Clinical trial results:
Tacrolimus as Treatment of Breast Cancer-Related Lymphedema

Summary

EudraCT number	2020-000877-25
Trial protocol	DK
Global end of trial date	03 February 2022

Results information

Result version number	v1 (current)
This version publication date	18 December 2022
First version publication date	18 December 2022

Trial information

Trial identification

Sponsor protocol code	Tacrolimus2020

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04541290
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Odense University Hospital
Sponsor organisation address	J.B. Winsløwsvej 4, Odense C, Denmark, 5000
Public contact	Frederik C. Gulmark Hansen, Dept. of Plastic Surgery, Odense University Hospital, 0045 21734450, Jens.sorensen@rsyd.dk
Scientific contact	Jens Ahm Sørensen, Dept. of Plastic Surgery, Odense University Hospital, 0045 65412436, Jens.sorensen@rsyd.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	01 December 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 February 2022
Global end of trial reached?	Yes
Global end of trial date	03 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of Tacrolimus treatment on breast cancer-related lymphedema and how it influences quality of life in patients.

Protection of trial subjects:

Prior to the injection of indocyanine green (ICG) into the subcutaneous tissue of the patients' hands, we injected local anesthesia so the participants would not feel the pain of the following injections and the possible itching sensation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 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: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	20
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The patients were recruited through an internal waiting for participating in experimental lymphedema treatment trials.

Pre-assignment

Screening details:

Initially, we screened the patients according to the following eligibility criteria: sex (female), age (30-65 years), breast cancer-related lymphedema, ISL stage I-II (yes), ipsilateral ALND (yes), bilateral breast cancer (no), allergy for tacrolimus or other macrolides (no), diagnosed immunodeficiency (no), psychiatric illness (no) and reduced kid

Pre-assignment period milestones

Number of subjects started	20
Number of subjects completed	20

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Treatment

Arm description:

This is a single arm trial with only the treatment group

Arm type	Experimental
Investigational medicinal product name	protopic (0,1% tacrolimus)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Cutaneous use

Dosage and administration details:

The participants were given 13 tubes of Protopic (0.1 % tacrolimus) (Leo Pharma, Ballerup, Denmark) at baseline. They were instructed to apply the ointment in a thin layer covering the armpit, entire arm, and hand once daily for six months.

Number of subjects in period 1	Treatment
Started	20
Completed	20

Period 2

Period 2 title	3 months
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Treatment

Arm description:

This is a single arm trial with only the treatment group

Arm type	Experimental
Investigational medicinal product name	protopic (0,1% tacrolimus)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Cutaneous use

Dosage and administration details:

The participants were given 13 tubes of Protopic (0.1 % tacrolimus) (Leo Pharma, Ballerup, Denmark) at baseline. They were instructed to apply the ointment in a thin layer covering the armpit, entire arm, and hand once daily for six months.

Number of subjects in period 2	Treatment
Started	20
Completed	18
Not completed	2
Consent withdrawn by subject	1
Adverse event, non-fatal	1

Period 3

Period 3 title	6 months
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Treatment

Arm description:

This is a single arm trial with only the treatment group

Arm type	Experimental
Investigational medicinal product name	protopic (0,1% tacrolimus)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Cutaneous use

Dosage and administration details:

The participants were given 13 tubes of Protopic (0.1 % tacrolimus) (Leo Pharma, Ballerup, Denmark) at baseline. They were instructed to apply the ointment in a thin layer covering the armpit, entire arm, and hand once daily for six months.

Number of subjects in period 3	Treatment
Started	18
Completed	18

Period 4

Period 4 title	12 months
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Treatment

Arm description:

This is a single arm trial with only the treatment group

Arm type	Experimental
Investigational medicinal product name	protopic (0,1% tacrolimus)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Cutaneous use

Dosage and administration details:

The participants were given 13 tubes of Protopic (0.1 % tacrolimus) (Leo Pharma, Ballerup, Denmark) at baseline. They were instructed to apply the ointment in a thin layer covering the armpit, entire arm, and hand once daily for six months.

Number of subjects in period 4	Treatment
Started	18
Completed	16
Not completed	2
Consent withdrawn by subject	2

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	20	20	
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			
arithmetic mean	55.28		
standard deviation	± 4.6	-	
Gender categorical Units: Subjects			
Female	20	20	
Male	0	0	
Type of surgery			
Type of surgery for breast cancer treatment			
Units: Subjects			
Mastectomy	10	10	
Lumpectomy	10	10	
BMI Units: kg/m^2			
arithmetic mean	27.24		
standard deviation	± 5.78	-	
Number of lymph nodes removed Units: lymph nodes			
arithmetic mean	19		
standard deviation	± 7.13	-	
Difference in arm volume			
Difference in volume between lymphedema arm and healthy arm			
Units: mL			
arithmetic mean	491.5		
standard deviation	± 227.55	-	
Time since lymphedema diagnosis Units: years			

arithmetic mean	7.33		
standard deviation	± 5.13	-	

End points

End points reporting groups

Reporting group title	Treatment
Reporting group description:	
This is a single arm trial with only the treatment group	
Reporting group title	Treatment
Reporting group description:	
This is a single arm trial with only the treatment group	
Reporting group title	Treatment
Reporting group description:	
This is a single arm trial with only the treatment group	
Reporting group title	Treatment
Reporting group description:	
This is a single arm trial with only the treatment group	

Primary: Lymphedema arm volume

End point title	Lymphedema arm volume
End point description:	
End point type	Primary
End point timeframe:	
Baseline, 3, 6 and 12 months	

End point values	Treatment	Treatment	Treatment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	16	
Units: millilitre(s)				
arithmetic mean (standard deviation)	3194 (± 833)	3069 (± 746)	2133 (± 754)	

Statistical analyses

Statistical analysis title	Paired t test
Comparison groups	Treatment v Treatment v Treatment
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05 [1]
Method	t-test, 2-sided

Notes:

[1] - Significant difference was seen from baseline to 6 months. Non significant changes were seen at 3 and 12 months

Primary: Healthy arm volume

End point title	Healthy arm volume

End point description:

End point type	Primary

End point timeframe:

Baseline, 3, 6 and 12 months

End point values	Treatment	Treatment	Treatment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	16	
Units: millilitre(s)				
arithmetic mean (standard deviation)	2723 (± 772)	2671 (± 750)	2680 (± 729)	

Statistical analyses

Statistical analysis title	Paired t test
Comparison groups	Treatment v Treatment v Treatment
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	> 0.05
Method	t-test, 2-sided

Notes:

[2] - Paired t test was performed. There was no significant changes in healty arm volume in the group

Secondary: L-Dex Score

End point title	L-Dex Score

End point description:

End point type	Secondary

End point timeframe:

Baseline, 3, 6 and 12 months

End point values	Treatment	Treatment	Treatment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	16	
Units: N/A				
arithmetic mean (standard deviation)	21.2 (± 12.5)	17.9 (± 9.8)	20 (± 12.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: LYMPH ICF

End point title	LYMPH ICF

End point description:

End point type	Secondary

End point timeframe:

Baseline, 3, 6 and 12 months

End point values	Treatment	Treatment	Treatment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	16	
Units: N/A				
arithmetic mean (standard deviation)	33.9 (± 17.4)	25.7 (± 17.2)	25.3 (± 15.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: DASH

End point title	DASH

End point description:

End point type	Secondary

End point timeframe:

Baseline, 3, 6 and 12 months

End point values	Treatment	Treatment	Treatment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	16	
Units: N/A				
arithmetic mean (standard deviation)	22.3 (± 11.3)	16.9 (± 12)	18.3 (± 11.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36

End point title	SF-36

End point description:

End point type	Secondary

End point timeframe:

Baseline, 3, 6, and 12 months

End point values	Treatment	Treatment	Treatment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	16	
Units: N/A				
arithmetic mean (standard deviation)	72.8 (± 19.8)	77.4 (± 16.9)	72.1 (± 19.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: ICG-L

End point title	ICG-L

End point description:

End point type	Secondary

End point timeframe:

Baseline, 6 and 12 months

End point values	Treatment	Treatment	Treatment	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	13	
Units: N/A				
number (not applicable)				
Stage 0	0	0	0	

Stage 1	0	0	0	
Stage 2	0	3	2	
Stage 3	9	6	6	
Stage 4	9	9	5	
Stage 5	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: SEP 2020 - MAR 2022	
Assessment type	Systematic
Dictionary used	
Dictionary name	none
Dictionary version	0
Reporting groups	
Reporting group title	Treatment
Reporting group description: This is a single arm trial with only the treatment group	

Serious adverse events	Treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 20 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Skin and subcutaneous tissue disorders			
Cellulitis			
subjects affected / exposed	5 / 20 (25.00%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 20 (30.00%)		
Skin and subcutaneous tissue disorders			
Flushing			
subjects affected / exposed	6 / 20 (30.00%)		
occurrences (all)	6		

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.

Lack of control group

Notes: