Clinical trial results:
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

Summary

EudraCT number	2021-005029-26
Trial protocol	DE FR NL CZ IT PL
Global end of trial date	18 November 2024

Results information

Result version number	v1 (current)
This version publication date	03 July 2025
First version publication date	03 July 2025

Trial information

Trial identification

Sponsor protocol code	KF7039-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05248386
WHO universal trial number (UTN)	U1111-1268-7314

Notes:

Sponsors

Sponsor organisation name	Grünenthal GmbH
Sponsor organisation address	Zieglerstr. 6, Aachen, Germany, 52099
Public contact	Grünenthal Trial Information Desk, Grünenthal GmbH, Clinical-Trials@grunenthal.com
Scientific contact	Grünenthal Trial Information Desk, Grünenthal GmbH, Clinical-Trials@grunenthal.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 November 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 November 2024
Global end of trial reached?	Yes
Global end of trial date	18 November 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

The trial was conducted according to Good Clinical Practice guidelines, the ethical principles that have their origin in the Declaration of Helsinki, and the applicable local laws and regulations. The applicable regulatory authorities approved the trial as required by national regulations, and the trial activities were only started when approval from the relevant independent ethics committee was available.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 August 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 35
Country: Number of subjects enrolled	Japan: 93
Country: Number of subjects enrolled	Mexico: 27
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Poland: 217
Country: Number of subjects enrolled	Czechia: 47
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	Germany: 32
Country: Number of subjects enrolled	Italy: 2
Worldwide total number of subjects	469
EEA total number of subjects	314

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	179
From 65 to 84 years	283
85 years and over	7

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 9 countries (including Canada, Czech Republic, France, Germany, Italy, Japan, Mexico, Netherlands, and Poland) between 26 Aug 2022 (first-subject-in) and 18 Nov 2024 (last-subject-out).

Pre-assignment

Screening details:

A total of 902 subjects were screened in the study, of which 469 subjects were enrolled in the study (Randomized Set – all subjects who were randomized, based on treatment as randomized).

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	RTX-GRT7039

Arm description:

Intra-articular RTX-GRT7039 400 ng injections. Full Analysis Set: 234 RTX-GRT7039; Safety Analysis Set: 234 RTX-GRT7039.

Arm type	Experimental
Investigational medicinal product name	RTX-GRT7039
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

Fifteen minutes following intra-articular injection of 5 mL ropivacaine 0.5% as local anesthetic, 5 mL (400 ng) RTX-GRT7039 were injected into the joint of the index knee.

Arm title	Placebo

Arm description:

Intra-articular injections of matching placebo. Full Analysis Set: 232 placebo; Safety Analysis Set: 232 placebo.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

Fifteen minutes following intra articular injection of 5 mL ropivacaine 0.5% as local anesthetic, 5 mL of matching placebo were injected into the joint of the index knee.

Number of subjects in period 1[1]	RTX-GRT7039	Placebo
Started	234	232
Completed	202	204
Not completed	32	28
technical problems	-	1
Consent withdrawn by subject	15	10
Physician decision	-	1
Adverse event, non-fatal	2	4
Not specified	1	-
Lack of efficacy	14	12

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Reporting groups (Full Analysis Set and Safety Analysis Set) corresponds to all subjects with an Investigational medicinal product (IMP) administration (including incomplete administrations), based on actual treatment received. In Placebo Arm, three (3) subjects were randomized but not exposed to IMP.

Baseline characteristics

Reporting groups	
Reporting group title	Overall study (overall period)

Reporting group description:

Reporting group values	Overall study (overall period)	Total	
Number of subjects	466	466	
Age categorical Units: Subjects			
18 - 35	0	0	
36 - 64	178	178	
>=65	288	288	
Age continuous Units: years			
median	67.0		
full range (min-max)	41 to 94	-	
Gender categorical Units: Subjects			
Female	337	337	
Male	129	129	

End points

End points reporting groups

Reporting group title	RTX-GRT7039
Reporting group description:	
Intra-articular RTX-GRT7039 400 ng injections. Full Analysis Set: 234 RTX-GRT7039; Safety Analysis Set: 234 RTX-GRT7039.	

Reporting group title	Placebo
Reporting group description:	
Intra-articular injections of matching placebo. Full Analysis Set: 232 placebo; Safety Analysis Set: 232 placebo.	

Primary: LS-mean (SE) change from baseline in WOMAC pain subscale score at Week 12

End point title	LS-mean (SE) change from baseline in WOMAC pain subscale score at Week 12
End point description:	
Difference in mean change from baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale score at Week 12 in the index knee using an 11-point (0-10) numeric rating scale (NRS) between RTX-GRT7039 and placebo.	
End point type	Primary
End point timeframe:	
At week 12	

End point values	RTX-GRT7039	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	232		
Units: LS-mean (SE) change				
least squares mean (standard error)	-2.959 (± 0.15)	-2.847 (± 0.15)		

Statistical analyses

Statistical analysis title	Mixed model repeated measures (MMRM) analysis
Comparison groups	Placebo v RTX-GRT7039
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.569
Method	MMRM

Secondary: LS-mean (SE) change from baseline in WOMAC pain subscale score at Week 26

End point title	LS-mean (SE) change from baseline in WOMAC pain subscale score at Week 26

End point description:

Difference in mean change from baseline in WOMAC pain subscale score at Week 26 in the index knee using an 11-point (0-10) numeric rating scale (NRS) between RTX-GRT7039 and placebo.

End point type	Secondary

End point timeframe:

At Week 26

End point values	RTX-GRT7039	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	232		
Units: LS-mean (SE) change				
least squares mean (standard error)	-2.564 (± 0.15)	-2.597 (± 0.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: LS-mean (SE) change from baseline in WOMAC pain subscale score at Week 52

End point title	LS-mean (SE) change from baseline in WOMAC pain subscale score at Week 52

End point description:

Difference in mean change from baseline in WOMAC pain subscale score at Week 52 in the index knee using an 11-point (0-10) numeric rating scale (NRS) between RTX-GRT7039 and placebo.

End point type	Secondary

End point timeframe:

At week 52

End point values	RTX-GRT7039	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	232		
Units: LS-mean (SE) change				
least squares mean (standard error)	-2.686 (± 0.18)	-2.823 (± 0.18)		

Statistical analyses

No statistical analyses for this end point

Secondary: LS-mean (SE) change from baseline in WOMAC physical function subscale score at Week 12

End point title	LS-mean (SE) change from baseline in WOMAC physical function subscale score at Week 12

End point description:

Difference in mean change from baseline in WOMAC physical function subscale score at Week 12 in the index knee using an 11-point (0-10) numeric rating scale (NRS) between RTX-GRT7039 and placebo.

End point type	Secondary

End point timeframe:

At week 12

End point values	RTX-GRT7039	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	232		
Units: LS-mean (SE) change				
least squares mean (standard error)	-2.802 (± 0.14)	-2.740 (± 0.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: LS-mean (SE) change from baseline in WOMAC physical function subscale score at Week 26

End point title	LS-mean (SE) change from baseline in WOMAC physical function subscale score at Week 26

End point description:

Difference in mean change from baseline in WOMAC physical function subscale score at Week 26 in the index knee using an 11-point (0-10) numeric rating scale (NRS) between RTX-GRT7039 and placebo

End point type	Secondary

End point timeframe:

At week 26

End point values	RTX-GRT7039	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	232		
Units: LS-mean (SE) change				
least squares mean (standard error)	-2.503 (± 0.14)	-2.552 (± 0.15)		

Statistical analyses

No statistical analyses for this end point

Secondary: LS-mean (SE) change from baseline in WOMAC physical function subscale score at Week 52

End point title	LS-mean (SE) change from baseline in WOMAC physical function subscale score at Week 52

End point description:

Difference in mean change from baseline in WOMAC physical function subscale score at Week 52 in the index knee using an 11-point (0-10) numeric rating scale (NRS) between RTX-GRT7039 and placebo

End point type	Secondary

End point timeframe:

At Week 52

End point values	RTX-GRT7039	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	232		
Units: LS-mean (SE) change				
least squares mean (standard error)	-2.664 (± 0.16)	-2.728 (± 0.16)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were documented from the time of enrollment (i.e., the time the informed consent form is signed) up to the time of the last protocol scheduled contact.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	RTX-GRT7039

Reporting group description:

Intra-articular RTX-GRT7039 400 ng injections.
Full Analysis Set: 234 RTX-GRT7039
Safety Analysis Set: 234 RTX-GRT7039

Reporting group title	Placebo

Reporting group description:

Intra-articular injections of matching placebo. Full Analysis Set: 232 placebo; Safety Analysis Set: 232 placebo.

Serious adverse events	RTX-GRT7039	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 234 (7.26%)	14 / 232 (6.03%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 234 (0.43%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	1 / 234 (0.43%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoma			
subjects affected / exposed	0 / 234 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural			

complications			
Femoral neck fracture			
subjects affected / exposed	0 / 234 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 234 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 234 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	0 / 234 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 234 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	1 / 234 (0.43%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	0 / 234 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 234 (0.85%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 234 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 234 (0.43%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 234 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	1 / 234 (0.43%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Large intestine polyp			
subjects affected / exposed	1 / 234 (0.43%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varices oesophageal			
subjects affected / exposed	0 / 234 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Vaginal prolapse			
subjects affected / exposed	0 / 234 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			

subjects affected / exposed	1 / 234 (0.43%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin lesion			
subjects affected / exposed	1 / 234 (0.43%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	4 / 234 (1.71%)	3 / 232 (1.29%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	1 / 234 (0.43%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	2 / 234 (0.85%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondyloarthropathy			
subjects affected / exposed	1 / 234 (0.43%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 234 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 234 (0.43%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Intervertebral discitis			
subjects affected / exposed	0 / 234 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	RTX-GRT7039	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 234 (22.65%)	40 / 232 (17.24%)	
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	31 / 234 (13.25%)	9 / 232 (3.88%)	
occurrences (all)	40	9	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	13 / 234 (5.56%)	20 / 232 (8.62%)	
occurrences (all)	18	26	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	10 / 234 (4.27%)	12 / 232 (5.17%)	
occurrences (all)	11	14	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 July 2022	This global amendment incorporates changes that have been implemented as requested by the health authorities during their review of the clinical trial application, including update IMP administration, exclusion criteria, concomitant treatments, imputation methods, storage conditions, documentation requirements, contraception definitions, and editorial adjustments.
01 December 2022	This amendment incorporates changes that have been implemented in order to enhance trial feasibility and recruitment, including correction and clarifications on safety endpoints, eligibility criteria, no re-injection in case of pregnancy, addition of re-screening procedures, addition of important medical events definition, and editorial updates.
01 February 2023	This amendment incorporates an update on the qualification of the person administering IMP

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study failed to meet its primary endpoint and is not intended to contribute to the evaluation of product effectiveness.

Notes: