Clinical trial results:
Effect of topical rhGM-CSF on the healing of venous leg ulcers: a randomized, placebo-controlled, double-blind, clinical phase II study

Summary

EudraCT number	2019-001483-30
Trial protocol	DK
Global end of trial date	30 January 2025

Results information

Result version number	v1 (current)
This version publication date	15 February 2026
First version publication date	15 February 2026
Summary attachment (see zip file)	Synopsis of study results_Repogel-01 (Synopsis of study results_Repogel-01_Final.pdf)

Trial information

Trial identification

Sponsor protocol code	BBH-GMCSF-01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Reponex Pharmaceuticals A/S
Sponsor organisation address	Slotsmarken 12, 1.th. , Hørsholm, Denmark,
Public contact	Reponex Pharmaceuticals A/S, Reponex Pharmaceuticals A/S, vp@reponex.dk
Scientific contact	Reponex Pharmaceuticals A/S, Reponex Pharmaceuticals A/S, vp@reponex.dk

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	22 January 2026
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 January 2025
Global end of trial reached?	Yes
Global end of trial date	30 January 2025
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To study the effect of rhGM-CSF on ulcer size reduction, when applied directly in the wound bed of difficult-to-heal venous leg ulcers, given on top of standard care. This was evaluated by measuring the ulcer area change after 4 weeks of treatment compared to placebo.

Protection of trial subjects:

For safety reasons, the study drug /placebo was applied in the outpatient wound clinic at the hospital with close monitoring of pain and immediate adverse events. During the treatment period with the study drug/placebo participants also received standard care by highly experienced wound care nurses a the center.

Participants were compensated for traveling expenses in accordance with the reimbursement policy.

Analgesics were offered in the case of pain.

Background therapy:

The following standard of care was performed twice a week in all participants (placebo/Repogel):
1. Ulcer debridement: mechanical or sharp debridement e.g. with a curette, performed at each visit, unless the procedure was too painful.
2. Ulcer irrigation: performed at every study visit with clean tap water
3. Dressing: Ulcers were dressed with a neutral non-medicated dressing at each visit accord-ing to the clinical routine in the department, reflecting the stage and needs of the individual wound. A preference list of dressing choices were made before inclusion. Active dressings such as silver-impregnated dressings or dressings with ibuprofen were not allowed. Dressing type was registered in the eCRF.
4. Compression therapy: Bandages with Coban 2TM, 3MTM were used. CobanTM (“Coban I”) was also accepted
5. Periwound skin treatment: The use of moisturizing creams and protecting the wound bor-der from maceration were used if clinically indicated

Home nurse visits: Some of the dressing changes were performed by the home care nurses or at nurses’ clinics in the follow-up period (in accordance with clinical routines).

Evidence for comparator: -	
Actual start date of recruitment	13 April 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	Denmark: 6

Worldwide total number of subjects	6
EEA total number of subjects	6

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)	2
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at the Department of Dermatology and Copenhagen Wound Healing Center, Bispebjerg Hospital, Denmark. The first patient was randomized 13-04-2021 and the last patient finished the study 19-10-2021.

Pre-assignment

Screening details:

The target population consisted of adult patients suffering from difficult-to-heal venous leg ulcers, with an ulcer duration of ≥2 months and ≤3 years and an ulcer size 2-75 cm2 at the randomization day.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Hydrogel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical

Dosage and administration details:

Twice weekly for 4 weeks topically in the wound bed

Arm title	Repogel

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Repogel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical

Dosage and administration details:

Repogel containing rhGM-CSF (molgramostim) in a hydrogel with an aimed concentration of 50 mikrgram molgramostim per mL of hydrogel. The treatment was adminstered locally in the wound bed twice weekly for 4 weeks with a dosage of 5 mikrogram/cm2 rhGM-CSF of wound bed. The ulcer area was calculated by means of Silhouette Star (Aranz medical) at every treatment visit, and the ulcer area at that visit determined the individual dose to be applied to the ulcer. The study drug/placebo was supplied in a transparent syringe of 10 mL, indicating the volume used.
The maximal dosage of molgramostim that could be given at each administration was 375 mikrogram.

Number of subjects in period 1	Placebo	Repogel
Started	3	3
Completed	3	3

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Repogel
Reporting group description: -	

Reporting group values	Placebo	Repogel	Total
Number of subjects	3	3	6
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)	1	1	2
From 65-84 years	2	2	4
85 years and over	0	0	0
Age continuous Units: years			
median	73	67	
inter-quartile range (Q1-Q3)	63.0 to 74.5	62.5 to 74.5	-
Gender categorical Units: Subjects			
Female	0	1	1
Male	3	2	5
Ulcer duration Units: Months			
median	6	8	
inter-quartile range (Q1-Q3)	4.0 to 7.7	5.5 to 11.0	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Repogel
Reporting group description: -	

Primary: Primary endpoint

End point title	Primary endpoint
End point description:	
Proportion of patients reaching a 40% ulcer area reduction, or more, 4 weeks after initiation of the study drug treatment/placebo	
End point type	Primary
End point timeframe:	
4 weeks after randomization	

End point values	Placebo	Repogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Number of subjects				
number (not applicable)	1	0		

Statistical analyses

Statistical analysis title	No statistical analysis
Statistical analysis description:	
Too small sample size (n=6). For this reason, test of statistical significance was deemed as inappropriate.	
Comparison groups	Repogel v Placebo
Number of subjects included in analysis	6
Analysis specification	Post-hoc
Analysis type	other[1]
P-value	≤ 0.05 [2]
Method	No statistical testing

Notes:

[1] - Too small sample size (n=6). For this reason, test of statistical significance was deemed as inappropriate.
[2] - Originally planned

Secondary: Absolute ulcer area change 4 weeks after randomization (cm2)

End point title	Absolute ulcer area change 4 weeks after randomization (cm2)
End point description:	

End point type	Secondary

End point timeframe:

4 weeks after randomization

End point values	Placebo	Repogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: cm2				
arithmetic mean (standard deviation)	4.5 (± 5.3)	-0.8 (± 1.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute ulcer area change 8 weeks after randomization (cm2)

End point title	Absolute ulcer area change 8 weeks after randomization (cm2)

End point description:

End point type	Secondary

End point timeframe:

8 weeks after randomization

End point values	Placebo	Repogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: cm2				
arithmetic mean (standard deviation)	6.3 (± 5.3)	-5.2 (± 8.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage reduction of the ulcer area 4 weeks after randomization

End point title	Percentage reduction of the ulcer area 4 weeks after randomization

End point description:

A negative value indicates an increase in wound size

End point type	Secondary

End point timeframe:

4 weeks after randomization

End point values	Placebo	Repogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Percentage area reduction				
arithmetic mean (standard deviation)	26.5 (± 33.7)	1.8 (± 10.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage reduction of the ulcer area 8 weeks after randomization

End point title	Percentage reduction of the ulcer area 8 weeks after randomization

End point description:

A negative values indicates an increase in wound size

End point type	Secondary

End point timeframe:

8 weeks after randomization

End point values	Placebo	Repogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Percentage area reduction				
arithmetic mean (standard deviation)	65 (± 20.1)	-10.5 (± 56.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Complete ulcer healing (full epithelialization and no drainage of wound fluid) 4 and 8 weeks after randomization

End point title	Complete ulcer healing (full epithelialization and no drainage of wound fluid) 4 and 8 weeks after randomization

End point description:

End point type	Secondary

End point timeframe:

4 and 8 weeks after randomization

End point values	Placebo	Repogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Number of participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to complete ulcer healing

End point title	Time to complete ulcer healing

End point description:

No participant in any study group experienced complete ulcer healing

End point type	Secondary

End point timeframe:

During study period

End point values	Placebo	Repogel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Number og subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From the screening visit to the end-of-trial visit.	
Assessment type	Systematic
Dictionary used	
Dictionary name	SNOMED CT
Dictionary version	2025-09-30
Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Repogel
Reporting group description: -	

Serious adverse events	Placebo	Repogel	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Placebo	Repogel	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	2 / 3 (66.67%)	
Cardiac disorders			
Hypertension	Additional description: Worsening of hypertension		
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Serology abnormal	Additional description: Increasing alkaline phosphatase		
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Vitamin D deficiency			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			

Wound	Additional description: New wound (small) developed on index leg. Unknown cause.		
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Wound infection bacterial	Additional description: Wound infection (streptococci)		
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Wound complication	Additional description: Worsening of wounds on index leg		
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Dermatitis allergic	Additional description: Allergic exanthema after a wound care product (not placebo/Repogel)		
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Muscle discomfort	Additional description: Muscular lumbar pain; participant slipped at work		
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Bursitis	Additional description: Bursitis olcecrani, right arm		
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
08 November 2021	The current study was temporarily stopped by the Danish Medicines Agency 08. Nov. 2021, following an inspection at sponsors site, due to insufficient validation of the analysis methods of the study drug in the dosage form (Repogel) in batch BA055HBMH. rhGM-CSF in the hydrogel dosage form used in the study were shown as physically not stable due to the hypothesis of stress during manu-facturing process caused alteration of peptide chain over the time. As subjects were included sequentially and participating in the study over a 6-month period, the content of rhGM-CSF may have varied significantly between the patients. At this timepoint six patients were included in the study. With the necessary documentation, the study could be continued. Despite multiple attempts, it was observed that Repogel dosage form was not robust enough and quantification of rhGM-CSF was not reproducible. It was concluded that to achieve the necessary validation/documentation was not possible and therefore it was decided to stop the study and report on the six patients included. Finally a closure of the study was filed in January 2025 with the results of six patients only and without any statistically analysis due to very small sample size (n=6). A dose of 5 mikrogram of rhGM-CSF (molgramostim) per cm2 of wound bed was aimed at being used in the study. The study drug was administered twice a week for 4 consecutive weeks. The maximal dosage of molgramostim that could be given at each administration in our trial, 375 mikrogram.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

No firm conclusions about the efficacy and safety of rhGM-CSF can be drawn from this study due to insufficient data and very few number of enrolled patients (n=6).

Notes: