Clinical trial results:
A prospective, single center, randomized, double-blind, placebo controlled study in two phases to evaluate the safety and efficacy of ATx201 as a topical antibiotic agent

Summary

EudraCT number	2016-003501-33
Trial protocol	AT
Global end of trial date	12 March 2018

Results information

Result version number	v1 (current)
This version publication date	31 October 2019
First version publication date	31 October 2019

Trial information

Trial identification

Sponsor protocol code	DECOLAD

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	UNION therapeutics A/S (formerly AntibioTx A/S)
Sponsor organisation address	Tuborg Havnevej 18, Hellerup, Denmark,
Public contact	UNION therapeutics A/S (formerly AntibioTx A/S), UNION therapeutics A/S (formerly AntibioTx A/S), +45 40103044, rasmus.toft-kehler@uniontherapeutics.com
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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	11 January 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to demonstrate the safety and tolerability of topical formulations of ATx201 in healthy volunteers and in patients with atopic dermatitis (AD), and to assess efficacy of ATx201 in eradicating S. aureus compared to vehicle after 4 and 7 days of treatment.
To determine the local and systemic exposure of ATx201 (Part 1 and 2) and best tolerable formulation to advance into Part 2 and to assess the impact of ATx201 on AD lesions (Part 2).

Protection of trial subjects:

Safety and tolerability endpoints (Part 1 and 2): Physical exam, vital signs, ECG (Part 1 only), safety laboratory, number, type and severity of (serious) adverse events (AE), local tolerability assessment scores compared to vehicle.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2016
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	Austria: 66
Worldwide total number of subjects	66
EEA total number of subjects	66

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)	66
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In part 1, 6 additional healthy volunteers were not exposed to the IP and were planned and enrolled for bioanalytical method validation.

Pre-assignment

Screening details:

The study was conducted in two Phases. In both Phases of the study subjects were screened at a Screening Visit. Part 1 (Phase 1) consisted of the screening Visit, a 7-day treatment period, and an end of study (EOS) visit on Day 15. Part 2 (Phase 2) consisted of a screening Visit, a 7-day treatment period, and an EOS visit on Day 14.

Period 1

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

Blinding implementation details:

Unblinded due to their profession were • Responsible staff for preparation of code break envelopes and • Responsible persons for production and labeling of the IP. On Day 8 of Part 1, blinding was broken before biopsy sampling, to detect areas that received active treatment. Routine unblinding of study subjects was prohibited, except for Part 1 in subjects undergoing biopsy sampling. Safety assessments were performed in the morning of Day 8. Biopsy samples were taken after the last application.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment arm 1

Arm description:

Consisted of the screening Visit, a 7-day treatment period (subjects received two formulations of ATx201 and vehicle), and an end of study (EOS) visit on Day 15. Subjects were treated in 4 separate areas, 2 on the right arm and 2 on the right or left arm, twice daily at the study site. For the subjects biopsies were set on Day 8, one hour after 15th application (±10 minutes) of the IP.

Arm type	Experimental
Investigational medicinal product name	ATx201 Anhydrous Cream 2%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Each subject in Part 1 was treated with four formulations (two active formulations and their corresponding vehicles). The IPs were applied to defined skin areas in the dorsal arms twice daily. The body area to be treated was circle marked with a skin marker and had a size of 5 cm in diameter. The expected dose of 80-200 mg of the dermal formulation corresponds to 1.6-4.0 mg active substance/day.

Investigational medicinal product name	ATx201 Anhydrous Cream Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Each subject in Part 1 was treated with four formulations (two active formulations and their corresponding vehicles). The IPs were applied to defined skin areas in the dorsal arms twice daily. The body area to be treated was circle marked with a skin marker and had a size of 5 cm in diameter. The expected dose of 80-200 mg of the dermal formulation corresponds to 1.6-4.0 mg active substance/day.

Investigational medicinal product name	ATx201 GEL 2%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

Each subject in Part 1 was treated with four formulations (two active formulations and their corresponding vehicles). The IPs were applied to defined skin areas in the dorsal arms twice daily. The body area to be treated was circle marked with a skin marker and had a size of 5 cm in diameter. The expected dose of 80-200 mg of the dermal formulation corresponds to 1.6-4.0 mg active substance/day.

Investigational medicinal product name	ATx201 GEL Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

Each subject in Part 1 was treated with four formulations (two active formulations and their corresponding vehicles). The IPs were applied to defined skin areas in the dorsal arms twice daily. The body area to be treated was circle marked with a skin marker and had a size of 5 cm in diameter. The expected dose of 80-200 mg of the dermal formulation corresponds to 1.6-4.0 mg active substance/day.

Arm title	Treatment arm 2

Arm description:

Consisted of the screening Visit, a 7-day treatment period (subjects received two formulations of ATx201 and vehicle), and an end of study (EOS) visit on Day 15. Subjects were treated in 4 separate areas, 2 on the right arm and 2 on the right or left arm, twice daily at the study site. For the subjects biopsies were set on Day 8, one hour after 15th application (±10 minutes) of the IP.

Arm type	Experimental
Investigational medicinal product name	ATx201 Anhydrous Cream 2%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Each subject in Part 1 was treated with four formulations (two active formulations and their corresponding vehicles). The IPs were applied to defined skin areas in the dorsal arms twice daily. The body area to be treated was circle marked with a skin marker and had a size of 5 cm in diameter. The expected dose of 80-200 mg of the dermal formulation corresponds to 1.6-4.0 mg active substance/day.

Investigational medicinal product name	ATx201 Anhydrous Cream Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Each subject in Part 1 was treated with four formulations (two active formulations and their corresponding vehicles). The IPs were applied to defined skin areas in the dorsal arms twice daily. The body area to be treated was circle marked with a skin marker and had a size of 5 cm in diameter. The expected dose of 80-200 mg of the dermal formulation corresponds to 1.6-4.0 mg active substance/day.

Investigational medicinal product name	ATx201 Cream 2%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Each subject in Part 1 was treated with four formulations (two active formulations and their corresponding vehicles). The IPs were applied to defined skin areas in the dorsal arms twice daily. The body area to be treated was circle marked with a skin marker and had a size of 5 cm in diameter. The

expected dose of 80-200 mg of the dermal formulation corresponds to 1.6-4.0 mg active substance/day.

Investigational medicinal product name	ATx201 Cream Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Each subject in Part 1 was treated with four formulations (two active formulations and their corresponding vehicles). The IPs were applied to defined skin areas in the dorsal arms twice daily. The body area to be treated was circle marked with a skin marker and had a size of 5 cm in diameter. The expected dose of 80-200 mg of the dermal formulation corresponds to 1.6-4.0 mg active substance/day.

Arm title	Treatment arm 3

Arm description:

Consisted of the screening Visit, a 7-day treatment period (subjects received two formulations of ATx201 and vehicle), and an end of study (EOS) visit on Day 15. Subjects were treated in 4 separate areas, 2 on the right arm and 2 on the right or left arm, twice daily at the study site. For the subjects biopsies were set on Day 8, one hour after 15th application (±10 minutes) of the IP.

Arm type	Experimental
Investigational medicinal product name	ATx201 GEL 2%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

Each subject in Part 1 was treated with four formulations (two active formulations and their corresponding vehicles). The IPs were applied to defined skin areas in the dorsal arms twice daily. The body area to be treated was circle marked with a skin marker and had a size of 5 cm in diameter. The expected dose of 80-200 mg of the dermal formulation corresponds to 1.6-4.0 mg active substance/day.

Investigational medicinal product name	ATx201 GEL Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

Each subject in Part 1 was treated with four formulations (two active formulations and their corresponding vehicles). The IPs were applied to defined skin areas in the dorsal arms twice daily. The body area to be treated was circle marked with a skin marker and had a size of 5 cm in diameter. The expected dose of 80-200 mg of the dermal formulation corresponds to 1.6-4.0 mg active substance/day.

Investigational medicinal product name	ATx201 Cream 2%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Each subject in Part 1 was treated with four formulations (two active formulations and their corresponding vehicles). The IPs were applied to defined skin areas in the dorsal arms twice daily. The body area to be treated was circle marked with a skin marker and had a size of 5 cm in diameter. The expected dose of 80-200 mg of the dermal formulation corresponds to 1.6-4.0 mg active substance/day.

Investigational medicinal product name	ATx201 Cream Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Each subject in Part 1 was treated with four formulations (two active formulations and their corresponding vehicles). The IPs were applied to defined skin areas in the dorsal arms twice daily. The

body area to be treated was circle marked with a skin marker and had a size of 5 cm in diameter. The expected dose of 80-200 mg of the dermal formulation corresponds to 1.6-4.0 mg active substance/day.

Arm title	Method testing arm
Arm description:	
Six healthy volunteers were enrolled for method testing.	
Arm type	method testing- non IMP arm
No investigational medicinal product assigned in this arm	

Number of subjects in period 1[1]	Treatment arm 1	Treatment arm 2	Treatment arm 3
Started	10	10	10
Completed	10	10	10

Number of subjects in period 1[1]	Method testing arm
Started	6
Completed	6

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: In part 1 36 healthy subjects were enrolled, in part 2 36 patients with atopic dermatitis. In total 72 patients were enrolled in trial.

Period 2

Period 2 title	Part 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

On Day 8 of Part 1, blinding was broken before biopsy sampling, in order to detect the areas that received active treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment arm 1
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	ATx201 GEL 2%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:	
Each patient applied ATx201 GEL 2% and matching vehicle to defined treatment areas between 10-200 cm2 once daily.	
Investigational medicinal product name	ATx201 GEL Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use
Dosage and administration details:	
Each patient applied ATx201 GEL 2% and matching vehicle to defined treatment areas between 10-200 cm2 once daily.	
Arm title	Treatment arm 2
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	ATx201 GEL 2%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use
Dosage and administration details:	
Each patient applied ATx201 GEL 2% and matching vehicle to defined treatment areas between 10-200 cm2 twice daily.	
Investigational medicinal product name	ATx201 GEL Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use
Dosage and administration details:	
Each patient applied ATx201 GEL 2% and matching vehicle to defined treatment areas between 10-200 cm2 twice daily.	

Number of subjects in period 2	Treatment arm 1	Treatment arm 2
Started	18	18
Completed	18	18

Baseline characteristics

Reporting groups	
Reporting group title	Treatment arm 1
Reporting group description:	
Consisted of the screening Visit, a 7-day treatment period (subjects received two formulations of ATx201 and vehicle), and an end of study (EOS) visit on Day 15. Subjects were treated in 4 separate areas, 2 on the right arm and 2 on the right or left arm, twice daily at the study site. For the subjects biopsies were set on Day 8, one hour after 15th application (±10 minutes) of the IP.	
Reporting group title	Treatment arm 2
Reporting group description:	
Consisted of the screening Visit, a 7-day treatment period (subjects received two formulations of ATx201 and vehicle), and an end of study (EOS) visit on Day 15. Subjects were treated in 4 separate areas, 2 on the right arm and 2 on the right or left arm, twice daily at the study site. For the subjects biopsies were set on Day 8, one hour after 15th application (±10 minutes) of the IP.	
Reporting group title	Treatment arm 3
Reporting group description:	
Consisted of the screening Visit, a 7-day treatment period (subjects received two formulations of ATx201 and vehicle), and an end of study (EOS) visit on Day 15. Subjects were treated in 4 separate areas, 2 on the right arm and 2 on the right or left arm, twice daily at the study site. For the subjects biopsies were set on Day 8, one hour after 15th application (±10 minutes) of the IP.	
Reporting group title	Method testing arm
Reporting group description:	
Six healthy volunteers were enrolled for method testing.	

Reporting group values	Treatment arm 1	Treatment arm 2	Treatment arm 3
Number of subjects	10	10	10
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)	10	10	10
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	4	2	3
Male	6	8	7

Reporting group values	Method testing arm	Total	
Number of subjects	6	36	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	

Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	6	36	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	0	9	
Male	6	27	

Subject analysis sets

Subject analysis set title	Part 1
Subject analysis set type	Per protocol

Subject analysis set description:

30 healthy subjects received three formulations of ATx201 and vehicle. The treatment part of Part 1 consisted of a screening visit (Day 0), a randomization visit (Day 1, first treatment), a treatment period of 7 consecutive days (Days 1-7), a PK visit (Day 8), and an EOS (end of study) visit (Day 15±2 days).

Subject analysis set title	Part 2
Subject analysis set type	Per protocol

Subject analysis set description:

36 patients (18 patients per group (once-daily vs twice-daily group) with a randomization ratio 1:1 with AD and colonized by S. aureus were enrolled.

Reporting group values	Part 1	Part 2	
Number of subjects	30	36	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	30	36	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	9	18	
Male	21	18	

End points

End points reporting groups

Reporting group title	Treatment arm 1
Reporting group description:	
Consisted of the screening Visit, a 7-day treatment period (subjects received two formulations of ATx201 and vehicle), and an end of study (EOS) visit on Day 15. Subjects were treated in 4 separate areas, 2 on the right arm and 2 on the right or left arm, twice daily at the study site. For the subjects biopsies were set on Day 8, one hour after 15th application (±10 minutes) of the IP.	
Reporting group title	Treatment arm 2
Reporting group description:	
Consisted of the screening Visit, a 7-day treatment period (subjects received two formulations of ATx201 and vehicle), and an end of study (EOS) visit on Day 15. Subjects were treated in 4 separate areas, 2 on the right arm and 2 on the right or left arm, twice daily at the study site. For the subjects biopsies were set on Day 8, one hour after 15th application (±10 minutes) of the IP.	
Reporting group title	Treatment arm 3
Reporting group description:	
Consisted of the screening Visit, a 7-day treatment period (subjects received two formulations of ATx201 and vehicle), and an end of study (EOS) visit on Day 15. Subjects were treated in 4 separate areas, 2 on the right arm and 2 on the right or left arm, twice daily at the study site. For the subjects biopsies were set on Day 8, one hour after 15th application (±10 minutes) of the IP.	
Reporting group title	Method testing arm
Reporting group description:	
Six healthy volunteers were enrolled for method testing.	
Reporting group title	Treatment arm 1
Reporting group description: -	
Reporting group title	Treatment arm 2
Reporting group description: -	
Subject analysis set title	Part 1
Subject analysis set type	Per protocol
Subject analysis set description:	
30 healthy subjects received three formulations of ATx201 and vehicle. The treatment part of Part 1 consisted of a screening visit (Day 0), a randomization visit (Day 1, first treatment), a treatment period of 7 consecutive days (Days 1-7), a PK visit (Day 8), and an EOS (end of study) visit (Day 15±2 days).	
Subject analysis set title	Part 2
Subject analysis set type	Per protocol
Subject analysis set description:	
36 patients (18 patients per group (once-daily vs twice-daily group) with a randomization ratio 1:1 with AD and colonized by S. aureus were enrolled.	

Primary: Primary efficacy endpoint Day 4 (Part 2) ATx201 GEL 2%

End point title	Primary efficacy endpoint Day 4 (Part 2) ATx201 GEL 2%[1]
End point description:	
Treatment success was defined as a 100-fold reduction in the S. aureus CFU/cm2 of samples skin lesion on Day 4. Once-daily group is Treatment arm 1 and the Twice-daily group is Treatment arm 2. Treatment for both treatment arms: ATx201 Gel 2%.	
End point type	Primary
End point timeframe:	
After 4 days of treatment.	

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: No statistical hypotheses were tested.

End point values	Treatment arm 1	Treatment arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: Treatment success				
Treatment success	10	13		
Total	18	18		

Statistical analyses

No statistical analyses for this end point

Primary: Primary safety and tolerability endpoint

End point title	Primary safety and tolerability endpoint[2]

End point description:

Neither Part 1 or Part 2 demonstrated any safety concerns. The safety endpoint was achieved. No systemic AEs were reported related to the study treatment. Skin reactions were reported as related to the study treatment.

End point type	Primary

End point timeframe:

Overall trial

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: No statistical hypotheses were tested.

End point values	Part 1	Part 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	36		
Units: Related skin reactions				
Skin reactions	0	6		

Statistical analyses

No statistical analyses for this end point

Primary: Primary efficacy endpoint Day 7 (Part 2) ATx201 GEL 2%

End point title	Primary efficacy endpoint Day 7 (Part 2) ATx201 GEL 2%[3]

End point description:

Treatment success was defined as a 100-fold reduction in the S. aureus CFU/cm2 of samples skin lesion on Day 7. Once-daily group is treatment arm 1 and the twice-daily group is treatment arm 2. Treatment for both treatment arms: ATx201 Gel 2%.

End point type	Primary

End point timeframe:

After 7 days of treatment.

Notes:

[3] - 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: No statistical hypotheses were tested.

End point values	Treatment arm 1	Treatment arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: Treatment success				
Treatment success	9	17		
Total	18	18		

Statistical analyses

No statistical analyses for this end point

Primary: Primary efficacy endpoint Day 4 (Part 2) Vehicle

End point title	Primary efficacy endpoint Day 4 (Part 2) Vehicle[4]

End point description:

Treatment success was defined as a 100-fold reduction in the S. aureus CFU/cm2 of samples skin lesion on Day 4. Once-daily group is Treatment arm 1 and the Twice-daily group is Treatment arm 2. Treatment for both treatment arms: Vehicle.

End point type	Primary

End point timeframe:

After 4 days of treatment.

Notes:

[4] - 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: No statistical hypotheses were tested.

End point values	Treatment arm 1	Treatment arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: Treatment success	3	9		

Statistical analyses

No statistical analyses for this end point

Primary: Primary efficacy endpoint Day 7 (Part 2) Vehicle

End point title	Primary efficacy endpoint Day 7 (Part 2) Vehicle[5]

End point description:

Treatment success was defined as a 100-fold reduction in the S. aureus CFU/cm2 of samples skin lesion on Day 7. Once-daily group is Treatment arm 1 and the Twice-daily group is Treatment arm 2. Treatment for both treatment arms: Vehicle.

End point type	Primary

End point timeframe:

After 7 days of treatment.

Notes:

[5] - 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: No statistical hypotheses were tested.

End point values	Treatment arm 1	Treatment arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: Treatment success	6	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary efficacy endpoint (Part 2)

End point title	Secondary efficacy endpoint (Part 2)

End point description:

Relative decrease of S. aureus colonies/cm2 on treated skin after treatment of the active groups, relative to their vehicles as well as relative to the untreated area. The Once-daily group is the Treatment arm 1 and the Twice-daily group is the Treatment arm 2.

End point type	Secondary

End point timeframe:

The ratio of colony count was measured on Day 7 compared to Baseline.

End point values	Treatment arm 1	Treatment arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: ratio of colony count				
arithmetic mean (standard deviation)				
Active	16377 (± 32181)	143305.8 (± 455680.7)		
Vehicle	978 (± 3648)	23787.9 (± 91357.9)		
Untreated	23 (± 28)	83.6 (± 220.9)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Overall trial (Part 1 and Part 2).	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21
Reporting groups	
Reporting group title	Part 1
Reporting group description: -	
Reporting group title	Part 2
Reporting group description: -	

Serious adverse events	Part 1	Part 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 36 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Part 1	Part 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 30 (33.33%)	26 / 36 (72.22%)	
Injury, poisoning and procedural complications			
Road traffic accident			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 30 (3.33%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	3 / 30 (10.00%)	5 / 36 (13.89%)	
occurrences (all)	3	5	
Blood and lymphatic system disorders			

Leukocytosis			
subjects affected / exposed	0 / 30 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Burning sensation			
subjects affected / exposed	0 / 30 (0.00%)	3 / 36 (8.33%)	
occurrences (all)	0	3	
Inflammation			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 30 (3.33%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 30 (3.33%)	2 / 36 (5.56%)	
occurrences (all)	1	3	
Vomiting			
subjects affected / exposed	1 / 30 (3.33%)	1 / 36 (2.78%)	
occurrences (all)	1	2	
Reproductive system and breast disorders			
Menstrual disorder			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 30 (3.33%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Viral upper respiratory tract infection			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	3 / 30 (10.00%)	1 / 36 (2.78%)	
occurrences (all)	3	1	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 30 (0.00%)	12 / 36 (33.33%)	
occurrences (all)	0	13	
Pruritus			
subjects affected / exposed	0 / 30 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	3	
Rash			

subjects affected / exposed	0 / 30 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	2	
Erythema			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 30 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Back pain			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 30 (3.33%)	0 / 36 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 April 2017	The address of the sponsor was amended. Additional 10 patients were planned for an extended pharmokinetic study. Therefore these patients got a higher payment for participation. Additional inclusion criteria were added, i.e. colonisation of lesions with S. aureus. Inclusion criteria were canceled, i.e. caffeine and tobacco consumption. Exclusion criteria were amended, i.e. concomitant medication was extended. Additional two co-workers were added to the protocol.
30 May 2017	Participation time of patients was reduced for two days. The overall time of the clinical trial was reduced for one month. Additional inclusion criteria were defined. Additional 3 co-workers were included. The number of S.aureus swabs was increased.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported