Clinical trial results:
A Randomized double-blind study of testosterone replacement therapy or placebo in testicular cancer survivors with mild Leydig Cell Insufficiency (Einstein-intervention)

Summary

EudraCT number	2015-001452-30
Trial protocol	DK
Global end of trial date	06 June 2019

Results information

Result version number	v1 (current)
This version publication date	07 January 2021
First version publication date	07 January 2021

Trial information

Trial identification

Sponsor protocol code	010815testis

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02991209
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Copenhagen University hospital Rigshospitalet
Sponsor organisation address	Blegdamsvej 9, Copenhagen, Denmark,
Public contact	Clinical Research Unit Information, Copenhagen University Hospital Rigshospitalet, mikkel.bandak@regionh.dk
Scientific contact	Clinical Research Unit Information, Copenhagen University Hospital Rigshospitalet, mikkel.bandak@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:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 June 2019
Global end of trial reached?	Yes
Global end of trial date	06 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Investigation of changes in insulin sensitivity after 12 months treatment with testosterone substitution

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 October 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	Denmark: 69
Worldwide total number of subjects	69
EEA total number of subjects	69

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)	69
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Between October 2016 and February 2018, 140 patients were screened for eligibility and 69 were subsequently randomized to receive testosterone (n=35) or placebo (n=34)

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Testosterone

Arm description:

Active treatment

Arm type	Placebo
Investigational medicinal product name	testosterone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Transdermal use

Dosage and administration details:

Tostran 10 mg a day to a max dose of 40 mg a day, transdermally

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	t
Other name	
Pharmaceutical forms	Gel
Routes of administration	Transdermal use

Dosage and administration details:

Transdermal gel

Number of subjects in period 1	Testosterone	Placebo
Started	35	34
Completed	35	34

Baseline characteristics

Reporting groups	
Reporting group title	Testosterone
Reporting group description: Active treatment	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Testosterone	Placebo	Total
Number of subjects	35	34	69
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	42	44	
inter-quartile range (Q1-Q3)	35 to 47	37 to 49	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	35	34	69

End points

End points reporting groups	
Reporting group title	Testosterone
Reporting group description: Active treatment	
Reporting group title	Placebo
Reporting group description: -	

Primary: Delta 2-hour glucose	
End point title	Delta 2-hour glucose
End point description:	
End point type	Primary
End point timeframe: 12-months	

End point values	Testosterone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	31		
Units: mmol/L				
median (inter-quartile range (Q1-Q3))	-0.2 (-1.2 to 0.7)	0.1 (-0.75 to 0.95)		

Statistical analyses

Statistical analysis title	mixed effect linear model
Comparison groups	Testosterone v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Mixed models analysis

Secondary: Delta 2-hour insulin	
End point title	Delta 2-hour insulin
End point description:	
End point type	Secondary

End point timeframe:
12-months

End point values	Testosterone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	31		
Units: pmol/L				
median (inter-quartile range (Q1-Q3))	-0.2 (-1.2 to 0.70)	0.1 (-0.75 to 0.95)		

Statistical analyses

Statistical analysis title	mixed effect linear model
Comparison groups	Testosterone v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Mixed models analysis

Secondary: Systolic blood pressure

End point title	Systolic blood pressure

End point description:

End point type	Secondary

End point timeframe:
12-months

End point values	Testosterone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	31		
Units: mmHG				
median (inter-quartile range (Q1-Q3))	132 (128 to 137)	130 (124 to 135)		

Statistical analyses

Statistical analysis title	mixed effect linear model
Comparison groups	Testosterone v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (net)

Secondary: Diastolic blood pressure	
End point title	Diastolic blood pressure
End point description:	

End point type	Secondary
End point timeframe:	
12- monhts	

End point values	Testosterone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	31		
Units: Mm Hg				
median (inter-quartile range (Q1-Q3))	84 (77 to 88)	82 (78 to 87)		

Statistical analyses

Statistical analysis title	Mixed effect linear model
Comparison groups	Testosterone v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)

Secondary: triglycerides	
End point title	triglycerides
End point description:	

End point type	Secondary

End point timeframe:
12-months

End point values	Testosterone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	29		
Units: mmol/L				
median (inter-quartile range (Q1-Q3))	1.23 (0.92 to 1.71)	1.32 (0.89 to 1.92)		

Statistical analyses

No statistical analyses for this end point

Secondary: HDL

End point title	HDL

End point description:

End point type	Secondary

End point timeframe:
12-months

End point values	Testosterone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	31		
Units: mmol/L				
median (inter-quartile range (Q1-Q3))	1.35 (1.18 to 1.44)	1.36 (1.08 to 1.46)		

Statistical analyses

No statistical analyses for this end point

Secondary: waist circumference

End point title	waist circumference

End point description:

End point type	Secondary

End point timeframe:
12 months

End point values	Testosterone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	31		
Units: cm				
median (inter-quartile range (Q1-Q3))	92 (89 to 101)	96 (90 to 101)		

Statistical analyses

No statistical analyses for this end point

Secondary: Fasting blood glucose

End point title	Fasting blood glucose

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Testosterone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	31		
Units: mmol/L				
median (inter-quartile range (Q1-Q3))	5.4 (5.00 to 5.55)	5.3 (4.95 to 5.6)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Overall period	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTC
Dictionary version	4.0

Reporting groups	
Reporting group title	Testosterone
Reporting group description:	
Active treatment	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Testosterone	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 35 (0.00%)	0 / 34 (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: 5 %

Non-serious adverse events	Testosterone	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 35 (25.71%)	5 / 34 (14.71%)	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	2 / 35 (5.71%)	2 / 34 (5.88%)	
occurrences (all)	2	2	
increased nail growth			
subjects affected / exposed	6 / 35 (17.14%)	3 / 34 (8.82%)	
occurrences (all)	6	3	
Psychiatric disorders			
agressive behavoiur			
subjects affected / exposed	1 / 35 (2.86%)	0 / 34 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 November 2017	The amendment allowed inclusion of patients with serum free testosterone level between -3 SD and the age-adjusted upper limit of normal (+2 SD) in combination with serum LH above +1 SD

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported