# A single (assessor) blinded, randomized, parallel-group, monotherapy trial to evaluate the pharmacokinetics and safety of tralokinumab in children (age 6 to <12 years) with moderate to-severe atopic dermatitis.

Published: 09-05-2022
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Primary objective: To establish the PK profile after multiple SC administrations of tralokinumab in children with moderate-to-severe AD.Secondairy objectives: - To assess the safety and tolerability of multiple SC administrations of tralokinumab in...

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Epidermal and dermal conditions |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON53683

**Source**
ToetsingOnline

**Brief title**
TRAPEDS 1

### Condition

- Epidermal and dermal conditions

**Synonym**
Atopic dermatitis

**Research involving**

Human

## Sponsors and support

**Primary sponsor:** Leo Pharma
**Source(s) of monetary or material Support:** LEO Pharma

## Intervention

**Keyword:** children, Pediatric, Tralokinumab

## Outcome measures

### Primary outcome

• Ctrough at Week 16.

• Cmax between Week 12-Week 14 for Q2W (Week 12-Week 16 for Q4W).

• AUC between Week 12-Week 14 for Q2W (Week 12-Week 16 for Q4W).

• Tmax between Week 12-Week14 for Q2W (Week 12-Week 16 for Q4W).

### Secondary outcome

• Number of treatment*emergent adverse events in the initial treatment period (Week 0-Week 16).

• Anti-drug antibodies (status) in the initial treatment period (Week 0-Week 16).

• Number of treatment*emergent adverse events in the open-label treatment period (Week 16-Week 68).

• Anti-drug antibodies (status) in the open-label treatment period (Week 16-Week 68).

• Change in SCORAD from Week 0 - Week 68.

• Change in POEM from Week 0 - Week 68.

• Change in EASI from Week 0 to Week 68.

# Study description

### Background summary

In this study, the main purpose is to investigate what happens to the trial drug in the body and to confirm that it is safe when used in children. The medicine being tested is called Tralokinumab. It is approved in the European Union, the United Kingdom and by the FDA for the treatment of moderate-to-severe atopic dermatitis (also called eczema) in adults.

Tralokinumab is an antibody, a type of a biological drug, which binds to a human protein called IL-13. IL-13 is involved in the body*s immune responses to fight diseases. By binding to IL-13, tralokinumab may improve or clear the symptoms of eczema.
Tralokinumab has already been tested in 26 clinical trials with more than 4,700 persons exposed to tralokinumab, including more than 300 adolescents. These subjects were either healthy or had eczema or other chronic inflammatory diseases.

### Study objective

Primary objective: To establish the PK profile after multiple SC administrations of tralokinumab in children with moderate-to-severe AD.

Secondairy objectives:
- To assess the safety and tolerability of multiple SC administrations of tralokinumab in children with moderate to-severe AD.
- To evaluate the efficacy of tralokinumab on severity and extent of AD, and on patient-reported outcomes, in children with moderate-to-severe AD.

other objectives:
- To evaluate the efficacy of tralokinumab on severity and extent of AD, and on patient-reported outcomes, in children with moderate-to-severe AD.

### Study design

This is a single (assessor) blinded, randomized, parallel-group, monotherapy trial to evaluate the PK and safety of tralokinumab in children (aged 6 to <12 years) with moderate-to-severe AD.
The trial will consist of a 2- to 6-week screening period, a 16-week initial treatment period, a 52 week open-label treatment period, and a 14-week safety follow-up period.

Subjects will be enrolled in 2 sequential age cohorts (cohort 1: 6 to <12 years; cohort 2: 2 to <6 years).

Screening period (Week -6/-2 to Week 0)
The screening period has a duration of 2 to 6 weeks depending on the need for wash-out. Eligibility will be assessed at the screening visit and at baseline prior to start of treatment.

Initial washout period: During the initial washout period the below atopic dermatitis treatments are disallowed at the indicated timepoints prior to baseline:
Not allowed 4 weeks prior to baseline: Use of tanning beds or phototherapy, systemic immunosuppressive/immunomodulating drugs, systemic corticosteroid us (excludes topical, inhaled, or intranasal delivery) and three or more bleach baths during any week.
Not allowed 2 weeks prior to baseline: Topical PDE 4 inhibitors.
During the entire washout period, up untill start of the initial treat-ment period at week 0, topical treatment with both corticosteroids and calcineurin inhibitors would be allowed.

Initial treatment period (Week 0 to Week 16)
Approximately 28 subjects will enter baseline (6 to <12 years ) to receive either a low fixed dose or a high fixed dose of tralokinumab. There will be at least 24 subjects in the cohort. For each subject, the age and weight at baseline will determine the dose for the entire duration of the trial.
The low dose and the high dose will not necessarily be the same in the 2 cohorts.
After the 2- to 6 week screening period, each cohort will be randomized 1:1 to a 16 week treatment period. Doses will be administered by SC injection starting with a loading dose of tralokinumab followed by either Q2W or Q4W dosing.
Cohort 1 (aged 6 to <12 years):
• Tralokinumab low dose, 12 subjects.
• Tralokinumab high dose, 12 subjects.

In the initial treatment period (Week 0 to Week 16), topical corti-costeroids and topical calcineurin inhibitors are allowed as topical rescue treatment. If these would be deemed to be inadequate, as outlined in above, treatment with systemic corticosteroids is al-lowed as systemic rescue at the discretion of the investigators. Use of biological rescue treatment and the use of JAK inhibitors and non-steroidal systemic immunosuppressive drugs (cyclosporine, methotrexate, mycophenolate mofetil, azathioprine etc.) for res-cue treatment will be disallowed.

Open-label treatment period (Week 16 to Week 68)
After completion of Week 16 treatment, all subjects will roll-over to open-label tralokinumab treatment with optional TCS (Panel 10). Subjects can use mild to moderate strength TCS and/or TCI on lesional skin as needed at the

investigator's discretion. Subjects, who in the opinion of the subject, the subject's caregiver, or the investigator have unacceptable treatment effect of tralokinumab may discontinue treatment at any timepoint and enter the safety follow up period.

In the open-label treatment period (Week 16 to Week 68), partic-ipants are allowed to use mild to moderate topical corticosteroids and topical calcineurin as needed, whereas high potency topical corticosteroids are allowed as topical rescue treatment. If these would be deemed to be inadequate, as outlined in above, treat-ment with systemic corticosteroids is allowed as systemic rescue at the discretion of the investigators. Use of biological rescue treat-ment and the use of JAK inhibitors and non-steroidal systemic immunosuppressive drugs (cyclosporine, methotrexate, mycophe-nolate mofetil, azathioprine etc.) for rescue treatment will be disallowed.

Long-term extension treatment period
After Week 68, subjects will continue in a long-term extension treatment period until a global end-of-treatment visit on approximately 15-Jan-2026. Treatment will be the same as during the open-label treatment period (open-label tralokinumab treatment [150 mg Q2W] with optional TCS). Subjects can use mild to moderate strength TCS and/or TCI on lesional skin as needed at the investigator's discretion. Subjects, who in the opinion of the subject, the subject's caregiver, or the investigator have unacceptable treatment effect of tralokinumab may discontinue treatment at any timepoint and enter the safety follow-up period. Visits will be performed every 6 weeks. Site visits will be interchanged with phone
visits. Tralokinumab will be administered at home in between site visits, and tralokinumab will be dispensed for this purpose at the site visits.

Safety follow-up period (Week 68 to 82)
After treatment completion or discontinuation of trial product, subjects will enter a 14 week off-drug safety follow-up period for assessment of safety and immunogenicity. During follow up, subjects will be allowed to receive standard AD care (excluding biological treatments and JAK inhibitors) at the investigator*s discretion, if needed.

14-week off-drug safety follow-up (Week 68 to Week 82), partici-pants are allowed to use topical corticosteroids of any potency. In addition, other topical medications used for the treatment of atopic dermatitis, such as topical canlcineurin inhibitors, JAK inhibi-tors and PDE-4 inhibitors would be allowed. Below atopic dermati-tis treatments would also be options during the off-drug safety follow up:
1. Use of UVA or UVB, psoralen + UVA, other pho-totherapy, or tanning beds
2. 3 or more bleach baths per week
3. Systemic corticosteroid
4. Systemic treatment for AD with an immuno-suppressive/immunomodulating agent (exam-ples include cyclosporine, mycophenolate mo-fetil, azathioprine,

methotrexate, and interfer-on-gamma)

**Intervention**

Name of IMP: Tralokinumab
Active substance:
Dosage form: Syringe/vials
Concentration: 150mg/mL
Dose and method of administration:

Dose regimen for cohort 1 (6 to <12 years)
Dose level Low
dose High dose
Subject weight 17-<40 kg >=40 kg 17-<40
kg >=40 kg
Loading dose (Visit 3/Week 0) 300 mg 300 mg 300 mg 600 mg
Initial treatment period 150 mg Q4W 150 mg Q2W 150 mg Q2W 300 mg Q2W
Open-label treatment period 150 mg Q2W
Long term extension period 150mg Q2W

**Study burden and risks**

With more than 4,200 subjects exposed to tralokinumab in the completed clinical trials in AD and additional diseases investigated, the benefit-risk ratio is considered favorable and supports the administration of tralokinumab in adult and adolescent subjects with moderate-to-severe AD.
In both the adult and the adolescent population, tralokinumab demonstrated substantial improvements in a number of AD-relevant clinical parameters, including improvements in IGA, EASI, SCORAD, and POEM. It is therefore hypothesized that treatment with tralokinumab will result in similar improvements in a younger population, such as children aged 2 to <12 years.

Based on the extensive clinical experience, a reassuring safety profile of tralokinumab has been observed. No major safety concerns have been identified and the use of tralokinumab has been well-tolerated. Generally, the overall incidence of AEs reported for tralokinumab has been similar to that for placebo in controlled clinical trials and the adverse drug reactions observed were mainly non-serious and mild or moderate in severity. ADA have been detected in only few adult subjects with AD exposed to tralokinumab for up to 1 year. Subsequently to having demonstrated a favorable safety and efficacy profile in adults, the efficacy and safety of tralokinumab has been investigated in an adolescent population (age 12 to <18 years) in which 276 subjects were dosed with tralokinumab. In this younger population, the safety profile was found to be similar to what has previously been observed in the adult population.

In the present trial, subjects will be enrolled in 1 age cohorts, initially

securing exposure and safety data for subjects aged 6 to <12 years.

Appropriate measures have been instituted in this trial to protect subjects from potential risks, such as:
• Exclusion of subjects with active or suspected endoparasitic infections, or high risk of endoparasitic infection, unless clinical and (if necessary) laboratory assessment have ruled out active infection before randomization; neutralization of IL-13 might theoretically cause a worsening of parasitic infestation, in particular prevention of expulsion of gastrointestinal worms (helminths).
• Exclusion of subjects with active chronic or acute infection requiring treatment with systemic antibiotics, antivirals, antifungals, or antiprotozoals within 2 weeks before the baseline visit.

Altogether, the risks associated with participating in this trial are considered low and outweighed by the benefit of potentially being able to treat children with moderate-to-severe AD with tralokinumab. Pediatric patients treated with dupilumab have been shown to have better outcomes than those not treated with dupilumab. Considering the similar mechanisms of action with tralokinumab and dupilumab and the demonstrated efficacy of tralokinumab in the adult and adolescent populations, tralokinumab is expected to offer a similar benefit in pediatric patients as that observed with dupilumab.

## Contacts

**Public**
Leo Pharma

Delflandlaan 1
Amsterdam 1062 EA
NL
**Scientific**
Leo Pharma

Delflandlaan 1
Amsterdam 1062 EA
NL

## Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Children (2-11 years)

## Inclusion criteria

• Diagnosis of AD (as defined by Hanifin and Rajka criteria for AD).
• Age 6 to <12 years.
• Body weight at baseline:
o >=17 kg for children aged 6 to <12 years at screening.
• History of AD for:
o >= 12 months for children aged 6 to <12 years at screening.
• History of TCS and/or TCI treatment failure (due to inadequate response or intolerance) or subjects for whom these topical AD treatments are medically inadvisable.
• AD involvement of >=10% body surface area at screening and baseline.
• An EASI score of >=16 at screening and at baseline.
• An IGA score of >=3 at screening and at baseline.
• Emollient twice daily (or more) for at least 14 days prior to baseline.

## Exclusion criteria

• Active dermatologic conditions that may confound the diagnosis of AD or would interfere with assessment of treatment.
• Treatment with topical PDE-4 inhibitor within 2 weeks prior to randomization.
• Treatment with the following immunomodulatory medications or bleach baths within 4 weeks prior to baseline:
o Systemic immunosuppressive/immunomodulating drugs (e.g. methotrexate, cyclosporine, azathioprine, mycophenolate mofetil, JAK inhibitors).
o Systemic corticosteroid use (excludes topical, inhaled, ophthalmic, or intranasal delivery).
o 3 or more bleach baths during any week within the 4 weeks.
• Receipt of any marketed biological therapy or investigational biologic agents (including immunoglobulin, anti-IgE, or dupilumab):
o Any cell-depleting agents, including but not limited to rituximab: within 6 months prior to baseline, or until lymphocyte count returns to normal, whichever is longer.
o Other biologics (including dupilumab): within 3 months or 5 half-lives,

whichever is longer, prior to baseline.
• Active chronic or acute infection requiring treatment with systemic antibiotics, antivirals, antifungals, or antiprotozoals within 2 weeks before the baseline visit.
• History of malignancy at any time before the baseline visit.
• History of anaphylaxis following any biological therapy.
• History of immune complex disease.
• Active or suspected endoparasitic infections.
• History of past or current tuberculosis or other mycobacterial infection.
• Established diagnosis of a primary immunodeficiency disorder.

# Study design

## Design

| | |
|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Masking: | Single blinded (masking used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 07-09-2022 |
| Enrollment: | 6 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Registration: | No |
| Product type: | Medicine |
| Brand name: | Tralokinumab |
| Generic name: | N/A |

## Ethics review

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|---|---|
| Approved WMO Date: | 09-05-2022 |
| Application type: | First submission |
| Review commission: | METC NedMec |
| Approved WMO Date: | 14-06-2022 |
| Application type: | First submission |
| Review commission: | METC NedMec |
| Approved WMO Date: | 11-02-2023 |
| Application type: | Amendment |
| Review commission: | METC NedMec |
| Approved WMO Date: | 09-03-2023 |
| Application type: | Amendment |
| Review commission: | METC NedMec |
| Approved WMO Date: | 21-11-2023 |
| Application type: | Amendment |
| Review commission: | METC NedMec |
| Approved WMO Date: | 05-12-2023 |
| Application type: | Amendment |
| Review commission: | METC NedMec |
| Approved WMO Date: | 16-02-2024 |
| Application type: | Amendment |
| Review commission: | METC NedMec |
| Approved WMO Date: | 26-03-2024 |
| Application type: | Amendment |
| Review commission: | METC NedMec |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2021-005573-12-NL |
| ClinicalTrials.gov | NCT05388760 |
| CCMO | NL80673.041.22 |