)	
Investigations			
Weight loss			
subjects affected / exposed	9 / 84 (10.71%)	4 / 85 (4.71%)	
occurrences (all)	9	4	
Investigations - Other, specify	Additional description: Increased liver enzymes		
subjects affected / exposed	2 / 84 (2.38%)	23 / 85 (27.06%)	
occurrences (all)	2	23	
Creatinine increased			
subjects affected / exposed	1 / 84 (1.19%)	5 / 85 (5.88%)	
occurrences (all)	1	5	
Vascular disorders			
Hot flashes			
subjects affected / exposed	16 / 84 (19.05%)	13 / 85 (15.29%)	
occurrences (all)	16	13	
Hypertension			
subjects affected / exposed	18 / 84 (21.43%)	14 / 85 (16.47%)	
occurrences (all)	18	14	
Nervous system disorders			
Nervous system disorders - Other, specify	Additional description: Restless legs syndrome		
subjects affected / exposed	15 / 84 (17.86%)	8 / 85 (9.41%)	
occurrences (all)	15	8	
Headache			

subjects affected / exposed occurrences (all)	7 / 84 (8.33%) 7	1 / 85 (1.18%) 1	
Amnesia subjects affected / exposed occurrences (all)	7 / 84 (8.33%) 7	0 / 85 (0.00%) 0	
Dizziness subjects affected / exposed occurrences (all)	14 / 84 (16.67%) 14	3 / 85 (3.53%) 3	
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	35 / 84 (41.67%) 35	20 / 85 (23.53%) 20	
Edema limbs subjects affected / exposed occurrences (all)	6 / 84 (7.14%) 6	3 / 85 (3.53%) 3	
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	3 / 84 (3.57%) 3	4 / 85 (4.71%) 4	
Constipation subjects affected / exposed occurrences (all)	5 / 84 (5.95%) 5	8 / 85 (9.41%) 8	
Diarrhea subjects affected / exposed occurrences (all)	4 / 84 (4.76%) 4	0 / 85 (0.00%) 0	
Dyspepsia subjects affected / exposed occurrences (all)	2 / 84 (2.38%) 2	9 / 85 (10.59%) 9	
Respiratory, thoracic and mediastinal disorders			
Dyspnea subjects affected / exposed occurrences (all)	0 / 84 (0.00%) 0	4 / 85 (4.71%) 4	
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	4 / 84 (4.76%) 4	2 / 85 (2.35%) 2	

Renal and urinary disorders Urinary tract obstruction subjects affected / exposed occurrences (all)	3 / 84 (3.57%) 3	6 / 85 (7.06%) 6	
Endocrine disorders Endocrine disorders - Other, specify subjects affected / exposed occurrences (all)	Additional description: Diabetes Mellitus Type II - glycated hemoglobin increase to 48mmol/mol		
	0 / 84 (0.00%) 0	8 / 85 (9.41%) 8	
Musculoskeletal and connective tissue disorders Generalized muscle weakness subjects affected / exposed occurrences (all)	4 / 84 (4.76%) 4	4 / 85 (4.71%) 4	
Myalgia subjects affected / exposed occurrences (all)	3 / 84 (3.57%) 3	4 / 85 (4.71%) 4	
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	4 / 84 (4.76%) 4	7 / 85 (8.24%) 7	
Metabolism and nutrition disorders Anorexia subjects affected / exposed occurrences (all)	Additional description: Loss of appetite		
	5 / 84 (5.95%) 5	2 / 85 (2.35%) 2	
Hypercalcaemia subjects affected / exposed occurrences (all)	6 / 84 (7.14%) 6	5 / 85 (5.88%) 5	
Hypocalcaemia subjects affected / exposed occurrences (all)	3 / 84 (3.57%) 3	11 / 85 (12.94%) 11	
Hypercholesterolaemia subjects affected / exposed occurrences (all)	18 / 84 (21.43%) 18	14 / 85 (16.47%) 14	
Hypokalemia subjects affected / exposed occurrences (all)	3 / 84 (3.57%) 3	17 / 85 (20.00%) 17	



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/35709600>