Clinical trial results:
Phase III, Open-label, Uncontrolled, Multicenter Study to Assess Efficacy, Pharmacokinetics and Safety of IMMUNORHO in the Prevention of RhD Isoimmunization in Rh(D) negative Women Pregnant with Rh(D) positive Foetuses

Summary

EudraCT number	2020-003570-49
Trial protocol	HU CZ PL IT
Global end of trial date	23 March 2024

Results information

Result version number	v1 (current)
This version publication date	26 March 2025
First version publication date	26 March 2025
Summary attachment (see zip file)	Pharmacokinetics (PK) Results (Pop-PK report for EudraCT submission.pdf)

Trial information

Trial identification

Sponsor protocol code	KB065

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Kedrion S.p.A.
Sponsor organisation address	Loc. Ai Conti, Castelvecchio Pascoli, Barga (LU), Italy, 55051
Public contact	Clinical Trial Manager, Kedrion S.p.A., +39 0538767324, a.lotti@kedrion.com
Scientific contact	Clinical Trial Manager, Kedrion S.p.A., +39 0538767324, a.lotti@kedrion.com

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	14 June 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 March 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Efficacy objective: To assess the efficacy of IMMUNORHO in the prevention of Rh(D) isoimmunization in Rh(D) negative women pregnant with a Rh(D) positive foetus (including D, Dweak and Dpartial), as measured by the incidence rate of anti-D antibodies at 24 weeks (corresponding to the 6 months timepoint in the EMA guideline) after last treatment administered.

Safety objective: To assess the safety of IMMUNORHO in the prevention of Rh(D) isoimmunization in Rh(D) negative women pregnant with a Rh(D) positive foetus (including D, Dweak and Dpartial) from baseline visit to 24 weeks (corresponding to 6 months) after last treatment administered.

Pharmacokinetic objective: To characterize the pharmacokinetics (PK) of anti-D immunoglobulins after IMMUNORHO administration in Rh(D) negative pregnant women.

Protection of trial subjects:

This study was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines including the Declaration of Helsinki, Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines, applicable International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines, and other applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 March 2021
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	Poland: 137
Country: Number of subjects enrolled	Czechia: 29
Country: Number of subjects enrolled	Hungary: 48
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Russian Federation: 24
Worldwide total number of subjects	255
EEA total number of subjects	231

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)	255
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted between 31-March-2021 (first subject first visit) to 23-March-2024 (last subject last visit) at 21 initiated study sites, of which 20 sites recruited subjects in Europe and Russia.

Pre-assignment

Screening details:

The screening visit was performed between Week 25 (day 0-6) up to Week 26 (day 0-6) of pregnancy. In total, 504 subjects were screened for the study. Out of this, 255 were enrolled and 249 were screen failed subjects.
Subjects who met the inclusion criteria and none of the exclusion criteria were enrolled to the study.

Period 1

Period 1 title	Baseline (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	BMI Group 1

Arm description:

Non-obese subjects (BMI < 30 kg/m²) received IMMUNORHO as an intramuscular injection both antenatal [at Week 28 (from day0 to day7) of pregnancy] and postnatal (within 72 hours after delivery).

Arm type	Experimental
Investigational medicinal product name	IMMUNORHO
Investigational medicinal product code	
Other name	Human Anti-D Immunoglobulin
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

IMMUNORHO was provided as a single dose (2 mL solution) pre-filled syringe for intramuscular injection administration both antenatal and postnatal.

Arm title	BMI Group 2

Arm description:

Obese subjects (BMI ≥ 30 kg/m²) received IMMUNORHO as an intramuscular injection both antenatal [at Week 28 (from day0 to day7) of pregnancy] and postnatal (within 72 hours after delivery).

Arm type	Experimental
Investigational medicinal product name	IMMUNORHO
Investigational medicinal product code	
Other name	Human Anti-D Immunoglobulin
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

IMMUNORHO was provided as a single dose (2 mL solution) pre-filled syringe for intramuscular injection administration both antenatal and postnatal.

Number of subjects in period 1[1]	BMI Group 1	BMI Group 2
Started	206	48
Completed	164	40
Not completed	42	8
Consent withdrawn by subject	11	2
Other	8	-
Use of another Anti-D immunoglobulin	18	4
Lost to follow-up	5	2

Notes:

[1] - 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: One treated subject did not have a baseline height reported, therefore, the BMI of that subject could not be calculated. That subject was not assigned to either BMI group but was included in the Overall Treatment population.

Baseline characteristics

Reporting groups	
Reporting group title	BMI Group 1
Reporting group description:	
Non-obese subjects (BMI < 30 kg/m²) received IMMUNORHO as an intramuscular injection both antenatal [at Week 28 (from day0 to day7) of pregnancy] and postnatal (within 72 hours after delivery).	
Reporting group title	BMI Group 2
Reporting group description:	
Obese subjects (BMI ≥ 30 kg/m²) received IMMUNORHO as an intramuscular injection both antenatal [at Week 28 (from day0 to day7) of pregnancy] and postnatal (within 72 hours after delivery).	

Reporting group values	BMI Group 1	BMI Group 2	Total
Number of subjects	206	48	254
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)	206	48	254
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	32.2	33.1	
standard deviation	± 4.71	± 5.43	-
Gender categorical Units: Subjects			
Female	206	48	254
Male	0	0	0

End points

End points reporting groups

Reporting group title	BMI Group 1

Reporting group description:

Non-obese subjects (BMI < 30 kg/m²) received IMMUNORHO as an intramuscular injection both antenatal [at Week 28 (from day0 to day7) of pregnancy] and postnatal (within 72 hours after delivery).

Reporting group title	BMI Group 2

Reporting group description:

Obese subjects (BMI ≥ 30 kg/m²) received IMMUNORHO as an intramuscular injection both antenatal [at Week 28 (from day0 to day7) of pregnancy] and postnatal (within 72 hours after delivery).

Primary: Incidence rate of anti-D antibodies at 24 weeks after treatment

End point title	Incidence rate of anti-D antibodies at 24 weeks after

End point description:

Prevention of Isoimmunization at 24 weeks (Corresponding to 6 months timepoint in EMA Guideline) was measured by the "Incidence of Anti-D Antibodies using the Indirect Antiglobulin (Coombs) Test.
The full analysis set (FAS) comprised all subjects that successfully met the Inclusion/Exclusion Criteria and were cleared for treatment by the investigator. The FAS was based upon the Intention-to-Treat principle.

Based on the observed data, of 201 subjects with Coombs test results, there were 0 active immunizations due to anti-D antibodies. There were 7 passive immunizations (including one with missing data at 24 weeks where results were imputed from the 12-week results); these were weak detectable anti-D antibodies reported with an anti-D antibody titration value of <2. Due to no alloimmunization events, incidence rate of alloimmunization and its associated 95% CI were not analysed.

End point type	Primary

End point timeframe:

At 24 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no events of alloimmunisation identified, therefore the incidence rate of alloimmunisation and its associated 95% CI were not analysed. Hence, no statistical analysis was performed for this endpoint.

End point values	BMI Group 1	BMI Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	40		
Units: Subjects				
Actively Immunized	0	0		
Passively Immunized	6	0		
Not Applicable	155	40		
Missing	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence rate of anti-D antibodies at 12 weeks after treatment

End point title	Incidence rate of anti-D antibodies at 12 weeks after treatment

End point description:

Prevention of Isoimmunization at 12 weeks (Corresponding to 3 months timepoint in EMA Guideline) was measured by the "Incidence of Anti-D Antibodies using the Indirect Antiglobulin (Coombs) Test.
The FAS comprised all subjects that successfully met the Inclusion/Exclusion Criteria and were cleared for treatment by the investigator. The FAS was based upon the Intention-to-Treat principle.

Based on observed data, of 185 subjects with Coombs test results, there were 0 active immunisations due to anti-D antibodies. There were 146 passive immunisations; these were weak detectable anti-D antibodies reported with an anti-D antibody titration value of <2. Due to no alloimmunisation events, incidence rate of alloimmunisation and its associated 95% CI were not analysed.

End point type	Secondary

End point timeframe:

At 12 weeks

End point values	BMI Group 1	BMI Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	36		
Units: Subjects				
Actively Immunized	0	0		
Passively Immunized	124	22		
Not Applicable	24	14		
Missing	4	1		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of subjects with adverse events (AEs) and serious AEs

End point title	Number of subjects with adverse events (AEs) and serious AEs

End point description:

The safety analysis set (SAF) comprised all subjects who had received at least one dose of study medication. In this study, the SAF and FAS were coincident as no randomization occurred.
The safety of IMMUNORHO in the prevention of Rh(D) isoimmunisation in Rh(D) negative women pregnant with a Rh(D) positive foetus (including D, Dweak and Dpartial) from Baseline visit to 24 weeks (corresponding to 6 months) after last treatment administered was assessed.
A related TEAE was a TEAE with Related, Certainly Related, Probably Related, or Possibly Related as relationship to study drug.

End point type	Other pre-specified

End point timeframe:

Baseline [(Week 28 (from day 0 to day 7) of pregnancy] to 24 weeks after last dose administered

End point values	BMI Group 1	BMI Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	48		
Units: Subjects				
AE	123	33		
Treatment Emergent AE (TEAE)	121	32		
Treatment Related TEAE	4	0		
Study Procedure Related TEAE	0	0		
TEAE due to Potentially sensitising event (PSE)	4	0		
TEAE of Special Interest	9	2		
TEAE about Worsening from a Pre-existing Condition	1	2		
Serious AEs (SAEs)	48	16		
AE leading to Death	0	0		
AE Leading to Study Discontinuation	1	0		
AE Leading to Hospitalisation	24	6		
AE Leading to Study Drug Withdrawal	1	0		
AE Leading to Study Drug Dose Delayed	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline [(Week 28 (from day 0 to day 7) of pregnancy] to 24 weeks after last dose administered

Adverse event reporting additional description:

The SAF comprised all subjects who had received at least one dose of study medication. In this study, the SAF and FAS were coincident as no randomization occurred.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	BMI Group 2

Reporting group description:

Obese subjects received IMMUNORHO as an intramuscular injection both antenatal [at Week 28 (from day0 to day7) of pregnancy] and postnatal (within 72 hours after delivery).

Reporting group title	BMI Group 1

Reporting group description:

Non-obese subjects received IMMUNORHO as an intramuscular injection both antenatal [at Week 28 (from day0 to day7) of pregnancy] and postnatal (within 72 hours after delivery).

Serious adverse events	BMI Group 2	BMI Group 1	
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 48 (35.42%)	51 / 206 (24.76%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Vascular disorders			
Venous thrombosis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial rupture			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Meconium in amniotic fluid			

subjects affected / exposed	1 / 48 (2.08%)	5 / 206 (2.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Threatened labour			
subjects affected / exposed	1 / 48 (2.08%)	4 / 206 (1.94%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gestational hypertension			
subjects affected / exposed	1 / 48 (2.08%)	2 / 206 (0.97%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gestational diabetes			
subjects affected / exposed	3 / 48 (6.25%)	6 / 206 (2.91%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oligohydramnios			
subjects affected / exposed	0 / 48 (0.00%)	3 / 206 (1.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature separation of placenta			
subjects affected / exposed	0 / 48 (0.00%)	3 / 206 (1.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix dystocia			
subjects affected / exposed	1 / 48 (2.08%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal growth restriction			
subjects affected / exposed	0 / 48 (0.00%)	2 / 206 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
High risk pregnancy			

subjects affected / exposed	0 / 48 (0.00%)	2 / 206 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prolonged labour			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical cord around neck			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical cord compression			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine atony			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature rupture of membranes			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature labour			
subjects affected / exposed	1 / 48 (2.08%)	0 / 206 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature delivery			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyhydramnios			

subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Placental insufficiency			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Placenta accreta			
subjects affected / exposed	1 / 48 (2.08%)	0 / 206 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperemesis gravidarum			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal arm prolapse			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pre-eclampsia			
subjects affected / exposed	2 / 48 (4.17%)	0 / 206 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine hypotonus			
subjects affected / exposed	1 / 48 (2.08%)	0 / 206 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			

Neonatal asphyxia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Foetal monitoring abnormal			
subjects affected / exposed	0 / 48 (0.00%)	2 / 206 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal heart rate abnormal			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Uterine rupture			
subjects affected / exposed	0 / 48 (0.00%)	2 / 206 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electric shock			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulvovaginal injury			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Foetal heart rate deceleration abnormality			
subjects affected / exposed	4 / 48 (8.33%)	4 / 206 (1.94%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia foetal			

subjects affected / exposed	1 / 48 (2.08%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia foetal			
subjects affected / exposed	1 / 48 (2.08%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombocytosis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 206 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia of pregnancy			
subjects affected / exposed	1 / 48 (2.08%)	0 / 206 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deafness neurosensory			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal rigidity			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholestasis of pregnancy			

subjects affected / exposed	1 / 48 (2.08%)	2 / 206 (0.97%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 48 (0.00%)	2 / 206 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Urinary tract infection bacterial			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometritis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 48 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	BMI Group 2	BMI Group 1	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 48 (39.58%)	55 / 206 (26.70%)	
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	7 / 48 (14.58%)	18 / 206 (8.74%)	
occurrences (all)	8	21	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 48 (6.25%)	18 / 206 (8.74%)	
occurrences (all)	3	49	

Pregnancy, puerperium and perinatal conditions			
Gestational hypertension			
subjects affected / exposed	4 / 48 (8.33%)	0 / 206 (0.00%)	
occurrences (all)	4	0	
Afterbirth pain			
subjects affected / exposed	3 / 48 (6.25%)	15 / 206 (7.28%)	
occurrences (all)	3	15	
Blood and lymphatic system disorders			
Anaemia of pregnancy			
subjects affected / exposed	4 / 48 (8.33%)	17 / 206 (8.25%)	
occurrences (all)	4	17	
Anaemia			
subjects affected / exposed	3 / 48 (6.25%)	5 / 206 (2.43%)	
occurrences (all)	3	5	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	3 / 48 (6.25%)	5 / 206 (2.43%)	
occurrences (all)	3	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2021	o Clarifications added regarding standard of care procedures for PSEs and FMH across different countries/sites. o Added collection of subject's height and weight at baseline to calculate BMI, as requested by Russian Ministry of Health. o Specified that anti-D antibody testing includes indirect antiglobulin test, red blood cell alloantibodies identification, and anti-D titration/microtitration. o Added reporting of Coronavirus Disease 2019 (COVID-19) related AEs as an Adverse Event of Special Interest (AESI). o Added section on collecting AEs in neonates/breastfeeding infants exposed to the study drug. o Clarified definition of EOS as Last Patient Last Visit. o Added details on handling of PK samples and analysis. o Removed planned interim analysis. o Clarified that missing data will not be imputed for primary/secondary efficacy analyses. o Added analysis by BMI groups (obese vs non-obese) for efficacy endpoints. o Made minor wording changes and corrections throughout to improve clarity.
13 May 2022	o Enrolment period of the study was prolonged. o Number of subjects to be screened was increased due to the high screening failure rate. o Added the possibility to use the Home Health Care agency. o Some clarifying wording for visits description added.
27 July 2022	o Contact information: A new Sponsor's Medical Expert had been appointed for the study, and their contact details were added. o Blood typing correction: References to "ABO/RhD" have been changed to just "RhD" throughout the document (Tables 1-4, Sections 2.3, 7.2.3, 8.1, and 9.2). o Clarification in Section 7.2.3: A statement was added to clarify the exception of ABO/RhD blood group testing for mothers, fathers, and newborns.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported