Clinical trial results:
A Phase 2, Multicenter, Non-Randomized, Open-Label Study of RVT-1401 for the Treatment of Patients with Warm Autoimmune Hemolytic Anemia

Summary

EudraCT number	2019-003924-19
Trial protocol	ES GB HU PL BG
Global end of trial date	01 April 2021

Results information

Result version number	v1 (current)
This version publication date	03 August 2022
First version publication date	03 August 2022

Trial information

Trial identification

Sponsor protocol code	RVT-1401-2003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04253236
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Immunovant Sciences GmbH
Sponsor organisation address	320 West, 37th Street, 6th Floor, New York, United States, 10018
Public contact	Central Study Contact, Immunovant Sciences GmbH, 1 800-797-0414, clinicaltrials@immunovant.com
Scientific contact	Central Study Contact, Immunovant Sciences GmbH, 1 800-797-0414, clinicaltrials@immunovant.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	11 May 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 April 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To examine the effect of RVT-1401 on proportion of responders (defined as Hb level ≥10g/dL with at least a ≥2 g/dL increase from baseline without rescue therapy or blood transfusions in the previous two weeks). To assess the safety and tolerability of RVT-1401 in participants with warm autoimmune hemolytic anemia.

Protection of trial subjects:

The study was conducted in accordance with the principles of the Declaration of Helsinki (as amended in Edinburgh, Tokyo, Venice, Hong Kong, and South Africa), International Council for Harmonisation (ICH) guidelines, and all of the applicable basic principles of "Good Clinical Practice," as outlined in 21 CFR 312, subpart D, "Responsibilities of Sponsors and Investigators," 21 CFR, part 50, 1998, and 21 CFR, part 56, 1998. These standards were consistent with the requirements of the European Community Directive 2001/20/EC.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 August 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	United Kingdom: 1
Country: Number of subjects enrolled	Korea, Republic of: 3
Country: Number of subjects enrolled	Thailand: 1
Worldwide total number of subjects	5
EEA total number of subjects	0

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)	4
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 11 participants were screened, of which 5 participants were enrolled into the study. Due to the small number of participants (n=5) enrolled in the study, efficacy and safety conclusions could not be drawn and Pharmacokinetics/Pharmacodynamics (PK/PD) data were limited.

Pre-assignment

Screening details:

The study was terminated early prior to completion of dosing all participants in Cohort 1 and prior to initiating Cohort 2 due to a voluntary program-wide dosing pause to investigate unanticipated abnormalities in lipid levels observed in Thyroid Eye Disease patients enrolled in Study RVT-1401-2001 (NCT03938545).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Cohort 1: RVT-1401 680 mg/Week

Arm description:

Participants received RVT-1401 680 milligram (mg) subcutaneous (SC) injection weekly for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	RVT-1401
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 680 mg in two syringes of 2 milliliters (mL) RVT-1401 for a total of 4 mL.

Number of subjects in period 1	Cohort 1: RVT-1401 680 mg/Week
Started	5
Completed	2
Not completed	3
Adverse event, non-fatal	1
Safety Concerns	1
Study Terminated by Sponsor	1

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: RVT-1401 680 mg/Week
Reporting group description:	
Participants received RVT-1401 680 milligram (mg) subcutaneous (SC) injection weekly for 12 weeks.	

Reporting group values	Cohort 1: RVT-1401 680 mg/Week	Total	
Number of subjects	5	5	
Age categorical Units: Subjects			
Adults (18-64 years)	4	4	
From 65-84 years	1	1	
Gender categorical Units: Subjects			
Female	3	3	
Male	2	2	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	4	4	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	1	1	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	5	5	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Cohort 1: RVT-1401 680 mg/Week

Reporting group description:

Participants received RVT-1401 680 milligram (mg) subcutaneous (SC) injection weekly for 12 weeks.

Primary: Number of Responders at Week 13

End point title	Number of Responders at Week 13[1]

End point description:

Responders were defined as the participants with level of hemoglobin (Hb) >=10 grams per deciliter (g/dL) with at least a >=2 g/dL increase from Baseline without rescue therapy or blood transfusions in the previous two weeks. Safety population: All participants who enrolled in the study and received at least 1 dose of study treatment. Data was not collected for Cohort 2 due to early termination of the trial.

End point type	Primary

End point timeframe:

Week 13

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: Statistical Analysis is not available.

End point values	Cohort 1: RVT-1401 680 mg/Week			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Any Treatment-emergent Adverse Event (TEAE), Serious AE (SAE), Treatment-related Adverse Event (AE), and Death

End point title	Number of Participants With Any Treatment-emergent Adverse Event (TEAE), Serious AE (SAE), Treatment-related Adverse Event (AE), and Death[2]

End point description:

AEs were defined as any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Clinically significant changes determined by the Investigator such as vital signs, Electrocardiograms (ECGs), and clinical laboratory values were also reported as AEs. TEAEs were defined as AEs that either started on or after the date of the first dose of study drug. SAEs were defined as any untoward medical occurrence that, at any dose: resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity, was a congenital anomaly/birth defect, or was an important medical event that may have jeopardized the participant or may have required medical or surgical intervention to prevent one of the other outcomes listed in the definition. Safety Population.Data was not collected for Cohort 2.

End point type	Primary

End point timeframe:

Up to Week 20

Notes:

[2] - 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: Only descriptive analysis was performed for this safety endpoint.

End point values	Cohort 1: RVT-1401 680 mg/Week			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants				
TEAEs	5			
SAEs	1			
Treatment-related AEs	4			
Deaths	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response

End point title	Time to Response

End point description:

The time to response was defined as the amount of time to achieve response (Hb levels >=10 g/dL with at least a >=2 g/dL increase from Baseline without rescue therapy or blood transfusions in the previous 2 weeks). Safety Population. Only those participants with data available at the specified time points were analyzed. Data was not collected for Cohort 2 due to early termination of the trial.

End point type	Secondary

End point timeframe:

Up to Week 13

End point values	Cohort 1: RVT-1401 680 mg/Week			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Weeks				
number (not applicable)	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Achieving Hb Levels in the Normal Range

End point title	Time to Achieving Hb Levels in the Normal Range

End point description:

Time to achieving Hb levels in the normal range was assessed. Safety Population. Only those participants with data available at the specified time points were analyzed. Data was not collected for Cohort 2 due to early termination of the trial.

End point type	Secondary

End point timeframe:

Up to Week 13

End point values	Cohort 1: RVT-1401 680 mg/Week			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Weeks				
number (not applicable)	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change in Functional Assessment of Chronic Illness Therapy-fatigue (FACIT-F) Score

End point title	Number of Participants With Change in Functional Assessment of Chronic Illness Therapy-fatigue (FACIT-F) Score

End point description:

The FACIT-F scale was a validated scale which measured the physical, emotional and social implications of fatigue, one of the key clinical manifestations of warm autoimmune hemolytic anemia. Scores ranged from 0-52, a higher score indicated a higher quality of life. A score of less than 30 indicated severe fatigue. The scale took approximately 5-10 minutes to complete. Safety Population. Data was not collected for Cohort 2 due to early termination of the trial.

End point type	Secondary

End point timeframe:

Up to Week 13

End point values	Cohort 1: RVT-1401 680 mg/Week			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change in Medical Research Council (MRC) Breathlessness Scale

End point title	Number of Participants With Change in Medical Research Council (MRC) Breathlessness Scale

End point description:

The MRC Breathlessness scale is a questionnaire that consisted of 5 statements about perceived Breathlessness and the focus of the scale was to quantify the disability associated with breathlessness. Score ranged from Grade 0 (limited to no disability) to Grade 4 (severe disability); higher score indicated severe disability. Safety Population. Data was not collected for Cohort 2 due to early termination of the trial.

End point type	Secondary

End point timeframe:

Up to Week 13

End point values	Cohort 1: RVT-1401 680 mg/Week			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change in Euro Quality-5 dimension-3 level (EQ-5D-3L) Score

End point title	Number of Participants With Change in Euro Quality-5 dimension-3 level (EQ-5D-3L) Score

End point description:

The EQ-5D-3L is a validated measurement of health-related quality of life. The scale consists of 2 components, the EQ-5D descriptive system and the EQ visual analogue scale (VAS). The descriptive system evaluates mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 3 levels: 1=no problems, 2=some problems, and 3=extreme problems; a lower score indicated better quality of life. The EQ VAS records the participant's self-rated health on a vertical visual analogue scale where the endpoints are labelled 'Best imaginable health state' (100) and 'Worst imaginable health state' (0). Safety Population. Data was not collected for Cohort 2 due to early termination of the trial.

End point type	Secondary

End point timeframe:

Up to Week 20

End point values	Cohort 1: RVT-1401 680 mg/Week			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of RVT-1401 Pre-dose

End point title	Concentration of RVT-1401 Pre-dose

End point description:

Blood samples were planned to be collected at indicated time points to measure the concentration of RVT-1401 pre-dose (Ctrough) as an assessment of the pharmacokinetic (PK) RVT-1401. Safety Population. Data could not be calculated due to high proportion of non-quantifiable values (>30% of values were imputed). Data was not collected for Cohort 2 due to early termination of the trial. 99999 indicates data is not available.

End point type	Secondary

End point timeframe:

Pre-dose, Weeks 1, 2, 3, 4, 5, 6, 8, 10, 12 and 13 post-dose

End point values	Cohort 1: RVT-1401 680 mg/Week			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Milligrams per liter				
geometric mean (geometric coefficient of variation)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Presence of Anti-RVT 1401 Antibodies

End point title	Number of Participants With Presence of Anti-RVT 1401 Antibodies

End point description:

Blood samples were collected at indicated time points to determine presence of anti-RVT 1401 antibodies. Participants with presence of anti-RVT 1401 antibodies is reported. Safety population. Data was not collected for Cohort 2 due to early termination of the trial.

End point type	Secondary

End point timeframe:

Pre-dose on Weeks 1, 3, 5, 8, 13 and Week 20

End point values	Cohort 1: RVT-1401 680 mg/Week			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change in Levels of Total Immunoglobulin (Ig)G and IgG Subclasses (1-4)

End point title	Number of Participants With Change in Levels of Total Immunoglobulin (Ig)G and IgG Subclasses (1-4)

End point description:

Blood samples were collected at indicated time points for pharmacodynamic (PD) analysis of serum total IgG and IgG subclasses (1-4) concentrations. Participants with changes in levels of Total IgG and IgG Subclasses (1-4) is reported. Safety Population. Data was not collected for Cohort 2 due to early termination of the trial.

End point type	Secondary

End point timeframe:

Up to Week 20

End point values	Cohort 1: RVT-1401 680 mg/Week			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants				
Total IgG	5			
IgG Subclasses (1-4)	5			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
All-cause mortality, non-serious TEAEs and SAEs were collected up to Week 20 in Cohort 1.	
Adverse event reporting additional description:	
Safety Population. Only data for Cohort 1 is presented as the study was terminated in Part 1; hence, Cohort 2 was not initiated.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	Cohort 1: RVT-1401 680 mg/Week
Reporting group description:	
Participants received a RVT-1401 680 milligram (mg) subcutaneous (SC) injection weekly for 12 weeks.	

Serious adverse events	Cohort 1: RVT-1401 680 mg/Week		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Immune thrombocytopenia			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cohort 1: RVT-1401 680 mg/Week		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)		
Investigations			
Blood cholesterol increased			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Nervous system disorders			

Paraesthesia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Non-cardiac chest pain subjects affected / exposed occurrences (all) Oedema subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all)	 2 / 5 (40.00%) 3 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 2 / 5 (40.00%) 2		
Eye disorders Cataract subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Gingival bleeding subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1		
Musculoskeletal and connective tissue disorders			

Muscle spasms subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Infections and infestations Rhinitis subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Metabolism and nutrition disorders Hypoalbuminaemia subjects affected / exposed occurrences (all) Hypocalcaemia subjects affected / exposed occurrences (all)	3 / 5 (60.00%) 3 1 / 5 (20.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 October 2019	• Added anti-D, anti-Band 3, and/or anti-glycophorin antibodies to the Time and Events Table • Updated the pregnancy follow up language to create consistency with the safety management plan.
23 December 2019	• Updated WAIHA overview to provide clarity regarding worsening and refractory disease. • Updated Study Rationale to provide clarity regarding worsening and refractory disease. • Revised management criteria for hypoalbuminemia. • Added Exploratory Endpoint to evaluate transfusion burden • Updated to define therapy failure. • Revised to reflect management criteria for Grade 2-4 albumin levels. • Updated management criteria for infection • Updated management criteria for Grade 3 and 4 events to include study drug interruption and study drug discontinuation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
02 February 2021	In January 2021, Immunovant became aware of unanticipated abnormalities in lipid levels in Thyroid Eye Disease (TED) patients enrolled in Study RVT-1401-2001 (NCT03938545) during the conduct of the study and therefore, implemented a voluntary program-wide dosing pause to investigate the potential for batoclimab to affect lipids. Immunovant notified the FDA of the voluntary dosing pause in February 2021 and within this communication, committed to discussing a path forward with the Agency prior to resuming dosing in the batoclimab clinical development program. As a result of this voluntary pause, RVT-1401-2003 was paused, and an interim data cut occurred on 21 February 2021 to evaluate all efficacy and safety data and to inform the batoclimab program.	-

Notes:

Limitations and caveats

None reported