Clinical trial results:
A Single-blind, Placebo-controlled, Single-center Study Investigating the Dose of Human Anti-Human Platelet Antigen (HPA)-1a Immune Globulin (NAITgam) Needed to Eliminate HPA-1a Positive Platelets Transfused to HPA-1a Negative Healthy Male Volunteers

Summary

EudraCT number	2019-003459-12
Trial protocol	DE
Global end of trial date	04 April 2022

Results information

Result version number	v1 (current)
This version publication date	11 October 2024
First version publication date	11 October 2024

Trial information

Trial identification

Sponsor protocol code	RB-NAIT-01-01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Rallybio IPA, LLC
Sponsor organisation address	234 Church Street, New Haven, United States, Suite 1020
Public contact	Head of Regulatory and Quality, Rallybio IPA, LLC, regulatory@rallybio.com
Scientific contact	Head of Regulatory and Quality, Rallybio IPA, LLC, regulatory@rallybio.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	04 April 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 April 2022
Global end of trial reached?	Yes
Global end of trial date	04 April 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To establish the dose of human anti-human platelet antigen (HPA)-1a immune globulin (NAITgam) needed to markedly (10-fold or greater) accelerate the clearance of HPA-1a positive platelets transfused to HPA-1a negative healthy volunteers

Protection of trial subjects:
Not Applicable
Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	21 September 2020
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	Germany: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	12
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Results from Cohorts 1 and 1B demonstrated that 1,000 IU NAITgam markedly accelerated the elimination of transfused platelets compared to placebo (10-fold or greater) and that proof of concept (PoC) criteria were met. It was determined by the sponsor that Cohorts 2 and 3 were not required and study was terminated following completion of Cohort 1B.

Pre-assignment

Screening details:

A total of 12 participants were enrolled at a single site in Germany.

Pre-assignment period milestones

Number of subjects started	12
Number of subjects completed	12

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 NAITgm 1000 IU

Arm description:

Participants received a single IV dose of NAITgam 1000 IU on Day 1 that was administered 1 hour following completion of a HPA-1a positive platelet transfusion, followed by a 24-week safety follow-up period.

Arm type	Experimental
Investigational medicinal product name	NAITgam
Investigational medicinal product code	
Other name	Human Anti-Human Platelet Antigen (HPA)-1a Immune Globulin
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intravenous use

Dosage and administration details:

Participants received a single IV dose of NAITgam 1000 IU.

Arm title	Cohort 1B NAITgam 1000 IU

Arm description:

Participants received a single IV dose of NAITgam 1000 IU on Day 1 followed by a HPA-1a positive platelet transfusion on Day 8, with a 25-week safety follow-up period from day of NAITgam administration.

Arm type	Experimental
Investigational medicinal product name	NAITgam
Investigational medicinal product code	
Other name	Human Anti-Human Platelet Antigen (HPA)-1a Immune Globulin
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intravenous use

Dosage and administration details:

Participants received a single IV dose of NAITgam 1000 IU.

Arm title	Cohort 1 and Cohort 1B Placebo

Arm description:

Cohort 1: Participants received a single IV administration of placebo 1 hour following completion of a HPA-1a positive platelet transfusion, followed by a 24-week safety follow-up period.
Cohort 1B: Participants received a single IV administration of placebo on Day 1 followed by a HPA-1a positive platelet transfusion on Day 8, with a 25-week follow- up period from day of placebo administration.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Sodium chloride injection, 0.9% (saline)
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants received a single administration of placebo IV.

Number of subjects in period 1	Cohort 1 NAITgm 1000 IU	Cohort 1B NAITgam 1000 IU	Cohort 1 and Cohort 1B Placebo
Started	6	3	3
Completed	6	3	3

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1 NAITgm 1000 IU
Reporting group description:	
Participants received a single IV dose of NAITgam 1000 IU on Day 1 that was administered 1 hour following completion of a HPA-1a positive platelet transfusion, followed by a 24-week safety follow-up period.	
Reporting group title	Cohort 1B NAITgam 1000 IU
Reporting group description:	
Participants received a single IV dose of NAITgam 1000 IU on Day 1 followed by a HPA-1a positive platelet transfusion on Day 8, with a 25-week safety follow-up period from day of NAITgam administration.	
Reporting group title	Cohort 1 and Cohort 1B Placebo
Reporting group description:	
Cohort 1: Participants received a single IV administration of placebo 1 hour following completion of a HPA-1a positive platelet transfusion, followed by a 24-week safety follow-up period. Cohort 1B: Participants received a single IV administration of placebo on Day 1 followed by a HPA-1a positive platelet transfusion on Day 8, with a 25-week follow- up period from day of placebo administration.	

Reporting group values	Cohort 1 NAITgm 1000 IU	Cohort 1B NAITgam 1000 IU	Cohort 1 and Cohort 1B Placebo
Number of subjects	6	3	3
Age categorical Units: Subjects			
Adults (18-64 years)	6	3	3
Age continuous Units: years			
arithmetic mean	46.8	46.7	39.0
standard deviation	± 11.27	± 12.50	± 17.09
Gender categorical Units: Subjects			
Male	6	3	3
Race Units: Subjects			
White	6	3	3

Reporting group values	Total		
Number of subjects	12		
Age categorical Units: Subjects			
Adults (18-64 years)	12		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Male	12		

Race Units: Subjects			
White	12		

End points

End points reporting groups

Reporting group title	Cohort 1 NAITgm 1000 IU
Reporting group description:	
Participants received a single IV dose of NAITgam 1000 IU on Day 1 that was administered 1 hour following completion of a HPA-1a positive platelet transfusion, followed by a 24-week safety follow-up period.	
Reporting group title	Cohort 1B NAITgam 1000 IU
Reporting group description:	
Participants received a single IV dose of NAITgam 1000 IU on Day 1 followed by a HPA-1a positive platelet transfusion on Day 8, with a 25-week safety follow-up period from day of NAITgam administration.	
Reporting group title	Cohort 1 and Cohort 1B Placebo
Reporting group description:	
Cohort 1: Participants received a single IV administration of placebo 1 hour following completion of a HPA-1a positive platelet transfusion, followed by a 24-week safety follow-up period. Cohort 1B: Participants received a single IV administration of placebo on Day 1 followed by a HPA-1a positive platelet transfusion on Day 8, with a 25-week follow- up period from day of placebo administration.	

Primary: Elimination half-life (t 1/2) of transfused HPA-1a positive platelets

End point title	Elimination half-life (t 1/2) of transfused HPA-1a positive platelets[1]
End point description:	
Half-life of transfused HPA-1a positive platelets in circulation in HPA-1a negative participants after IV administration of NAITgam or placebo, determined by flow cytometry. Proof of concept was elimination of HPA-1a positive platelets by 10-fold or greater compared to placebo, as defined by platelet elimination half-life.	
End point type	Primary
End point timeframe:	
Cohort 1: Day 1 to Day 8 Cohort 1B: Day 8 to Day 15	

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: No statistical analysis was performed for this endpoint.

End point values	Cohort 1 NAITgm 1000 IU	Cohort 1B NAITgam 1000 IU	Cohort 1 and Cohort 1B Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	3	3	
Units: Hours				
median (full range (min-max))	0.33 (0.28 to 0.37)	0.59 (0.42 to 2.60)	59.94 (49.34 to 71.11)	

Statistical analyses

No statistical analyses for this end point

Secondary: Serious treatment emergent adverse events (serious TEAEs) and non-serious TEAEs

End point title	Serious treatment emergent adverse events (serious TEAEs) and non-serious TEAEs

End point description:

Treatment-emergent adverse events (TEAEs) were defined as adverse events that occurred from the time of study drug administration through 25 weeks of follow-up. The incidence of TEAEs were reported by seriousness (serious and non-serious). Safety analysis set (SAS) comprised of all participants randomly assigned to study intervention and who received platelets and/or study drug.

End point type	Secondary

End point timeframe:

Cohort 1: 24 weeks from day of study drug administration
Cohort 1B: 25 weeks from day of study drug administration

End point values	Cohort 1 NAITgm 1000 IU	Cohort 1B NAITgam 1000 IU	Cohort 1 and Cohort 1B Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	3	3	
Units: Participants				
number (not applicable)				
Serious TEAEs	0	0	0	
non-Serious TEAEs	5	3	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Vital signs, clinical laboratory values and electrocardiogram (ECG)

End point title	Vital signs, clinical laboratory values and electrocardiogram (ECG)

End point description:

Vital signs included pulse rate and blood pressure measurements. Clinical laboratory evaluations included of hematology, clinical chemistry, coagulation, and urinalysis; ECGs

End point type	Secondary

End point timeframe:

Cohort 1: 24 weeks from day of study drug administration
Cohort 1B: 25 weeks from day of study drug administration

End point values	Cohort 1 NAITgm 1000 IU	Cohort 1B NAITgam 1000 IU	Cohort 1 and Cohort 1B Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	3	3	
Units: Participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment for anti-HPA-1a Alloantibodies

End point title	Assessment for anti-HPA-1a Alloantibodies

End point description:

Assessment for alloimmune response to HPA-1a positive platelets.

End point type	Secondary

End point timeframe:

Cohort 1: 24 weeks from day of study drug administration
Cohort 1B: 25 weeks from day of study drug administration

End point values	Cohort 1 NAITgm 1000 IU	Cohort 1B NAITgam 1000 IU	Cohort 1 and Cohort 1B Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	3	3	
Units: Participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Cohort 1: 24 weeks from day of study drug administration
Cohort 1B: 25 weeks from day of study drug administration

Adverse event reporting additional description:

Serious TEAEs and TEAEs were collected based on all participants randomly assigned to study intervention and who received platelets and/or study drug.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Cohort 1 1000 International Units (IU) NAITgam

Reporting group description:

Participants received 1000 IU NAITgam IV 1 hour after completion of HPA-1a positive platelet transfusion on Day 1, with a 24-week follow-up period.

Reporting group title	Cohort 1B 1000 IU NAITgam

Reporting group description:

Participants received 1000 IU NAITgam IV 7 days prior to HPA-1a positive platelet transfusion, with a 25-week follow-up period from day of NAITgam administration.

Reporting group title	Placebo (Cohort 1 and Cohort 1B)

Reporting group description:

For Cohort 1, participants received single IV administration of placebo 1 hour after completion of HPA-1a positive platelet transfusion with a 24-week follow-up period. For Cohort 1B, participants received single IV administration of placebo 7 days prior to HPA-1a positive platelet transfusion, with a 25-week follow-up period from day of NAITgam administration.

Serious adverse events	Cohort 1 1000 International Units (IU) NAITgam	Cohort 1B 1000 IU NAITgam	Placebo (Cohort 1 and Cohort 1B)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Cohort 1 1000 International Units (IU) NAITgam	Cohort 1B 1000 IU NAITgam	Placebo (Cohort 1 and Cohort 1B)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	3 / 3 (100.00%)	3 / 3 (100.00%)

Injury, poisoning and procedural complications			
Skin laceration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscle strain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Vascular disorders			
Vasodilatation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Sciatica			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	2 / 6 (33.33%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	2	2	3
Migraine			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ageusia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Anosmia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Nasal polyps			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Psychiatric disorders			
Alcoholic hangover			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Joint swelling			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Coccydynia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tendonitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Muscle tightness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Osteonecrosis			

subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Otitis media			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Bronchitis bacterial			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gingivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 June 2020	Updates to address review comments from the Ethics Committee and for administrative/editorial changes.
29 June 2020	Updates to address Health Authority review comments and for administrative/editorial changes.
07 August 2020	Updates to harmonize both Ethics Committee and Health Authority review comments in single protocol.
11 May 2021	Inclusion of Cohort 1B to characterize the duration of the observed pharmacodynamic effect of NAITgam and to assess whether NAITgam retains the ability to efficiently clear platelets in the days after administration of NAITgam.
18 October 2021	Eligibility criteria updated for clarification purposes; editorial changes to Guidance on remote Source Data Verification; Serious Adverse Event reporting guidance updated to align with General Data Protection Regulation guidelines.

Notes:

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.

None reported. Trial ended prematurely having established proof-of-concept at the lowest NAITgam dose (1000 IU)

Notes: