



## Clinical trial results:

### Intravenous immunoglobulin and prednisolone to women with unexplained recurrent pregnancy loss after assisted reproductive technology treatment: a randomised, double-blind, placebo-controlled trial

#### Summary

EudraCT number	2020-000256-35
Trial protocol	DK
Global end of trial date	18 April 2024

#### Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

#### Trial information

##### Trial identification

Sponsor protocol code	CNPOBC2020
-----------------------	------------

##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04701034
WHO universal trial number (UTN)	U1111-1273-8585

Notes:

#### Sponsors

Sponsor organisation name	Aalborg University Hospital
Sponsor organisation address	Reberbansgade 15, Aalborg, Denmark, 9000
Public contact	Ole B. Christiansen, Aalborg University Hospital , +45 26821960, olbc@rn.dk
Scientific contact	Ole B. Christiansen, Aalborg University Hospital , +45 26821960, olbc@rn.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	28 June 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 April 2024
Global end of trial reached?	Yes
Global end of trial date	18 April 2024
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

In a randomized, double-blinded placebo-controlled trial we aim to investigate whether treatment with prednisolone and IVIg before and in early pregnancy improves the chance of a live birth in women undergoing treatment with artificial reproductive technologies (ART) after previous recurrent pregnancy losses after ART.

Protection of trial subjects:

The study has been conducted in accordance with ICH-GCP guideline

Background therapy:

Intravenous immunoglobulin (Privigen 10%) 25-35g per infusion at the time of embryo transfer and maximum 3 times in early pregnancy or similar intravenous placebo (human Albumin 5%) given after same protocol in addition to 5-10 g prednisolone or similar placebo tablets given daily from start of ART cycle to gestational week 8 in participants who became pregnant

Evidence for comparator:

The comparators (Human Albumin and oral placebo) had similar visual appearance as the active drugs (Privigen and prednisolone) and were given with same doses and frequency as the active drugs.

Actual start date of recruitment	28 January 2021
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: 80
Worldwide total number of subjects	80
EEA total number of subjects	80

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)	80
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Patients with  $\geq 2$  consecutive early pregnancy losses after ART treatment who were referred to the Centre for Recurrent Pregnancy Loss of Western Denmark between 28th January 2021 and 23rd February 2024

### Pre-assignment

Screening details:

All patients were screened for uterine anomalies by hysteroscopy, water hysterosonography or 3D vaginal ultrasound and in addition they were screened for a series of antiphospholipid antibodies, thyroid dysfunction by TSH, ovarian insufficiency by anti-Müllerian hormone and total IgA was measured to detect possible IgA deficiency

### 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, Monitor, Data analyst, Carer

Blinding implementation details:

The randomization list was only held at the Hospital Pharmacy of the North Denmark Region, Aalborg and at the Department of Clinical Immunology, Aalborg University Hospital, which were the two sites preparing the oral and intravenous trial drugs. The investigators, caretakers, monitors and patients had no access to the list, The active trial drugs and the placebos had complete similar appearances.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Intravenous immunoglobulin and prednisolone

Arm description:

A maximum of 4 Privigen infusions from time of embryo transfer and to gestational week 7 of pregnancy and prednisolone tablets from start of ART cycle to gestational week 8 in pregnant participants

Arm type	Experimental
Investigational medicinal product name	privigen
Investigational medicinal product code	J06BA02
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

Information provided previously

Investigational medicinal product name	prednisolone
Investigational medicinal product code	H02AB06
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Information provided previously

<b>Arm title</b>	Intravenous (Human Albumin) and peroral placebo
------------------	---

Arm description:

A maximum of 4 albumin infusions from time of embryo transfer and to gestational week 7 of pregnancy and placebo tablets from start of ART cycle to gestational week 8 in pregnant participants

Arm type	Placebo
----------	---------

Investigational medicinal product name	Albumin
Investigational medicinal product code	B05AA01
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use
Dosage and administration details:	
Information provided previously	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

0 mg coated tablet administered daily from the start of the ART cycle to gestational week 8.

<b>Number of subjects in period 1</b>	Intravenous immunoglobulin and prednisolone	Intravenous (Human Albumin) and peroral placebo
Started	40	40
Completed	37	37
Not completed	3	3
Protocol deviation	3	3

## Baseline characteristics

### Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	80	80	
Age categorical Units: Subjects			
Adults (18-64 years)	80	80	
Age continuous Units: years median inter-quartile range (Q1-Q3)	34.75 30.5 to 37.25	-	
Gender categorical Units: Subjects			
Female	80	80	
Male	0	0	
Number of previous consecutive pregnancy losses Units: number median inter-quartile range (Q1-Q3)		-	

### Subject analysis sets

Subject analysis set title	ARM 1 Experimental
Subject analysis set type	Per protocol
Subject analysis set description: Per protocol 1	
Subject analysis set title	ARM 2 (Placebo)
Subject analysis set type	Per protocol
Subject analysis set description: Per protocol 2	

Reporting group values	ARM 1 Experimental	ARM 2 (Placebo)	
Number of subjects	37	37	
Age categorical Units: Subjects			
Adults (18-64 years)	37	37	
Age continuous Units: years median inter-quartile range (Q1-Q3)	33.5 30.0 to 37.0	35.0 31.0 to 37.5	
Gender categorical Units: Subjects			
Female	40	40	
Male	0	0	

Number of previous consecutive pregnancy losses			
Units: number			
median	3	4	
inter-quartile range (Q1-Q3)	3 to 4	3 to 4	

---

## End points

### End points reporting groups

Reporting group title	Intravenous immunoglobulin and prednisolone
Reporting group description: A maximum of 4 Privigen infusions from time of embryo transfer and to gestational week 7 of pregnancy and prednisolone tablets from start of ART cycle to gestational week 8 in pregnant participants	
Reporting group title	Intravenous (Human Albumin) and peroral placebo
Reporting group description: A maximum of 4 albumin infusions from time of embryo transfer and to gestational week 7 of pregnancy and placebo tablets from start of ART cycle to gestational week 8 in pregnant participants	
Subject analysis set title	ARM 1 Experimental
Subject analysis set type	Per protocol
Subject analysis set description: Per protocol 1	
Subject analysis set title	ARM 2 (Placebo)
Subject analysis set type	Per protocol
Subject analysis set description: Per protocol 2	

### Primary: Ongoing pregnancy rates in all participants and among those who conceived

End point title	Ongoing pregnancy rates in all participants and among those who conceived
End point description:	
End point type	Primary
End point timeframe: End of study	

End point values	Intravenous immunoglobulin and prednisolone	Intravenous (Human Albumin) and peroral placebo	ARM 1 Experimental	ARM 2 (Placebo)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	40	40	40	40
Units: number				
Category 1: Number of ongoing pregnancies/all part	10	6	10	6
Category 2: Number of ongoing pregnancies /partici	10	6	10	6

### Statistical analyses

Statistical analysis title	Ongoing pregnancy rate in reporting group 1 vs rep
Statistical analysis description: Chi-square analysis	
Comparison groups	ARM 1 Experimental v ARM 2 (Placebo)



Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.26
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	4.15
Variability estimate	Standard deviation

<b>Statistical analysis title</b>	Ongoing pregnancy rate in reporting group 1 vs rep
Comparison groups	ARM 1 Experimental v ARM 2 (Placebo)
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	3.75

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the first day of taking study medicine until 6 months after last intravenous infusion in participants not achieving pregnancy or until the day of delivery in pregnant participants

Assessment type	Systematic
-----------------	------------

### Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	28
--------------------	----

### Reporting groups

Reporting group title	Reporting group 1
-----------------------	-------------------

Reporting group description:

Active treatment

Reporting group title	Reporting group 2
-----------------------	-------------------

Reporting group description:

Placebo treatment

Serious adverse events	Reporting group 1	Reporting group 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 37 (2.70%)	1 / 37 (2.70%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Pregnancy, puerperium and perinatal conditions			
Vaginal haemorrhage in gestational week 11	Additional description: The pregnancy continued		
subjects affected / exposed	1 / 37 (2.70%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postpartum chorioamnionitis in the mother and newborn child	Additional description: Both recovered without sequelae		
subjects affected / exposed	1 / 37 (2.70%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postpartum seizures and signs of cerebral ischemia in the child	Additional description: The child is one year old healthy without signs of brain damage		
subjects affected / exposed	0 / 37 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

<b>Non-serious adverse events</b>	Reporting group 1	Reporting group 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 37 (54.05%)	16 / 37 (43.24%)	
Pregnancy, puerperium and perinatal conditions			
Potentially infusion-related	Additional description: Headache, fatigue, nausea, skin rash, dizziness, flu-like symptoms, muscle/joint pain		
subjects affected / exposed	20 / 37 (54.05%)	16 / 37 (43.24%)	
occurrences (all)	20	16	
Nervous system disorders			
Event term Potentially tablet-related	Additional description: Insomnia, mood-swings		
subjects affected / exposed	6 / 37 (16.22%)	1 / 37 (2.70%)	
occurrences (all)	6	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