Clinical trial results:
Open Phase IV Study to Assess the Impact of Tirbanibulin on the Wellbeing of Patients With Actinic Keratoses (TIRBASKIN)

Summary

EudraCT number	2022-001251-16
Trial protocol	IT ES
Global end of trial date	19 January 2024

Results information

Result version number	v1 (current)
This version publication date	29 January 2025
First version publication date	29 January 2025

Trial information

Trial identification

Sponsor protocol code	M-14789-42

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05741294
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Almirall S.A.
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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	19 January 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 January 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to assess treatment satisfaction on Day 57 in subjects with AK of the face or scalp following treatment with tirbanibulin ointment 1 percent (%) administered once daily for 5 consecutive days.

Protection of trial subjects:

This trial was conducted in accordance with the recommendations guiding physicians in biomedical research involving human patients adopted by the 18th World Medical Assembly of Helsinki (1964), as amended in Fortaleza, Brazil (2013), as well as in compliance with ICH GCP E6 (R2) guidelines, and local laws of the Countries in which the trial centres were located.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 January 2023
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	Italy: 72
Country: Number of subjects enrolled	Spain: 262
Worldwide total number of subjects	334
EEA total number of subjects	334

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)	38
From 65 to 84 years	264

85 years and over	32

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 37 sites in Europe (7 in Italy and 30 in Spain) from 20 January 2023 to 19 January 2024.

Pre-assignment

Screening details:

A total of 340 subjects were screened, of which 334 subjects enrolled in this study.

Period 1

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

Arms

Arm title	Tirbanibulin 2.5 mg

Arm description:

Subjects applied tirbanibulin ointment- topically at a dose of 2.5 milligrams (mg) once daily for 5 consecutive days on the face or scalp.

Arm type	Experimental
Investigational medicinal product name	Tirbanibulin
Investigational medicinal product code	M-14789-42
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Cutaneous use

Dosage and administration details:

Subjects applied tirbanibulin ointment- topically once daily to a contiguous area of up to 25 square centimeter (cm^2) area of the face or scalp.

Number of subjects in period 1	Tirbanibulin 2.5 mg
Started	334
Evaluable Population	328
LC-OCT Population	12 [1]
Safety Population	334
Completed	327
Not completed	7
Consent withdrawn by subject	1
Lost to follow-up	3
Protocol deviation	3

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestones in this study were added as per the analysis population set.

Baseline characteristics

Reporting groups	
Reporting group title	Tirbanibulin 2.5 mg
Reporting group description:	
Subjects applied tirbanibulin ointment- topically at a dose of 2.5 milligrams (mg) once daily for 5 consecutive days on the face or scalp.	

Reporting group values	Tirbanibulin 2.5 mg	Total	
Number of subjects	334	334	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	74.9		
standard deviation	± 8.51	-	
Gender categorical Units: Subjects			
Female	56	56	
Male	278	278	
Race Units: Subjects			
Caucasian	334	334	

End points

End points reporting groups

Reporting group title	Tirbanibulin 2.5 mg

Reporting group description:

Subjects applied tirbanibulin ointment- topically at a dose of 2.5 milligrams (mg) once daily for 5 consecutive days on the face or scalp.

Primary: Treatment Satisfaction Questionnaire for Medication Version 9 (TSQM-9) Total Score of Each Components at Day 57

End point title	Treatment Satisfaction Questionnaire for Medication Version 9 (TSQM-9) Total Score of Each Components at Day 57[1]

End point description:

TSQM-9 was a 9-item clinically validated psychometric instrument developed from the TSQM 1.4. TSQM-9 measures subject satisfaction with the medication in 3 domains: Effectiveness, convenience, and global satisfaction. The scores were computed by adding items for each domain (1 to 3 for effectiveness, 4 to 6 for convenience, and 7 to 9 for global satisfaction). The lowest possible score (1 for each item and 3 for all 3 subscales) was subtracted from the composite score and divided by the greatest possible score range. The greatest range was (7-1) x 3 items = 18 for effectiveness and convenience, and (5-1) x 3 items = 12 for global satisfaction. This provided a transformed score between 0 and 1 that was multiplied by 100. TSQM-9 domain scores range from 0 to 100, with higher scores indicating greater satisfaction for that domain. A positive change from baseline indicates improvement. Evaluable population.

End point type	Primary

End point timeframe:

At Day 57

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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Tirbanibulin 2.5 mg			
Subject group type	Reporting group			
Number of subjects analysed	328			
Units: score on a scale				
arithmetic mean (confidence interval 95%)				
Effectiveness Total Score Value	73.64 (71.28 to 76.01)			
Convenience Total Score Value	82.81 (81.28 to 84.34)			
Global Satisfaction Total Score Value	76.94 (74.89 to 78.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Skindex-16 Questionnaire Symptoms Sub-Score at Day 57

End point title	Change From Baseline in Skindex-16 Questionnaire Symptoms Sub-Score at Day 57

End point description:

Skindex-16 was used for subjects to rate skin conditions that have occurred within the previous week. The Skindex-16 consisted of 16 items that were divided into three sub-scores: Symptoms (four items, range 0-24), Emotions (seven items, range 0-42), and Functioning (five items, range 0-30). Subject were asked to respond on how much their skin condition bothered them in the week prior to administration of the Skindex-16. Each item was scored on a scale ranged from 0 (never bothered) to 6 (always bothered), where higher score indicated continued/more botheration. Item scores are transformed to 0 to 100 scale, and domain scores are calculated as the average of the item scores comprising the domain. Net positive changes in respective subscale scoring indicates improvement in that particular Quality of life assessment (i.e., Symptoms, Emotions, Functioning), while net negative changes in scoring indicates decrease in that particular Quality of life assessment. Evaluable population.

End point type	Secondary

End point timeframe:

Baseline, Day 57

End point values	Tirbanibulin 2.5 mg			
Subject group type	Reporting group			
Number of subjects analysed	328			
Units: score on a scale				
arithmetic mean (confidence interval 95%)				
Symptoms Sub-Score: Change at Day 57	-10.49 (-12.55 to -8.44)			
Emotions Sub-Score: Change at Day 57	-11.56 (-13.56 to -9.55)			
Functioning Sub-Score: Change at Day 57	-2.49 (-3.98 to -1.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Organoleptic Properties of Tirbanibulin Assessed on a Likert Scale at Day 8

End point title	Percentage of Subjects With Organoleptic Properties of Tirbanibulin Assessed on a Likert Scale at Day 8

End point description:

Likert scale was an instrument used to measure the individual's degree of agreement and disagreement with a variety of statements about some attitude, options, or their feelings. In this study, the product's organoleptic properties are evaluated with Likert scale. The questionnaire was built with questions related to the product's characteristics namely appearance, color, convenience, texture, smell, and the feelings experienced during drug application. The Likert scale offers 7 possible answers, from "totally agree",' In agreement", "Somewhat agree", "Neither agree nor disagree", "Something in disagreement", "In disagreement" and "totally in disagreement". Evaluable population. Here "number of subjects analyzed" signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At Day 8

End point values	Tirbanibulin 2.5 mg			
Subject group type	Reporting group			
Number of subjects analysed	327			
Units: Percentage of subjects				
number (confidence interval 95%)				
General appearance(good): Totally agree	52.60 (43.75 to 61.34)			
General appearance(good): In agreement	38.23 (29.91 to 47.04)			
General appearance(good): Somewhat agree	3.06 (0.85 to 7.22)			
General appearance(good): Neither agree/disagree	5.20 (2.11 to 10.15)			
Generalappearance(good): Something in disagreement	0.31 (0.00 to 2.76)			
General appearance(good): In disagreement	0.61 (0.00 to 3.36)			
General appearance(good): Totally in disagreement	0.0 (0.0 to 0.0)			
Overall assessment: Totally agree	36.70 (27.64 to 46.33)			
Overall assessment: In agreement	38.53 (29.35 to 48.21)			
Overall assessment: Somewhat agree	8.26 (3.75 to 14.57)			
Overall assessment: Neither agree/disagree	10.40 (5.28 to 17.23)			
Overall assessment: Something in disagreement	1.53 (0.00 to 5.18)			
Overall assessment: In disagreement	3.36 (0.74 to 8.01)			
Overall assessment: Totally in disagreement	1.22 (0.00 to 4.66)			
Would recommend: Totally agree	34.86 (25.95 to 44.43)			
Would recommend: In agreement	33.64 (24.83 to 43.15)			
Would recommend: Somewhat agree	5.81 (2.13 to 11.40)			
Would recommend: Neither agree/disagree	18.04 (11.25 to 26.22)			
Would recommend: Something in disagreement	1.22 (0.00 to 4.66)			
Would recommend: In disagreement	3.06 (0.59 to 7.56)			
Would recommend: Totally in disagreement	3.36 (0.74 to 8.01)			
Color: Totally agree	36.70 (29.37 to 44.55)			
Color: In agreement	36.09 (28.80 to 43.92)			
Color: Somewhat agree	5.81 (2.90 to 10.47)			
Color: Neither agree/disagree	20.80 (14.96 to 27.79)			
Color: Something in disagreement	0.0 (0.0 to 0.0)			

Color: In disagreement	0.61 (0.02 to 3.17)			
Color: Totally in disagreement	0.0 (0.0 to 0.0)			
Texture (Nice): Totally agree	48.93 (40.14 to 57.76)			
Texture (Nice): In agreement	40.37 (31.92 to 49.21)			
Texture (Nice): Somewhat agree	5.20 (2.11 to 10.15)			
Texture (Nice): Neither agree/disagree	4.28 (1.54 to 8.93)			
Texture (Nice): Something in disagreement	0.61 (0.00 to 3.36)			
Texture (Nice): In disagreement	0.61 (0.00 to 3.36)			
Texture (Nice): Totally in disagreement	0.00 (0.00 to 0.00)			
Texture (Watery): Totally agree	12.84 (7.12 to 20.18)			
Texture (Watery): In agreement	18.65 (11.76 to 26.91)			
Texture (Watery): Somewhat agree	9.79 (4.83 to 16.48)			
Texture (Watery): Neither agree/disagree	15.90 (9.52 to 23.76)			
Texture (Watery): Something in disagreement	8.26 (3.75 to 14.57)			
Texture (Watery): In disagreement	19.88 (12.77 to 28.29)			
Texture (Watery): Totally in disagreement	14.68 (8.54 to 22.34)			
Texture (oily): Totally agree	11.31 (5.96 to 18.35)			
Texture (oily): In agreement	15.90 (9.52 to 23.76)			
Texture (oily): Somewhat agree	9.48 (4.61 to 16.10)			
Texture (oily): Neither agree/disagree	16.82 (10.26 to 24.82)			
Texture (oily): Something in disagreement	6.73 (2.72 to 12.61)			
Texture (oily): In disagreement	20.49 (13.28 to 28.97)			
Texture (oily): Totally in disagreement	19.27 (12.26 to 27.60)			
Texture (creamy): Totally agree	40.06 (30.78 to 49.77)			
Texture (creamy): In agreement	41.28 (31.93 to 51.01)			
Texture (creamy): Somewhat agree	7.03 (2.92 to 13.00)			
Texture (creamy): Neither agree/disagree	7.34 (3.13 to 13.40)			
Texture (creamy): Something in disagreement	1.53 (0.00 to 5.18)			
Texture (creamy): In disagreement	1.83 (0.08 to 5.68)			
Texture (creamy): Totally in disagreement	0.92 (0.00 to 4.11)			
Skin was greasy: Totally agree	12.84 (7.12 to 20.18)			

Skin was greasy: In agreement	25.08 (17.20 to 34.03)			
Skin was greasy: Somewhat agree	14.68 (8.54 to 22.34)			
Skin was greasy: Neither agree/disagree	8.56 (3.96 to 14.95)			
Skin was greasy: Something in disagreement	3.98 (1.06 to 8.89)			
Skin was greasy: In disagreement	17.13 (10.50 to 25.17)			
Skin was greasy: Totally in disagreement	17.74 (11.00 to 25.87)			
Product smell: Totally agree	23.85 (16.14 to 32.70)			
Product smell: In agreement	23.55 (15.88 to 32.36)			
Product smell: Somewhat agree	7.65 (3.33 to 13.79)			
Product smell: Neither agree/disagree	42.51 (33.09 to 52.25)			
Product smell: Something in disagreement	0.61 (0.00 to 3.53)			
Product smell: In disagreement	0.92 (0.00 to 4.11)			
Product smell: Totally in disagreement	0.92 (0.00 to 4.11)			
Pleasant product: Totally agree	27.22 (19.07 to 36.35)			
Pleasant product: In agreement	30.28 (21.79 to 39.61)			
Pleasant product: Somewhat agree	10.70 (5.50 to 17.60)			
Pleasant product: Neither agree/disagree	21.10 (13.80 to 29.66)			
Pleasant product: Something in disagreement	1.83 (0.08 to 5.68)			
Pleasant product: In disagreement	5.50 (1.95 to 10.99)			
Pleasant product: Totally in disagreement	3.36 (0.74 to 8.01)			
Product refreshing: Totally agree	18.35 (11.50 to 26.56)			
Product refreshing: In agreement	20.80 (13.54 to 29.32)			
Product refreshing: Somewhat agree	11.31 (5.96 to 18.35)			
Product refreshing: Neither agree/disagree	22.94 (15.36 to 31.69)			
Product refreshing: Something in disagreement	5.81 (2.13 to 11.40)			
Product refreshing: In disagreement	10.09 (5.06 to 16.86)			
Product refreshing: Totally in disagreement	10.70 (5.50 to 17.60)			
Protective feeling: Totally agree	20.80 (13.54 to 29.32)			
Protective feeling: In agreement	25.38 (17.47 to 34.36)			
Protective feeling: Somewhat agree	9.48 (4.61 to 16.10)			
Protective feeling: Neither agree/disagree	30.28 (21.79 to 39.61)			

Protective feeling: Something in disagreement	3.06 (0.59 to 7.56)			
Protective feeling: In disagreement	5.81 (2.13 to 11.40)			
Protective feeling: Totally in disagreement	5.20 (1.76 to 10.58)			
Easy to apply: Totally agree	66.36 (56.85 to 75.17)			
Easy to apply: In agreement	27.22 (19.07 to 36.35)			
Easy to apply: Somewhat agree	3.67 (0.89 to 8.45)			
Easy to apply: Neither agree/disagree	0.92 (0.00 to 4.11)			
Easy to apply: Something in disagreement	0.92 (0.00 to 4.11)			
Easy to apply: In disagreement	0.31 (0.00 to 2.90)			
Easy to apply: Totally in disagreement	0.61 (0.00 to 3.53)			
Product distributed: Totally agree	64.53 (55.79 to 72.66)			
Product distributed: In agreement	29.05 (21.48 to 37.50)			
Product distributed: Somewhat agree	4.28 (1.54 to 8.93)			
Product distributed: Neither agree/disagree	0.61 (0.00 to 3.36)			
Product distributed: Something in disagreement	0.92 (0.00 to 3.91)			
Product distributed: In disagreement	0.61 (0.00 to 3.36)			
Product distributed: Totally in disagreement	0.0 (0.0 to 0.0)			
Application area: Totally agree	57.19 (47.44 to 66.62)			
Application area: In agreement	29.97 (21.52 to 39.29)			
Application area: Somewhat agree	6.12 (2.33 to 11.81)			
Application area: Neither agree/disagree	2.75 (0.44 to 7.11)			
Application area: Something in disagreement	2.14 (0.19 to 6.17)			
Application area: In disagreement	0.61 (0.00 to 3.53)			
Application area: Totally in disagreement	1.22 (0.00 to 4.66)			
Product packaging: Totally agree	50.76 (41.06 to 60.43)			
Product packaging: In agreement	33.94 (25.11 to 43.47)			
Product packaging: Somewhat agree	6.12 (2.33 to 11.81)			
Product packaging: Neither agree/disagree	3.06 (0.59 to 7.56)			
Product packaging: Something in disagreement	2.14 (0.19 to 6.17)			
Product packaging: In disagreement	3.36 (0.74 to 8.01)			
Product packaging: Totally in disagreement	0.61 (0.00 to 3.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Satisfaction Questionnaire for Medication Version 1.4 (TSQM 1.4) Components Scores at Day 57

End point title	Treatment Satisfaction Questionnaire for Medication Version 1.4 (TSQM 1.4) Components Scores at Day 57

End point description:

TSQM 1.4 was a 14-item robust instrument that psychometrically evaluates the treatment satisfaction of the administered medication. The instrument is designed with 4 scales consisting of 14 questions. These 14 questions were derived from an original set of 55 questions extracted from exhaustive literature review and treatment groups through multistep iterative process. The 4 scales focused on effectiveness (questions: 1-3), side effects (questions: 4-8), convenience (questions: 9-11), global satisfaction (questions:12-14). Global Satisfaction- Question 12 scored as 1 (not at all confident) to 5 (extremely confident); question 13 scored as 1 (not at all certain) to 5 (extremely certain); and question 14 scored as 1 (extremely dissatisfied) to 7 (extremely satisfied). The scores of the domain were added together and an algorithm was used to create a score of 0 to 100. Higher scores indicated greater satisfaction. Evaluable population.

End point type	Secondary

End point timeframe:

At Day 57

End point values	Tirbanibulin 2.5 mg			
Subject group type	Reporting group			
Number of subjects analysed	328			
Units: score on a scale				
arithmetic mean (confidence interval 95%)				
Effectiveness score value at Day 57	73.64 (71.28 to 76.01)			
Convenience score value at Day 57	82.81 (81.28 to 84.34)			
Side Effects score value at Day 57	97.47 (96.59 to 98.34)			
Global satisfaction score value at Day 57	76.94 (74.89 to 78.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients who Answered Expert Panel Questionnaire (EPQ) (Question 1 to Question 9) at Day 57

End point title	Percentage of Patients who Answered Expert Panel Questionnaire (EPQ) (Question 1 to Question 9) at Day 57

End point description:

Expert panel on consensus developed a questionnaire directed to patients consisting of 9 simple items using a qualitative modified delphi method and agreed to ask 9 specific items; 1: Overall appearance of the skin (much worse to much improved); 2: Treatment satisfaction of skin looks (extremely dissatisfied to extremely satisfied); 3: Treatment satisfaction of skin texture (extremely dissatisfied to extremely satisfied); 4: Duration of skin reactions (much shorter to much longer); 5: rate the severity of skin reactions (much better to much worse); 6: impact on your daily activities due to skin reactions (much better to much worse); 7: rate the convenience/ease of use (much better to much worse); 8: rate your overall satisfaction (much better to much worse); 9: You need to be retreated for AK, how likely are you to consider tirbanibulin (very unlikely to very likely). Evaluable population. Here, "n" signifies subjects who were evaluable at specific category.

End point type	Secondary

End point timeframe:

At Day 57

End point values	Tirbanibulin 2.5 mg			
Subject group type	Reporting group			
Number of subjects analysed	328			
Units: Percentage of patients				
number (confidence interval 95%)				
Overall appearance: Much worse (n=318)	0.31 (0.00 to 2.68)			
Overall appearance: Somewhat worse (n=318)	0.31 (0.00 to 2.68)			
Overall appearance: No change (n=318)	6.92 (3.66 to 11.94)			
Overall appearance: Somewhat improved (n=318)	24.84 (18.45 to 32.27)			
Overall appearance: Much improved (n=318)	67.61 (59.78 to 74.72)			
Skin look: Extremely Dissatisfied (n=318)	0 (0 to 0)			
Skin look: Very Dissatisfied (n=318)	0.63 (0.00 to 3.45)			
Skin look: Dissatisfied (n=318)	2.83 (0.71 to 6.97)			
Skin look: Somewhat Satisfied (n=318)	7.23 (3.43 to 12.86)			
Skin look: Satisfied (n=318)	25.79 (18.47 to 34.14)			
Skin look: Very Satisfied (n=318)	30.19 (22.40 to 38.82)			
Skin look: Extremely Satisfied (n=318)	33.33 (25.26 to 42.12)			
Skin texture: Extremely Dissatisfied (n=321)	0 (0 to 0)			
Skin texture: Very Dissatisfied (n=321)	1.25 (0.05 to 4.51)			
Skin texture: Dissatisfied (n=321)	2.80 (0.70 to 6.91)			
Skin texture: Somewhat Satisfied (n=321)	7.17 (3.40 to 12.75)			
Skin texture: Satisfied (n=321)	30.84 (23.03 to 39.47)			

Skin texture: Very Satisfied (n=321)	27.73 (20.23 to 36.17)			
Skin texture: Extremely Satisfied (n=321)	36.17 (22.46 to 38.81)			
Duration of skin reactions: Much shorter (n=186)	44.62 (34.53 to 55.09)			
Duration of skin reactions:Somewhatshorter (n=186)	23.66 (15.73 to 33.40)			
Duration of skin reactions: Same (n=186)	18.82 (11.74 to 28.04)			
Duration of skin reactions:Somewhatlonger (n=186)	9.14 (4.42 to 16.67)			
Duration of skin reactions: Much longer (n=186)	3.76 (1.11 to 9.60)			
Severity (skin reactions): Much better (n=187)	51.34 (40.98 to 61.60)			
Severity (skin reactions): Somewhat better (n=187)	21.93 (14.30 to 31.47)			
Severity (skin reactions): Same (n=187)	16.58 (9.97 to 25.48)			
Severity (skin reactions): Somewhat worse (n=187)	8.02 (3.68 to 15.24)			
Severity (skin reactions): Much worse (n=187)	2.14 (0.37 to 7.18)			
Daily activities: Much better (n=189)	49.74 (39.48 to 60.00)			
Daily activities: Somewhat better (n=189)	13.76 (7.81 to 22.16)			
Daily activities: Same (n=189)	31.75 (22.79 to 41.94)			
Daily activities: Somewhat worse (n=189)	3.70 (1.09 to 9.46)			
Daily activities: Much worse (n=189)	1.06 (0.04 to 5.39)			
Convenience/ease: Much better (n=207)	57.97 (48.02 to 67.42)			
Convenience/ease: Somewhat better (n=207)	19.81 (12.86 to 28.63)			
Convenience/ease: Same (n=207)	19.81 (12.86 to 28.63)			
Convenience/ease: Somewhat worse (n=207)	1.93 (0.34 to 6.51)			
Convenience/ease: Much worse (n=207)	0.48 (0.00 to 4.08)			
Overall satisfaction: Much better (n=209)	60.29 (50.40 to 69.54)			
Overall satisfaction: Somewhat better (n=209)	21.53 (14.32 to 30.49)			
Overall satisfaction: Same (n=209)	13.40 (7.77 to 21.28)			
Overall satisfaction: Somewhat worse (n=209)	3.83 (1.24 to 9.26)			
Overall satisfaction: Much worse (n=209)	0.96 (0.04 to 4.89)			
Retreated for AK: Very unlikely (n=328)	3.66 (1.49 to 7.67)			
Retreated for AK: Somewhat unlikely (n=328)	2.44 (0.78 to 5.98)			
Retreated for AK: Neutral (n=328)	7.62 (4.21 to 12.72)			
Retreated for AK: Somewhat likely (n=328)	18.60 (13.08 to 25.37)			

Retreated for AK: Very likely (n=328)	67.68 (59.98 to 74.69)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Physician Who Answered Expert Panel Questionnaire (EPQ) (Question 1 to Question 10) at Day 57

End point title	Percentage of Physician Who Answered Expert Panel Questionnaire (EPQ) (Question 1 to Question 10) at Day 57

End point description:

Expert panel on consensus developed a questionnaire directed to physicians consisting of 10 simple items using a qualitative modified delphi method and agreed to ask 10 specific items-1: Overall appearance of the skin (much worse to much improved); 2: Treatment satisfaction of skin looks (extremely dissatisfied-extremely satisfied); 3: Treatment satisfaction of skin texture (extremely dissatisfied-extremely satisfied); 4: Duration of skin reactions (much shorter-much longer); 5: rate the severity of skin reactions (much better-much worse); 6: impact on patient's daily activities due to skin reactions (much better-much worse); 7: rate the convenience/ease of use (much better-much worse); 8: rate your overall satisfaction (much better-much worse); 9: patient needs to be retreated for AK, how likely to consider tirbanibulin (very unlikely-very likely);10: severity of skin photodamage in the original AK treated area (absent-severe). Evaluable population.

End point type	Secondary

End point timeframe:

At Day 57

End point values	Tirbanibulin 2.5 mg			
Subject group type	Reporting group			
Number of subjects analysed	326			
Units: Percentage of physician				
number (confidence interval 95%)				
Overall appearance: Much worse (n=326)	1.23 (0.21 to 4.19)			
Overall appearance: Somewhat worse (n=326)	1.23 (0.21 to 4.19)			
Overall appearance: No change (n=326)	1.23 (0.21 to 4.19)			
Overall appearance: Somewhat improved (n=326)	21.78 (15.81 to 28.87)			
Overall appearance: Much improved (n=326)	74.54 (67.17 to 80.93)			
Skin look: Extremely Dissatisfied (n=324)	0.31 (0.00 to 2.93)			
Skin look: Very Dissatisfied (n=324)	0.31 (0.00 to 2.93)			
Skin look: Dissatisfied (n=324)	0.31 (0.00 to 2.93)			
Skin look: Somewhat Satisfied (n=324)	6.79 (2.75 to 12.72)			
Skin look: Satisfied (n=324)	25.31 (17.37 to 34.33)			

Skin look: Very Satisfied (n=324)	31.48 (22.84 to 40.93)			
Skin look: Extremely Satisfied (n=324)	35.49 (26.49 to 45.13)			
Skin texture: Extremely Dissatisfied (n=325)	0.31 (0.00 to 2.92)			
Skin texture: Very Dissatisfied (n=325)	0.31 (0.00 to 2.92)			
Skin texture: Dissatisfied (n=325)	0.92 (0.00 to 4.14)			
Skin texture: Somewhat Satisfied (n=325)	6.77 (2.74 to 12.68)			
Skin texture: Satisfied (n=325)	27.69 (19.47 to 36.89)			
Skin texture: Very Satisfied (n=325)	32.92 (24.16 to 42.43)			
Skin texture: Extremely Satisfied (n=325)	31.08 (22.49 to 40.49)			
Duration of skin reactions: Much shorter (n=223)	60.09 (50.51 to 69.08)			
Duration of skin reactions:Somewhatshorter (n=223)	27.35 (19.54 to 36.48)			
Duration of skin reactions: Same (n=223)	8.52 (4.29 to 15.14)			
Duration of skin reactions:Somewhatlonger (n=223)	3.14 (0.92 to 8.06)			
Duration of skin reactions: Much longer (n=223)	0.90 (0.03 to 4.60)			
Severity (skin reactions): Much better (n=222)	64.86 (55.36 to 73.15)			
Severity (skin reactions): Somewhat better (n=222)	22.07 (14.96 to 30.80)			
Severity (skin reactions): Same (n=222)	9.01 (4.63 to 15.76)			
Severity (skin reactions): Somewhat worse (n=222)	3.60 (1.16 to 8.74)			
Severity (skin reactions): Much worse (n=222)	0.45 (0.00 to 3.81)			
Daily activities: Much better (n=214)	59.81 (50.04 to 69.00)			
Daily activities: Somewhat better (n=214)	19.63 (12.81 to 28.27)			
Daily activities: Same (n=214)	19.63 (12.81 to 28.27)			
Daily activities: Somewhat worse (n=214)	0.47 (0.00 to 3.95)			
Daily activities: Much worse (n=214)	0.47 (0.00 to 3.95)			
Convenience/ease: Much better (n=225)	65.78 (57.55 to 73.16)			
Convenience/ease: Somewhat better (n=225)	25.33 (18.82 to 33.17)			
Convenience/ease: Same (n=225)	5.33 (2.66 to 10.42)			
Convenience/ease: Somewhat worse (n=225)	3.56 (1.52 to 8.10)			
Convenience/ease: Much worse (n=225)	0.0 (0.00 to 0.00)			
Overall satisfaction: Much better (n=227)	50.66 (41.25 to 60.03)			
Overall satisfaction: Somewhat better (n=227)	37.00 (28.30 to 46.45)			

Overall satisfaction: Same (n=227)	11.01 (6.14 to 18.11)			
Overall satisfaction: Somewhat worse (n=227)	0.88 (0.03 to 4.52)			
Overall satisfaction: Much worse (n=227)	0.44 (0.00 to 3.73)			
Retreated for AK: Very unlikely (n=326)	3.68 (1.50 to 7.71)			
Retreated for AK: Somewhat unlikely (n=326)	1.53 (0.34 to 4.66)			
Retreated for AK: Neutral (n=326)	7.67 (4.24 to 12.79)			
Retreated for AK: Somewhat likely (n=326)	23.01 (16.89 to 30.20)			
Retreated for AK: Very likely (n=326)	64.11 (56.26 to 71.39)			
Skin photodamage: Absent (n=326)	24.85 (19.38 to 31.26)			
Skin photodamage: Mild (n=326)	46.63 (39.85 to 53.53)			
Skin photodamage: Moderate (n=326)	27.61 (21.89 to 34.17)			
Skin photodamage: Severe (n=326)	0.92 (0.24 to 3.44)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Complete (100%) Clearance of All Lesions Within the Application Area at Day 57

End point title	Percentage of Subjects With Complete (100%) Clearance of All Lesions Within the Application Area at Day 57

End point description:

Complete clearance of all AK lesions within the application area, is defined as a reduction from baseline in the number of lesions = 100% at Day 57. Percentage of subjects with complete clearance with a reduction of 100% (i.e., clearance percentage = 100% from Baseline) in the number of lesions within the application area were reported. Evaluable population.

End point type	Secondary

End point timeframe:

At Day 57

End point values	Tirbanibulin 2.5 mg			
Subject group type	Reporting group			
Number of subjects analysed	328			
Units: Percentage of subjects				
number (confidence interval 95%)	54.27 (48.71 to 59.75)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Partial Clearance (Reduction of at Least >=75% to <100%) of All Lesions Within the Application Area at Day 57

End point title	Percentage of Subjects With Partial Clearance (Reduction of at Least >=75% to <100%) of All Lesions Within the Application Area at Day 57

End point description:

Subjects with partial clearance were patients with a reduction of >=75% (i.e., clearance percentage <=-75% from Baseline) to <100% in the number of lesions within the application area at final visit. Evaluable population.

End point type	Secondary

End point timeframe:

At Day 57

End point values	Tirbanibulin 2.5 mg			
Subject group type	Reporting group			
Number of subjects analysed	328			
Units: Percentage of subjects				
number (confidence interval 95%)	22.56 (18.15 to 27.47)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Mean Number of Old and New AK Lesions at Day 57

End point title	Percent Change From Baseline in Mean Number of Old and New AK Lesions at Day 57

End point description:

Percent change from baseline in number of old and new AK lesions at Day 57 was reported. Number of lesions at Day 57 was calculated considering both old and new lesions, as: N lesions at Baseline - N lesions at Day 57/ N lesions at Baseline * 100%. Evaluable population.

End point type	Secondary

End point timeframe:

At Day 57

End point values	Tirbanibulin 2.5 mg			
Subject group type	Reporting group			
Number of subjects analysed	328			
Units: Percent change				
arithmetic mean (standard deviation)	-82.22 (± 26.367)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects by Olsen characterization at Baseline and Day 57

End point title	Percentage of Subjects by Olsen characterization at Baseline and Day 57

End point description:

The lesions in the identified treatment area will be classified based on Olsen characterization. Classification of AK lesions according to Olsen grade of baseline lesions: Olsen Grade I: Early AK appear as single or few, differently sized, rough, blurred, less visible than palpable, red, rough spots or very flat, non-edged plaques which reach into the reddish color; Olsen grade II: describes advanced AK as clearly visible and palpable, flat, and irregularly raised, with sharp or blurred boundaries, red, rough keratinized surface. If the surface is more strongly keratinized, the AK can also be white, yellow, or light brown. After scratching effects, a black or blue-black shade may appear; Olsen grade III: denotes "late" AK that have existed for a longer period of time and are firmly anchored on the lower surface, with an irregular, humpy surface, also wart-like and of different colors (white, brown, black). Evaluable population.

End point type	Secondary

End point timeframe:

Baseline (Day 0) and Day 57

End point values	Tirbanibulin 2.5 mg			
Subject group type	Reporting group			
Number of subjects analysed	328			
Units: Percentage of subjects				
number (confidence interval 95%)				
Olsen Grade I: Baseline	62.80 (54.95 to 70.15)			
Olsen Grade I: Day 57	39.33 (30.95 to 48.15)			
Olsen Grade II: Baseline	8.84 (5.12 to 14.19)			
Olsen Grade II: Day 57	3.66 (1.18 to 8.06)			
Olsen Grade III: Baseline	0 (0 to 0)			
Olsen Grade III: Day 57	0.30 (0.00 to 2.75)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Performed Line-field Confocal Optical Coherence Tomography (LC-OCT) for Clinical and Sub Clinical Lesions Assessment at Each Timepoint

End point title	Percentage of Subjects Who Performed Line-field Confocal Optical Coherence Tomography (LC-OCT) for Clinical and Sub Clinical Lesions Assessment at Each Timepoint

End point description:

LC-OCT was a novel non-invasive imaging technique that enables in vivo visualization of the skin. It has been used for diagnosing and monitoring the treatment of skin disorders, including actinic keratosis. The use of LC-OCT in AK treatment progression allows for lesion classification based on histological features without the need for a biopsy. The histopathology of the skin was evaluated based on the estimated atypia score at cellular level of the LC-OCT images of clinical and subclinical lesions. Percentage of participants who performed LC-OCT for clinical and subclinical lesions assessment at each timepoint were reported. LC-OCT population consisted of FAS participants who performed at least one valid LC-OCT assessment.

End point type	Secondary

End point timeframe:

Baseline, Day 8, Day 15, Day 29, and Day 57

End point values	Tirbanibulin 2.5 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of subjects				
number (not applicable)				
At Baseline	100.00			
At Day 8	91.67			
At Day 15	91.67			
At Day 29	91.67			
At Day 57	100.00			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs) and Severity of TEAEs

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs) and Severity of TEAEs

End point description:

An adverse event (AE) is as any untoward medical occurrence associated with the use of an intervention in humans after providing written informed consent for subjects in the study until the end of study visit, whether considered intervention-related or not. A TEAE is defined as an AE with an onset that occurs after receiving study drug. Severity of TEAEs is graded as follows: Grade 1 Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated. Grade 2 Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate activities of daily living. Grade 3 Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living. Grade 4 Life-threatening consequences; urgent intervention indicated. Safety population consisted of FAS subjects.

End point type	Secondary

End point timeframe:

From start of study administration up to Day 57

End point values	Tirbanibulin 2.5 mg			
Subject group type	Reporting group			
Number of subjects analysed	334			
Units: Subjects				
Subjects with TEAEs	153			
Severity of TEAEs: Grade 1	131			
Severity of TEAEs: Grade 2	17			
Severity of TEAEs: Grade 3	3			
Severity of TEAEs: Grade 4	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of study administration up to Day 57	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0
Reporting groups	
Reporting group title	Tirbanibulin 2.5 mg
Reporting group description:	
Participants applied tirbanibulin ointment- topically at a dose of 2.5 mg once daily for 5 consecutive days on the face or scalp.	

Serious adverse events	Tirbanibulin 2.5 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 334 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Tirbanibulin 2.5 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	153 / 334 (45.81%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	3 / 334 (0.90%)		
occurrences (all)	3		
Neoplasm			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	2		
Hypotension			

subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
General disorders and administration site conditions			
Application site hypersensitivity			
subjects affected / exposed	2 / 334 (0.60%)		
occurrences (all)	2		
Application site pain			
subjects affected / exposed	3 / 334 (0.90%)		
occurrences (all)	5		
Asthenia			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Burning sensation			
subjects affected / exposed	17 / 334 (5.09%)		
occurrences (all)	19		
Chills			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	6 / 334 (1.80%)		
occurrences (all)	6		
Inflammation			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	31 / 334 (9.28%)		
occurrences (all)	34		
Temperature intolerance			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	2		
Tenderness			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Immune system disorders			

Hypersensitivity subjects affected / exposed occurrences (all)	6 / 334 (1.80%) 6		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) Fall subjects affected / exposed occurrences (all) Skin injury subjects affected / exposed occurrences (all) Wound subjects affected / exposed occurrences (all)	 1 / 334 (0.30%) 1 2 / 334 (0.60%) 2 1 / 334 (0.30%) 1 2 / 334 (0.60%) 2		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all)	 2 / 334 (0.60%) 2 13 / 334 (3.89%) 13 2 / 334 (0.60%) 2 1 / 334 (0.30%) 1		
Ear and labyrinth disorders Deafness neurosensory subjects affected / exposed occurrences (all)	 1 / 334 (0.30%) 1		
Eye disorders Conjunctival haemorrhage			

subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Eye swelling			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	2 / 334 (0.60%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	2 / 334 (0.60%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	5 / 334 (1.50%)		
occurrences (all)	5		
Cellulite			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Dermatitis allergic			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Pain of skin			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Photodermatosis			

subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	92 / 334 (27.54%)		
occurrences (all)	96		
Skin burning sensation			
subjects affected / exposed	2 / 334 (0.60%)		
occurrences (all)	2		
Thermal burn			
subjects affected / exposed	4 / 334 (1.20%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 334 (0.60%)		
occurrences (all)	2		
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	2 / 334 (0.60%)		
occurrences (all)	2		
Pharyngitis			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 334 (0.30%)		
occurrences (all)	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