A randomized, double-blind, placebo-controlled, Phase III trial to evaluate the efficacy and safety of intra-articular injections of RTX-GRT7039 in adult subjects with pain associated with osteoarthritis of the knee

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Primary objective:Demonstrate the analgesic efficacy of intra-articular RTX-GRT7039 compared with placebo.Secondary objective:• Demonstrate the analgesic efficacy of intra-articular RTX-GRT7039 compared with placebo.• Demonstrate the efficacy of...

Ethical review	Approved WMO
Status	Completed
Health condition type	Tendon, ligament and cartilage disorders
Study type	Interventional

Summary

ID

NL-OMON51845

Source
ToetsingOnline

Brief title
Grunenthal KF7039-01 (RTX GRT7039); 0389/0073

Condition

- Tendon, ligament and cartilage disorders

Synonym
moderate to severe pain associated with osteoarthritis of the knee

Research involving
Human

Sponsors and support

Primary sponsor: Grunenthal
Source(s) of monetary or material Support: Grünenthal GmbH

Intervention

Keyword: Comparison of RTX-GRT7039 and placebo Intra-articular injections, Pain associated with osteoarthritis of the knee

Outcome measures

Primary outcome

Change from baseline in Western Ontario and McMaster Universities

Osteoarthritis Index (WOMAC) pain subscale score in the index knee to the score

at Week 12.

The WOMAC pain subscale, which consists of 5 questions, will be assessed and

reported in the electronic patient reported outcomes (ePRO) device once weekly

with a 48-hour recall, using an 11-point numeric rating scale (NRS, from 0 = no

pain to 10 = pain as bad as you can imagine).

Timeframe for the assessment: from baseline (assessment at V2) to V5 (Week

12/Day 84).

Estimand

The primary comparison of interest is the difference in mean change from

baseline in 48-hour WOMAC pain subscale score at Week 12 in the index knee

using an 11-point (0-10) NRS between RTX-GRT7039 and placebo, in subjects who

initiate treatment, as if substantial changes in background medication or

addition of new analgesics were not available.

Secondary outcome

See protocol section 1.2

Study description

Background summary

Osteoarthritis is the most common chronic joint disease affecting millions of people worldwide and a leading cause of pain and disability. Despite the available analgesic medications, not all patients with osteoarthritis, particularly those with advanced degenerative disease, achieve adequate pain relief with currently available treatment options.

Grünenthal is developing RTX GRT7039 for intra-articular injection of the novel analgesic RTX for the treatment of pain associated with osteoarthritis of the knee.

The purpose of this Phase III trial is to confirm the efficacy and safety of RTX GRT7039, administered as repeated intra-articular injections (i.e., second injection at 26 weeks) of 400 ng RTX GRT7039 in subjects with moderate to severe pain associated with osteoarthritis of the knee despite receiving continued treatment with optimal SoC or who are unable to receive SoC treatment due to contraindications or intolerability.

This pivotal trial is intended to be an integral part of the overall efficacy and safety assessment of RTX GRT7039 and will be used to support a marketing authorization application.

Study objective

Primary objective:

Demonstrate the analgesic efficacy of intra-articular RTX-GRT7039 compared with placebo.

Secondary objective:

• Demonstrate the analgesic efficacy of intra-articular RTX-GRT7039 compared with placebo.
• Demonstrate the efficacy of intra-articular RTX-GRT7039 on function compared with placebo.
• To assess the safety and tolerability of intra-articular RTX-GRT7039.

Study design

This is an interventional, Phase III, double-blind, randomized, placebo-controlled, parallel-group, multi-site, clinical trial to confirm the efficacy and safety of repeated intra-articular injections of RTX-GRT7039 versus placebo in subjects who have moderate to severe pain associated with osteoarthritis of the knee despite receiving continued treatment with optimal standard of care (SoC) or who are unable to receive SoC treatment due to contraindications or intolerability.

Approximately 450 subjects will be randomized to receive either RTX-GRT7039 or placebo in a 1:1 ratio. In addition to continued SoC treatment, subjects will receive 1 of the following treatments:

• Intra-articular RTX-GRT7039 400 ng injections.
• Placebo to match intra-articular RTX-GRT7039 injections.

Subjects will receive IMP into the index knee as identified by inclusion and exclusion criteria in Section 1.3 of the protocol. Subjects will receive IMP in 1 knee only.

This trial comprises a Screening Period and a double-blind Treatment and Follow-up Period (including a Final Visit of the Treatment and Follow-up Period at Week 52). Each subject is expected to be in the trial for up to 56 weeks (i.e., the Screening Period of up to 30 days followed by the 52-week Treatment and Follow-up Period).

Subjects will each receive 2 injections of investigational medicinal product (IMP) during the double-blind Treatment Period (on Day 1 and at Week 26). For the second injection, subjects will receive the same IMP that was administered at the first injection, in a double-blind manner.

Intervention

A total of 5 mL of IMP will be injected 15 minutes after ropivacaine administration into the knee joint. Fifteen minutes prior to the intra-articular injection of IMP, a 5 mL intra-articular injection of ropivacaine 0.5% will be administered.

The IMP must be administered by a qualified physician experienced in the

administration of intra articular injection.

It is strongly recommended that the injection is assisted by ultrasound. If ultrasound is unavailable, aspiration of synovial fluid is strongly recommended. Once completed, the needle and syringe will be removed, and an adhesive bandage applied.Once completed, the needle and syringe will be removed, and an adhesive bandage applied.

The first IMP injection will occur at the Randomization Visit (V2/Day 1) and a second injection of IMP will be administered at 6 months (V6/Week 26). Re-injection is not allowed if the subject did not tolerate previous IMP injection as judged by the investigator or if they developed hypersensitivity to the IMP.

Study burden and risks

Potential benefits to subjects participating in this trial may include a reduction in knee pain as well as the benefits of medical supervision from being in a clinical trial. Risks to subjects participating in this trial are primarily related to the currently known side effects of RTX as well as the administration of local anesthetic (Las). In addition to drug-specific risks, there are also the risks of the procedures used in the trial.

Given the observed reductions in knee pain, and improvements in WOMAC subscale scores, it is anticipated that RTX-GRT7039 will be efficacious in the proposed trial population outlined in this protocol: subjects who still have moderate to severe pain associated with osteoarthritis of the knee despite receiving continued treatment with optimal SoC treatment or who are unable to receive SoC treatment due to contraindications or intolerability, an indication for which there is currently an unmet medical need.

Across the 3 clinical trials, there was no treatment-emergent adverse events (TEAE) related to RTX-GRT7039 resolving with sequalae, of life-threatening intensity or leading to hospitalization or death.

For more details refer to the protocol section 8.2

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• >= 18 years of age at the screening visit.
• Body Mass Index (BMI) <= 40.0 kg/m2.
• Diagnosis of osteoarthritis of the knee based on American College of Rheumatology criteria and functional capacity class of I-III.
• Moderate to severe osteoarthritis at baseline.
• Documented history indicating that subject has insufficient pain relief with optimal standard of care (SoC).
• The investigator does not consider that any additional benefit can reasonably be expected from further adjustments to the patient's pain treatment.

For the list of complete inclusion criteria refer to the protocol.

Exclusion criteria

• The subject had an intra-articular injection of either corticosteroid or intra-articular visco-supplementation (i.e., hyaluronic acid) into the index knee within 3 months.
• The subject had an injection of platelet-rich plasma into the index knee within 6 months.

• The subject applied topical capsaicin on the index knee within 3 months.
• Pre-existing rapidly progressing osteoarthritis (RPOA) Type I or Type II, osteonecrosis, subchondral insufficiency fracture, atrophic osteoarthritis, or the subject has knee pain attributable to disease other than osteoarthritis.
• Other conditions that could confound discrimination of pain assessment in the index knee.
• Clinically significant disease(s) or condition(s) that may affect efficacy or safety assessments, or any other reason which, in the investigator's opinion, may preclude the subject's participation in the full duration of the trial.
• History of severe allergic or anaphylactic reactions.
• History of significant trauma or surgery, or surgery planned during the trial period, related to the knee.

For the complete list of exclusion criteria refer to the protocol.

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):	28-02-2023
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	RTX-GRT1076857

Generic name:	resiniferatoxin

Ethics review

Approved WMO Date:	21-04-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-06-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-03-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-03-2023
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-06-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-10-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2021-005029-26-NL
ClinicalTrials.gov	NCT05248386
CCMO	NL80659.056.22