



Clinical trial results:

An exploratory randomized, intra-individual controlled trial of the cutaneous healing properties of Petrolatum versus the vehicle for Oleogel-S10 versus no treatment when applied topically to mechanically induced partial thickness wounds in healthy volunteers

Summary

EudraCT number	2019-002081-12
Trial protocol	DE
Global end of trial date	04 March 2020

Results information

Result version number	v1 (current)
This version publication date	10 June 2021
First version publication date	10 June 2021

Trial information

Trial identification

Sponsor protocol code	AHV-18-A
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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 Dublin2, Dublin 2, Ireland, D04 W2F1
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	04 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 March 2020
Global end of trial reached?	Yes
Global end of trial date	04 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe and to measure cutaneous healing of mechanically induced wounds with application of vehicle of Oleogel-S10, petrolatum, and no treatment in healthy volunteers in a wound healing model of mechanically induced wounds.

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	23 January 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: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	12
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Adult healthy volunteers (n = 6 male, n = 6 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 first visit was 23-Jan-2020 and the last patient last visit was 04-Mar-2020.

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 for which 12 proceeded to the recruitment.

Period 1

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

Blinding implementation details:

Study personnel who administered the intervention and the subjects who received the interventions were not blinded. The Investigators and study staff who performed the wound assessments were blinded to treatment.

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 21 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®Film) from Day 1 through Day 10 immediately after product application.

Arm title	Petrolatum (ALLERGIKA® – BASISSALBE)
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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 21 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®Film) from Day 1 through Day 10 immediately after product application.

Arm title	Untreated control
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Arm description:

No topical treatment applied. Covered with a non adhesive wound dressing with a non adherent pad (Mepitel®Film) from Day 1 through Day 10.

Arm type	No intervention
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No investigational medicinal product assigned in this arm

Number of subjects in period 1	Control Gel	Petrolatum (ALLERGIKA® – BASISSALBE)	Untreated control
Started	12	12	12
Completed	11	11	11
Not completed	1	1	1
Lost to follow-up	1	1	1

Baseline characteristics

Reporting groups

Reporting group title	Overall period
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Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	12	12	
Age categorical			
Units: Subjects			
Adults (18-64 years)	12	12	
Gender categorical			
Units: Subjects			
Female	6	6	
Male	6	6	

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)	
Reporting group title	Untreated control
Reporting group description:	
No topical treatment applied. Covered with a non adhesive wound dressing with a non adherent pad (Mepitel®Film) from Day 1 through Day 10.	

Primary: Complete wound healing according to Clinical Score

End point title	Complete wound healing according to Clinical Score ^[1]
End point description:	
A six 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=Greater than 75% re epithelialisation, but not complete healing, 5=100% re epithelialisation [complete healing]).	
End point type	Primary
End point timeframe:	
Wound healing was assessed from Day 1 through Day 28.	

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: As this was an exploratory study, only descriptive statistical methods were applied. The investigational medicinal products (IMPs) and the untreated control were not compared using a statistical test; no null hypotheses were tested.

End point values	Control Gel	Petrolatum (ALLERGIKA® – BASISSALBE)	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	11	
Units: Days to complete wound healing				
number (confidence interval 95%)	13.3 (12.3 to 14.2)	13.4 (12.4 to 14.3)	13.3 (12.3 to 14.3)	

Statistical analyses

No statistical analyses for this end point

Primary: Complete wound healing according to Planimetry

End point title	Complete wound healing according to Planimetry ^[2]
End point description:	
Wound healing measurements (planimetry) were performed by computerised image analysis using the software ImageJ.	

End point type	Primary
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End point timeframe:

Wound healing was assessed from Day 1 through Day 28.

Notes:

[2] - 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: As this was an exploratory study, only descriptive statistical methods were applied. The investigational medicinal products (IMPs) and the untreated control were not compared using a statistical test; no null hypotheses were tested.

End point values	Control Gel	Petrolatum (ALLERGIKA® – BASISSALBE)	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	11	
Units: Days to complete wound healing				
number (confidence interval 95%)	10.6 (9.8 to 11.4)	10.5 (9.6 to 11.3)	10.6 (9.5 to 11.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Adverse Events

End point title	Adverse Events
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End point description:

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

End point type	Secondary
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End point timeframe:

Adverse events (AEs) were monitored throughout the study from the time of informed consent through Day 28.

End point values	Control Gel	Petrolatum (ALLERGIKA® – BASISSALBE)	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	12	12	
Units: Adverse Events				
Medical device site papule	7	7	7	
Application site papules	4	1	2	
Medical device site pustule	1	1	1	
Epistaxis	1	1	1	
Nasopharyngitis	1	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Score Per Day

End point title	Clinical Score Per Day
End point description: A six 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=Greater than 75% re epithelialisation, but not complete healing, 5=100% re epithelialisation [complete healing])	
End point type	Secondary
End point timeframe: Wound healing was assessed from Day 1 through Day 28.	

End point values	Control Gel	Petrolatum (ALLERGIKA® - BASISSALBE)	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	11	
Units: Clinical Score per Day				
median (full range (min-max))				
Day 2	0 (0 to 1)	0 (0 to 0)	0 (0 to 0)	
Day 3	1 (0 to 1)	1 (0 to 1)	1 (0 to 2)	
Day 4	1 (1 to 1)	1 (1 to 1)	1 (1 to 2)	
Day 5	1 (1 to 2)	1 (1 to 2)	1 (1 to 2)	
Day 6	2 (1 to 4)	2 (1 to 3)	2 (1 to 3)	
Day 7	2.5 (2 to 4)	3 (2 to 4)	3 (1 to 4)	
Day 8	3 (2 to 4)	3.5 (2 to 4)	3 (2 to 4)	
Day 9	3.5 (3 to 4)	3.5 (3 to 4)	4 (3 to 4)	
Day 10	4 (3 to 4)	4 (3 to 4)	4 (4 to 4)	
Day 11	4 (4 to 5)	4 (3 to 5)	4 (4 to 5)	
Day 12	4 (4 to 5)	4 (4 to 5)	4 (4 to 5)	
Day 13	4.5 (4 to 5)	5 (4 to 5)	4.5 (4 to 5)	
Day 14	5 (4 to 5)	5 (4 to 5)	5 (4 to 5)	
Day 15	5 (5 to 5)	5 (4 to 5)	5 (4 to 5)	
Day 16 to 28	5 (5 to 5)	5 (5 to 5)	5 (5 to 5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean TEWL Per Wound

End point title	Mean TEWL Per Wound
End point description: TEWL was measured according to international guidelines.	
End point type	Secondary
End point timeframe: Transepidermal water loss (TEWL) was assessed from Day 1 through Day 28.	

End point values	Control Gel	Petrolatum (ALLERGIKA® – BASISSALBE)	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12 ^[3]	12 ^[4]	12 ^[5]	
Units: TEWL Per Day (g/m ² /h)				
arithmetic mean (standard deviation)				
Day 1	76.2 (± 9.4)	75.5 (± 11.0)	77.4 (± 6.7)	
Day 3	73.3 (± 7.7)	74.6 (± 6.7)	76.1 (± 4.8)	
Day 5	58.2 (± 13.4)	62.6 (± 12.2)	60.3 (± 13.7)	
Day 7	23.7 (± 15.6)	26.5 (± 19.5)	25.1 (± 18.4)	
Day 9	14.0 (± 13.9)	15.1 (± 18.0)	15.5 (± 17.9)	
Day 11	9.0 (± 2.7)	11.2 (± 9.4)	11.3 (± 8.3)	
Day 13	10.7 (± 1.9)	10.8 (± 2.9)	12.8 (± 3.4)	
Day 15	12.8 (± 3.6)	11.4 (± 2.9)	13.8 (± 3.9)	
Day 17	11.4 (± 3.1)	10.2 (± 3.2)	11.5 (± 2.1)	
Day 19	10.4 (± 2.4)	9.0 (± 1.5)	10.1 (± 1.9)	
Day 21	10.3 (± 3.3)	9.0 (± 1.7)	9.9 (± 1.6)	
Day 23	8.8 (± 1.8)	8.7 (± 2.1)	8.8 (± 1.6)	
Day 28	9.9 (± 2.7)	10.3 (± 3.0)	10.0 (± 2.8)	

Notes:

[3] - Day 1 to 13: N=12; Day 15 to 28: N=11

[4] - Day 1 to 13: N=12; Day 15 to 28: N=11

[5] - Day 1 to 13: N=12; Day 15 to 28: N=11

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Wound Surface Area According to Planimetry

End point title	Mean Wound Surface Area According to Planimetry
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End point description:

For measurement of wound area, standardised photographs of each wound were taken; at least two photographs were taken at each timepoint and the best image (after assessment for clarity and quality) was stored for subsequent image analysis. Wound healing measurements (planimetry) were performed by computerised image analysis using the software ImageJ.

End point type	Secondary
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End point timeframe:

Wound healing was assessed from Day 1 through Day 28.

End point values	Control Gel	Petrolatum (ALLERGIKA® – BASISSALBE)	Untreated control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12 ^[6]	12 ^[7]	12 ^[8]	
Units: Wound Surface Area Per Day (mm ²)				
arithmetic mean (standard deviation)				

Day 1	43.2 (± 8.1)	44.2 (± 5.5)	42.9 (± 5.8)	
Day 3	32.3 (± 7.3)	35.1 (± 5.8)	34.1 (± 5.7)	
Day 5	18.6 (± 6.2)	19.1 (± 4.9)	20.8 (± 8.2)	
Day 7	8.1 (± 6.7)	6.6 (± 4.0)	7.8 (± 7.4)	
Day 9	1.4 (± 1.9)	1.9 (± 2.5)	4.2 (± 9.9)	
Day 11	0.1 (± 0.2)	0.4 (± 1.0)	0.2 (± 0.6)	
Day 13 to 28	0.0 (± 0.0)	0.0 (± 0.0)	0.0 (± 0.0)	

Notes:

[6] - Day 1 to 9: N=12; Day 11 to 28: N=11

[7] - Day 1 to 9: N=12; Day 11 to 28: N=11

[8] - Day 1 to 9: N=12; Day 11 to 28: N=11

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were monitored throughout the study from the time of informed consent through Day 28.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Petrolatum (ALLERGIKA® – BASISSALBE)
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Reporting group description:

Treatment with Petrolatum (ALLERGIKA® – BASISSALBE)

Reporting group title	Untreated control
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Reporting group description:

No topical treatment applied. Covered with a non adhesive wound dressing with a non adherent pad (Mepitel®Film) from Day 1 through Day 10.

Reporting group title	Control Gel
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Reporting group description:

Treatment with Control Gel

Serious adverse events	Petrolatum (ALLERGIKA® – BASISSALBE)	Untreated control	Control Gel
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (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	Petrolatum (ALLERGIKA® – BASISSALBE)	Untreated control	Control Gel
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 12 (58.33%)	8 / 12 (66.67%)	9 / 12 (75.00%)
General disorders and administration site conditions			
Medical device site papule			
subjects affected / exposed	6 / 12 (50.00%)	6 / 12 (50.00%)	6 / 12 (50.00%)
occurrences (all)	7	7	7
Application site papules			

subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	2 / 12 (16.67%) 2	4 / 12 (33.33%) 4
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 12 (8.33%) 1	1 / 12 (8.33%) 1
Infections and infestations Medical device site pustule subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1 1 / 12 (8.33%) 1	1 / 12 (8.33%) 1 1 / 12 (8.33%) 1	1 / 12 (8.33%) 1 1 / 12 (8.33%) 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? No

Limitations and caveats

None reported