Clinical trial results:
Effect of treatment with testosterone undecaonat in patients with Diabetes Mellitus Type 1 (DM-1) and hipogonadotrophic hypogonadism

Summary

EudraCT number	2012-000291-42
Trial protocol	ES
Global end of trial date	31 July 2015

Results information

Result version number	v1 (current)
This version publication date	21 February 2020
First version publication date	21 February 2020
Summary attachment (see zip file)	Summary TEST-DM1 (Summary TEST-DM1.docx)

Trial information

Trial identification

Sponsor protocol code	TEST-DM1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Parc de Salut Mar
Sponsor organisation address	Passeig Maritim 23, Barcelona, Spain,
Public contact	Servicio de Endocrinología, Hospital del Mar, 0034 932483902, JChillaron@parcdesalutmar.cat
Scientific contact	Servicio de Endocrinología, Hospital del Mar, 0034 932483902, JChillaron@parcdesalutmar.cat

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	04 April 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 July 2015
Global end of trial reached?	Yes
Global end of trial date	31 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the effectiveness of testosterone replacement therapy in patients with DM1 and hypogonadotropic hypogonadism on insulin sensitivity, measured by eGDR (estimated Glucose Disposal Rate) and evaluate the effectiveness of testosterone replacement therapy in patients with DM1 and hypogonadotropic hypogonadism on the control anthropometric parameters glycemic blood pressure and lipid profile.

Protection of trial subjects:

The three injections administered during the trial were administered according to the usual technique, trying to minimize pain in the area.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2012
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: 13
Worldwide total number of subjects	13
EEA total number of subjects	13

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)	13
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment process: July 2012-Feb 2015 in 3 endocrinology departments (Hospital del Mar, Hospital Dos de Maig, Hospital Moisès Broggi)

Pre-assignment

Screening details:

Screening was performed in 202 T1D patients of whom 21 had hypogonadotropic hypogonadism, constituting a prevalence of 10.4% (95% CI: 6.2-14.6%). Six patients were excluded owing to contraindications for TU treatment (5 benign prostatic hyperplasia, 1 polyglobulia), one had an empty sella on MRI and one refused to give his consent.

Period 1

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

Blinding implementation details:

Reandron/placebo had exactly the same appearance

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Baseline, 6 and 16 week.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Placebo administration by intramuscular route at 0, 6 and 16 weeks

Arm title	Undecanoate testosterone

Arm description:

1000 mg undecanoate testosterone at baseline, 6 and 16 weeks

Arm type	Active comparator
Investigational medicinal product name	Testosterone undecanoate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1000 mg at baseline, 6 and 16 week.

Number of subjects in period 1	Placebo	Undecanoate testosterone
Started	7	6
Completed	6	5
Not completed	1	1
Lost to follow-up	1	1

Period 2

Period 2 title	22 weeks
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Reandron/placebo had exactly the same appearance

Arms

Are arms mutually exclusive?	Yes
Arm title	Undecanoate testosterone

Arm description:

1000 mg testosterone undecanoate at week 0, 6 and 16 weeks

Arm type	Experimental
Investigational medicinal product name	Undecanoate testosterone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection/infusion
Routes of administration	Intramuscular use

Dosage and administration details:

1000 mg undecanoate testosterone

Arm title	Placebo

Arm description:

Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection at 0, 6 and 16 weeks

Number of subjects in period 2	Undecanoate testosterone	Placebo
Started	5	6
Completed	5	6

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial
Reporting group description:	
Overall group	

Reporting group values	Overall trial	Total	
Number of subjects	13	13	
Age categorical			
Recruited patients were 30-65 years old			
Units: Subjects			
30-65	13	13	
Age continuous			
46.3 +- 9.8 y			
Units: years			
arithmetic mean	46.3		
standard deviation	± 9.8	-	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	13	13	

End points

End points reporting groups	
Reporting group title	Placebo
Reporting group description: Baseline, 6 and 16 week.	
Reporting group title	Undecanoate testosterone
Reporting group description: 1000 mg undecanoate testosterone at baseline, 6 and 16 weeks	
Reporting group title	Undecanoate testosterone
Reporting group description: 1000 mg testosterone undecanoate at week 0, 6 and 16 weeks	
Reporting group title	Placebo
Reporting group description: Placebo	

Primary: Insulin sensitivity	
End point title	Insulin sensitivity
End point description:	
End point type	Primary
End point timeframe: Change at 22 weeks	

End point values	Placebo	Undecanoate testosterone	Undecanoate testosterone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	5	6
Units: mg/Kg*min				
arithmetic mean (standard deviation)	4.9 (± 1.3)	6.12 (± 2.2)	6.42 (± 1.8)	5.05 (± 1.3)

Statistical analyses

Statistical analysis title	t Student
Comparison groups	Placebo v Undecanoate testosterone v Placebo v Undecanoate testosterone
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.276
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Primary: Glycemic control-HbA1c

End point title	Glycemic control-HbA1c

End point description:

End point type	Primary

End point timeframe:

Change at 22 weeks

End point values	Placebo	Undecanoate testosterone	Undecanoate testosterone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	5	6
Units: %				
arithmetic mean (standard deviation)	8.6 (± 1.7)	7.6 (± 0.5)	7.2 (± 0.7)	7.7 (± 0.5)

Statistical analyses

Statistical analysis title	t Student
Comparison groups	Placebo v Undecanoate testosterone v Undecanoate testosterone v Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.977
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

Primary: Body mass index

End point title	Body mass index

End point description:

Testosterone undecanoate + 0.13 +- 1.1
Placebo +0.28 +- 0.3

P 0.753

End point type	Primary

End point timeframe:

Change at 22 weeks

End point values	Placebo	Undecanoate testosterone	Undecanoate testosterone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	5	6
Units: Kg/m2				
arithmetic mean (standard deviation)	34.5 (± 8.5)	30.2 (± 3.3)	30.3 (± 2.8)	37.1 (± 6.3)

Statistical analyses

Statistical analysis title	t Student
Comparison groups	Placebo v Undecanoate testosterone v Undecanoate testosterone v Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.753
Method	t-test, 2-sided
Parameter estimate	Median difference (final values)

Primary: Systolic blood pressure

End point title	Systolic blood pressure
End point description: Testosterone undecanoate -9.6 +- 11.9 Placebo + 8.8 +- 22.8 P 0.138	
End point type	Primary
End point timeframe: Change at 22 weeks	

End point values	Placebo	Undecanoate testosterone	Undecanoate testosterone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	5	6
Units: mm Hg				
arithmetic mean (standard deviation)	139.9 (± 15.6)	144.8 (± 12.9)	135.2 (± 23.7)	149.5 (± 14.4)

Statistical analyses

Statistical analysis title	t student
Comparison groups	Placebo v Undecanoate testosterone v Undecanoate testosterone v Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.138
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

Primary: Diastolic blood pressure

End point title	Diastolic blood pressure
End point description: Testosterone undecanoate +1.0 +- 4.5 Placebo +8.8 +- 22.8 P 0.819	
End point type	Primary
End point timeframe: Change at 22 weeks	

End point values	Placebo	Undecanoate testosterone	Undecanoate testosterone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	5	6
Units: mm Hg				
arithmetic mean (standard deviation)	83.4 (± 13.3)	81.4 (± 1.1)	76.4 (± 6.5)	86.2 (± 14.6)

Statistical analyses

Statistical analysis title	t student
Comparison groups	Placebo v Undecanoate testosterone v Undecanoate testosterone v Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.819
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

Primary: LDL-cholesterol

End point title	LDL-cholesterol

End point description:

Testosterone undecanoate -30.2 +- 22.1
Placebo +10.5 +- 13.4

P 0.004

End point type	Primary

End point timeframe:

Change at 22 weeks

End point values	Placebo	Undecanoate testosterone	Undecanoate testosterone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	5	6
Units: mg/dL				
arithmetic mean (standard deviation)	118.9 (± 86.5)	114.2 (± 16.1)	84 (± 14.53)	97.7 (± 20.0)

Statistical analyses

Statistical analysis title	t student
Comparison groups	Placebo v Undecanoate testosterone v Undecanoate testosterone v Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	t-test, 2-sided
Parameter estimate	Median difference (final values)

Primary: HDL cholesterol

End point title	HDL cholesterol

End point description:

Testosterone undecanoate +2.2 +- 4.3
Placebo +0.9 +- 3.1

P 0.567

End point type	Primary

End point timeframe:

Change at 22 weeks

End point values	Placebo	Undecanoate testosterone	Undecanoate testosterone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	5	6
Units: mg/dL				
arithmetic mean (standard deviation)	42.0 (± 6.1)	39.8 (± 9.1)	42 (± 8.4)	42.8 (± 6.7)

Statistical analyses

Statistical analysis title	t student
Comparison groups	Placebo v Undecanoate testosterone v Undecanoate testosterone v Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.567
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

Primary: Triglycerides

End point title	Triglycerides
End point description:	
End point type	Primary
End point timeframe: 22 weeks	

End point values	Placebo	Undecanoate testosterone	Undecanoate testosterone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	5	6
Units: mg/dL				
median (full range (min-max))	105 (61 to 700)	105 (71 to 150)	66 (49 to 92)	108 (60 to 218)

Statistical analyses

Statistical analysis title	t student
Statistical analysis description: Change 22 weeks	
Comparison groups	Placebo v Undecanoate testosterone v Undecanoate testosterone v Placebo

Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

Secondary: International Index Erectile Function- 5 Test

End point title	International Index Erectile Function- 5 Test

End point description:

Testosterone undecanoate + 5.0 +- 7.5
Placebo +0.5 +- 2.1

P 0.800

End point type	Secondary

End point timeframe:

Change at 22 weeks

End point values	Placebo	Undecanoate testosterone	Undecanoate testosterone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	5	6
Units: Escale number				
arithmetic mean (standard deviation)	17.3 (± 4.9)	13.4 (± 7.3)	18.4 (± 7.6)	17.8 (± 5.1)

Statistical analyses

Statistical analysis title	t student
Comparison groups	Placebo v Undecanoate testosterone v Undecanoate testosterone v Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse event assessment was evaluated in each visit.	
Adverse event reporting additional description:	
One patient in the placebo group reported pain at the injection site, which resolved with conventional analgesia in less than 48 hours.	
Assessment type	Systematic

Dictionary used	
Dictionary name	SNOMED CT
Dictionary version	2012

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Pain at the injection site	

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)		
Skin and subcutaneous tissue disorders			
Pain at injection site			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		

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

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27452372