Clinical trial results:
Testosterone replacement therapy in hypogonadal men with nonalcoholic steatohepatitis (TEREPINS)

Summary

EudraCT number	2012-002564-27
Trial protocol	GB
Global end of trial date	30 December 2017

Results information

Result version number	v1 (current)
This version publication date	23 May 2021
First version publication date	23 May 2021
Summary attachment (see zip file)	Final study report (TEREPIN Report Final.pdf)

Trial information

Trial identification

Sponsor protocol code	STH16037

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01919294
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sheffield Teaching Hospitals NHS Foundation Trust
Sponsor organisation address	Trust Headquarters, 8 Beech Hill Road, Sheffield, United Kingdom, S10 2SB
Public contact	Dr Dipak Patel, Sheffield Teaching Hospitals NHS Foundation Trust, sth.ResearchAdministration@nhs.net
Scientific contact	Dr Dipak Patel, Sheffield Teaching Hospitals NHS Foundation Trust, sth.ResearchAdministration@nhs.net

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	30 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 December 2017
Global end of trial reached?	Yes
Global end of trial date	30 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

In hypogonadal men with non-alcoholic steatohepatitis (NASH), does Testosterone Replacement Therapy (TRT), given for 12 months, improve severity of steatosis assessed by liver biopsy?

Protection of trial subjects:

All participants were given a participant information sheet to read and consider for at least 24 hours. Participants were reviewed by a clinician who was delegated to this task, according to the strict inclusion and exclusion criteria. All participants give written informed consent prior to enrolment to the study.

Background therapy: -

Evidence for comparator:

Single arm. No comparators were used.

Actual start date of recruitment	06 February 2013
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	United Kingdom: 3
Worldwide total number of subjects	3
EEA total number of subjects	3

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)	2
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Men with NAFLD and some inflammation or scarring (proven on liver biopsy performed for clinical diagnosis) and who had mildly reduced testosterone levels were recruited from NHS clinics in Sheffield, UK.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	3
Number of subjects completed	3

Period 1

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

Blinding implementation details:

Not blinded. All participants received the same treatment.

Arms

Arm title	Treatment, baseline results

Arm description:

As per EudraCT FAQs dated 24Nov2020, this arm represents participant's baseline results.

Guidance: In order to report a statistical analysis related to a specific endpoint it is required to define at least two comparison groups. In order to report a single arm trial, a workaround needs to be performed. One of the two comparison groups can be defined in the subject disposition, and the other(s) in section "baseline characteristics" within the "Subject analysis set" functionality. You can then select both comparison groups in each "Endpoint definition" section. Please note that this is a workaround in order to accommodate reporting of single arm trials results.

Arm type	Experimental
Investigational medicinal product name	Nebido
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Testosterone Undecanoate (1 g in 4 ml oily base) was given as slow (2 minute) intramuscular injections (Nebido, manufactured by Bayer-Schering). Given at time zero (baseline visit 2) and after 6, 18, 30 and 42 weeks.

Number of subjects in period 1	Treatment, baseline results
Started	3
Completed	3

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	3	3	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	2	2	
From 65-84 years	1	1	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	0	0	
Male	3	3	

End points

End points reporting groups

Reporting group title	Treatment, baseline results

Reporting group description:

As per EudraCT FAQs dated 24Nov2020, this arm represents participant's baseline results.

Guidance: In order to report a statistical analysis related to a specific endpoint it is required to define at least two comparison groups. In order to report a single arm trial, a workaround needs to be performed. One of the two comparison groups can be defined in the subject disposition, and the other(s) in section "baseline characteristics" within the "Subject analysis set" functionality. You can then select both comparison groups in each "Endpoint definition" section. Please note that this is a workaround in order to accommodate reporting of single arm trials results.

Subject analysis set title	Treatment, 52 weeks results
Subject analysis set type	Intention-to-treat

Subject analysis set description:

As per EudraCT FAQs 24 November 2020, this group represents participant's data at 52 weeks.

Guidance: In order to report a statistical analysis related to a specific endpoint it is required to define at least two comparison groups. In order to report a single arm trial, a workaround needs to be performed. One of the two comparison groups can be defined in the subject disposition, and the other(s) in section "baseline characteristics" within the "Subject analysis set" functionality. You can then select both comparison groups in each "Endpoint definition" section. Please note that this is a workaround in order to accommodate reporting of single arm trials results.

Primary: Change in steatosis

End point title	Change in steatosis[1]

End point description:

As per EudraCT FAQs 24 November 2020, the group 'subject disposition, period one overall trial' represents the baseline data for participants and the group 'baseline characteristics/subject analysis set' represents the data at 52 weeks for participants.

Guidance: In order to report a statistical analysis related to a specific endpoint it is required to define at least two comparison groups. In order to report a single arm trial, a workaround needs to be performed. One of the two comparison groups can be defined in the subject disposition, and the other(s) in section "baseline characteristics" within the "Subject analysis set" functionality. You can then select both comparison groups in each "Endpoint definition" section. Please note that this is a workaround in order to accommodate reporting of single arm trials results.

End point type	Primary

End point timeframe:

Baseline to 52 weeks

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: There is no statistical analysis provided for this endpoint as the trial recruited only three participants and therefore performing formal statistics is not justified; the calculations lack sufficient power.

End point values	Treatment, baseline results	Treatment, 52 weeks results		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	3	3		
Units: Graded 1-3				
median (full range (min-max))	2 (2 to 2)	1 (1 to 1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Hepatocyte ballooning

End point title	Hepatocyte ballooning

End point description:

As per EudraCT FAQs 24 November 2020, the group 'subject disposition, period one overall trial' represents the baseline data for participants and the group 'baseline characteristics/subject analysis set' represents the data at 52 weeks for participants.

Guidance: In order to report a statistical analysis related to a specific endpoint it is required to define at least two comparison groups. In order to report a single arm trial, a workaround needs to be performed. One of the two comparison groups can be defined in the subject disposition, and the other(s) in section "baseline characteristics" within the "Subject analysis set" functionality. You can then select both comparison groups in each "Endpoint definition" section. Please note that this is a workaround in order to accommodate reporting of single arm trials results.

End point type	Secondary

End point timeframe:

Baseline to 52 weeks

End point values	Treatment, baseline results	Treatment, 52 weeks results		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	3	3		
Units: Graded 1-3				
median (full range (min-max))	3 (2 to 3)	1 (1 to 1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Brunt (inflammatory grade)

End point title	Brunt (inflammatory grade)

End point description:

As per EudraCT FAQs 24 November 2020, the group 'subject disposition, period one overall trial' represents the baseline data for participants and the group 'baseline characteristics/subject analysis set' represents the data at 52 weeks for participants.

Guidance: In order to report a statistical analysis related to a specific endpoint it is required to define at least two comparison groups. In order to report a single arm trial, a workaround needs to be performed. One of the two comparison groups can be defined in the subject disposition, and the other(s) in section "baseline characteristics" within the "Subject analysis set" functionality. You can then select both comparison groups in each "Endpoint definition" section. Please note that this is a workaround in order to accommodate reporting of single arm trials results.

End point type	Secondary

End point timeframe:

Baseline to 52 weeks

End point values	Treatment, baseline results	Treatment, 52 weeks results		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	3	3		
Units: inflammatory grade				
median (full range (min-max))	3 (2 to 3)	1 (1 to 1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Fibrosis (central)

End point title	Fibrosis (central)

End point description:

As per EudraCT FAQs 24 November 2020, the group 'subject disposition, period one overall trial' represents the baseline data for participants and the group 'baseline characteristics/subject analysis set' represents the data at 52 weeks for participants.

Guidance: In order to report a statistical analysis related to a specific endpoint it is required to define at least two comparison groups. In order to report a single arm trial, a workaround needs to be performed. One of the two comparison groups can be defined in the subject disposition, and the other(s) in section "baseline characteristics" within the "Subject analysis set" functionality. You can then select both comparison groups in each "Endpoint definition" section. Please note that this is a workaround in order to accommodate reporting of single arm trials results.

End point type	Secondary

End point timeframe:

Baseline to 52 weeks

End point values	Treatment, baseline results	Treatment, 52 weeks results		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	3	3		
Units: Central grading				
median (full range (min-max))	5 (4 to 5)	2 (2 to 2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in liver enzymes - ALT

End point title	Change in liver enzymes - ALT

End point description:

As per EudraCT FAQs 24 November 2020, the group 'subject disposition, period one overall trial' represents the baseline data for participants and the group 'baseline characteristics/subject analysis set' represents the data at 52 weeks for participants.

Guidance: In order to report a statistical analysis related to a specific endpoint it is required to define at least two comparison groups. In order to report a single arm trial, a workaround needs to be performed. One of the two comparison groups can be defined in the subject disposition, and the other(s) in section "baseline characteristics" within the "Subject analysis set" functionality. You can then select both comparison groups in each "Endpoint definition" section. Please note that this is a workaround in order to accommodate reporting of single arm trials results.

End point type	Secondary

End point timeframe:

Baseline to 52 weeks

End point values	Treatment, baseline results	Treatment, 52 weeks results		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	3	3		
Units: international unit(s)/litre				
median (inter-quartile range (Q1-Q3))	77 (56 to 98)	88 (51 to 133)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in liver enzymes - Alk-Phos

End point title	Change in liver enzymes - Alk-Phos

End point description:

As per EudraCT FAQs 24 November 2020, the group 'subject disposition, period one overall trial' represents the baseline data for participants and the group 'baseline characteristics/subject analysis set' represents the data at 52 weeks for participants.

Guidance: In order to report a statistical analysis related to a specific endpoint it is required to define at least two comparison groups. In order to report a single arm trial, a workaround needs to be performed. One of the two comparison groups can be defined in the subject disposition, and the other(s) in section "baseline characteristics" within the "Subject analysis set" functionality. You can then select both comparison groups in each "Endpoint definition" section. Please note that this is a workaround in order to accommodate reporting of single arm trials results.

End point type	Secondary

End point timeframe:

Baseline to week 52

End point values	Treatment, baseline results	Treatment, 52 weeks results		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	3	3		
Units: international unit(s)/litre				
median (inter-quartile range (Q1-Q3))	165 (79 to 184)	136 (75 to 150)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in HOMA

End point title	Change in HOMA

End point description:

As per EudraCT FAQs 24 November 2020, the group 'subject disposition, period one overall trial' represents the baseline data for participants and the group 'baseline characteristics/subject analysis set' represents the data at 52 weeks for participants.

Guidance: In order to report a statistical analysis related to a specific endpoint it is required to define at least two comparison groups. In order to report a single arm trial, a workaround needs to be performed. One of the two comparison groups can be defined in the subject disposition, and the other(s) in section "baseline characteristics" within the "Subject analysis set" functionality. You can then select both comparison groups in each "Endpoint definition" section. Please note that this is a workaround in order to accommodate reporting of single arm trials results.

End point type	Secondary

End point timeframe:

Baseline to 52 weeks

End point values	Treatment, baseline results	Treatment, 52 weeks results		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	3	3		
Units: HOMA index				
median (inter-quartile range (Q1-Q3))	19.5 (12.5 to 73.8)	14.4 (13.2 to 15.5)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From informed consent until 4 weeks after the end of participant's involvement in trial	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Overall trial
Reporting group description: All participants throughout trial	

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)		
Blood and lymphatic system disorders			
Polycythaemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Infections and infestations			
Chest infection			
subjects affected / exposed	1 / 3 (33.33%)		
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

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

Three participants were recruited whereas it was initially intended that there would be 10 recruits.

Notes: