Clinical trial results:
Emicizumab in Patients with Acquired Hemophilia A: Multicenter, Single-Arm, Open-Label Clinical Trial

Summary

EudraCT number	2019-004430-42
Trial protocol	DE AT
Global end of trial date	04 January 2023

Results information

Result version number	v1 (current)
This version publication date	06 March 2024
First version publication date	06 March 2024

Trial information

Trial identification

Sponsor protocol code	AHA-EMI

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04188639
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GWT-TUD GmbH
Sponsor organisation address	Freiberger Str. 33, Dresden, Germany, 01067
Public contact	Medical Consulting, GWT-TUD GmbH, +49 35125933100, medical.consulting@g-wt.de
Scientific contact	Medical Consulting, GWT-TUD GmbH, +49 35125933172, medical.consulting@g-wt.de

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 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 January 2023
Global end of trial reached?	Yes
Global end of trial date	04 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the present study is to evaluate the efficacy of prophylactic emicizumab administered on a scheduled basis to prevent bleeds in patients with acquired hemophilia A (AHA).

Protection of trial subjects:

An independent data monitoring committee / Data safety monitoring board (DSMB/DMC) will be formed to oversee the safety of the trial subjects in the clinical trial by periodically assessing the safety of the trial therapy. The DSMB will consist at least of two physicians who are not involved in the trial and who are external to the sponsor. The study DSMB charter will elaborate the guidelines for the DSMB. The DSMB will meet according to the intervals mentioned in the DSMB Charter.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 March 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	Austria: 9
Country: Number of subjects enrolled	Germany: 38
Worldwide total number of subjects	47
EEA total number of subjects	47

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)	10
From 65 to 84 years	32

85 years and over	5

Subject disposition

Recruitment

Recruitment details:

From 25 Mar 2021 through 10 Jun 2022, a total of 49 patients were screened at 11 study sites in Germany and 2 study sites in Austria.

Pre-assignment

Screening details:

47 of 49 screened patients entered the study and received at least one dose of the study drug emicizumab. Overall, 42 patients completed 12 weeks of
treatment and 43 started the FU period.

Period 1

Period 1 title	Emicizumab treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Treatment period

Arm description:

Day 1 (6 mg/kg body weight (bw) subcutaneously)
Day 2 (3 mg/kg bw)
Maintenance dose: 1.5 mg/kg bw SC weekly starting week 2 (day 8 to 10) up to week 12

Arm type	Experimental
Investigational medicinal product name	Emicizumab
Investigational medicinal product code	
Other name	Hemlibra®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Emicizumab will be given on day 1 (6 mg/kg body weight (bw) subcutaneously) and day 2 (3 mg/kg bw), followed by maintenance doses of 1.5 mg/kg bw weekly starting week 2 (day 8 to 10) and up to week 12.
Emicizumab treatment will be discontinued in case of achieving spontaneous partial remission of AHA, defined as FVIII activity (chromogenic test with bovine components) increased to >50% of normal.

Number of subjects in period 1	Treatment period
Started	47
Completed	42
Not completed	5
partial remission	1
Consent withdrawn by subject	1
Physician decision	2
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups

Reporting group title	Emicizumab treatment

Reporting group description: -

Reporting group values	Emicizumab treatment	Total	
Number of subjects	47	47	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	10	10	
From 65-84 years	32	32	
85 years and over	5	5	
Gender categorical Units: Subjects			
Female	23	23	
Male	24	24	

Subject analysis sets

Subject analysis set title	PPS
Subject analysis set type	Per protocol

Subject analysis set description:

The PPS consisted of all patients who were treated for at least 12 weeks without major protocol deviations.

Reporting group values	PPS		
Number of subjects	35		
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)	8		
From 65-84 years	23		
85 years and over	4		

Gender categorical Units: Subjects			
Female	19		
Male	16		

End points

End points reporting groups

Reporting group title	Treatment period
Reporting group description:	
Day 1 (6 mg/kg body weight (bw) subcutaneously) Day 2 (3 mg/kg bw) Maintenance dose: 1.5 mg/kg bw SC weekly starting week 2 (day 8 to 10) up to week 12	
Subject analysis set title	PPS
Subject analysis set type	Per protocol
Subject analysis set description:	
The PPS consisted of all patients who were treated for at least 12 weeks without major protocol deviations.	

Primary: number of clinically significant new bleeds per patient-week

End point title	number of clinically significant new bleeds per patient-week
End point description:	
The primary endpoint was the number of clinically significant new bleeds per patient-week after the first dose of emicizumab until Week 12 after starting emicizumab treatment or dropout, whatever occurred first.	
End point type	Primary
End point timeframe:	
12 weeks	

End point values	Treatment period	PPS		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	47	35		
Units: bleeding rate				
number (not applicable)	22	11		

Statistical analyses

Statistical analysis title	Full Analysis
Comparison groups	Treatment period v PPS
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Chi-squared
Parameter estimate	likelihood-ratio test
Confidence interval	
level	Other: 2.5 %
sides	1-sided
upper limit	0.061
Variability estimate	Standard deviation
Dispersion value	0.0704

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 12 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Overall

Reporting group description: -

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 47 (34.04%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Contusion			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural hemorrhage			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transfusion-related circulatory overload			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Traumatic hemorrhage			

subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Traumatic intracranial hemorrhage				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Shock hemorrhage				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hematoma				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Anal hemorrhage				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal hemorrhage				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal ischemia				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intra-abdominal hemorrhage				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Retroperitoneal hemorrhage				

subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Covid-19			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Diverticulitis			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infected dermal cyst			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperglycemia			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Overall		
Total subjects affected by non-serious adverse events subjects affected / exposed	32 / 47 (68.09%)		
Vascular disorders Hematoma subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 4		
Hypertension subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Surgical and medical procedures Catheter placement subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Debridement subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Skin graft subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Wound treatment subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
General disorders and administration site conditions nflammation subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Vessel puncture site thrombosis subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Immune system disorders Anaphylactic shock subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Drug hypersensitivity			

subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Hypogammaglobulinemia			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Dyspnea			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Blood potassium decreased			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		

C-reactive protein increased subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Hemoglobin decreased subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Red blood cell count decreased subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 3		
Contusion subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 2		
Head injury subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Overdose subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Skin abrasion subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Skin laceration subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Toxicity to various agents subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Congenital, familial and genetic disorders			
Phimosis subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Cardiac disorders			

Atrial fibrillation subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Bradycardia subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Cardiac failure subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 3		
Extrapyramidal disorder subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Paresthesia subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Peroneal nerve palsy subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Blood and lymphatic system disorders			
Anemia subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Eye disorders			
Dry eye subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Eye hemorrhage subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Gastrointestinal disorders			

Diarrhea subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 3		
Constipation subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2		
Diverticulum subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2		
Abdominal pain subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Barrett's esophagus subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Chronic gastritis subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Gastritis subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Gastroesophageal reflux disease subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Ileus subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Proctitis ulcerative subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Skin and subcutaneous tissue disorders			

Rash subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2		
Dermal cyst subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Erythema subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Skin hemorrhage subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Urticaria subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2		
Bladder disorder subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Renal cyst subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Ureterolithiasis subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Urinary incontinence subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Muscle hemorrhage			

subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 47 (4.26%)		
occurrences (all)	2		
Bacteriuria			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Clostridium difficile infection			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Device related infection			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Laryngitis			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Urosepsis			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		

Metabolism and nutrition disorders			
Hyperkalemia			
subjects affected / exposed	2 / 47 (4.26%)		
occurrences (all)	2		
Fluid overload			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Hyperglycemia			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Hyperuricemia			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Hypocalcemia			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Hyponatremia			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Hypokalemia			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Lactic acidosis			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Vitamin K deficiency			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 March 2022	Version 3.0 dated 01 Mar 2022 including new safety information from updated Investigator´s Brochure and adaptation of study procedures

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported