A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Nemolizumab (CD14152) in Subjects with Moderate-to-Severe Atopic Dermatitis

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Primary objective: The primary objective is to assess the efficacy and safety of nemolizumab (CD14152) after a 16-week treatment period in adult and adolescent subjects with moderate-to-severe atopic dermatitis (AD) not adequately controlled with...

Ethical review	Approved WMO
Status	Completed
Health condition type	Epidermal and dermal conditions
Study type	Interventional

Summary

ID

NL-OMON52453

Source
ToetsingOnline

Brief title
Nemolizumab vs. placebo in atopic dermatitis (ARCADIA RD.06.SPR.118161)

Condition

- Epidermal and dermal conditions

Synonym
atopic dermatitis, chronic skin inflammation

Research involving
Human

Sponsors and support

Primary sponsor: Galderma
Source(s) of monetary or material Support: industry;Galderma SA

Intervention

Keyword: atopic dermatitis, nemolizumab

Outcome measures

Primary outcome

Co-Primary Endpoints:

• Proportion of subjects with an IGA success (defined as an IGA of 0 [clear] or

1 [almost clear] and a >= 2-point reduction from baseline) at Week 16

• Proportion of subjects with EASI-75 (>= 75% improvement in EASI from baseline)

at Week 16

Secondary outcome

Key Secondary Endpoints:

• Proportion of subjects with an improvement of PP NRS >= 4 at Week 16

• Proportion of subjects with PP NRS < 2 at Week 16

• Proportion of subjects with an improvement of sleep disturbance NRS (SD NRS)

>= 4 at Week 16

• Proportion of subjects with an improvement of PP NRS >= 4 at Week 4

• Proportion of subjects with PP NRS < 2 at Week 4

• Proportion of subjects with an improvement of PP NRS >= 4 at Week 2

• Proportion of subjects with an improvement of PP NRS >= 4 at Week 1

• Proportion of subjects with EASI-75 and improvement of PP NRS >= 4 at Week 16

• Proportion of subjects with IGA success and improvement of PP NRS >= 4 at Week

Both primary and key secondary endpoints will be evaluated for the following

populations:

• Baseline PP NRS >= 4 (full population)

• Baseline PP NRS >= 7

For further secondary endpoints, safety endpoints and other endpoints please

refer to sections 7.5 to 7.7 of the protocol.

Study description

Background summary

Topical medications are the mainstay of atopic dermatitis (AD) therapy. Treatment options are however limited for patients with moderate-to-severe AD whose disease cannot be adequately controlled with topical medications. Nemolizumab may present a new treatment option for AD in pediatric as well as adult patients. AD patients with associated pruritus and an insufficient response to topical therapies could particularly benefit from such a therapy.

Study objective

Primary objective: The primary objective is to assess the efficacy and safety of nemolizumab (CD14152) after a 16-week treatment period in adult and adolescent subjects with moderate-to-severe atopic dermatitis (AD) not adequately controlled with topical treatments.

Secondary objective: The secondary objective is to evaluate the efficacy and safety of maintenance treatment with nemolizumab (CD14152) for up to an additional 32 weeks.

Study design

This is a randomized, double-blind, placebo-controlled, multicenter, parallel-group study in adult and adolescent subjects with moderate-to-severe

AD. Eligible subjects must have a documented history of inadequate response to topical AD medication(s).

Approximately 750 total subjects will be randomized (2:1) to receive either nemolizumab (CD14152) or placebo, stratified by baseline disease severity (Investigator*s Global Assessment [IGA]; moderate: IGA = 3; severe: IGA = 4) and peak pruritus numeric rating scale (PP NRS) severity (PP NRS >= 7; PP NRS < 7). A minimum of 250 subjects will be randomized in each PP NRS strata. Clinical responders at Week 16 (ie, the end of initial treatment/beginning of maintenance) will be rerandomized (1:1:1) to different treatment regimens (injections every 4 weeks [Q4W] or every 8 weeks [Q8W] of nemolizumab [CD14152] or placebo Q4W).

Subjects will apply a moisturizer at least once daily, beginning at screening. Subjects will also be provided or prescribed background topical therapy for AD (including a medium-potency topical corticosteroid [TCS] for the body and a low-potency TCS or topical calcineurin inhibitor (TCI) for sensitive areas such as the face, neck, intertriginous areas, etc for use throughout the study. If deemed to be medically necessary by the investigator (eg, to control intolerable AD signs/symptoms), rescue therapies can be prescribed to the subjects during the study, except during the run-in period (ie, at least 2 weeks [14 days] before Day 1/baseline).

The study consists of 4 periods over approximately 60 weeks: screening (including run-in), initial treatment, maintenance, and follow-up (unless the subject is a non-responder at Week 16, at which their participation could last up to 28 weeks).

An independent data monitoring committee (IDMC) will review and monitor subject safety throughout the study, and an adjudication committee (AC) will review all asthma-related events throughout the study. Details on the IDMC and AC, including the plan of analysis for outputs; the composition of the committees; and the procedures, roles, responsibilities, and communications are provided in the respective IDMC and AC charters.

Intervention

Nemolizumab (CD14152) or placebo will be provided as lyophilized powder in a dual-chamber syringe (DCS) for solution for injection.

During the initial treatment period, eligible subjects will be randomized to receive either 30 mg of nemolizumab (CD14152) in group 1 or placebo in group 2, administered as a subcutaneous injection only after reconstitution Q4W for 16 weeks (last injection at Week 12), with a loading dose of 60 mg on Day 1/baseline.

Subjects (and/or their caregivers) will have the option to self-inject study

drug while at the study center under staff supervision. Subjects (and/or their caregivers) will be trained on injecting the study drug at Day 1 and will be allowed to inject study drug at all subsequent visits, while at the study center, under staff supervision. If the subject (and/or caregivers) is unwilling to perform the injections, study staff can administer study drug at each visit.

In the maintenance period, group 1 subjects who are clinical responders will be re-randomized to receive either 30 mg of nemolizumab (CD14152) or placebo for 32 weeks. Subjects in group 1A will receive a subcutaneous injection of nemolizumab Q4W (last injection at Week 44); group 1B will receive an injection of nemolizumab Q8W, with alternating placebo Q8W (last active injection at Week 40 and last placebo injection at Week 44); and group 1C will receive placebo Q4W. Subjects in group 2 who are clinical responders will continue to receive placebo Q4W.

Patients will additionally use moisturizer daily, will be provided with topical background therapy and, if needed, will be provided with rescue therapy.

Study burden and risks

When completing the full study, patients will visit the research location at least 16 times over a period of 15 months. During the treatment period patients will receive study drug injections every four weeks. They will additionally use moisturizer daily and will be provided with topical background therapy and if needed with rescue therapy. During the study the following procedures will be done, among others: physical exam (9x), respiratory assessment (15x), completion of questionnaires (14x), blood draw (12x), urine collection (7x), ECG (4x). Patients will be asked to complete a daily electronic diary.

The study medication is a non-registered medication. Possible known side effects are described in the IB and patient information and can also occur during this study. There is also a risk that unknown side effects occur and there is a chance that the treatment will not be efficacious for the patient.

The more commonly occurring side effects with nemolizumab were:
- Worsening of AD (itching, rash, skin inflammation [irritation that can cause pain, swelling, redness and heat], skin swelling) - To try and prevent this, the study doctors will ask to apply daily moisturizer, topical corticosteroids, and/or topical calcineurin inhibitors.
- Asthma or worsening of asthma (difficulty breathing caused by narrowing of the airways)
- Infections (primarily nasopharyngitis [a cold] and upper respiratory tract [nose and throat] infection)
- Injection-related reactions (this can be a major or minor allergic reaction related to the injection [shot]; there may also be redness, swelling, pain and/or heat in or around the area where the injection was given)

- Headache

There are also less common side effects with nemolizumab and risks associated with the study procedures. Please refer to section 6 of the adult informed consent form for a listing of all risks and side effects.

Contacts

Public
Galderma

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Scientific
Galderma

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)

Inclusion criteria

1. Male or female subjects aged >= 12 years at the screening visit.
Note: Enrollment of subjects aged 12 to 17 years has been opened after the IDMC has assessed interim safety data from the phase 2 study (Protocol 116912) and provided recommendations to the sponsor, who then determined the eligibility of

this age group for enrollment in the study.
The sponsor sent a written communication to the site confirming that the study is open for enrollment of adolescents. Adolescents could not be enrolled in the study until such communication was received.
2. Chronic atopic dermatitis (AD) for at least 2 years before the screening visit, and confirmed according to American Academy of Dermatology Consensus Criteria at the time of the screening visit.
3. EASI score >= 16 at both the screening and baseline visits.
4. IGA score >= 3 (based on the IGA scale ranging from 0 to 4, in which 3 is moderate and 4 is severe) at both the screening and baseline visits.
5. AD involvement >= 10% of body surface area (BSA) at both the screening and baseline visits.
6. Peak (maximum) pruritus NRS score of at least 4.0 at the screening and baseline visit.
7. Documented recent history (within 6 months before the screening visit) of inadequate response to topical medications (TCS with or without TCI).
8. Agree to apply a moisturizer throughout the study from the screening visit; agree to apply authorized topical therapy from the screening visit and throughout the study as determined appropriate by the investigator.
9. Female subjects of childbearing potential (ie, fertile, following menarche and until becoming postmenopausal unless permanently sterile) must agree either to commit to true abstinence throughout the study and for 12 weeks after the last study drug injection, when this is in line with the preferred and usual lifestyle of the subject, or to use an adequate and approved method of contraception
throughout the study and for 12 weeks after the last study drug injection. This criterion also applies to a prepubertal female subject who begins menses during the study. *In Germany only, if a subject has reached Tanner stage 3 breast development, even if not having menarche, the subject will be considered a female of childbearing potential.
Adequate and approved methods of contraception applicable for the subject and/or her partner are defined below:
- Progestogen-only oral hormonal contraception;
- Combination of male condom with cap, diaphragm, or sponge with spermicide (double barrier methods) (*In Germany only, double barrier methods are not considered a highly effective method of contraception);
Note: *Double barrier methods* refers to simultaneous use of a physical barrier by each partner. Use of a single barrier method (eg, condom) together with a spermicide is not acceptable.
- Combined (estrogen- and progestogen-containing) oral, intravaginal, or transdermal hormonal contraception;
- Injectable or implanted hormonal contraception;
- Intrauterine devices or intrauterine hormone-releasing system;
- Bilateral tubal ligation or tube insert (such as the Essure system) at least 3 months before the study;
- Bilateral vasectomy of partner at least 3 months before the study

10. Female subjects of non-childbearing potential must meet one of the following criteria:
•Absence of menstrual bleeding for 1 year prior to screening without any other medical reason, confirmed with follicle-stimulating hormone (FSH) level in the postmenopausal range
•Documented hysterectomy or bilateral salpingectomy at least 3 months before screening
Note: Bilateral tubal ligation is not accepted as a reason for non-childbearing potential
11. Subject (and guardian, when applicable) willing and able to comply with all of the time commitments and procedural requirements of the clinical study protocol, including daily diary recordings by the subject using an electronic handheld device provided for this study.
12. Understand and sign an informed consent form (and assent form, when applicable) before any investigational procedure(s) are performed.

Exclusion criteria

1. Body weight < 30 kg.
2. Subjects meeting 1 or more of the following criteria at screening or baseline:
2a. Had an exacerbation of asthma requiring hospitalization in the preceding 12 months.
2b. Reporting asthma that has not been well-controlled (ie, symptoms occurring on >2 days per week, nighttime awakenings > 2 or more times per week, or some interference with normal activities) during the preceding 3 months.
2c. Asthma Control Test <= 19 (only for subjects with a history of asthma).
2d. Peak expiratory flow < 80% of the predicted value.
3. Subjects with a current medical history of chronic obstructive pulmonary disease and/or chronic bronchitis.
4. Cutaneous infection within 1 week before the baseline visit, any infection requiring treatment with oral or parenteral antibiotics, antivirals, antiparasitics or antifungals within 2 weeks before the baseline visit, or any confirmed or suspected coronavirus disease (COVID)-19 infection within 2 weeks before the screening or baseline visit. Subjects may be rescreened once the infection has resolved. Resolution of COVID-19 infection can be confirmed by recovery assessment methods, as described in Section 8.3.4.2;
Note: Subjects with chronic, stable use of prophylactic treatment for recurrent herpes viral infection can be included in this study.
5. Requiring rescue therapy for atopic dermatitis (AD) during the run-in period or expected to require rescue therapy within 2 weeks following the baseline visit.
6. Positive serology results (hepatitis B surface antigen [HBsAg] or hepatitis B core antibody [HBcAb], hepatitis C antibody, or human immunodeficiency virus

antibody) at the screening visit.
7. Having received any of the treatments specified in Table 6 reported in the protocol within the specified timeframe before the baseline visit.
8. Previous treatment with Nemolizumab.
9. Subjects who, after a full treatment course of 16 weeks with dupilumab, experienced worsening of their AD or failed to achieve minimal improvement (eg, <= 10% reduction in EASI or no reduction in
IGA)
10. Pregnant women (positive serum pregnancy test result at the screening visit or positive urine pregnancy test at the baseline visit), breastfeeding women, or women planning a pregnancy during the clinical study.
11. History of lymphoproliferative disease or history of malignancy of any organ system within the last 5 years, except for (1) basal cell carcinoma, squamous cell carcinoma in situ (Bowen's disease), or carcinomas in situ of the cervix that have been treated and have no evidence of recurrence in the last 12 weeks before the baseline visit, or (2) actinic keratoses that have been treated.
12. History of hypersensitivity (including anaphylaxis) to an immunoglobulin product (plasma-derived or recombinant, eg, monoclonal antibody) or to any of the study drug excipients.
13. History of intolerance to TCS or for whom TCS is not advisable (eg, hypersensitivity, significant skin atrophy).
14. Known active or untreated latent tuberculosis infection.
Note: Subjects who have a documented history of completion of an appropriate TB treatment regimen for active or latent TB with no history of re-exposure to TB since their treatment was completed are eligible to participate in the study.
15. Known or suspected immunosuppression or unusually frequent, recurrent, severe, or prolonged infections as per investigator judgment.
16. Presence of confounding skin condition that may interfere with study assessments (eg, Netherton syndrome, psoriasis, cutaneous Tcell lymphoma [mycosis fungoides or Sezary syndrome], contact dermatitis, chronic actinic dermatitis, dermatitis herpetiformis).
17. Any medical or psychological condition or any clinically relevant laboratory abnormalities, such as but not limited to elevated ALT or AST (> 3 × upper limit of normal [ULN]) in combination with elevated bilirubin (> 2 × ULN), during the screening period that may put the subject at significant risk according to the investigator*s judgment, if he/she participates in the clinical study, or may interfere with study assessments (eg, poor venous access or needle-phobia).
18. Planned or expected major surgical procedure during the clinical study.
19. Subjects unwilling to refrain from using prohibited medications during the clinical study.
20. Currently participating or participated in any other study of a drug or device, within the past 8 weeks before the screening visit, (or 5 half-lives of the investigational drug, whichever is longer), or is in an exclusion period (if verifiable) from a previous study.
21.History of alcohol or substance abuse within 6 months of the screening

visit.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	18-11-2020
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nemolizumab
Generic name:	CD14152

Ethics review

Approved WMO

Date:	08-01-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	26-03-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-09-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-10-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-10-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-02-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-04-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-08-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-03-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	08-06-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2019-001887-31-NL
ClinicalTrials.gov	NCT03985943
CCMO	NL71974.078.19

Study results

Date completed:	11-08-2022
Results posted:	18-03-2024

First publication
06-03-2024

URL result
URL
Type
int
Naam
M2.2 Samenvatting voor de leek

URL

Internal documents
File