



Clinical trial results: Prevention of breast cancer-related lymphedema with tacrolimus Summary

EudraCT number	2018-003416-50
Trial protocol	DK
Global end of trial date	22 November 2022

Results information

Result version number	v1 (current)
This version publication date	21 October 2023
First version publication date	21 October 2023

Trial information

Trial identification

Sponsor protocol code	2018-BCRL-TACRO
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04390685
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Odense university Hospital
Sponsor organisation address	J.B. Winsløws vej 4, Odense, Denmark, 5000
Public contact	Dept. of Plastic Surgery, Odense University Hospital, 0045 65412436 , jens.sorensen@rsyd.dk
Scientific contact	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	Interim
Date of interim/final analysis	28 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 November 2022
Global end of trial reached?	Yes
Global end of trial date	22 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study will evaluate the feasibility of tacrolimus ointment in preventing lymphedema after breast cancer treatment.

Protection of trial subjects:

The protection of clinical trial subjects is consistent with the principles set out in the Declaration of Helsinki

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 February 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: 61
Worldwide total number of subjects	61
EEA total number of subjects	61

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)	49
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited at Odense University Hospital, Lillebælt Hospital Vejle, and Hospital of Southwest Jutland in Esbjerg from February 2020 to June 2022. Patients included at Odense University hospital were assigned to the treatment group, and patients included at Vejle and Esbjerg were allocated to the control group.

Pre-assignment

Screening details:

Inclusion took place 1-4 days prior to the scheduled axillary lymph node dissection surgery. During the course of breast cancer treatment, potential participants were screened for eligibility criteria at the outpatient clinic for each participating study site by clinical staff.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Tacrolimus (0.1 % tacrolimus)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Cutaneous use

Dosage and administration details:

1 thin layer on the axilla, arm and hand daily for 12 months

Arm title	Control
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Arm description:

Control group not receiving any treatment

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Intervention	Control
Started	22	39
3 months	19	38
6 months	19	39
9 months	19	37
12 months	18	37
Completed	18	37
Not completed	4	2

Consent withdrawn by subject	3	-
Lost to follow-up	1	2

Baseline characteristics

Reporting groups

Reporting group title	Overall period
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Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	61	61	
Age categorical			
Units: Subjects			
Adults (18-64 years)	11	11	
From 65-84 years	50	50	
Age continuous			
Units: years			
arithmetic mean	53.89		
standard deviation	± 10.60	-	
Gender categorical			
Units: Subjects			
Female	61	61	
Male	0	0	
Body mass index			
Units: kg/m ²			
arithmetic mean	26.49		
standard deviation	± 4.70	-	

End points

End points reporting groups

Reporting group title	Intervention
Reporting group description: -	
Reporting group title	Control
Reporting group description: Control group not receiving any treatment	
Subject analysis set title	Endpoints
Subject analysis set type	Per protocol
Subject analysis set description: Data was analyzed per protocol.	

Primary: Lymphedema diagnosis

End point title	Lymphedema diagnosis
End point description:	
End point type	Primary
End point timeframe: Observed at 12 months follow up	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	37		
Units: subjects				
Yes	7	13		
No	11	24		

Statistical analyses

Statistical analysis title	Paired t-test
Comparison groups	Intervention v Control
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.05
Method	t-test, 2-sided

Secondary: Lymphedema criteria met?

End point title	Lymphedema criteria met?
End point description: Was a change of at least 10% seen in the arm at-risk	

End point type	Secondary
End point timeframe: baseline to 12 months	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	37		
Units: subjects				
Yes	3	4		
No	15	33		

Statistical analyses

Statistical analysis title	Paired t-test
Comparison groups	Intervention v Control
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.05
Method	t-test, 2-sided

Secondary: Change in arm volume difference

End point title	Change in arm volume difference
End point description: Change in difference in arm volume for each patient fra baseline to 12 months	
End point type	Secondary
End point timeframe: Baseline to 12 months	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	37		
Units: millilitre(s)				
arithmetic mean (standard deviation)	95.22 (± 34.93)	76.26 (± 24.18)		

Statistical analyses

Statistical analysis title	Paired t-test
Comparison groups	Intervention v Control
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	t-test, 2-sided

Secondary: LYMPH ICF

End point title	LYMPH ICF
End point description:	
Change in LYMPH ICF scores	
End point type	Secondary
End point timeframe:	
baseline to 12 months	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	37		
Units: Arbitrary unit				
arithmetic mean (standard deviation)	5.14 (± 3.40)	10.80 (± 2.37)		

Statistical analyses

Statistical analysis title	Paired t-test
Comparison groups	Intervention v Control
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	t-test, 2-sided

Secondary: DASH

End point title	DASH
End point description:	
change in DASH scores	
End point type	Secondary
End point timeframe:	
Baseline to 12 months	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	37		
Units: Arbitrary unit				
arithmetic mean (standard deviation)	8.51 ($\pm$ 2.18)	7.41 ($\pm$ 1.53)		

Statistical analyses

Statistical analysis title	Paired t-test
Comparison groups	Intervention v Control
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	t-test, 2-sided

Secondary: L-Dex

End point title	L-Dex ^[1]
End point description:	
Any assessed for the intervention group	
End point type	Secondary
End point timeframe:	
baseline to 12 months	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only the intervention group was assessed with l-dex

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Arbitrary unit				
arithmetic mean (standard deviation)	5.98 ($\pm$ 2.51)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

0-12 months

Adverse event reporting additional description:

Data collected throughout the study

Assessment type	Systematic
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Dictionary used

Dictionary name	none
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Dictionary version	0
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Reporting groups

Reporting group title	intervention
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Reporting group description:

The intervention group was instructed to apply a thin layer of 0.1% tacrolimus ointment to the arm, hand, and axilla for a period. of 12 months starting from the day after surgery.

Serious adverse events	intervention		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (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	intervention		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 22 (22.73%)		
Skin and subcutaneous tissue disorders			
Flushing	Additional description: In relation to alcohol intake		
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Folliculitis			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Infection	Additional description: postoperative skin infection in the axilla		
subjects affected / exposed	1 / 22 (4.55%)		
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