



Clinical trial results:

Factor XII-associated cold autoinflammatory syndrome (FACAS) linked tokallikrein-kinin pathology: Proof of concept treatment with Lanadelumab (DX-2930)

Short title: LANA-FXII

Summary

EudraCT number	2019-001235-31
Trial protocol	DE
Global end of trial date	10 June 2024

Results information

Result version number	v1 (current)
This version publication date	15 January 2026
First version publication date	15 January 2026

Trial information

Trial identification

Sponsor protocol code	DEALSZ-2019-001
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Charité Universitätsmedizin Berlin
Sponsor organisation address	Charitéplatz 1, Berlin, Germany, 10117
Public contact	Karoline Krause, Institute of Allergology, Campus Benjamin Franklin, 0049 30450518043, ifa@charite.de
Scientific contact	Karoline Krause, Institute of Allergology, Campus Benjamin Franklin, 0049 30450518043, ifa@charite.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 January 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 June 2024
Global end of trial reached?	Yes
Global end of trial date	10 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of Lanadelumab on the clinical signs and symptoms of FXII-associated cold autoinflammatory syndrome (reduction in symptomatic days with urticarial rash, arthralgia, headache, chills)

Protection of trial subjects:

The study was conducted in accordance with the ICH E6 (R2) Guideline for Good Clinical Practice (GCP), with applicable local regulations (including European Directive 2001/20/EC, German Medicinal Products Act (AMG)), and with the ethical principles that have their origins in the Declaration of Helsinki (version 2013).

Background therapy:

Factor XII is a serine protease with diverse functions that participates in coagulation, fibrinolysis, complement, and contact system activation. So far, mutations in the factor XII gene have been linked to the rare coagulation disorder Hagemann factor deficiency and hereditary angioedema (FXII-HAE). We recently identified a novel Factor FXII (FXII) mutation in a 4-generation family with an autoinflammatory clinical phenotype. Affected family members show severe cold-associated symptoms (urticarial rash, chills, joint and bone pain, headache, fatigue), that worsen with age and partially respond to IL-1 receptor antagonist anakinra. Genetic analysis revealed no pathogenic mutations in classic autoinflammatory genes such as NLRP3, NLRP12, or others; however, we observed a novel heterozygous mutation affecting the FXII-kallikrein-kinin pathway. Neither angioedema attacks nor coagulation disorders were reported. In all affected family members, plasma levels of FXIIa were upregulated, and prekallikrein consecutively downregulated.

Lanadelumab is a fully human, monoclonal antibody (IgG1/ κ -light chain) that inhibits active plasma kallikrein proteolytic activity, providing sustained control of plasma kallikrein activity and thereby limiting bradykinin generation. The primary objective of this study was to assess the effect of Lanadelumab on the clinical signs and symptoms (patient-reported disease activity) of FACAS. Thus, the change in patient reported disease activity total score (mean of weeks 9 to 12 compared to mean of weeks -4 to -1 (baseline)) was determined as the primary endpoint. In addition, the effect of Lanadelumab on inflammation markers (such as CRP, ESR, SAA, S100A8/9), as well as on patients' quality of life, was aimed to be investigated.

Evidence for comparator: -

Actual start date of recruitment	02 October 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: 4
Worldwide total number of subjects	4
EEA total number of subjects	4

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)	1
Adults (18-64 years)	2
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at one site at Charité.

Pre-assignment

Screening details:

Four persons were assessed for eligibility (screened), no re-screening was necessary. All 4 of them were enrolled in the study and were allocated to the treatment intervention and received the IMP.

Period 1

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

Blinding implementation details:

this study was planned and conducted as an open-label, singlearm trial

Arms

Arm title	Treatment
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Lanadelumab
Investigational medicinal product code	CAS Number 1426055-14-2
Other name	Takzhyro
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients received an injection of 300 mg Lanadelumab every 2 weeks.

Number of subjects in period 1	Treatment
Started	4
Completed	4

Baseline characteristics

Reporting groups

Reporting group title	overall trial
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Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	4	4	
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)	1	1	
Adults (18-64 years)	2	2	
From 65-84 years	1	1	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	3	3	
Male	1	1	

End points

End points reporting groups

Reporting group title	Treatment
Reporting group description: -	

Primary: Change in patient-reported disease activity (PR-DA)

End point title	Change in patient-reported disease activity (PR-DA) ^[1]
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End point description:

Analysis of efficacy:

The PR-DA total score declined from a mean value of 15.47 (SD = 5.92) at baseline (weeks -4 to -1), to a mean value of 3.60 (SD = 7.16) at weeks 9 to 12. This is a change of -11.87 units (SD = 4.70, p-value = 0.050).

End point type	Primary
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End point timeframe:

from baseline up to 12 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: A limitation of the study is the small sample size of n=4. No statistical analysis for the primary endpoint was conducted.

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: score				
arithmetic mean (standard deviation)				
baseline (weeks -4 to -1)	15.47 (± 5.92)			
weeks 9 -12	3.6 (± 7.16)			

Attachments (see zip file)	charts_primary and secondary endpoints/DEALZ-2019-
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Statistical analyses

No statistical analyses for this end point

Secondary: Change in PR-DA total score at weeks 24 to 28

End point title	Change in PR-DA total score at weeks 24 to 28
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End point description:

Analysis of efficacy

The PR-DA total score declined from a mean value of 15.47 (SD = 5.92) at baseline (weeks -4 to -1), to a mean value of 1.65 (SD = 3.30) at weeks 25 to 28. This is a change of -13.82 units (SD = 4.03, p-value = 0.050). P

End point type	Secondary
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End point timeframe:

from baseline to weeks 24-28

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: score				
arithmetic mean (standard deviation)				
baseline	15.47 (± 5.92)			
weeks 24-28	1.65 (± 3.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PR-DA urticarial rash score

End point title	Change in PR-DA urticarial rash score
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End point description:

The PR-DA Urticarial Rash Score declined from a mean value of 3.92 (SD = 1.34) at baseline (weeks -4 to -1), over a mean value of 0.00 (SD = 0.00) at weeks 9 to 12, to a mean value of 0.00 (SD = 0.00) at weeks 25 to 28. This is a change of -3.92 units (SD = 1.34, p-value = 0.050) from baseline to weeks 9 to 12, versus a change of -3.92 units (SD = 1.34, p-value = 0.050) from baseline to weeks 25 to 28.

End point type	Secondary
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End point timeframe:

from baseline up to week 28

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: score				
arithmetic mean (standard deviation)				
weeks 9 to 12	0 (± 0)			
weeks 25 to 28	0 (± 0)			
baseline	3.92 (± 1.34)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PR-DA fatigue score

End point title	Change in PR-DA fatigue score
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End point description:

End point type	Secondary
End point timeframe:	
from baseline to 28 weeks	

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: score				
arithmetic mean (standard deviation)				
baseline	3.88 (± 1.39)			
weeks 9 to 12	1.4 (± 2.81)			
weeks 25 to 28	0.59 (± 1.18)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

overall trial

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27
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Reporting groups

Reporting group title	treatment
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Reporting group description: -

Serious adverse events	treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
Injury, poisoning and procedural complications			
Pansynovitis with secondary bleeding			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Injection site urticaria			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		

Ear and labyrinth disorders Sudden hearing loss subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Infections and infestations Pharyngitis subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 November 2019	update protocol version 1.1 • Additional information was added to background and overall study rationale
04 December 2019	update protocol version 1.2: • Changes in Information on contraception
07 December 2022	update protocol 1.3: • Inclusion of Adolescents
15 August 2023	update protocol 2.0: • Adjustment of applicable legislation (no reference to US law) • Adaptation of administrative structure • Update of Database Management and Quality Control (section 10.4) as well as Data Analysis (section 11) – paper CRF and SPSS will be used

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.

A limitation of the study is the small sample size of n=4. Based on the results of the study, Lanadelumab may be considered as an effective treatment option in FACAS patients.

Notes: