Clinical trial results:
Childhood atopic dermatitis : allergic sensitisation, long-term treatment, and genetics

Summary

EudraCT number	2012-002412-95
Trial protocol	FI
Global end of trial date	18 June 2024

Results information

Result version number	v1 (current)
This version publication date	25 January 2025
First version publication date	25 January 2025

Trial information

Trial identification

Sponsor protocol code	Atopia

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Miia Perälä, HUS, Skin and allergy Hospital
Sponsor organisation address	PL 160, Helsinki, Finland, 00029
Public contact	Anita Remitz, Iho-ja allergiasairaala/SKin and Allergy Hospital, 358 9471 86355, anita.remitz@hus.fi
Scientific contact	Anita Remitz, Iho-ja allergiasairaala, 358 9471 86355, anita.remitz@hus.fi

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	18 June 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 June 2024
Global end of trial reached?	Yes
Global end of trial date	18 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Long-term treatment of moderate-to severe childhood atopic eczema with two different treatment regimens.

Protection of trial subjects:

Informend concents from caregivers, right to withdraw fro the study at any time point with no implications. Study plan approved of national ethics committee. Right to contact study nurse/investigator at any time point. Previously studied treatment (ointments) used.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2013
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	Finland: 152
Worldwide total number of subjects	152
EEA total number of subjects	152

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)	152
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

1-3 year-old children with moderate-to-severe atopic eczema.

Pre-assignment

Screening details:

Moderate-to severe atopic eczema based on Rajka-Langeland criteria.
2 weeks wash-out perriod before baseline
152 patients enrolled

Pre-assignment period milestones

Number of subjects started	152
Number of subjects completed	152

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	TAC-group

Arm description:

Treatment with tacrolimus

Arm type	Experimental
Investigational medicinal product name	Protopic 0,03%
Investigational medicinal product code	
Other name	Tacrolimus
Pharmaceutical forms	Ointment
Routes of administration	Cutaneous use

Dosage and administration details:

Treatment was twice daily until clearance was achieved, after which it continued as twice-weekly maintenance therapy.

Investigational medicinal product name	Protopic 0,1%
Investigational medicinal product code	
Other name	Tacrolimus
Pharmaceutical forms	Ointment
Routes of administration	Cutaneous use

Dosage and administration details:

treatment was twice daily until clearance was achieved, after which it continued as twice-weekly maintenance therapy.

Arm title	TCS-group

Arm description:

Treatment with corticosteroids

Arm type	Active comparator

Investigational medicinal product name	Hydrocortison 1%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Twice daily for 3-7 days, followed by a treatment pause lasting a minimum of 3-7 days. Treatment was restarted in case of a flare-up based on parents' or caregiver's decision.

Investigational medicinal product name	Bucort 0,1%
Investigational medicinal product code	
Other name	Hydrocortison-17-butyrate
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

In case of Hyrcostison was inneffective, twice daily for 3-7 days, followed by a treatment pause lasting a minimum of 3-7 days. Treatment was restarted in case of a flare-up based on parents' or caregiver's decision.

Number of subjects in period 1	TAC-group	TCS-group
Started	77	75
Completed	77	75

Period 2

Period 2 title	Overall trial
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	TCS-group

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Hydrocortison 1%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Twice daily for 3-7 days, followed by a treatment pause lasting a minimum of 3-7 days. Treatment was restarted in case of a flare-up based on parents' or caregiver's decision.

Investigational medicinal product name	Bucort 0,1%
Investigational medicinal product code	
Other name	Hydrocortison-17-butyrate
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

In case of Hyrcostison was inneffective, twice daily for 3-7 days, followed by a treatment pause lasting a minimum of 3-7 days. Treatment was restarted in case of a flare-up based on parents' or caregiver's decision.

Arm title	TAC-group

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Protopic 0,03%
Investigational medicinal product code	
Other name	Tacrolimus
Pharmaceutical forms	Ointment
Routes of administration	Cutaneous use

Dosage and administration details:

Treatment was twice daily until clearance was achieved, after which it continued as twice-weekly maintenance therapy.

Investigational medicinal product name	Protopic 0,1%
Investigational medicinal product code	
Other name	Tacrolimus
Pharmaceutical forms	Ointment
Routes of administration	Cutaneous use

Dosage and administration details:

treatment was twice daily until clearance was achieved, after which it continued as twice-weekly maintenance therapy.

Number of subjects in period 2	TCS-group	TAC-group
Started	75	77
Completed	62	60
Not completed	13	17
Consent withdrawn by subject	-	3
Moving away	1	2
Lost to follow-up	4	4
Lack of efficacy	5	6
Protocol deviation	3	2

Baseline characteristics

Reporting groups	
Reporting group title	TAC-group
Reporting group description: Treatment with tacrolimus	
Reporting group title	TCS-group
Reporting group description: Treatment with corticosteroids	

Reporting group values	TAC-group	TCS-group	Total
Number of subjects	77	75	152
Age categorical Units: Subjects			
Children (2-11 years)			0
Age continuous			
Age at baseline			
Units: years arithmetic mean standard deviation	 1.8 ± 0.7	 1.8 ± 0.7	 -
Gender categorical Units: Subjects			
Female	42	31	73
Male	35	44	79
BSA %			
Eczema area			
Units: 0-100 % arithmetic mean standard deviation	 29.4 ± 24.8	 25.7 ± 30.0	 -
EASI			
Eczema severity assesment			
Units: 0-72 arithmetic mean standard deviation	 13.3 ± 10.3	 11.4 ± 7.7	 -

End points

End points reporting groups	
Reporting group title	TAC-group
Reporting group description: Treatment with tacrolimus	
Reporting group title	TCS-group
Reporting group description: Treatment with corticosteroids	
Reporting group title	TCS-group
Reporting group description: -	
Reporting group title	TAC-group
Reporting group description: -	

Primary: EASI_36 months	
End point title	EASI_36 months
End point description:	
End point type	Primary
End point timeframe: 36 months	

End point values	TAC-group	TCS-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	57		
Units: 0-72	57	57		

Statistical analyses

Statistical analysis title	EASI_36
Statistical analysis description: Difference in eczema severity between the treatment groups at 36 months	
Comparison groups	TAC-group v TCS-group
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	Mean difference (final values)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	1.8

Variability estimate	Standard deviation
Dispersion value	1.3

Notes:
[1] - mean fifference

Primary: BSA_36 months

End point title	BSA_36 months

End point description:

End point type	Primary

End point timeframe:
36 months

End point values	TAC-group	TCS-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: %	60	60		

Statistical analyses

Statistical analysis title	EASI_36

Statistical analysis description:
Eczema severity difference at 36 months between treatment groups

Comparison groups	TCS-group v TAC-group
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	1.8
Variability estimate	Standard deviation
Dispersion value	1.3

Statistical analysis title	BSA_36

Statistical analysis description:
Eczema area difference (%) at 36 months

Comparison groups	TAC-group v TCS-group

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	4.2
Variability estimate	Standard deviation
Dispersion value	0.7

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From baseline to 36 months	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0
Reporting groups	
Reporting group title	TAC-group
Reporting group description: tac-treated patients	
Reporting group title	TCS-group
Reporting group description: Corticosteroid-treated patients	

Serious adverse events	TAC-group	TCS-group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 77 (0.00%)	0 / 75 (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: 4.6 %

Non-serious adverse events	TAC-group	TCS-group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 77 (9.09%)	1 / 75 (1.33%)	
Skin and subcutaneous tissue disorders			
Burning sensation			
subjects affected / exposed	7 / 77 (9.09%)	0 / 75 (0.00%)	
occurrences (all)	7	0	
Endocrine disorders			
Cortisol decreased	Additional description: S-cortisol was decreased, but follwing ACTH test was normal.		
subjects affected / exposed	0 / 77 (0.00%)	1 / 75 (1.33%)	
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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The restricted cohort size can be seen as a limitation. The cohort size was due to the study being a single-centre investigator-initiated clinical study with young infants and relatively frequent follow-up visits.

Notes: