



Clinical trial results:

A Phase 3, Randomized, Double-blind, Placebo-controlled Multicenter Study to Evaluate the Efficacy and Safety of Pegcetacoplan in Patients with Cold Agglutinin Disease (CAD)

Summary

EudraCT number	2021-003160-27
Trial protocol	DE NO HU AT IT BG ES FI BE
Global end of trial date	11 September 2024

Results information

Result version number	v1 (current)
This version publication date	20 June 2025
First version publication date	20 June 2025
Summary attachment (see zip file)	Sobi.PEGCET-101_CSR Final_v1.0_28Mar2025 (Sobi.PEGCET-101_CSR Final_v1.0_28Mar2025.pdf)

Trial information

Trial identification

Sponsor protocol code	Sobi.PEGCET-101
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Swedish Orphan Biovitrum AB (publ)
Sponsor organisation address	SE-112 76 , Stockholm, Sweden,
Public contact	Sobi Global Medical, Swedish Orphan Biovitrum AB (publ), 0046 86972000 , medical.info@sobi.com
Scientific contact	Sobi Global Medical, Swedish Orphan Biovitrum AB (publ), 0046 86972000 , medical.info@sobi.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 September 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 September 2024
Global end of trial reached?	Yes
Global end of trial date	11 September 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of twice-weekly subcutaneous (s.c.) 1080-mg infusions of pegcetacoplan compared with that of placebo in patients with CAD

Protection of trial subjects:

Vaccination was mandatory unless documented evidence existed that patients were non responders to vaccination. Vaccinations were to be administered following the ACIP recommendations for adults or children with complement deficiencies and/or immunocompromising conditions

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 September 2022
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	Netherlands: 2
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Georgia: 2
Country: Number of subjects enrolled	Japan: 4
Country: Number of subjects enrolled	United Kingdom: 4
Worldwide total number of subjects	24
EEA total number of subjects	14

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	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 38 patients were screened, with 14 patients failing screening. Of the 24 patients eligible for the study, 16 patients were randomized to pegcetacoplan and 8 patients to placebo.

Pre-assignment

Screening details:

Patients experiencing acute hemolytic crisis may have received blood cell transfusions during the Screening period. The dosing was started at least 7 days after receiving the last transfusion. As needed and after consultation with the medical monitor, the Screening period was extended by up to 2 additional weeks

Pre-assignment period milestones

Number of subjects started	24
Number of subjects completed	24

Period 1

Period 1 title	Part A
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Pegcetacoplan

Arm description: -

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

Dosage and administration details:

1080 mg twice weekly via SC infusion

Arm title	Placebo
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo infusion twice weekly

Number of subjects in period 1	Pegcetacoplan	Placebo
Started	16	8
Completed	14	7
Not completed	2	1
Adverse event, non-fatal	2	-
Investigator decision	-	1

Period 2

Period 2 title	Part B
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

All patients who completed the 24-week double-blind treatment period were eligible to enter the open-label treatment period, during which they received pegcetacoplan 1080 mg twice weekly for up to 24 weeks (Week 48)

Arms

Arm title	Open-label Treatment Period
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Pegcetacoplan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1080 mg twice weekly via SC injection

Number of subjects in period 2	Open-label Treatment Period
Started	21
Completed	11
Not completed	10
Sponsor terminated	9
Lack of efficacy	1

Period 3

Period 3 title	Part C
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Open-label maintenance period
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Pegcetacoplan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1080 mg twice weekly via SC injection

Number of subjects in period 3	Open-label maintenance period
Started	11
Completed	0
Not completed	11
Sponsor terminated study	10
Lack of efficacy	1

Baseline characteristics

Reporting groups

Reporting group title	Pegcetacoplan
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Pegcetacoplan	Placebo	Total
Number of subjects	16	8	24
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	1	4
From 65-84 years	13	7	20
85 years and over	0	0	0
Age continuous Units: years			
median	76.0	73.0	-
standard deviation	± 7.25	± 6.73	
Gender categorical Units: Subjects			
Female	10	6	16
Male	6	2	8

Subject analysis sets

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
included all patients who received at least 1 dose of IMP. Patients were analyzed according to the treatment they received	
Subject analysis set title	ITT Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
included all randomized patients. Patients were analyzed according to their assigned treatment, regardless of the treatment they actually received. The ITT set was used for all efficacy analyses	
Subject analysis set title	PK Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The PK set included all patients in the ITT set who received IMP and had at least 1 evaluable post dose PK measurement	
Subject analysis set title	PD Set

Subject analysis set type	Intention-to-treat
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Subject analysis set description:

The PD set included all patients in the ITT set who received IMP and had at least 1 evaluable post dose PD measurement

Reporting group values	Safety Set	ITT Set	PK Set
Number of subjects	24	24	24
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	4	4	4
From 65-84 years	20	20	20
85 years and over	0	0	0
Age continuous Units: years			
median	73.5	73.5	73.5
standard deviation	± 7.08	± 7.08	± 7.08
Gender categorical Units: Subjects			
Female	16	16	16
Male	8	8	8

Reporting group values	PD Set		
Number of subjects	24		
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)	4		
From 65-84 years	20		
85 years and over	0		
Age continuous Units: years			
median	73.5		
standard deviation	± 7.08		
Gender categorical Units: Subjects			
Female	16		
Male	8		

End points

End points reporting groups

Reporting group title	Pegcetacoplan
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Open-label Treatment Period
Reporting group description: -	
Reporting group title	Open-label maintenance period
Reporting group description: -	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description: included all patients who received at least 1 dose of IMP. Patients were analyzed according to the treatment they received	
Subject analysis set title	ITT Set
Subject analysis set type	Intention-to-treat
Subject analysis set description: included all randomized patients. Patients were analyzed according to their assigned treatment, regardless of the treatment they actually received. The ITT set was used for all efficacy analyses	
Subject analysis set title	PK Set
Subject analysis set type	Intention-to-treat
Subject analysis set description: The PK set included all patients in the ITT set who received IMP and had at least 1 evaluable post dose PK measurement	
Subject analysis set title	PD Set
Subject analysis set type	Intention-to-treat
Subject analysis set description: The PD set included all patients in the ITT set who received IMP and had at least 1 evaluable post dose PD measurement	

Primary: To demonstrate the efficacy of twice-weekly SC 1080 mg infusions of pegcetacoplan compared with that of placebo in patients with CAD

End point title	To demonstrate the efficacy of twice-weekly SC 1080 mg infusions of pegcetacoplan compared with that of placebo in patients with CAD
End point description:	
End point type	Primary
End point timeframe: The primary endpoint was response to treatment at Week 24	

End point values	Pegcetacoplan	Placebo	ITT Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	8	24	
Units: p-value	16	8	24	

Statistical analyses

Statistical analysis title	Response to Week 24
Comparison groups	Pegcetacoplan v Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.05
Method	t-test, 2-sided
Parameter estimate	Odds ratio (OR)
Confidence interval	
level	90 %
sides	2-sided
lower limit	5
upper limit	90
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the study

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.1
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Reporting groups

Reporting group title	Part A
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Reporting group description:

Treatment-emergent adverse events (TEAEs) were defined as those AEs that start on or after the first dose of IMP and up to 8 weeks after the last dose of study medication

Reporting group title	Part B
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Reporting group description:

Treatment-emergent adverse events (TEAEs) were defined as those AEs that start on or after the first dose of IMP and up to 8 weeks after the last dose of study medication.

Serious adverse events	Part A	Part B	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 24 (29.17%)	7 / 21 (33.33%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events		0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 24 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breakthrough haemolysis			

subjects affected / exposed	0 / 24 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cold type haemolytic anaemia			
subjects affected / exposed	0 / 24 (0.00%)	2 / 21 (9.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolysis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic anaemia			
subjects affected / exposed	1 / 24 (4.17%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Syncope			
subjects affected / exposed	1 / 24 (4.17%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Cholecystitis			
subjects affected / exposed	1 / 24 (4.17%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonia			
subjects affected / exposed	1 / 24 (4.17%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	0 / 24 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteonecrosis of jaw			
subjects affected / exposed	0 / 24 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Covid-19			
subjects affected / exposed	1 / 24 (4.17%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal sepsis			
subjects affected / exposed	1 / 24 (4.17%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Part A	Part B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 24 (100.00%)	8 / 21 (38.10%)	
Blood and lymphatic system disorders			
Cold type haemolytic anaemia			
subjects affected / exposed	2 / 24 (8.33%)	3 / 21 (14.29%)	
occurrences (all)	2	3	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 24 (12.50%)	0 / 21 (0.00%)	
occurrences (all)	3	0	
Oedema peripheral			
subjects affected / exposed	6 / 24 (25.00%)	0 / 21 (0.00%)	
occurrences (all)	6	0	
Respiratory, thoracic and mediastinal			

disorders			
Dyspnoea			
subjects affected / exposed	2 / 24 (8.33%)	0 / 21 (0.00%)	
occurrences (all)	2	0	
Pleural effusion			
subjects affected / exposed	2 / 24 (8.33%)	0 / 21 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Pruritis			
subjects affected / exposed	2 / 24 (8.33%)	1 / 21 (4.76%)	
occurrences (all)	2	1	
Infections and infestations			
Covid-19			
subjects affected / exposed	4 / 24 (16.67%)	3 / 21 (14.29%)	
occurrences (all)	4	3	
Upper respiratory tract infection			
subjects affected / exposed	3 / 24 (12.50%)	1 / 21 (4.76%)	
occurrences (all)	3	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 October 2021	<p>This amendment included the following changes to the clinical study protocol version 1.0, dated 02 August 2021.</p> <ul style="list-style-type: none">• Addition of patient stopping criteria.• Addition of study stopping criteria.• Change of stratification definition regarding prior transfusions.• Removal of the requirement to have a prior rituximab-based therapy.• Change of inclusion criterion regarding liver dysfunction.• Addition of a subgroup analysis on rituximab-experienced/naïve patients for primary and key secondary endpoints.• Change of the instructions for documentation of temperature control of the study drug at the patient's residence.
10 December 2021	<p>This protocol amendment serves to remove the exploratory measurements of activity/movement by the use of Actigraphy at Baseline, Week 24 and Week 48. In addition, C3 deposition on red blood cells (RBCs) by flow cytometry, which was already included in the study protocol as an assessment, was also described among exploratory endpoints.</p>
28 April 2022	<p>This amendment to the protocol adds the following inclusion and exclusion criteria:</p> <p>Added inclusion criterion</p> <ul style="list-style-type: none">• An absolute neutrophil count ≥ 1500 cells/mm³ at Screening. <p>Added exclusion criteria</p> <ul style="list-style-type: none">• Protected adults (guardianship, trusteeship) who are unable to express their consent and persons under court protection.• Hypersensitivity to pegcetacoplan or to any of the excipients or placebo compounds.• Unresolved infection caused by encapsulated bacteria including <i>Neisseria meningitidis</i>, <i>Streptococcus pneumoniae</i> and <i>Haemophilus influenzae</i>.• Known or suspected hereditary fructose intolerance. <p>The study endpoints were modified as follows:</p> <ul style="list-style-type: none">• The key secondary endpoints were displayed in a different order.• For Hb, LDH, indirect bilirubin, ARC and haptoglobin levels, only time to first normalization from Baseline to Week 24 will be measured, and time from Baseline to Weeks, 48 and 96 was removed.• Addition of separate analysis of the subset of questions in the FACIT-Fatigue scale. <p>In addition, the exploratory objective to evaluate change in patient activity level and energy expenditure has been removed.</p>

13 March 2023	<p>Inclusion criteria was adjusted to clarify:</p> <ul style="list-style-type: none"> o It was noted that the diagnosis of primary cold agglutinin disease (CAD) should be on the basis of the presence of all the criteria at Screening. o The restriction that patients who were not previously vaccinated should not receive multiple vaccines on the same day was removed and replaced with a reminder that vaccinations should be administered following the Advisory Committee on Immunization Practices (ACIP) recommendations for adults or children with complement deficiencies and/or immunocompromising conditions, as was already noted elsewhere in the protocol. <p>• Exclusion criteria was adjusted to clarify:</p> <ul style="list-style-type: none"> o The exclusion period for sutimlimab was changed from within 4 weeks prior to randomization to within 15 weeks prior to randomization. Patients previously treated with >1 dose of sutimlimab but who have not had experienced a documented increase in hemoglobin (Hb) \geq 1.0 g/dL during sutimlimab treatment was added as exclusionary. o Belimumab and anti-CD20 antibody other than rituximab were added as exclusionary treatments, and the exclusionary period from other treatments, as monotherapy or in combination, had been set to 16 weeks prior to randomization. o For diagnosis of systemic lupus erythematosus or other autoimmune diseases with antinuclear antibodies, it was noted that antinuclear antibodies of long-standing duration without associated clinical symptoms will be adjudicated on a case-by-case basis. o For cold agglutinin syndrome secondary to Mycoplasma pneumoniae, Epstein-Barr virus or other specific causative infection, it was added that patients with long history of CAD, positive IgM titer and IgG titer without associated clinical symptoms will be adjudicated on a case-by-case basis.
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported