Clinical trial results:
Gonadal dysfunction in male long-term survivors of malignant lymphoma

Summary

EudraCT number	2020-002140-22
Trial protocol	DK
Global end of trial date	10 November 2022

Results information

Result version number	v1 (current)
This version publication date	22 July 2023
First version publication date	22 July 2023

Trial information

Trial identification

Sponsor protocol code	Vitality

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Copenhagen University hospital,Rigshospitalet
Sponsor organisation address	Blegdamsvej 9, kbh Ø, Denmark, 2100
Public contact	Department of hematology, Copenhagen University hospital,Rigshospitalet, +45 35453545, signe.micas.pedersen@regionh.dk
Scientific contact	Department of hematology, Copenhagen University hospital,Rigshospitalet, +45 35453545, signe.micas.pedersen@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 July 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 November 2022
Global end of trial reached?	Yes
Global end of trial date	10 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The approach to surveillance and treatment of gonadal dysfunction following remission with first line therapy for malignant lymphoma remains controversial. With a paucity of evidence whether follow-up programs and treatment are effective, evidence-based guidelines for follow-up and treatment of gonadal dysfunction are needed. The main purpose of the current study is to assess the extent of sexual dysfunction, quality of life (QoL) and reduced levels of testosterone in male patients with Hodgkin lymphoma (HL) and diffuse large B-cell lymphoma (DLBCL). Furthermore, in a prospective phase 2 study, to test the impact on QoL before and after substitution with testosterone in patients with reduced levels of testosterone.

Protection of trial subjects:

Approval of the study was obtained from both the regional ethics commitee and the danish medicines agency. An independant monitor was involved during the study. All patients were screened for in- and exclusion criteria, making sure that no contraindications for treatment with the study drug was present.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 7
Worldwide total number of subjects	7
EEA total number of subjects	7

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)	7
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from a study screening for testosterone deficiency. Men treated for malignant lymphoma at least one year prior, were screened with measurements of serum total testosterone. If concentration were below age adjusted reference levels, they were informed about the current study and offered treatment for the deficiency.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	7
Number of subjects completed	7

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Overall study

Arm description:

All patients were offered the same treatment with Testogel.

Arm type	Experimental
Investigational medicinal product name	Testogel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Cutaneous use

Dosage and administration details:

Sachets of tesotserone gel was applied in the morning on arms og thighs. One sachet was initial dose, which could be increased to two sachets upon lack of efficacy.

Number of subjects in period 1	Overall study
Started	7
Control visit 1 month	7
Control visit 3 months	7
Control visit 6 months	5
Control visit 12 months	4
Completed	4
Not completed	3
Consent withdrawn by subject	1
Adverse event, non-fatal	2

Baseline characteristics

Reporting groups

Reporting group title	Overall study

Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	7	7	
Age categorical Units: Subjects			
Adults (18-64 years)	7	7	
Gender categorical			
all male participants			
Units: Subjects			
Female	0	0	
Male	7	7	

Subject analysis sets

Subject analysis set title	Vitality patients
Subject analysis set type	Intention-to-treat

Subject analysis set description:

7 patients with testosterone deficiency were included, to evaluate tolerance, hormonal response and sexual and general quality of life during one year of treatment with Testogel. 4 survivors completed the study with good results on both hormonal status, general quality of life and sexual health. All 4 were referred for further endocrinological treatment. One was stopped because of increased hemotacrit, one was stopped because of unrelated adverse event, and one wished to terminate treatment because of lack of effect. During the year of treatment, subjects were treated with daily Testogel, had blood samples drawn and filled in questionnaires at preplanned control visits.

Reporting group values	Vitality patients		
Number of subjects	7		
Age categorical Units: Subjects			
Adults (18-64 years)	7		
Gender categorical			
all male participants			
Units: Subjects			
Female	0		
Male	7		

End points

End points reporting groups

Reporting group title	Overall study

Reporting group description:

All patients were offered the same treatment with Testogel.

Subject analysis set title	Vitality patients
Subject analysis set type	Intention-to-treat

Subject analysis set description:

7 patients with testosterone deficiency were included, to evaluate tolerance, hormonal response and sexual and general quality of life during one year of treatment with Testogel. 4 survivors completed the study with good results on both hormonal status, general quality of life and sexual health. All 4 were referred for further endocrinological treatment. One was stopped because of increased hemotacrit, one was stopped because of unrelated adverse event, and one wished to terminate treatment because of lack of effect. During the year of treatment, subjects were treated with daily Testogel, had blood samples drawn and filled in questionnaires at preplanned control visits.

Primary: Effect of testosterone on QLQ C-30 score

End point title	Effect of testosterone on QLQ C-30 score[1]

End point description:

score change during treatment with testogel

End point type	Primary

End point timeframe:

one year

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: Because only 7 patients were enrolled in the study, statistical analyses is not possible.

End point values	Overall study	Vitality patients		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	7	7		
Units: questionnaire score				
number (not applicable)	7	7		

Attachments (see zip file)	Treatment effect/Vitality- charts of treatment effect.PNG

Statistical analyses

No statistical analyses for this end point

Secondary: Effect of testosterone on QLQ SHQ-22 score

End point title	Effect of testosterone on QLQ SHQ-22 score

End point description:

Score change during treatment with Testogel

End point type	Secondary

End point timeframe:

one year

End point values	Overall study	Vitality patients		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	7	7		
Units: Questionnaire score				
number (not applicable)	7	7		

Attachments (see zip file)	Treatment effect/Vitality- charts of treatment effect.PNG

Statistical analyses

No statistical analyses for this end point

Secondary: Effect of testosterone on IIEF-5 score

End point title	Effect of testosterone on IIEF-5 score
End point description: score change during treatment with Testogel	
End point type	Secondary
End point timeframe: one year	

End point values	Overall study	Vitality patients		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	7	7		
Units: questionnaire score				
number (not applicable)	7	7		

Attachments (see zip file)	Treatment effect/Vitality- charts of treatment effect.PNG

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

one year

Adverse event reporting additional description:

During the one year of treatment patients were controlled for adverse events in the study settings. After cessation of treatment, patients were controlled for events after one week. Patients continuing on Testogel after the end of study was follow-up by an endocrinologist.

Assessment type	Non-systematic

Dictionary used

Dictionary name	CTC
Dictionary version	4

Reporting groups

Reporting group title	Overall study

Reporting group description:

All patients were offered the same treatment with Testogel.

Serious adverse events	Overall study		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Atrioventricular block complete			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Increased hemotocrit			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Overall study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)		
General disorders and administration site conditions			
Nightsweats	Additional description: Checked for malignancy without an concerns and continued on Testogel.		
alternative assessment type: Systematic			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Mild rash	Additional description: Unrelated to application site		
subjects affected / exposed	1 / 4 (25.00%)		
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.

Only 7 patients enrolled, why significant conclusions could not be made.

Notes: