



## 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 consents 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 period 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       |
| <b>Arm title</b>             | 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.

|                  |           |
|------------------|-----------|
| <b>Arm title</b> | 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 ineffective, 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               |
| <b>Arm title</b>                       | 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 ineffective, 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.

|                                        |                   |
|----------------------------------------|-------------------|
| <b>Arm title</b>                       | 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.

| <b>Number of subjects in period 2</b> | 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           | 1.8       | 1.8       |       |
| standard deviation        | ± 0.7     | ± 0.7     | -     |
| Gender categorical        |           |           |       |
| Units: Subjects           |           |           |       |
| Female                    | 42        | 31        | 73    |
| Male                      | 35        | 44        | 79    |
| BSA %                     |           |           |       |
| Eczema area               |           |           |       |
| Units: 0-100 %            |           |           |       |
| arithmetic mean           | 29.4      | 25.7      |       |
| standard deviation        | ± 24.8    | ± 30.0    | -     |
| EASI                      |           |           |       |
| Eczema severity assesment |           |           |       |
| Units: 0-72               |           |           |       |
| arithmetic mean           | 13.3      | 11.4      |       |
| standard deviation        | ± 10.3    | ± 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 <sup>[1]</sup>           |
| 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 difference

### 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

|                                   |         |
|-----------------------------------|---------|
| <b>Statistical analysis title</b> | 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                            |

|                                   |        |
|-----------------------------------|--------|
| <b>Statistical analysis title</b> | 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 following 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

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### 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: