Clinical trial results:
A randomised, intra-individual controlled trial of the cutaneous healing properties of petrolatum versus the vehicle for Oleogel-S10 when applied topically to mechanically induced partial thickness wounds in healthy volunteers

Summary

EudraCT number	2020-002358-26
Trial protocol	DE
Global end of trial date	16 June 2021

Results information

Result version number	v1 (current)
This version publication date	10 June 2022
First version publication date	10 June 2022

Trial information

Trial identification

Sponsor protocol code	AHV-18-B

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Amryt Research Ltd
Sponsor organisation address	45 Mespil Road, Dublin 4, Ireland,
Public contact	Head of Clinical Development, Amryt Research Ltd., 353 15180200, janet.boylan@amrytpharma.com
Scientific contact	Head of Clinical Development, Amryt Research Ltd., 353 15180200, janet.boylan@amrytpharma.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	28 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 June 2021
Global end of trial reached?	Yes
Global end of trial date	16 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the vehicle for Oleogel-S10 is non-inferior to petrolatum with regards to time to achieve cutaneous healing of mechanically induced partial thickness wounds in healthy volunteers

Protection of trial subjects:

This study was conducted in compliance with the ethical principles derived from the principles of Good Clinical Practices (GCP) and the declaration of Helsinki (1964) including all amendments up to the October 2013 revision. All local regulatory requirements pertinent to the safety of trial subjects were followed during the conduct of the trial. Patients attended daily throughout the trial and adverse events were monitored throughout the study.

Background therapy:

None

Evidence for comparator:

Topically applied leave-on products may be helpful to enhance cutaneous healing and re-epithelization of cutaneous wounds. An occlusive and ‘protective’ effect seems to be responsible for this phenomenon, but the performance of products depends on the overall composition and possible active ingredients. Amryt Pharma developed a vehicle of Oleogel-S10 to be used in a clinical phase III study comparing the efficacy of Oleogel-S10 to vehicle for the treatment of Epidermolysis bullosa (EB). Petrolatum is considered an example of a standard topical product to promote cutaneous healing in the management of wounds caused by EB. It is expected that the vehicle gel, that has been developed for use as a blinded comparator in the EB study, has similar beneficial effects on wound healing to those associated with the use of petrolatum.

Actual start date of recruitment	12 April 2021
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: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	16
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Adult healthy volunteers (n = 8 male, n = 8 female) were enrolled in the trial at the Clinical Research Center for Hair and Skin Science (CRC), Department of Dermatology and Allergy, Charité-Universitätsmedizin Berlin, Germany. The first patient fist visit was 12-Apr-2021 and the last patient last visit was 16-Jun-2021.

Pre-assignment

Screening details:

Subjects underwent assessments to determine eligibility at the Initial Screening Visit (Day-14 to Day-3). A total of 16 subjects entered the screening phase and all of them proceeded to the recruitment.

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind[1]
Roles blinded	Data analyst, Assessor[2]

Blinding implementation details:

The study was outcome-assessor blinded. Study personnel who administered the intervention and the subjects who received the interventions were not blinded. The Investigators who performed the wound assessments and standardised image analysis were blinded to treatment. To maintain the blind, the data manager, project manager and those preparing the analysis and results (programmers and statisticians) were blinded throughout the study until after database lock.

Arms

Are arms mutually exclusive?	No
Arm title	Control Gel

Arm description:

Treatment with Control Gel

Arm type	Experimental
Investigational medicinal product name	Control Gel
Investigational medicinal product code	
Other name	Vehicle for Oleogel-S10
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

Applied topically once daily for 16 days at a thickness of approximately 1 mm (0.04 inch) over the wound area (diameter 8 mm to cover the wound edges). The treated areas were covered with a non-adhesive wound dressing with a non-adherent pad (Mepitel® Border Lite) from Day 1 through Day 10 immediately after product application.

Arm title	Petrolatum (ALLERGIKA® – BASISSALBE)

Arm description:

Treatment with Petrolatum (ALLERGIKA® – BASISSALBE)

Arm type	Experimental
Investigational medicinal product name	Petrolatum (ALLERGIKA® – BASISSALBE)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

Applied topically once daily for 16 days at a thickness of approximately 1 mm (0.04 inch) over the wound area (diameter 8 mm to cover the wound edges). The treated areas were covered with a non-

adhesive wound dressing with a non-adherent pad (Mepitel® Border Lite) from Day 1 through Day 10 immediately after product application.

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.

Justification: The study was outcome-assessor blinded. Study personnel who administered the intervention and the subjects who received the interventions were not blinded. The Investigators who performed the wound assessments and standardised image analysis were blinded to treatment. To maintain the blind, the data manager, project manager and those preparing the analysis and results (programmers and statisticians) were blinded throughout the study until after database lock.

[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: The study was outcome-assessor blinded. Study personnel who administered the intervention and the subjects who received the interventions were not blinded. The Investigators who performed the wound assessments and standardised image analysis were blinded to treatment. To maintain the blind, the data manager, project manager and those preparing the analysis and results (programmers and statisticians) were blinded throughout the study until after database lock.

Number of subjects in period 1	Control Gel	Petrolatum (ALLERGIKA® – BASISSALBE)
Started	16	16
Completed	16	16

Baseline characteristics

Reporting groups	
Reporting group title	Control Gel
Reporting group description: Treatment with Control Gel	
Reporting group title	Petrolatum (ALLERGIKA® – BASISSALBE)
Reporting group description: Treatment with Petrolatum (ALLERGIKA® – BASISSALBE)	

Reporting group values	Control Gel	Petrolatum (ALLERGIKA® – BASISSALBE)	Total
Number of subjects	16	16	16
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)	16	16	16
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	8	8	8
Male	8	8	8

End points

End points reporting groups

Reporting group title	Control Gel
Reporting group description: Treatment with Control Gel	
Reporting group title	Petrolatum (ALLERGIKA® – BASISSALBE)
Reporting group description: Treatment with Petrolatum (ALLERGIKA® – BASISSALBE)	

Primary: Days until complete healing of mechanically induced wounds assessed by clinical score

End point title	Days until complete healing of mechanically induced wounds assessed by clinical score
End point description: Days until complete healing of mechanically induced wounds assessed by clinical score	
End point type	Primary
End point timeframe: Wound healing was assessed by clinical score from Day 1 through Day 16 and at the End of Study Visit.	

End point values	Control Gel	Petrolatum (ALLERGIKA® – BASISSALBE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	16		
Units: days				
arithmetic mean (confidence interval 95%)	14.19 (12.14 to 16.24)	12.50 (11.57 to 13.43)		

Statistical analyses

Statistical analysis title	Non-inferiority analysis
Statistical analysis description: The null hypothesis was that the control gel was inferior to petrolatum (i.e., H0: Mean difference ≥ NIM) and the alternative hypothesis was that the control gel was non-inferior to petrolatum (i.e., H1: Mean difference < NIM), where NIM was the non-inferiority margin which was equal to 1 day, and the difference corresponded to: Control gel - petrolatum.	
Comparison groups	Control Gel v Petrolatum (ALLERGIKA® – BASISSALBE)
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.7925 [1]
Method	t-test, 1-sided
Parameter estimate	Mean difference (net)
Point estimate	1.69

Confidence interval	
level	Other: 97.5 %
sides	1-sided
upper limit	3.44
Variability estimate	Standard deviation
Dispersion value	3.281

Notes:

[1] - A paired T-Test was fitted to days until complete healing with one-sided alpha of 0.025.

Secondary: Days until complete healing of mechanically induced wounds assessed by planimetry

End point title	Days until complete healing of mechanically induced wounds assessed by planimetry

End point description:

Planimetry was performed by computerised image analysis using the software ImageJ.
The wound area was reported in mm2 and the means of the 2 independent measurements were used.
Complete wound healing was defined as a mean wound area of 0 mm2.

End point type	Secondary

End point timeframe:

Wound healing was assessed by planimetry on Day 1, Day 3, and Day 5 through Day 16.

End point values	Control Gel	Petrolatum (ALLERGIKA® – BASISSALBE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	16		
Units: days				
arithmetic mean (confidence interval 95%)	8.56 (7.84 to 9.29)	8.88 (8.40 to 9.35)		

Statistical analyses

Statistical analysis title	Non-inferiority analysis

Statistical analysis description:

The null hypothesis was that the control gel was inferior to petrolatum (i.e., H0: Mean difference ≥ NIM) and the alternative hypothesis was that the control gel was non-inferior to petrolatum (i.e., H1: Mean difference < NIM), where NIM was the non-inferiority margin which was equal to 1 day, and the difference corresponded to: Control gel - petrolatum.

Comparison groups	Control Gel v Petrolatum (ALLERGIKA® – BASISSALBE)
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0004 [2]
Method	t-test, 1-sided
Parameter estimate	Mean difference (net)
Point estimate	-0.31

Confidence interval	
level	Other: 97.5 %
sides	1-sided
upper limit	0.35
Variability estimate	Standard deviation
Dispersion value	1.25

Notes:

[2] - A paired T-Test was fitted to days until complete healing with one-sided alpha of 0.025.

Secondary: Clinical score per day

End point title	Clinical score per day

End point description:

A 6-category clinical score was used to assess the degree of epithelialisation (0=0% [no healing], 1=1 to 25% re-epithelialisation, 2=26 to 50% re-epithelialisation, 3=51 to 75% re-epithelialisation, 4=>75% re-epithelialisation, but not complete healing, 5=100% re-epithelialisation [complete healing]).

End point type	Secondary

End point timeframe:

Wound healing was assessed by clinical score from Day 1 through Day 16 and at the End of Study Visit.

End point values	Control Gel	Petrolatum (ALLERGIKA® – BASISSALBE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	16		
Units: Clinical score per day				
median (full range (min-max))				
Day 1	0 (0 to 0)	0 (0 to 0)		
Day 2	0 (0 to 1.0)	0 (0 to 1.0)		
Day 3	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)		
Day 4	1.0 (1.0 to 2.0)	1.0 (1.0 to 2.0)		
Day 5	2.0 (1.0 to 4.0)	1.0 (1.0 to 2.0)		
Day 6	2.0 (1.0 to 3.0)	2.0 (1.0 to 3.0)		
Day 7	3.0 (2.0 to 4.0)	3.0 (2.0 to 3.0)		
Day 8	3.0 (2.0 to 4.0)	3.0 (2.0 to 4.0)		
Day 9	4.0 (3.0 to 5.0)	4.0 (2.0 to 4.0)		
Day 10	4.0 (3.0 to 5.0)	4.0 (3.0 to 5.0)		
Day 11	4.0 (3.0 to 5.0)	4.0 (3.0 to 5.0)		
Day 12	4.0 (3.0 to 5.0)	5.0 (4.0 to 5.0)		
Day 13	4.0 (4.0 to 5.0)	5.0 (4.0 to 5.0)		
Day 14	5.0 (4.0 to 5.0)	5.0 (4.0 to 5.0)		
Day 15	5.0 (4.0 to 5.0)	5.0 (4.0 to 5.0)		
Day 16	5.0 (4.0 to 5.0)	5.0 (5.0 to 5.0)		
End of Study Visit	5.0 (5.0 to 5.0)	5.0 (5.0 to 5.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Wound surface area in mm2 per day (assessed by planimetry)

End point title	Wound surface area in mm2 per day (assessed by planimetry)

End point description:

Wound surface area in mm2 per day (assessed by planimetry)

End point type	Secondary

End point timeframe:

Wound healing was assessed by planimetry on Day 1, Day 3, and Day 5 through Day 16.

End point values	Control Gel	Petrolatum (ALLERGIKA® – BASISSALBE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	16		
Units: mm2				
arithmetic mean (standard deviation)				
Day 1	42.97 (± 9.011)	42.15 (± 9.584)		
Day 3	33.04 (± 9.221)	33.82 (± 7.454)		
Day 5	17.47 (± 7.342)	19.39 (± 7.035)		
Day 6	7.98 (± 4.285)	11.37 (± 3.919)		
Day 7	2.71 (± 2.035)	5.27 (± 3.489)		
Day 8	0.87 (± 1.160)	1.61 (± 2.085)		
Day 9	0.40 (± 1.016)	0.25 (± 0.661)		
Day 10	0.02 (± 0.085)	0.07 (± 0.267)		
Day 11	0.00 (± 0.000)	0.00 (± 0.000)		
Day 12	0.00 (± 0.000)	0.00 (± 0.000)		
Day 13	0.00 (± 0.000)	0.00 (± 0.000)		
Day 14	0.00 (± 0.000)	0.00 (± 0.000)		
Day 15	0.00 (± 0.000)	0.00 (± 0.000)		
Day 16	0.00 (± 0.000)	0.00 (± 0.000)		

Statistical analyses

No statistical analyses for this end point

Secondary: Adverse Events

End point title	Adverse Events

End point description:

Incidence, severity, and causality of local tolerance AEs, and incidence, severity, and causality of all AEs.

End point type	Secondary

End point timeframe:

AEs were monitored throughout the study from the time of informed consent through Day 23±2 days.

End point values	Control Gel	Petrolatum (ALLERGIKA® – BASISSALBE)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	16		
Units: Adverse Events				
number (not applicable)				
Application site pain	1	0		
Application site pruritus	1	0		
Application site erosion	4	0		
Ligament sprain	1	1		
Nasopharyngitis	1	1		
Rhinitis allergic	1	1		
Pruritus	1	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: AEs were monitored throughout the study from the time of informed consent through Day 23±2 days.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1
Reporting groups	
Reporting group title	Control Gel
Reporting group description: Treatment with Control Gel	
Reporting group title	Petrolatum (ALLERGIKA® – BASISSALBE)
Reporting group description: Treatment with Petrolatum (ALLERGIKA® – BASISSALBE)	
Reporting group title	Not applicable
Reporting group description: AEs not associated with any of the IMPs.	

Serious adverse events	Control Gel	Petrolatum (ALLERGIKA® – BASISSALBE)	Not applicable
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Control Gel	Petrolatum (ALLERGIKA® – BASISSALBE)	Not applicable
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 16 (18.75%)	0 / 16 (0.00%)	3 / 16 (18.75%)
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
General disorders and administration site conditions			

Application site pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Application site pruritus			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Application site erosion			
subjects affected / exposed	2 / 16 (12.50%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	4	0	0
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 September 2020	Protocol Amendment 1 Changes in this amendment included: - Inclusion of SARS-CoV-2 screening at the screening visit - Details relating to termination of the study added
28 April 2021	Protocol Amendment 2 Changes in this amendment included: - a shelf life extension due to updated stability data - a change of the sponsor’s address - updated estimated timelines in the protocol and - various further minor updates to the IMPD.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported