# A phase II, randomised, double-blind, placebo-controlled study to evaluate the safety and efficacy of lebrikizumab in patients with persistent moderate to severe atopic dermatitis that is inadequately controlled by topical corticosteroids

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EFFICACY OBJECTIVESThe primary efficacy objective for this study is to evaluate the efficacy of lebrikizumabused as adjunctive therapy with TCS compared with TCS in patients with persistentmoderate to severe AD, as measured by Eczema Area and...

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

## Summary

### ID

NL-OMON42001

**Source**
ToetsingOnline

**Brief title**
GS29250 AD

### Condition

- Epidermal and dermal conditions

**Synonym**
atopic dermatitis, eczema

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Roche Nederland B.V.
**Source(s) of monetary or material Support:** F. Hoffmann La Roche Inc.

## Intervention

**Keyword:** atopic dermatitis, Efficacy, Safety

## Outcome measures

### Primary outcome

The primary efficacy outcome measure is the percentage of patients achieving

EASI-50

(a 50% reduction in EASI score from baseline) at Week 12.

### Secondary outcome

Efficacy Outcome Measures

The secondary efficacy outcome measures for this study are as follows:

• Percent and absolute change from baseline in EASI score at Week 12

• Percent of patients achieving a 75% reduction from baseline in EASI score

(EASI-75)

at Week 12

• Percent of patients achieving an IGA score of 0 or 1 at Week 12

• Percent of patients with a >= 2 point reduction from baseline in IGA at Week 12

• Absolute change from baseline in IGA at Week 12

• Percent of patients achieving an IGSA score of 0 or 1 at Week 12

• Percent of patients with a >= 2 point reduction from baseline in IGSA at Week

12

• Absolute change from baseline in IGSA at Week 12

• Percent and absolute change from baseline in SCORAD at Week 12

• Percent of patients with a 50% or 75% reduction from baseline in SCORAD-50/75

at

Week 12

• Percent of patients achieving EASI-50 at Week 12 and maintaining EASI-50 at

Weeks 16 and 20

• Percent of patients achieving IGA score of 0 or 1 at Week 12 and maintaining

IGA score of 0 or 1 at Weeks 16 and 20

• Percent of patients achieving IGSA score of 0 or 1 at Week 12 and maintaining

IGSA score of 0 or 1 at Weeks 16 and 20

• Percent of patients achieving SCORAD-50 at Week 12 and maintaining

SCORAD-50 at Weeks 16 and 20

• Percent change from baseline in total % body surface area (BSA) affected at

Week 12

• Absolute- and percent-change from baseline in pruritus as measured by the

Pruritus

VAS (assessed as part of the SCORAD) at Week 12

• Absolute- and percent-change from baseline in pruritus as measured by the 5-D

Itch

Scale at Week 12

• Total use (grams) of TCS from baseline to Week 12

• Total use (grams) of TCS from Week 12 to end of study or early termination

• Number of disease flares from baseline to Week 12

• Change in AD symptoms from baseline to Week 12, as assessed by the ADSD

• Change in AD-specific health-related QoL from baseline to Week 12, as assessed

by the ADIQ

• Change in health-related QoL from baseline to Week 12, as measured by the DLQI

For more outcome measures see protocol section 3.4

# Study description

**Background summary**

Atopic dermatitis (AD) is a chronic relapsing and remitting inflammatory skin disorder
affecting all age groups. Clinically, AD is characterized by xerosis, erythematous
crusting rash, lichenification, an impaired skin barrier, and intense pruritus.

AD is one of the most common dermatologic diseases and the prevalence appears to have increased over the past two to three decades; 15% to 30% of children and 2% to
10% of adults are affected. Approximately 85% of all cases of AD
begin before 5 years of age with up to 70% of children having spontaneous remission
before adolescence.
Patients with AD have a high disease burden, and their quality of life (QoL) is significantly impacted. In one study, AD was shown to have a greater negative effect on
patient mental health than diabetes and hypertension. Patients
with moderate to severe AD have a higher prevalence of social dysfunction and sleep
impairment, which is directly related to severity of disease.
Depression, anxiety, and social dysfunction not only affect patients with AD but also their
caregivers. Compared with psoriasis, another common and
debilitating skin disease, AD patients have lower role-physical, vitality, social functioning,
role-emotional, and mental health subscale scores

Lebrikizumab is a humanized monoclonal immunoglobulin (Ig) G4 antibody (huIgG4)

with a mutation in the hinge region for increased stability. Lebrikizumab binds specifically to soluble human interleukin (IL) 13 with high affinity and neutralizes its functional activities with high potency. Lebrikizumab inhibits IL-13 signaling through the IL-4R*/IL-13R*1 receptor. It blocks the binding of IL-13 to IL-4R*, but does not block the binding of IL-13 to IL-13R*1 or IL-13R*2.
Lebrikizumab does not bind to mouse IL-13, the commonly used species for animal models of AD. Therefore, there are no nonclinical data available from in vivo lebrikizumab pharmacology/efficacy studies in animal models of AD. However, numerous nonclinical studies have been published that demonstrate increased expression of IL-13 in affected skin that support the use of an anti-IL-13 therapeutic for human AD (see Section 1.3 in the protocol).
To date, no dedicated studies have been conducted with lebrikizumab in patients with AD or other skin diseases; however, a small number of patients (approximately 69) with concomitant active AD (or eczema) have been exposed to lebrikizumab in Phase II asthma studies (Studies ILR4646g, GB27862, and GB27864) without evidence of an acute safety signal. In addition, results from a questionnaire completed by investigators in a Phase II asthma study showed improvements in AD disease in some asthma patients.

**Study objective**

EFFICACY OBJECTIVES
The primary efficacy objective for this study is to evaluate the efficacy of lebrikizumab
used as adjunctive therapy with TCS compared with TCS in patients with persistent
moderate to severe AD, as measured by Eczema Area and Severity Index (EASI)-50, defined as a 50% reduction in EASI score relative to baseline.
The secondary efficacy objectives for this study are as follows:
• To evaluate the efficacy of lebrikizumab used as adjunctive therapy with TCS compared with TCS in patients with persistent moderate to severe AD, as measured by EASI, Investigator*s Global Assessment (IGA), Investigator Global Signs Assessment (IGSA), and Severity Scoring of Atopic Dermatitis (SCORAD)
• To evaluate the efficacy of lebrikizumab used as adjunctive therapy with TCS compared with TCS in patients with persistent moderate to severe AD, as measured by total use (grams) of TCS
• To evaluate the efficacy of lebrikizumab used as adjunctive therapy with TCS compared with TCS in patients with persistent moderate to severe AD, as measured by AD symptoms and AD-specific health-related QoL, as assessed by the Atopic Dermatitis Symptom Diary (ADSD), Pruritus Visual Analogue Scale (VAS), 5-D Itch Scale, the Atopic Dermatitis Impact Questionnaire (ADIQ), and the Dermatology Life
Quality Index (DLQI)
SAFETY OBJECTIVES
The safety objectives for this study are as follows:
• To evaluate the safety of lebrikizumab used as adjunctive therapy with TCS

compared with TCS in patients with persistent moderate to severe AD focusing on the nature, frequency, and severity of serious and non-serious adverse events, as
well as effects on laboratory values, vital signs, electrocardiogram (ECG) parameters, or other safety biomarkers
• To characterize the immunogenic potential of lebrikizumab by measuring anti-lebrikizumab antibodies and assessing their relationship with other outcome measures
PHARMACOKINETIC OBJECTIVE
The pharmacokinetic (PK) objective for this study is to evaluate the pharmacokinetics of
lebrikizumab administered by subcutaneous (SC) injection in patients with persistent
moderate to severe AD.
EXPLORATORY OBJECTIVES
The exploratory objectives for this study are as follows:
• To evaluate IL-13-related and AD-related biomarkers and the effect of lebrikizumab
used as adjunctive therapy with TCS compared with TCS on their expression
• To evaluate the effect of lebrikizumab used as adjunctive therapy with TCS compared with TCS on health utilities as assessed by the Short-Form 36 health survey questionnaire (SF-36)
• To evaluate the effect of lebrikizumab used as adjunctive therapy with TCS compared with TCS on asthma control as assessed by the Asthma Control Questionnaire-5 (ACQ-5)
• To evaluate the effect of lebrikizumab used as adjunctive therapy with TCS compared with TCS on asthma control as assessed by the frequency of rescue inhaler use

## Study design

This is a Phase II global, randomized, double-blind, placebo-controlled study to evaluate the
efficacy and safety of lebrikizumab in adult patients (18*75 years of age) with persistent
moderate to severe AD, who are inadequately controlled by TCS.

## Intervention

Patients that participate in the study will be treated with a lebrikizumab or placebo sub cutaneous injection in a Q4W regimen

## Study burden and risks

For the study assessments, see Question E6 and E9 of this form.

SIDE EFFECTS KNOWN THAT THEY RELATED TO LEBRIKIZUMAB
In completed studies to date, local skin reactions (redness of the skin, itching, swelling around the injection site, rash) at the site of the injection were commonly seen in patients receiving lebrikizumab and were seen commonly in patients receiving placebo. Local injection-site reactions did not occur with every dose. Local injection site reactions rarely required treatment, and few patients discontinued lebrikizumab or placebo treatment due to the injection-site reactions.

Some side effects are rare or very rare. For more information, see the Informed Consent.

OTHER POTENTIAL RISKS OF THE INVESTIGATION IS NOT CAUSED BY LEBRIKIZUMAB or topical steroid creams

POSSIBLE RISKS AND DISADVANTAGES IN CONNECTION WITH BLOOD
During this study, small amounts of blood will be drawn from a vein and used for tests that allow your study doctors to see how you are doing. Drawing blood may cause pain where the needle is inserted, and there is a small risk of bruising or infection at the place where the needle is inserted. Some people experience dizziness, upset stomach, or fainting when their blood is drawn.

RISKS ECG
Possible side effects of the ECG are skin irritation from the ECG electrode pads or pain when the pads are taken off.

OPTIONAL SKIN BIOPSIES

The risks of skin biopsies include the following:
• Bleeding: During the procedure the patient will slightly bleeding after the procedure and there may be some oozing after the procedure.
• Bruising
• Pain:In most cases any discomfort is minimal. The patient can perceive a feeling of pressure in the area of the skin biopsy, but normally the patient will experience no pain.
• Healing problems: If the patient has a tendency to form large, overgrown scars (keloids), there is an increased risk of the occurrence of a similar lesion to the biopsy site. Smoking and some chronic medical conditions such as diabetes have a negative effect on the healing ability of the skin.
• Allergic reaction to the local anesthetic

# Contacts

**Public**

Roche Nederland B.V.

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NL
**Scientific**
Roche Nederland B.V.

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NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

- Age 18 to 75 years, inclusive, at the start of the run-in period
- AD diagnosed by the Hanifin/Rajka criteria and that has been present for at least 1 year at screening
- Moderate to severe AD as graded by the Rajka/Langeland criteria at screening
- History of inadequate response to a >= 1 month (within the 3 months prior to the screening visit) treatment regimen of at least daily TCS and regular emollient for treatment of AD
- EASI score >= 14 at screening
- IGA score >=3
- AD involvement of >=10% body surface area
- Pruritus Visual Analog Scale score >= 3

## Exclusion criteria

- Past and/or current use of any anti-IL-13 or anti-IL-4/IL-13 therapy, including lebrikizumab;- Use of an investigational agent within 4 weeks prior to screening or within 5 half-lives of the

investigational agent, whichever is longer;- History of a severe allergic reaction or anaphylactic reaction to a biologic agent or known hypersensitivity to any component of the lebrikizumab injection;- Use of any complementary, alternative, or homeopathic medicines including, but not limited to, phytotherapies, traditional or non-traditional herbal medications, essential fatty acids, or acupuncture within 7 days prior to the run-in period or need for such medications during the study;- Evidence of other skin conditions; including, but not limited to, T-cell lymphoma or allergic contact dermatitis;- Evidence of, or ongoing treatment (including topical antibiotics) for active skin infection at screening;- Other recent infections meeting protocol criteria;- Active tuberculosis requiring treatment within the 12 months prior to Visit 1;- Evidence of acute or chronic hepatitis or known liver cirrhosis;- Known immunodeficiency, including HIV infection;- Use of a topical calcineurin inhibitor (TCI) at the time of screening, unless the patient is willing to stop TCI use during the study (including the run-in period) and, in the investigators opinion, it is safe to do so;- Clinically significant abnormality on screening ECG or laboratory tests;- Known current malignancy or current evaluation for a potential malignancy, including basal or squamous cell carcinoma of the skin or carcinoma in situ;- History of malignancy within 5 years prior to screening, except for appropriately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, Stage I uterine cancer

# Study design

## Design

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| Study phase: | 2 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 26-08-2015 |
| Enrollment: | 10 |
| Type: | Actual |

### Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | nvt |
| Generic name: | lebrikizumab |

## Ethics review

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|---|---|
| Approved WMO Date: | 02-04-2015 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 20-07-2015 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 14-09-2015 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 18-09-2015 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 23-09-2015 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |

## 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 | EUCTR2014-000049-56-NL |
| ClinicalTrials.gov | NCT02340234 |
| CCMO | NL52334.041.15 |