Clinical trial results:
Determining the role of pre-existing factors, early diagnostic options and early treatment in the development of breast cancer related lymphedema.

Summary

EudraCT number	2017-002306-12
Trial protocol	BE
Global end of trial date	03 October 2024

Results information

Result version number	v1 (current)
This version publication date	25 January 2025
First version publication date	25 January 2025
Summary attachment (see zip file)	final results (final results DEARLY.pdf)

Trial information

Trial identification

Sponsor protocol code	S60382

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03210311
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Hospitals Leuven
Sponsor organisation address	Herestraat 49, Leuven, Belgium, 3000
Public contact	Secretariaat vaatheelkunde, University Hospitals Leuven, 0032 16346850, sarah.thomis@uzleuven.be
Scientific contact	Secretariaat vaatheelkunde, University Hospitals Leuven, 0032 0498296629, sarah.thomis@uzleuven.be

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	03 October 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 October 2024
Global end of trial reached?	Yes
Global end of trial date	03 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective entails detecting early development of lymphedema and establishing a decrease in the incidence of lymphedema and/or improvement or stabilization of the lymphofluoroscopic image when treatment is started early.

Protection of trial subjects:

In accordance with the Belgian Law relating to experiments on human persons dated May 7, 2004, Sponsor shall assume, even without fault, the responsibility of any damages incurred by a Study Patient and linked directly or indirectly to the participation to the Study, and shall provide compensation therefore through its insurance."

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 September 2017
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	Belgium: 128
Worldwide total number of subjects	128
EEA total number of subjects	128

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)	92
From 65 to 84 years	36

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients are recruited at the preoperative consultation of the Multidisciplinary Breast Clinic. Leaflet will be handed out and the trial will be explained.

Pre-assignment

Screening details:

Patients scheduled for breast surgery and either unilateral axillary lymph node dissection (ALND) or sentinel node biopsy (SNB) in the Multidisciplinary Breast Clinic in the University Hospitals Leuven (N=128) will be screened for participation in the study.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Arms

Are arms mutually exclusive?	Yes
Arm title	preventive treatment group

Arm description:

compression garment was added to the standard of care treatment

Arm type	Active comparator
Investigational medicinal product name	Indocyanine Green pulsion 25 mg
Investigational medicinal product code	3588 IE 1 F 0
Other name	Verdeye
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Injection , Intralymphatic use

Dosage and administration details:

0.2ml (of 25 mg ICG diluted in 25ml NaCl) in two injection sites of the hand

Arm title	standard of care group

Arm description:

patients received standard of care treatment consisting out of exercises, skin care

Arm type	No intervention

No investigational medicinal product assigned in this arm

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: the assessor was blinded, she dind't knew in which group the patient was allocated

Number of subjects in period 1[2]	preventive treatment group	standard of care group
Started	19	20
Completed	13	13
Not completed	6	7
Lost to follow-up	6	7

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: the total number of patients in the study was 128, but only 39 patients were randomized and analyzed

Baseline characteristics

Reporting groups	
Reporting group title	preventive treatment group
Reporting group description: compression garment was added to the standard of care treatment	
Reporting group title	standard of care group
Reporting group description: patients received standard of care treatment consisting out of exercises, skin care	

Reporting group values	preventive treatment group	standard of care group	Total
Number of subjects	19	20	39
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	12	17	29
From 65-84 years	7	3	10
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	19	20	39
Male	0	0	0

Subject analysis sets	
Subject analysis set title	Randomized patients
Subject analysis set type	Full analysis

Subject analysis set description:

- Patients in the treatment group will have a:
o Increase of the incidence of lymphedema of arm and hand (defined as 5% volume increase compared to the contralateral side)
o Improvement or stabilization of lymphatic transport visualized and measured by ICG fluoroscopy
- Patients with more aggressive breast-cancer treatment will have a higher chance of developing lymphedema.
- Early detection of lymphedema is possible by visualizing an abnormal pattern of ICG lymphofluoroscopy and/or by measuring lower velocity times of the lymph transport.
- Early detection of lymphedema is possible by measuring
o Change of volume measurements of the hand/arm
o Change of extracellular fluid in the arm

Reporting group values	Randomized patients		
Number of subjects	39		
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)	27		
From 65-84 years	10		
85 years and over	0		
Gender categorical Units: Subjects			
Female	37		
Male	0		

End points

End points reporting groups

Reporting group title	preventive treatment group
Reporting group description:	
compression garment was added to the standard of care treatment	
Reporting group title	standard of care group
Reporting group description:	
patients received standard of care treatment consisting out of exercises, skin care	
Subject analysis set title	Randomized patients
Subject analysis set type	Full analysis
Subject analysis set description:	
- Patients in the treatment group will have a: o Increase of the incidence of lymphedema of arm and hand (defined as 5% volume increase compared to the contralateral side) o Improvement or stabilization of lymphatic transport visualized and measured by ICG fluoroscopy - Patients with more aggressive breast-cancer treatment will have a higher chance of developing lymphedema. - Early detection of lymphedema is possible by visualizing an abnormal pattern of ICG lymphofluoroscopy and/or by measuring lower velocity times of the lymph transport. - Early detection of lymphedema is possible by measuring o Change of volume measurements of the hand/arm o Change of extracellular fluid in the arm	

Primary: Presence of clinical lymphedema

End point title	Presence of clinical lymphedema
End point description:	
presence of lymphedema measured with circumference measurements dan defined as > 5% volume difference	
End point type	Primary
End point timeframe:	
12M	

End point values	preventive treatment group	standard of care group	Randomized patients	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	13	13	26	
Units: 2	6	4	10	

Statistical analyses

Statistical analysis title	logistic regression analysis
Comparison groups	preventive treatment group v standard of care group

Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.508
upper limit	8.125

Primary: evolution of dermal backflow

End point title	evolution of dermal backflow
End point description: evolution of dermal backflow worsening = 1 stable or better = 0	
End point type	Primary
End point timeframe: 12M	

End point values	preventive treatment group	standard of care group	Randomized patients	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	13	13	26	
Units: 2	6	7	13	

Statistical analyses

Statistical analysis title	logistic regression analysis
Comparison groups	preventive treatment group v standard of care group
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	6.493

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

The sponsor shall ensure that all relevant information about suspected unexpected serious adverse reactions that are fatal or life-threatening is recorded and reported as soon as possible to the minister, to the competent authorities in all the Member Sta

Adverse event reporting additional description:

8.2.1 Definitions in Law of May 7, 2004 concerning experiments on the human person

Adverse reaction (AR): all untoward and unintended responses to an investigational medicinal product or to an experiment and, when an investigational product is concerned, related to any dose administered; Adverse event (AE): any untoward medical occurrence in a

Assessment type	Systematic

Dictionary used

Dictionary name	no AE reportes
Dictionary version	1

Reporting groups

Reporting group title	standard of care
Reporting group description: -	
Reporting group title	preventive treatment group

Reporting group description: -

Serious adverse events	standard of care	preventive treatment group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	standard of care	preventive treatment group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: there were no adverse events

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/39253841

http://www.ncbi.nlm.nih.gov/pubmed/36980660

http://www.ncbi.nlm.nih.gov/pubmed/33277289