



Clinical trial results:

The risk of an elevated intraocular pressure after treatment with topical corticosteroids in the periocular region

Summary

EudraCT number	2020-000252-35
Trial protocol	DK
Global end of trial date	31 August 2023

Results information

Result version number	v1 (current)
This version publication date	02 August 2025
First version publication date	02 August 2025

Trial information

Trial identification

Sponsor protocol code	DA-TCS-AD
-----------------------	-----------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Lone Skov
Sponsor organisation address	Gentofte Hospitalsvej 15, 1. floor, Gentofte, Denmark, 2820
Public contact	Department of Dermatology , Gentofte Hospital, diva.amiri@regionh.dk
Scientific contact	Department of Dermatology , Gentofte Hospital, lone.skov.02@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	Final
Date of interim/final analysis	19 March 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 August 2023
Global end of trial reached?	Yes
Global end of trial date	31 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective is to evaluate whether daily treatment with topical corticosteroids in the periorcular region causes a change in comparison to the control group.

Protection of trial subjects:

Participants would be monitored for any unacceptable side effects or increase in eye pressure. Monitoring would continue until the pressure had returned to normal. An additional follow-up examination would be offered if the participant wished for it.

If there was an increase in eye pressure, a slit-lamp examination would be offered and performed by Professor, Chief Physician, PhD Miriam Kolko. This examination would take place before the trial concluded.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2020
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	Denmark: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	24
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were included from October 2021 to August 2023 at Department of Dermatology and Allergy, Herlev-Gentofte Hospital.

Pre-assignment

Screening details:

Inclusion criteria were periorcular AD, age 18–75years and body mass index (BMI) <30kg/m². Exclusion criteria were systemic corticosteroid treatments within fourweeks before study start, pregnancy, corticosteroid-requiring inflammatory eye diseases, allergy towards interventions, diagnosed diseases that may affect or be affected by the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Hydrocortisone cream 1% (AD)

Arm description:

Patients with periorcular AD assessed with Eczema Area and Severity Index (EASI)

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

Dosage and administration details:

Third of an index fingertip unit of hydrocortisone cream 1% around the eyes once daily for four weeks.

Arm title	Hydrocortison-17-butytrat 0.1% (AD)
------------------	-------------------------------------

Arm description:

Patients with periorcular AD assessed with Eczema Area and Severity Index (EASI)

Arm type	Active comparator
Investigational medicinal product name	Locoid Lipid 0.1 % cream
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Third of an index fingertip unit of hydrocortisone-17-butytrat cream 0.1% cream around the eyes once daily for four weeks.

Arm title	Control
------------------	---------

Arm description:

Healthy untreated controls

Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Hydrocortisone cream 1% (Healthy)

Arm description:	
Healthy treated controls.	
Arm type	Active comparator
Investigational medicinal product name	Mildison Lipid 1% cream
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use
Dosage and administration details:	
Third of an index fingertip unit of hydrocortisone cream 1% around the eyes once daily for four weeks.	
Arm title	Hydrocortison-17-butytrat 0.1% (Healthy)

Arm description:	
Healthy treated controls	
Arm type	Active comparator
Investigational medicinal product name	Locoid Lipid 0.1 % cream
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use
Dosage and administration details:	
Third of an index fingertip unit of hydrocortisone-17-butytrat cream 0.1% cream around the eyes once daily for four weeks.	

Number of subjects in period 1	Hydrocortisone cream 1% (AD)	Hydrocortison-17-butytrat 0.1% (AD)	Control
Started	4	4	8
Completed	4	4	8

Number of subjects in period 1	Hydrocortisone cream 1% (Healthy)	Hydrocortison-17-butytrat 0.1% (Healthy)
Started	3	5
Completed	3	5

Baseline characteristics

Reporting groups

Reporting group title	Hydrocortisone cream 1% (AD)
Reporting group description:	
Patients with periorcular AD assessed with Eczema Area and Severity Index (EASI)	
Reporting group title	Hydrocortison-17-butytrat 0.1% (AD)
Reporting group description:	
Patients with periorcular AD assessed with Eczema Area and Severity Index (EASI)	
Reporting group title	Control
Reporting group description:	
Healthy untreated controls	
Reporting group title	Hydrocortisone cream 1% (Healthy)
Reporting group description:	
Healthy treated controls.	
Reporting group title	Hydrocortison-17-butytrat 0.1% (Healthy)
Reporting group description:	
Healthy treated controls	

Reporting group values	Hydrocortisone cream 1% (AD)	Hydrocortison-17-butytrat 0.1% (AD)	Control
Number of subjects	4	4	8
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	31.0	30.0	33.5
standard deviation	± 12.1	± 8.7	± 8.2
Gender categorical			
Units: Subjects			
Female	2	3	5
Male	2	1	3
Body Mass Index (BMI)			
Units: kg/m2			
arithmetic mean	23.8	23.6	24.0
standard deviation	± 1.5	± 4.0	± 3.0
Reporting group values	Hydrocortisone cream 1% (Healthy)	Hydrocortison-17-butytrat 0.1% (Healthy)	Total

Number of subjects	3	5	24
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	25.3	30.6	
standard deviation	± 3.5	± 10.1	-
Gender categorical			
Units: Subjects			
Female	2	3	15
Male	1	2	9
Body Mass Index (BMI)			
Units: kg/m2			
arithmetic mean	22.8	22.1	
standard deviation	± 4.4	± 5.8	-

End points

End points reporting groups

Reporting group title	Hydrocortisone cream 1% (AD)
Reporting group description:	
Patients with periorcular AD assessed with Eczema Area and Severity Index (EASI)	
Reporting group title	Hydrocortison-17-butytrat 0.1% (AD)
Reporting group description:	
Patients with periorcular AD assessed with Eczema Area and Severity Index (EASI)	
Reporting group title	Control
Reporting group description:	
Healthy untreated controls	
Reporting group title	Hydrocortisone cream 1% (Healthy)
Reporting group description:	
Healthy treated controls.	
Reporting group title	Hydrocortison-17-butytrat 0.1% (Healthy)
Reporting group description:	
Healthy treated controls	

Primary: Change in intraocular pressure

End point title	Change in intraocular pressure
End point description:	
The primary endpoint was change in intraocular pressure during four weeks of once daily periorcular treatment with hydrocortisone cream 1% or hydrocortisone-17-butytrat cream 0.1% in patients with periorcular AD and healthy adults.	
End point type	Primary
End point timeframe:	
Two, three and four weeks after the first visit intraocular pressure was measured	

End point values	Hydrocortisone cream 1% (AD)	Hydrocortison-17-butytrat 0.1% (AD)	Control	Hydrocortisone cream 1% (Healthy)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	8	3
Units: mmHg				
number (confidence interval 95%)	15.0 (12.3 to 17.7)	15.0 (12.3 to 17.7)	14.2 (11.5 to 16.9)	13.7 (11.0 to 16.3)

End point values	Hydrocortison-17-butytrat 0.1% (Healthy)			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: mmHg				
number (confidence interval 95%)	13.7 (11.0 to			

Statistical analyses

Statistical analysis title	Primary Endpoint – Change in IOP from Baseline
-----------------------------------	--

Statistical analysis description:

As recruitment was not met for this study, our analysis were performed by pooling the groups to the following:

Patients with atopic dermatitis treated with Hydrocortison 1%/Hydrocortison-17-butytrat 0.1%

Healthy treated controls treated with Hydrocortison 1%/Hydrocortison-17-butytrat 0.1%

Healthy untreated controls with no intervention.

Treatment difference in change from baseline in patients with atopic dermatitis and healthy treated controls compared to healthy untreated controls

Comparison groups	Hydrocortisone cream 1% (AD) v Hydrocortison-17-butytrat 0.1% (AD) v Control v Hydrocortisone cream 1% (Healthy) v Hydrocortison-17-butytrat 0.1% (Healthy)
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	< 0.05 ^[2]
Method	Mixed models analysis

Notes:

[1] - Changes in outcome between baseline and study days and estimated treatment difference were analyzed using a constrained linear mixed model with inherent baseline adjustment. An unstructured covariance was assumed to account for repeated measurements on study participants. Results were reported as baseline mean and mean differences with 95% CI for approximately normally distributed outcomes. Goodness of fit was assessed by residual diagnostics. Analyses were performed using SAS Enterprise.

[2] - Changes in outcome between baseline and study days and estimated treatment difference were analyzed using a constrained linear mixed repeated model with inherent baseline adjustment. An unstructured covariance was assumed to account for repeated measurements.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

October 2021 to August 2023

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	25.1
--------------------	------

Reporting groups

Reporting group title	Hydrocortison-17-butytrat 0.1% (AD)
-----------------------	-------------------------------------

Reporting group description: -

Serious adverse events	Hydrocortison-17-butytrat 0.1% (AD)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (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	Hydrocortison-17-butytrat 0.1% (AD)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)		
Infections and infestations			
Viral rhinitis			
subjects affected / exposed	1 / 4 (25.00%)		
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

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

Recruitment for this study was not met due to substantial reluctance among potential participants. Participants were concerned about use of TCS around the eyes, particularly the potential risk of inducing glaucoma.

Notes: