

A Multicenter, Parallel-group Study of Long-term Safety and Efficacy of CNTO 136 (sirukumab) for Rheumatoid Arthritis in Subjects Completing Treatment in Studies CNTO136ARA3002 (SIRROUND-D) and CNTO136ARA3003 (SIRROUND-T)

Published: 28-12-2013

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON40162

Source

ToetsingOnline

Brief title

SIRROUND-LTE

Condition

- Autoimmune disorders
- Joint disorders

Synonym

rheuma, rheumatoid arthritis

Research involving

Human

Sponsors and support

Primary sponsor: Janssen-Cilag

Source(s) of monetary or material Support: Janssen-Cilag

Intervention

Keyword: rheumatoid arthritis, sirukumab, subcutaneously

Outcome measures

Primary outcome

To evaluate the long-term safety of sirukumab in subjects with RA, who are refractory to disease modifying antirheumatic drugs (DMARD) or anti-TNF* agents.

Secondary outcome

The secondary objectives are to observe the following long-term effects of sirukumab in subjects with RA who are refractory to DMARDs or anti-TNF* agents on:

- * Efficacy
- * Pharmacokinetics
- * Immunogenicity
- * Pharmacodynamics
- * Pharmacogenetics
- * PFS-AI usability (as defined in a separate substudy protocol)

Study description

Background summary

This is a parallel-group long-term extension (LTE) trial of studies CNTO136ARA3002 and CNTO136ARA3003 to assess the long-term safety and efficacy of sirukumab in subjects with moderately to severely active RA. Subjects who have completed participation in studies CNTO136ARA3002 or CNTO136ARA3003 will be eligible to enroll in this study. Subjects are to continue to receive the identical sirukumab SC dose regimen of 100 mg every 2 (q2) weeks or 50 mg every 4 (q4) weeks that they were receiving upon completion of participation in studies CNTO136ARA3002 and CNTO136ARA3003.

Study objective

Primary Objective is to evaluate the long-term safety of sirukumab in subjects with RA who are refractory to DMARDs or anti-TNF* agents.

The secondary objectives are to observe the following long-term effects of sirukumab in subjects with RA who are refractory to DMARDs or anti-TNF* agents on:

- * Efficacy
- * Pharmacokinetics
- * Immunogenicity
- * Pharmacodynamics
- * Pharmacogenetics
- * PFS-AI Usability (as defined in separate substudy protocol)

Study design

Subjects will become eligible to participate in this LTE study when they have completed participation in studies CNTO136ARA3002 (104 weeks) or CNTO136ARA3003 (52 weeks). The purpose of this LTE study is to evaluate the safety, efficacy, and pharmacologic effects of sirukumab for a minimum duration of 1 additional year and a maximum total duration of approximately 5 years across the combined protocols (CNTO136ARA3002 (2 years) or CNTO136ARA3003 (1 year) + CNTO136ARA3004 (1 to 4 years) = maximum of 5 years treatment).

The SmartJect* Autoinjector (PFS-AI) is expected to be used by the majority of subjects in study CNTO136ARA3004. In the event PFS-AIs are unavailable at the time of a subject's enrollment in this protocol, sirukumab PFS-Ultrasafer (PFS-U), the same device used in the CNTO136ARA3002 and CNTO136ARA3003 studies, will be provided until such time as the PFS-AIs become available. Upon availability of PFS-AI trial supplies, subjects who are newly entering the CNTO136ARA3004 protocol will be trained on the operation of PFS-AI and perform self-administration of study agent using PFS-AI at the Week 2 study visit and return to the study site at Week 4 for self-administration with PFS-AI. In the event PFS-AIs are unavailable at the time of a subject's enrollment in this

protocol, training on the use of a PFS-AI will be provided at the next study visit when the PFS-AI is available.

During the Week 104 visit in CNTO136ARA3002 or the Week 52 visit in CNTO136ARA3003, subjects will sign the informed consent form (ICF) to enter study CNTO136ARA3004. As a result, the Week 104 visit in study CNTO136ARA3002 and the Week 52 visit in study CNTO136ARA3003 will correspond to the Week 0 visit in the CNTO136ARA3004 study.

After a minimum of 1 year treatment in CNTO136ARA3004 for subjects from study CNTO136ARA3002, or a minimum of 2 years of treatment in CNTO136ARA3004 for subjects from CNTO136ARA3003, and after sirukumab is approved for the treatment of RA in the subject's country of residence, the Sponsor may no longer offer study treatment in CNTO136ARA3004 for those specific subjects. At that point the subject will have the opportunity to discuss treatment options with their treating physician.

The maximum duration of participation in this study is 208 weeks, followed by approximately 16 weeks of safety and efficacy follow-up after the administration of the final study agent injection of sirukumab. The study will end with the last visit for the last subject participating in the study.

Study treatment will remain blinded in CNTO136ARA3004 until the following 3 conditions have been met: the Week 52 DBL occurs in study CNTO136ARA3002, the Week 24 DBL occurs in study CNTO136ARA3003, and the last AI usability substudy subject completes the Week 16 visit or terminates from the study. Thereafter treatment in study CNTO136ARA3004 becomes open-label, and placebo injections are discontinued in the SC sirukumab 50 mg treatment group.

Subject safety will be monitored and assessments will be done through the end of the study.

Only 1 DBL (at the end of the study) is planned. Additional data releases or locks may occur as needed.

An Independent Data Monitoring Committee (DMC) and Clinical Events Committee (CEC) will be commissioned for this study.

Intervention

The study medication (or placebo) is administered once per 2 weeks (1 ml) subcutaneously. Administration switches to once per 4 weeks (1 ml study medication) when study becomes open-label. Total period is maximal 208 weeks.

Study burden and risks

The risks, side effects and discomforts that have been reported from our

clinical studies with sirukumab. Also mentioned are side effects that have been reported with similar drugs, but not at this time with sirukumab.

Infections

Sirukumab is a drug that may change how the body fights infections. People given sirukumab as well as similar medicines have reported infections. Serious, possibly life-threatening infections that may require hospitalization have been reported.

Sirukumab may keep a subject from developing a fever when he/she has an infection and therefore, may hide a sign that he/she has one. The subject may have more infections while taking this medication. Signs of an infection may include:

- * fever
- * headache
- * cough
- * congestion
- * chills
- * change in urine frequency or burning feeling while passing urine
- * redness or swelling of the skin or a joint
- * night sweats

Blood

Sirukumab may lower the number of blood cells that help the body fight infection and stop bleeding. Sirukumab may increase certain types of cholesterol and may affect the liver.

The study doctor will monitor with blood tests for any abnormal results related to the following:

- * blood cells (help the body fight infection and stop bleeding)
- * liver tests
- * different type of cholesterol and triglycerides

Injection Site Reactions * specific for subcutaneous injections

Sirukumab will be given as an injection under the skin. After the injection, temporary and common reactions seen at the injection site could include:

- * redness
- * pain
- * itching
- * swelling

Allergic Reactions

Allergic reactions can happen from the study medication. Some may be severe. The following can be signs of an allergic reaction:

- * chills
- * rash or hives
- * nausea

- * flushing
- * light-headedness
- * irregular heartbeats
- * chest tightness or wheezing
- * difficulty breathing or swallowing
- * low blood pressure
- * swelling in face, lips, tongue and/or throat

Serious allergic reactions called anaphylaxis have been reported with sirukumab. These can be life threatening.

Vaccines

It is unknown at this time what effect sirukumab may have on vaccines. During this study or for 4 months after the last dose of study drug **live** vaccines such as FluMist®, Varicella, BCG may not be administered. Other kinds of vaccines, like tetanus and flu shots are allowed.

Antibodies to Sirukumab

Sometimes the body can make special antibodies that may increase the risk of an allergic reaction to either sirukumab or other antibody medicines. If the subject has an allergic reaction, he/she may not be able to have these types of medications in the future.

Additional Known Risks from a similar drug

In people taking a similar drug the following have been reported: gastrointestinal perforations (tears in the stomach or intestines) and a certain type of nervous system disorder which may include symptoms such as changes in vision, weakness, numbness or tingling. Medications like this lower the activity of the immune system, so there may be an increased risk of some types of cancers if the immune system cannot stop them.

Other Risks

There may be other discomforts or risks to subject from this study that are not yet known.

Risk of Procedures

The subject may experience discomfort when a needle is inserted into the vein to collect blood. There may be a

- * slight bruise
- * discoloration
- * swelling
- * scarring at the puncture site
- * fainting

Over the course of the entire study 325 ml blood will be collected from the subject.

Risks from use of the SmartJect Autoinjector (PFS-AI) device

In case of malfunction or improper use, the potential harms from the use of an autoinjector are as follows: unknown quantity or quality of drug delivered, drug contacts skin, drug swallowed, drug contacts eye, drug delivered too shallow, drug delivered too deep, needle hits bone, needle stick injury, pain, skin irritation, cuts, needle breaks, bruising, and air bubble under the skin.

Contacts

Public

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Scientific

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

1. Have completed the final study agent administrations in the primary study (Week 104 injection in CNTO136ARA3002 or Week 52 injection in CNTO136ARA3003) including all other assessments required for these visits. The subject will then be deemed to have completed participation in those studies and will be eligible to enroll in this long-term extension study.;2.

Sign an informed consent form (ICF) indicating that they understand the purpose of and procedures required for the study and are willing to participate in the study.;3. Sign an informed consent form (ICF) for pharmacogenetics research in order to participate in the optional pharmacogenetics component of this study, where local regulations permit. Refusal to give consent for this component does not exclude a subject from participation in this clinical study.

Exclusion criteria

1. Withdraws consent and/or discontinues participation in study CNTO136ARA3002 or CNTO136ARA3003 ;2. Is pregnant ;3. Has active diverticulitis ;4. Has any condition that, in the opinion of the investigator, would make participation not be in the best interest (eg, compromise the well-being) of the participant or that could prevent, limit, or confound the protocol-specified assessments

Study design

Design

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

Recruitment

NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	03-07-2014
Enrollment:	7
Type:	Actual

Medical products/devices used

Product type:	Medicine
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Brand name: CNTO 136
Generic name: sirukumab (50 and 100 mg)

Ethics review

Approved WMO
Date: 28-12-2013
Application type: First submission
Review commission: METC Leiden-Den Haag-Delft (Leiden)
metc-ldd@lumc.nl

Approved WMO
Date: 18-04-2014
Application type: First submission
Review commission: METC Leiden-Den Haag-Delft (Leiden)
metc-ldd@lumc.nl

Approved WMO
Date: 22-07-2014
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 12-08-2014
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 19-12-2014
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 07-04-2015
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 29-05-2015
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 08-06-2015
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 22-07-2015
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 23-07-2015
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 26-01-2016
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 17-02-2016
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 24-01-2017
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 21-02-2017
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 13-07-2017
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 27-11-2017
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 13-12-2017
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 09-01-2018
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 29-01-2018
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 05-04-2018
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 09-04-2018
Application type: Amendment
Review commission: METC Leiden-Den Haag-Delft (Leiden)
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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

EudraCT

ClinicalTrials.gov

CCMO

ID

EUCTR2012-001176-10-NL

NCT01856309

NL47332.098.13