Clinical trial results:
The Pathogenic Role Of Staphylococcus Aureus And The Skin Microbiome During Flare And Resolution Of Atopic Dermatitis

Summary

EudraCT number	2021-006883-25
Trial protocol	DK
Global end of trial date	13 June 2023

Results information

Result version number	v1 (current)
This version publication date	16 May 2025
First version publication date	16 May 2025

Trial information

Trial identification

Sponsor protocol code	AR-AB-AD

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05578482
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Jacob Thyssen
Sponsor organisation address	Bispebjerg Bakke 23, Dermato-Venerologisk afdeling D92, Nielsine Nielsens Vej 9, Enterance 4, Second, Copenhagen NV, Denmark, 2400
Public contact	Dermato-Venerologisk afdeling, Biepebjerg Hospital, 0045 38636173, jacob.pontoppidan.thyssen@regionh.dk
Scientific contact	Dermato-Venerologisk afdeling, Biepebjerg Hospital, 0045 38636173, jacob.pontoppidan.thyssen@regionh.dk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	29 April 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 June 2023
Global end of trial reached?	Yes
Global end of trial date	13 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

We hypothesize: use of oral systemic antibiotic treatment with dicloxacillin (1000 mg x 3 times a day) will decrease the time to AD improvement as well as the amount of S. aureus and its toxins and alter the skin microbiome.
Specifically, we aim to investigate the following research questions:

- RQ1: Does the addition of systemic dicloxacillin to TCS treatment result in a more rapid and deeper treatment response?
- RQ2: Does the addition of systemic dicloxacillin to TCS treatment affect the skin microbiome, the skin barrier and immune response during improvement of AD?
- RQ3: Does topical application of S. aureus or SEB increase the severity and rapidity of a flare?
- RQ4: Does topical application of S. aureus and SEB alter the skin microbiome, the skin barrier and immune response during a flare of AD?
- RQ5: Can changes in protein expression or metabolic pathways explain the modulated mechanisms in the host-microbial cross talk of AD?

Protection of trial subjects:

The study was monitored by the Good Clinical Practice (GCP) unit of Region H (https://gcp-enhed.dk/english/).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 October 2022
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	Denmark: 45
Worldwide total number of subjects	45
EEA total number of subjects	45

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)	45
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from the Department of Dermatology, Bispebjerg Hospital, other dermatology departments including private clinics in the area near Copenhagen. Further, patients were recruited through webpages pointed out and approved in the protocol.

Pre-assignment

Screening details:

Patients were screened prior to inclusion to ensure that they fulfilled the inclusion criterias e.g. Age 18 years or above, European ancestry, AD diagnosis according to Hanifin & Rajka criteria, AD for at least 3 years, AD that is moderate-to-severe defined as an EASI score of ≥ 7, AD in the sampled location that has an TLSS score of ≥ 5.

Period 1

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

Blinding implementation details:

All participants and investigators who were involved in the screening, clinical visits and analysis during the study were blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	Active

Arm description:

Dicloxacillin 1000 mg three times daily in five days + Elocon 0.1 % Topical Cream.

Arm type	Active comparator
Investigational medicinal product name	Dicloxacillin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

1000 mg dicloxacillin 3 times daily in five days.

Investigational medicinal product name	Mometasone futurate 0.1%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use, Topical use

Dosage and administration details:

All patients were instructed to use the TCS creme (mometasone futurate 0.1%) once daily at areas where AD is active. If the AD was located in the face or at intimate regions patients were instructed to use their regular treatment for this area (hydrocortisone, hydrocortison-17-butyrat, topical tacrolimus 0.1% or pimecrolimus 1%) instead. The tubes of mometasone futurate 0.1% were weighed prior to study start and in the end of day 5.

Arm title	Placebo

Arm description:

Placebo + TCS creme (mometasone futurate 0.1%) once daily at areas where AD is active. If the AD is located in the face or at intimate regions patients will be instructed to use their regular treatment for this area (hydrocortisone, hydrocortison-17-butyrat, topical tacrolimus 0.1% or pimecrolimus 1%) instead.

Arm type	Placebo
Investigational medicinal product name	Mometasone futurate 0.1%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use, Topical use

Dosage and administration details:

All patients were instructed to use the TCS creme (mometasone futurate 0.1%) once daily at areas where AD is active. If the AD was located in the face or at intimate regions patients were instructed to use their regular treatment for this area (hydrocortisone, hydrocortison-17-butyrat, topical tacrolimus 0.1% or pimecrolimus 1%) instead. The tubes of mometasone futurate 0.1% were weighed prior to study start and in the end of day 5.

Number of subjects in period 1[1]	Active	Placebo
Started	20	21
Completed	19	21
Not completed	1	0
Consent withdrawn by subject	1	-

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: A total of 41 patients were enrolled in the trial. One dropped out due to personal circumstances resulting in a total of 40 patients completing the trial.

Baseline characteristics

Reporting groups	
Reporting group title	Study period

Reporting group description: -

Reporting group values	Study period	Total	
Number of subjects	41	41	
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)	41	41	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	30	30	
Male	11	11	

End points

End points reporting groups

Reporting group title	Active
Reporting group description:	
Dicloxacillin 1000 mg three times daily in five days + Elocon 0.1 % Topical Cream.	
Reporting group title	Placebo
Reporting group description:	
Placebo + TCS creme (mometasone futurate 0.1%) once daily at areas where AD is active. If the AD is located in the face or at intimate regions patients will be instructed to use their regular treatment for this area (hydrocortisone, hydrocortison-17-butyrat, topical tacrolimus 0.1% or pimecrolimus 1%) instead.	

Primary: Effect of treatment on TLSS change over time

End point title	Effect of treatment on TLSS change over time
End point description:	
A mixed effects model was fit using the following formula: total_tlss ~ visit * treatment_unblinded + (visit | study_id). This formula included covariates for visit (continuous, 1-5) and treatment(Active/Placebo) including a random interaction term of patient for each study day. A significant effect of treatment was assumed if the interaction term between visit:treatment was	
End point type	Primary
End point timeframe:	
Day 1-5.	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Interaction effect				
number (confidence interval 95%)	-0.953 (-1.148 to -0.758)	-0.967 (-1.152 to -0.782)		

Statistical analyses

Statistical analysis title	Mixed effects model
Statistical analysis description:	
The analysis implemented the lmerTest method from the lmerTest package in R. This implements atterthwaite's degrees of freedom method for calculating p-values and confidence intervals for covariates in a linear mixed-effects model.	
Comparison groups	Active v Placebo

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.916 [1]
Method	Mixed models analysis
Parameter estimate	Slope
Point estimate	0.014
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.246
upper limit	0.274
Variability estimate	Standard error of the mean
Dispersion value	0.133

Notes:

[1] - This is the reported p-value of the interaction term (visit:treatment). Thus, we are unable to disprove the null hypothesis that docloxicicillin treatment does not significantly change the effect of corticosteroid treatment on TLSS severity.

Secondary: Daily change in EASI

End point title	Daily change in EASI

End point description:

A mixed effects model was fit using the following formula: total_easi ~ visit * treatment_unblinded + (visit | study_id). This formula included covariates for visit (continuous, 1-5) and treatment(Active/Placebo) including a random interaction term of patient for each study day. A significant effect of treatment was assumed if the interaction term between visit:treatment was

End point type	Secondary

End point timeframe:

Day 1-5.

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Estimated daily change in EASI				
number (confidence interval 95%)	-2.052 (-2.677 to -1.427)	-2.607 (-3.210 to -2.003)		

Statistical analyses

Statistical analysis title	Mixed effects model - EASI

Statistical analysis description:

The analysis implemented the lmerTest method from the lmerTest package in R. This implements atterthwaite's degrees of freedom method for calculating p-values and confidence intervals for covariates in a linear mixed-effects model.

Comparison groups	Placebo v Active

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.204 [2]
Method	Mixed models analysis
Parameter estimate	Slope
Point estimate	0.555
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.286
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	0.429

Notes:

[2] - This is the reported p-value of the interaction term (visit:treatment). Thus, we are unable to disprove the null hypothesis that docloxicicillin treatment does not significantly change the effect of corticosteroids on EASI change.

Secondary: Daily change in itch

End point title	Daily change in itch

End point description:

A mixed effects model was fit using the following formula: itch ~ visit * treatment_unblinded + (visit | study_id).

End point type	Secondary

End point timeframe:

Day 1-5

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Change in itch				
number (confidence interval 95%)	-1.23 (-1.5 to -1.0)	-0.95 (-1.2 to -0.7)		

Statistical analyses

Statistical analysis title	Mixed effects model - Itch NRS

Statistical analysis description:

The analysis implemented the lmerTest method from the lmerTest package in R. This implements atterthwaite's degrees of freedom methom for calculating p-values and confidence intervals for covariates in a linear mixed-effects model.

Comparison groups	Active v Placebo

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1 [3]
Method	Mixed models analysis
Parameter estimate	Slope
Point estimate	-0.279
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.046
Variability estimate	Standard error of the mean
Dispersion value	0.17

Notes:

[3] - This is the reported p-value of the interaction term (visit:treatment). Thus, we are unable to disprove the null hypothesis that docloxicicillin treatment does not significantly change the effect of corticosteroid treatment on Itch.

Secondary: Daily change in Sleep NRS

End point title	Daily change in Sleep NRS

End point description:

A mixed effects model was fit using the following formula: sleep ~ visit * treat-ment_unblinded + (visit | study_id).

End point type	Secondary

End point timeframe:

Day 1-5.

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Change in sleep				
number (confidence interval 95%)	-0.49 (-0.824 to -0.156)	-0.6 (-0.922 to -0.278)		

Statistical analyses

Statistical analysis title	Mixed effects model - Sleep

Statistical analysis description:

This formula included covariates for visit (continuous, 1-5) and treatment(Active/Placebo) including a random interaction term of patient for each study day. A significant effect of treatment was assumed if the interaction term between visit:treatment was significant.

Comparison groups	Active v Placebo

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.634 [4]
Method	Mixed models analysis
Parameter estimate	Slope
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.29

Notes:

[4] - This is the reported p-value of the interaction term (visit:treatment). Thus, we are unable to disprove the null hypothesis that dicloxacillin treatment does not significantly change the effect of corticosteroid treatment on sleep NRS.

Secondary: Daily change in pain-NRS

End point title	Daily change in pain-NRS

End point description:

A mixed effects model was fit using the following formula: pain ~ visit * treat-ment_unblinded + (visit | study_id).

End point type	Secondary

End point timeframe:

Day 1-5.

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Change in pain-NRS				
number (confidence interval 95%)	-0.945 (-1.195 to -0.694)	-0.99 (-1.227 to -0.744)		

Statistical analyses

Statistical analysis title	Mixed effects model - Pain NRS

Statistical analysis description:

This formula included covariates for visit (continuous, 1-5) and treatment(Active/Placebo) including a random interaction term of patient for each study day. A significant effect of treatment was assumed if the interaction term between visit:treatment was significant.

Comparison groups	Active v Placebo

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.81 [5]
Method	Mixed models analysis
Parameter estimate	Slope
Point estimate	-0.041
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.38
Variability estimate	Standard error of the mean
Dispersion value	0.17

Notes:

[5] - This is the reported p-value of the interaction term (visit:treatment). Thus, we are unable to disprove the null hypothesis that dicloxacillin treatment does not significantly change the effect of corticosteroid treatment on pain NRS.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
All reported adverse events are followed until dissolved or as clinically required. AE's from first administration of the trail medication to 24 hours after the last administration of the trial medicine.	
Adverse event reporting additional description:	
AE's were collected each day at a clinical visit.	
Assessment type	Systematic

Dictionary used	
Dictionary name	0
Dictionary version	0

Reporting groups	
Reporting group title	Active
Reporting group description:	
Active group receiving dicloxacillin 1000 mg x 3 times daily + topical mometasone furoate 0.1%.	
Reporting group title	Placebo
Reporting group description:	
Placebo group receiving placebo + topical mometasone furoate 0.1%	

Serious adverse events	Active	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (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: 0 %

Non-serious adverse events	Active	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 19 (15.79%)	3 / 21 (14.29%)	
Ear and labyrinth disorders			
Dizziness	Additional description: Dizziness during change of a plaster.		
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Social circumstances			
Fatigue			
subjects affected / exposed	0 / 19 (0.00%)	2 / 21 (9.52%)	
occurrences (all)	0	2	
Gastrointestinal disorders			

Nausea			
subjects affected / exposed	2 / 19 (10.53%)	0 / 21 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Urticaria	Additional description: Urticaria affecting the skin. No other additional symptoms.		
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported