Clinical trial results:
Fat transplantation enriched with ex vivo expanded adipose-derived autologous mesenchymal stem cells in reconstruction of the breast.

Summary

EudraCT number	2014-000510-59
Trial protocol	DK
Global end of trial date	01 August 2019

Results information

Result version number	v1 (current)
This version publication date	19 December 2020
First version publication date	19 December 2020

Trial information

Trial identification

Sponsor protocol code	01012014

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Copenhagen University Hospital, Righospitalet
Sponsor organisation address	Blegdamsvej 9, Copenhagen , Denmark, Dk-2100
Public contact	Rigshospitalet, Dept of Plastic Surgery, Breast Surgery & Burns, 45 35453545, Krysztof.T.Drzewiecki@regionh.dk
Scientific contact	Rigshospitalet, Dept of Plastic Surgery, Breast Surgery & Burns, 45 35453545, Krysztof.T.Drzewiecki@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	01 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 August 2019
Global end of trial reached?	Yes
Global end of trial date	01 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of the trial is to examine whether enrichment of a fat graft with autologous ASC injected into the breast tissue using traditional technique of 'small aliquot-injection' will significantly improve take of the graft and the result of a breast augmentation. The trial will compare fat grafting enriched with ex vivo expanded stem cells to the conventional fat grafting.

Protection of trial subjects:

Not relevant

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 December 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Ethical reason
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

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)	10
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In the process of screening potential participants for inclusion in the clinical study 306 potential candidates responded to our advertisements. Out of these potential candidates 221 women were excluded because they failed to meet the criteria of the study. Additionally 83 women either did not respond or declined to participate in the study.

Pre-assignment

Screening details:

Most frequent causes for exclusion during screening:
Breast ptosis
Large breasts
Participant not interested after detailed information about the study
Age below 30 or above 45
BMI below 22
Previous gastric bypass/gastric sleeve surgery
Familiy history of breast cancer

Pre-assignment period milestones

Number of subjects started	10
Number of subjects completed	10

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Blinding implementation details:

ASC enrichment was randomly allocated to the right or left breast of the included participants; their contralateral breast received non-enriched fat grafting (placebo). Allocation ratio between ASC enrichment and placebo was 1:1. The randomisation sequence was generated with www.randomization.com in a single block. An envelope for each participant was opened peroperatively behind a cover by a nurse who prepared the syringes with either ASC enricment or non-enriched fat according to the sequence.

Arms

Are arms mutually exclusive?	No
Arm title	ASC-enriched fat grafts

Arm description:

Fat grafts enriched with autologous ex-vivo expanded adipose-derived stromal cells, injected to the breast

Arm type	Experimental
Investigational medicinal product name	ex vivo expanded adipose-derived stromal cells
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution and suspension for suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

10 mio cells per mL fat graft, mixed with a fat graft peroperatively

Arm title	Non-enriched fat grafts (placebo)

Arm description:	
non-enriched normal fat grafts injected to the breast	
Arm type	Placebo
Investigational medicinal product name	normal fat graft
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

normal fat grafts injected to the breast, no cell enrichment

Number of subjects in period 1	ASC-enriched fat grafts	Non-enriched fat grafts (placebo)
Started	10	10
Completed	10	10

Baseline characteristics

Reporting groups	
Reporting group title	ASC-enriched fat grafts
Reporting group description:	
Fat grafts enriched with autologous ex-vivo expanded adipose-derived stromal cells, injected to the breast	
Reporting group title	Non-enriched fat grafts (placebo)
Reporting group description:	
non-enriched normal fat grafts injected to the breast	

Reporting group values	ASC-enriched fat grafts	Non-enriched fat grafts (placebo)	Total
Number of subjects	10	10	10
Age categorical Units: Subjects			
Adults (18-64 years)	10	10	20
Age continuous Units: years			
median	33	33	
inter-quartile range (Q1-Q3)	30.3 to 40.0	30.3 to 40.0	-
Gender categorical Units: Subjects			
Female	10	10	10
Male	0	0	0
Mean injected fat graft volume Units: millilitre(s)			
median	300	300	
inter-quartile range (Q1-Q3)	300 to 315	300 to 315	-

End points

End points reporting groups

Reporting group title	ASC-enriched fat grafts
Reporting group description:	
Fat grafts enriched with autologous ex-vivo expanded adipose-derived stromal cells, injected to the breast	
Reporting group title	Non-enriched fat grafts (placebo)
Reporting group description:	
non-enriched normal fat grafts injected to the breast	

Primary: 12 months fat graft retention

End point title	12 months fat graft retention
End point description:	
Residual volume of injected fat graft to the breast based on MRI	
End point type	Primary
End point timeframe:	
12 months post-op	

End point values	ASC-enriched fat grafts	Non-enriched fat grafts (placebo)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Percent				
arithmetic mean (confidence interval 95%)				
fat graft volume retention	54.0 (30.4 to 77.6)	55.9 (28.9 to 82.9)		

Statistical analyses

Statistical analysis title	Difference in mean retention, 12 months post-op
Statistical analysis description:	
Difference in mean retention, 12 months post-op	
Comparison groups	Non-enriched fat grafts (placebo) v ASC-enriched fat grafts
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence[1]
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-1.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.11
upper limit	5.31
Variability estimate	Standard error of the mean
Dispersion value	12.04

Notes:
[1] - paired t-test

Secondary: 4 months fat graft retention

End point title	4 months fat graft retention
End point description: based on MRI	
End point type	Secondary
End point timeframe: fat graft retention in the breast 4 months after surgery	

End point values	ASC-enriched fat grafts	Non-enriched fat grafts (placebo)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Percent				
arithmetic mean (confidence interval 95%)				
Fat graft volume retention	54.3 (39.4 to 69.2)	56.2 (42.7 to 69.6)		

Statistical analyses

Statistical analysis title	Difference in mean retention, 4 months post-op
Comparison groups	ASC-enriched fat grafts v Non-enriched fat grafts (placebo)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence[2]
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.86
upper limit	5.06
Variability estimate	Standard error of the mean
Dispersion value	7.6

Notes:

[2] - paired t-test

Secondary: Radiological changes in the breast after conventional and stem cell-enriched fat injection as based on mammography after 12 months

End point title	Radiological changes in the breast after conventional and stem cell-enriched fat injection as based on mammography after 12 months

End point description:

Radiological changes in the breast after conventional and stem cell-enriched fat injection as based on mammography after 12 months

End point type	Secondary

End point timeframe:

12 months post-op

End point values	ASC-enriched fat grafts	Non-enriched fat grafts (placebo)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Patients				
Oily cysts	9	9		
Fat necrosis	2	1		
Palpable changes	3	2		
Fine needle aspiration cytology + mammography/US	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Radiological changes in the breast after conventional and stem cell-enriched fat injection as based on MRI after lipoinjection to the breast after 4 months

End point title	Radiological changes in the breast after conventional and stem cell-enriched fat injection as based on MRI after lipoinjection to the breast after 4 months

End point description:

Radiological changes in the breast after conventional and stem cell-enriched fat injection as based on MRI four months after lipoinjection to the breast.

End point type	Secondary

End point timeframe:

4 months

End point values	ASC-enriched fat grafts	Non-enriched fat grafts (placebo)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Oily cysts				
Oily cysts	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Radiological changes in the breast after conventional and stem cell-enriched fat injection as based on MRI after lipoinjection to the breast after 12 months

End point title	Radiological changes in the breast after conventional and stem cell-enriched fat injection as based on MRI after lipoinjection to the breast after 12 months

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	ASC-enriched fat grafts	Non-enriched fat grafts (placebo)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Cysts				
Oily cysts	1	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Patients were assessed for adverse events after the study intervention 2 weeks, 4 months and 12 months postoperatively

Adverse event reporting additional description:

Assessment of adverse events took place at our outpatient clinic at Copenhagen University Hospital Rigshospitalet.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	1

Reporting groups

Reporting group title	All patients

Reporting group description: -

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)		
Renal and urinary disorders			
Urinary tract infection bacterial	Additional description: One trial participant had a urinary tract infection 11 months after study intervention and was admitted to intravenous antibiotics for two days. This event was assessed to have no relation to the intervention in the study.		
subjects affected / exposed	1 / 10 (10.00%)		
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

None reported