A Prospective, Multicenter, Long-Term Study to Assess the Safety and Efficacy of Nemolizumab (CD14152) in Subjects with Moderate-to-Severe Atopic Dermatitis.

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This study has been transitioned to CTIS with ID 2024-514404-13-00 check the CTIS register for the current data. The primary objective is to assess the long-term safety of nemolizumab (CD14152) in adult and adolescent subjects with moderate-to-...

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

Summary

ID

NL-OMON54779

Source
ToetsingOnline

Brief title
Long-term nemolizumab in atopic dermatitis (RD.06.SPR.118163)

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

Safety Endpoints:

- Incidence and severity of treatment-emergent AEs throughout the study

- Incidence of serious treatment-emergent AEs throughout the study

- Incidence and severity of AEs of special interest (AESIs) throughout the

study

Secondary outcome

Efficacy Endpoints:

- Proportion of subjects with IGA score = 0-1 at each visit through Week 200

- Proportion of subjects with EASI-75 response at each visit through Week 200

- Change and percent change from baseline in EASI at each visit through Week 200

- Proportion of subjects with low disease activity state (ie, IGA <= 2) at each

visit through Week 200

- Change and percent change from baseline in SCORing Atopic Dermatitis (SCORAD)

score at each visit through Week 200

- Change and percent change from baseline in subject-reported pruritus using

10-cm visual analogue scale (SCORAD sub-component)

- Change and percent change from baseline in subject-reported sleep loss using

10-cm visual analogue scale (SCORAD sub-component)

- Proportion of subjects reporting low disease activity state (clear, almost clear, or mild) based on Patient Global Assessment of Disease 5-point scale at each visit up to Week 200

- Proportion of subjects satisfied with study treatment (good, very good, or excellent) based on Patient Global Assessment of Treatment 5-point Likert scale at each visit up to Week 200

- Change from baseline in Dermatology Life Quality Index (DLQI) or Children*s DLQI (cDLQI) total score at each visit through Week 200

- Change from baseline in Patient-Oriented Eczema Measure (POEM) total score at each visit through Week 200

- Change from baseline in Hospital Anxiety and Depression Scale (HADS) for each subscale (i.e., depression and anxiety) at each visit through Week 200

- Change from baseline in Work Productivity and Activity Impairment: Atopic Dermatitis (WPAI:AD) for each subscale (i.e., work productivity and activity impairment) at each visit through Week 200

- Change from baseline in EuroQoL 5-Dimension (EQ-5D) at each visit through Week 200

- Proportion of subjects receiving any rescue therapy by rescue treatment type (e.g., topical, phototherapy, systemic) at any visit during the treatment period

- Time to first relapse (relapse is defined as: worsening of AD requiring rescue therapy, if judged to be medically necessary by the investigator [i.e, clinically significant worsening of signs and/or symptoms of AD])

- Duration of remission (time to first relapse in subjects with IGA=0 or 1 at

baseline in the LTE)

- Time to permanent study drug discontinuation

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

This study has been transitioned to CTIS with ID 2024-514404-13-00 check the CTIS register for the current data.

The primary objective is to assess the long-term safety of nemolizumab (CD14152) in adult and adolescent subjects with moderate-to-severe atopic dermatitis (AD).

The secondary objective is to assess the long-term efficacy of nemolizumab (CD14152) in adult and adolescent subjects with moderate-to-severe AD.

Study design

This is a prospective, multicenter, open-label, long-term extension study in adult and adolescent subjects with moderate-to-severe AD who had been previously enrolled in nemolizumab AD Phase 2b dose-ranging (SPR.114322), Phase 2 adolescent pharmacokinetics (PK)/safety (SPR.116912), Phase 2 vaccination safety (SPR.118380), Phase 2 Drug-Drug Interaction (SPR.201593), Phase 3 pivotal (SPR.118169, SPR.118161), Phase 3b (SPR.201591) studies,or new adolescents who had not previously participated in a nemolizumab study. Entry into the long-term extension (LTE) study is as follows:
• Subjects who completed a Phase 2 study (SPR.114322, SPR.116912, SPR.118380, SPR.201593):
o Subjects who completed the treatment period may be eligible to enroll into the LTE study.
o Subjects who discontinued study drug prior to completion of the treatment period but otherwise completed study visits may be eligible to enroll into the LTE study, based on investigator clinical judgment, unless the subject

experienced an adverse event (AE) that may present an unreasonable risk if study drug is continued.
• Subjects who participated in a Phase 3 pivotal study (SPR.118169, SPR.118161):
o Subjects completing the initial treatment period (Week 16 visit) who do not qualify for the maintenance period may be eligible to enroll immediately into the LTE study.
o Subjects completing the maintenance period (Week 48 visit) may be eligible to enroll immediately into the LTE study.
o Subjects who discontinued study drug prior to completion of the treatment period but completed requisite study visits may be considered for eligibility into the LTE study based on investigator clinical judgment. Subjects discontinuing study drug before the Week 16 visit will be required to continue study visits until the Week 16 visit is due before considering LTE study eligibility. Similarly, in the maintenance period, subjects discontinuing study drug before the Week 32 visit will be required to continue study visits until the Week 32 visit is due. Thereafter, subjects who discontinue study drug prematurely may be considered for LTE eligibility without a wait period. Subjects who experienced an AE that may present an unreasonable risk if study drug is continued are not eligible.
o Subjects who participated in a Phase 3b study (SPR.201591):
• Subjects completing the treatment period may be eligible to enroll immediately into the LTE study.
o New adolescent subjects (age 12-17) who had not participated in a previous nemolizumab study (selected countries/selected sites- See Appendix 3).

To maintain the blind of ongoing blinded lead-in studies, the interactive response technology (IRT) will not restrict enrollment into the LTE study based on prior treatment assigned in the lead-in study. Subjects who did not respond to treatment, who required rescue therapy, or who experienced an AE in a lead-in study should be closely monitored by the investigator to assess the benefit of continued participation compared to observed or potential risks (as there is a chance that these subjects were previously assigned to active drug in the lead-in study and therefore may not receive additional therapeutic benefit in the LTE study or may experience AE recurrence).
The LTE study includes up to a 4-week screening period, up to a 200-week treatment period, and an 8-week follow-up period (12 weeks after the last dose of study medication).

Intervention

Nemolizumab (CD14152) or placebo will be provided as lyophilized powder in a dual-chamber syringe (DCS) for solution for injection. The shots will be given in the abdomen or in an alternative injection site (such as the arms or thighs). A different area will be selected for each shot.

All subjects in the Netherlands will roll over from protocol RD.06.SPR.118161.

For these subjects, the first dose in the current protocol will consist of 2 injections. One of these will be nemolizumab (30 mg). The other injection will be either nemolizumab (30 mg) or placebo, depending on whether the subject received placebo or nemolizumab in protocol RD.06.SPR.118161. Subjects and investigators will be blinded for this first dose.

After the first dose, all subjects will continue to receive 1 open label injection of nemolizumab (30 mg) every 4 weeks.

Subjects (and/or their caregivers) will have the option to self-inject study drug while at the study center under staff supervision.

Subjects will additionally use moisturizer daily, will be provided or prescribed 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 up to 29 times over a period of 116 weeks. 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 (13x), respiratory assessment (13x, if needed), completion of questionnaires (12x), blood draw (12x), urine collection (11x), ECG (6x).

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

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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

See protocol page 11:
1. Adolescent subjects (aged 12-17) who have not participated in a previous nemolizumab study (selected countries/selected sites - See Appendix 3) or subjects who may benefit from study participation in the opinion of the investigator and had participated in a prior nemolizumab study for AD including:
a. Subjects who completed the initial treatment period (Week 16 visit) in a

Phase 3 pivotal study (SPR.118161 or SPR.118169) and do not qualify for the maintenance period;
OR
b. Subjects who completed the maintenance period (Week 48 visit) in a Phase 3 pivotal study (SPR.118161 or SPR.118169);
OR
c. Subjects who completed the treatment period (Week 16 visit) in the Phase 2 vaccination safety study (SPR.118380);
OR
d. Subjects who completed the treatment period (Week 16 visit) in the Phase 2 adolescent PK/safety study (SPR.116912);
OR
e. Subjects who completed the treatment period (Week 24 visit) in the Phase 2b dose-ranging study (SPR.114322) and remain insufficiently controlled on topical therapy alone;
OR
f. Subjects who discontinued study medication in a prior study and completed required study visits prior to LTE participation (Week 16 visit for SPR.118161 and SPR.118169 initial treatment period, Week 32 visit for SPR.118161 and SPR.118169 maintenance period; final study visits for SPR.118380 [Week 16], SPR.116912 [Week 16], SPR.114322 [Week 24], SPR.201591 [Week 16], and SPR.201593 [Week 13] , unless the subject experienced an AE that may present an unreasonable risk if study medication is continued.
OR
g. Subjects who completed the treatment period (Week 16) in the Phase 3b study (SPR.201591);
OR
h. Subjects who completed the treatment period (Week 13) in the Phase 2 DDI study (SPR.201593).

Note(s): For ongoing studies, transfer into the LTE study should occur as soon as possible to minimize gaps in study medication dosing. Subjects who satisfy inclusion criteria 1a through 1c are permitted to enroll immediately into the LTE study, provided other eligibility criteria are met.

Enrollment of subjects aged 12 to 17 years has been open after the IDMC has assessed interim safety data from the phase 2 study (SPR.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 study sites confirming that the study is open for enrollment of adolescents. Adolescents could not be enrolled in the study until such communication was received.

2. Agree to apply a moisturizer at least once daily throughout the study and agree to apply the authorized topical therapy, as determined appropriate by the investigator.

3. Women 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.

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). Note: *Double barrier methods* refers to simultaneous use of a physical barrier by each partner. Use of a single barrier method (e.g., 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

4. 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, bilateral salpingectomy, or bilateral oophorectomy at least 3 months before screening
NOTE: bilateral tubal ligation is not accepted as a reason for non-childbearing potential

5. Subject (and guardian, when applicable) willing and able to comply with all of the time commitments and procedural requirements of the clinical study protocol.

6. Understand and sign an informed consent form (and assent form, when applicable), before any investigational procedure(s) being performed.

Additional Inclusion Criteria: For adolescent subjects (age 12-17) who have not participated in a previous clinical study with nemolizumab only (selected countries/selected sites - See Appendix 3):

7. Chronic AD for at least 2 years before the screening visit, and confirmed according to American Academy of Dermatology Consensus Criteria (Appendix 1)2

at the time of the screening visit.

8. EASI score >= 16 at both the screening and baseline visits.

9. 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.

10. AD involvement >= 10% of body surface area (BSA) at both the screening and baseline visits.

11. SCORAD pruritus VAS score of at least 4.0 at the screening and baseline visit. SCORAD pruritus VAS is completed by the subject as a single assessment of their average pruritus symptoms over the past 3*days or nights on a scale from 0 to 10.

12. Documented recent history (within 6 months before the screening visit) of inadequate response to topical medications (TCS with or without TCI). All subjects must demonstrate inadequate response to TCS. All subjects who have used TCI within 6 months of the screening visit, or for whom TCI is selected as background therapy for sensitive areas, must also demonstrate inadequate response to TCI. Acceptable documentation includes patient records with information on TCS (with or without TCI) prescription and treatment outcome, or written documentation of the conversation with the subject*s treating physician, if different than the investigator.
Inadequate response to TCS treatments (with or without TCI) is defined as:
a. Failure to achieve or maintain remission or low disease activity (equivalent to IGA <= 2) despite treatment with a regimen of a medium or higher potency TCS (with or without TCI), applied for at least 4 weeks or for the maximum duration per prescribing information;
or
b. Requirement of a long-term treatment (> 4 weeks) with a high- or very high-potency TCS (with or without TCI) to achieve or maintain remission or low disease activity (equivalent to IGA <= 2);
or
c. If documentation of inadequate response to topical treatments is not available, subjects with a documented recent course of systemic treatment or phototherapy for AD (within 6 months before the visit) will also be considered as inadequate responders to topical treatments.

If documentation is inadequate, subjects may be re-screened after such documentation is obtained.

Exclusion criteria

See protocol page 12:

1. Subjects who, during their participation in a prior nemolizumab study, experienced an AE which in the opinion of the investigator could indicate that continued treatment with nemolizumab may present an unreasonable risk for the subject.
2. Having received any of the following treatments in Table 3 within the specified timeframe before the baseline visit.
3. Pregnant women (positive pregnancy test result at screening or baseline visit), breastfeeding women, or women planning a pregnancy during the clinical study.
4. Any medical or psychological condition at the screening visit 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).
5. Planning or expected to have a major surgical procedure during the clinical study.
6. Subjects unwilling to refrain from using prohibited medications during the clinical study (see Section 8.4.9.2).

Additional Exclusion Criteria: For new adolescent subjects or for subjects who do not rollover from a prior nemolizumab study within 28 days of completing final study assessments during the lead-in study:
7. Body weight < 30 kg.
8. Subjects meeting 1 or more of the following criteria at screening or baseline:
8a. Had an asthma exacerbation requiring hospitalization in the preceding 12 months;
8b. Reporting asthma that has been not 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;
8c. Asthma Control Test (ACT) <= 19 (only for subjects with a history of asthma);
8d. Peak expiratory flow < 80% of the predicted value.
Note: In the event that PEF is * 80% of the predicted value at the screening visit, PEF testing can be repeated once within 48 hours:
• For subjects without a history of asthma
• For subjects with a history of asthma but if the ACT score is >19 at screening.
9. Subjects with a current medical history of chronic obstructive pulmonary disease and/or chronic bronchitis.
10. 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 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 8.3.5.2.; Note: Subjects with chronic, stable use of prophylactic treatment for recurrent herpes viral infection can be included in this study.

11. Positive serology results (hepatitis B surface antigen [HBsAg] or hepatitis B core antibody, [HBcAb], hepatitis C [HCV] antibody with positive HCV RNA, or human immunodeficiency virus [HIV] antibody) at the screening visit.
Note: Subjects with a positive HBcAb and a negative HBsAg can be included if hepatitis B surface antibody is positive (considered immune after a natural infection). Subjects who are positive for HCV antibody and negative for HCV RNA may be enrolled.
In the event of rescreening, the serology tests results (eg, HBV, HCV, HIV) from the first screening can be used by the investigator to assess the eligibility of rescreened subjects if those tests were performed within 6 weeks prior to the baseline visit.
12. Subjects who, after a full treatment course of 16 weeks with dupilumab, experience worsening of their AD or failed to achieve minimal improvement (eg, <10% reduction in EASI or no reduction in IGA);
13. 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 carcinoma in situ of the cervix that have been treated and have no evidence of recurrence in the last 12 weeks before the screening visit, or 2) actinic keratoses that have been treated;
14. History of hypersensitivity (including anaphylaxis) to an immunoglobulin product (plasma-derived or recombinant, eg, monoclonal antibody) or to any of the study drug excipients.
15. History of intolerance to TCS or for whom TCS is not advisable (eg, hypersensitivity to TCS, significant skin atrophy, etc), unless TCS was not used as background therapy in the lead-in study, if applicable.
16. 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.
17. Known or suspected immunosuppression or unusually frequent, recurrent, severe, or prolonged infections as per investigator judgment.
18. Presence of or current confounding skin condition that may interfere with study assessments (eg, Netherton Syndrome, psoriasis, cutaneous T-cell lymphoma [Mycosis Fungoides or Sezary Syndrome], contact dermatitis, chronic actinic dermatitis, dermatitis herpetiformis).
19. Any clinically relevant laboratory abnormalities, such as but not limited to elevated ALT or AST (> 3 × upper limit of normal) in combination with elevated bilirubin (> 2 × upper limit of normal), 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.
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, other than the nemolizumab for AD studies (SPR.114322, SPR.116912, SPR.118380, SPR.118169, SPR.118161, SPR.201591, and SPR.201593).

21. History of alcohol or substance abuse within 6 months of the screening visit.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-06-2021
Enrollment:	15
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	23-06-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-09-2020

Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-11-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-02-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-04-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
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Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-12-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-02-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-03-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-01-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-04-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-05-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-05-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-08-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-11-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-03-2024
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-06-2024
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
EU-CTR	CTIS2024-514404-13-00
EudraCT	EUCTR2019-001889-15-NL
ClinicalTrials.gov	NCT03989206
CCMO	NL71983.078.20