



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
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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

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
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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
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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
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Subject analysis set type	Per protocol
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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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.0
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Reporting groups

Reporting group title	Overall
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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		

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	3 / 47 (6.38%)		
occurrences (all)	4		
Hypertension subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Surgical and medical procedures			
Catheter placement subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Debridement subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Skin graft subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Wound treatment subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
General disorders and administration site conditions			
Inflammation subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Vessel puncture site thrombosis subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Immune system disorders			
Anaphylactic shock subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Drug hypersensitivity			

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

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

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

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