



Clinical trial results:

A Danish, single centre, double-blind, randomized study evaluating allogeneic adipose tissue derived mesenchymal stromal cell therapy to reduce primary graft dysfunction after lung transplantation.

A phase I-II study

Summary

EudraCT number	2019-004848-30
Trial protocol	DK
Global end of trial date	10 July 2023

Results information

Result version number	v1 (current)
This version publication date	05 October 2024
First version publication date	05 October 2024

Trial information

Trial identification

Sponsor protocol code	12.12.2019
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Rigshospitalet
Sponsor organisation address	Blegdamsvej 9, Copenhagen, Denmark, 2100
Public contact	Jens Kastrup, Rigshospitalet, 45 35452819, jens.kastrup@regionh.dk
Scientific contact	Jens Kastrup, Rigshospitalet, 45 35452819, jens.kastrup@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	10 July 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 July 2023
Global end of trial reached?	Yes
Global end of trial date	10 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate safety of treatment with allogeneic adipose tissue-derived mesenchymal stromal cells (ASCs) in patients undergoing lung transplantation, to evaluate whether the treatment can reduce host immunological reaction towards the graft, and to reduce the ischemic reperfusion-injury after transplantation.

Protection of trial subjects:

The study was approved by the National Committee on Health Research Ethics, the Danish Health and Medicines Agency and the Data Inspectorate. The study responsible persons had access to health care data from the patient's records. This information was important to ensure that the patients fulfil all the protocol criteria and approvals from the authorities.

The study was monitored by the GCP-unit, Capital region of Denmark. Representatives from these authorities and the responsible for the clinical trial had access to all patient and study data. This control ensured that the clinical study was conducted in accordance with the approved protocol

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 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: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	26
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Ten women and 20 men were treated with 200 million ASCs (n=10), 100 million ASCs (n=10) or saline infusion (n=10). No statistically significant differences in major baseline characteristics were observed between the three groups except in forced vital capacity and quality of life activity score. Randomization was performed using an online tool.

Pre-assignment

Screening details:

Thirty-one patients were included from December 2020 to April 2023. During transplantation, one patient developed an unexpected need for extra corporal membrane oxygenation and thus was excluded before ASC/placebo treatment according to the in- and exclusion criteria.

Period 1

Period 1 title	Inclusion period (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:

Patients were randomized in blocks of six using a web program RANDOM.ORG - List Randomizer [Internet]. <https://www.random.org/lists/>
CSCC was responsible for the randomization code and for preparing the cell product in infusion bag, to assure blinding of the treatment for the clinical team. It was not possible to see whether it was 200 or 100 million ASCs or placebo (saline) in the prepared infusion bag.

Arms

Are arms mutually exclusive?	Yes
Arm title	ASC 200

Arm description:

Patients receiving 200 million ASCs

Arm type	Experimental
Investigational medicinal product name	ASC_CSCC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Allogeneic 200 million ASCs

Arm title	ASC 100
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Arm description:

Patients receiving 100 mio. ASCs

Arm type	Experimental
Investigational medicinal product name	ASC_CSCC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Allogeneic 100 million ASCs

Arm title	Placebo
Arm description:	
Saline infusion	
Arm type	Placebo
Investigational medicinal product name	Isotonic saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Isotonic saline infusion	

Number of subjects in period 1	ASC 200	ASC 100	Placebo
Started	10	10	10
Completed	10	10	10

Baseline characteristics

Reporting groups

Reporting group title	ASC 200
Reporting group description: Patients receiving 200 million ASCs	
Reporting group title	ASC 100
Reporting group description: Patients receiving 100 mio. ASCs	
Reporting group title	Placebo
Reporting group description: Saline infusion	

Reporting group values	ASC 200	ASC 100	Placebo
Number of subjects	10	10	10
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Age in years			
Units: years			
arithmetic mean	55.5	59.6	55.6
standard deviation	± 6.8	± 5.6	± 6.2
Gender categorical			
Gender M/F			
Units: Subjects			
Female	4	3	3
Male	6	7	7

Reporting group values	Total		
Number of subjects	30		
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			
Age in years			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Gender M/F			
Units: Subjects			
Female	10		
Male	20		

Subject analysis sets

Subject analysis set title	overall
Subject analysis set type	Per protocol

Subject analysis set description:

Statistical analysis was performed using SPSS version 29 (SPSS Inc., Chicago, Illinois). Continuous variables are presented as mean±standard deviation and categorical variables are presented as numbers and percentages. Categorical data are compared using Fisher's exact or Chi-square test as appropriate. Analysis of variances (Anova) is used to compare more than two groups for normal data distribution. A two-sided P-value of <0.05 is considered statistically significant. It was predefined in the protocol that the ASC groups would be analysed alone and combined against the placebo group.

Reporting group values	overall		
Number of subjects	30		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Age in years			
Units: years			
arithmetic mean	56.9		
standard deviation	± 6.3		
Gender categorical			
Gender M/F			
Units: Subjects			
Female	10		
Male	20		

End points

End points reporting groups

Reporting group title	ASC 200
Reporting group description: Patients receiving 200 million ASCs	
Reporting group title	ASC 100
Reporting group description: Patients receiving 100 mio. ASCs	
Reporting group title	Placebo
Reporting group description: Saline infusion	
Subject analysis set title	overall
Subject analysis set type	Per protocol
Subject analysis set description: Statistical analysis was performed using SPSS version 29 (SPSS Inc., Chicago, Illinois). Continuous variables are presented as mean±standard deviation and categorical variables are presented as numbers and percentages. Categorical data are compared using Fisher's exact or Chi-square test as appropriate. Analysis of variances (Anova) is used to compare more than two groups for normal data distribution. A two-sided P-value of <0.05 is considered statistically significant. It was predefined in the protocol that the ASC groups would be analysed alone and combined against the placebo group.	

Primary: PGD

End point title	PGD
End point description: PGD was defined according to the International Society for Heart and Lung Transplantation (ISHLT) as pulmonary infiltrates and hypoxemia occurring in the first 72 hours after transplantation. PGD was graded every 24 hours during the first 72 hours after transplantation. Time started at reperfusion of the second lung. PGD was analysed and graded by two independent consultants with expertise in lung transplantations and blinded to the patient's treatment status. If there was disagreement in PGD, consensus had to be reached.	
End point type	Primary
End point timeframe: 72 hours	

End point values	ASC 200	ASC 100	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: noon unit				
number (not applicable)	10	7	14	

Statistical analyses

Statistical analysis title	Per protocol
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Statistical analysis description:

Statistical analysis was performed using SPSS version 29 (SPSS Inc., Chicago, Illinois). Continuous variables are presented as mean±standard deviation and categorical variables are presented as numbers and percentages. Categorical data are compared using Fisher's exact or Chi-square test as appropriate. Analysis of variances (Anova) is used to compare more than two groups for normal data distribution. A two-sided P-value of <0.05 is considered statistically significant. It was predefined in the p

Comparison groups	ASC 200 v ASC 100 v Placebo
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Confidence interval	
level	90 %
sides	2-sided
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Final follow-up after 3 months

Adverse event reporting additional description:

Please see SAE section

Assessment type	Systematic
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Dictionary used

Dictionary name	Danish authorities
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Dictionary version	1
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Reporting groups

Reporting group title	ASC 200
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Reporting group description:

Patients receiving 200 million ASCs

Reporting group title	ASC 100
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Reporting group description:

Patients receiving 100 mio. ASCs

Reporting group title	Placebo
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Reporting group description:

Saline infusion

Serious adverse events	ASC 200	ASC 100	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 10 (60.00%)	4 / 10 (40.00%)	5 / 10 (50.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Cardiomyopathy acute	Additional description: Takotsubo cardiomyopathy		
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Acute cellular rejection	Additional description: Acute cellular rejection		
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 7	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastric ulcer			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Death			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pleural effusion	Additional description: Recurrent pleural effusion		
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
recurrent laryngeal nervous paresis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diaphragmatic disorder	Additional description: Diaphragm paralysis		
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Breast abscess			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Pneumonia	Additional description: pneumonia, bacterial, viral and fungal		
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 3	0 / 10	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	ASC 200	ASC 100	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
Respiratory, thoracic and mediastinal disorders			
Breast abscess	Additional description: Please see SAE section		
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

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.

A small phase I/II trial

Notes: