NOVARTIS

Clinical Development

LRX712

CLRX712A12201 / NCT04097379

A randomized, placebo-controlled, subject and investigatorblinded study investigating the safety, tolerability andpreliminary efficacy of 8-week treatment with intra-articular LRX712 to regenerate articular cartilage in patients with mild/moderate knee osteoarthritis

Statistical Analysis Plan (SAP)

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03-Mar-2022	Study Ongoing	Amendment based on protocol v04	Amendment v01	
12-Mar-2025	Study Ongoing	Amendment based on abbreviated/synoptic CSR format	Amendment v02	Section 1, 4.1.1, 8 and 10

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AE	Adverse event
BMI	Body Mass Index
CMO&PS	Chief Medical Office & Patient Safety
CSR	Clinical study report
CTC	Common Toxicity Criteria
CV	Coefficient of variation
ECG	Electrocardiogram
EDC	Electronic Data Capture
i.a.	Intraarticular
i.v.	Intravenous
CCI	[redacted]
LLN	Lower limit of normal
LLOQ	Lower limit of quantification
MedDRA	Medical dictionary for regulatory activities
mg	Milligram(s)
mL	Milliliter(s)
CCI	[redacted]
MRI	Magnetic Resonance Imaging
OA	Osteoarthritis
PD	Pharmacodynamic(s)
PK	Pharmacokinetic(s)
CCI	[redacted]
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SD	Standard deviation
ULN	Upper limit of normal
ULQ	Upper limit of quantification
WHO	World Health Organization
WPI	Widespread Pain Index

1 Introduction

Note: Data from the three participants who completed dosing with 75 mg will be included in all safety analyses. CCI [redacted].
Data from the three participants who completed dosing with the corresponding placebo will be pooled with the data from subjects enrolled after the implementation of protocol amendment 4.

1.1 Study design

This is an exploratory study, with approximately 7 weeks screening, 8 weeks treatment and 44 weeks followup periods, using a 3-treatment arms, parallel-group, randomized, double-blind, placebo-controlled clinical study design (Figure 1-1). Up to 45 patients will be randomized in the study, to ensure that at least 39 patients will complete the Week 28 assessments, assuming a 13% drop out rate until this time point. Additional participants may be enrolled if the dropout rate will exceed 13%.

Some of the key study assessments are knee X-ray, 7T MRI, triplicate 12-lead digitized ECGs, PK blood and synovial fluid collection, CCI [redacted] Please see Table 8-1 in the Protocol for further information.

The study consists of 3 periods:

Screening (Day -45 to Day -6)

Informed consent will be obtained prior to undertaking any study specific procedures. The Screening epoch begins at Day -45 and ends with randomization between Day -5 and Day -1. All entry criteria must be fulfilled before randomization (and latest on Day -6). In the case where a safety laboratory assessment at screening is outside of the range specified in the exclusion criteria, the assessment may be repeated once prior to randomization. If the repeat value remains outside of the specified ranges, the participant must be excluded from the study.

Due to the extensive preparation of the study medication, the randomization may be performed days before study drug administration on Day 1 (Day -1 to Day -5), once eligibility is confirmed and as near to Day 1 as possible. Eligible participants will be randomized in a 1:1:1 ratio to either i.a. LRX712 15 mg, LRX712 25 mg or placebo. Please see the SOM for further details on screening assessments.

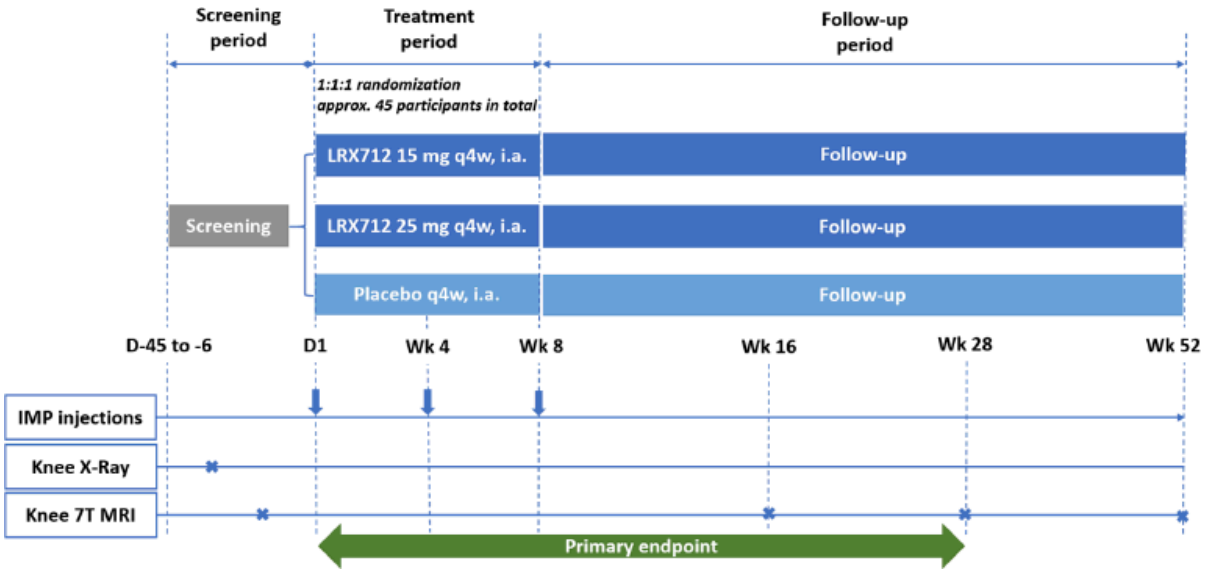
Treatment (8 weeks)

First dose of investigational treatment will be administered on Day 1. Each participant will receive 3 i.a. doses, one every 4 weeks. The third and last dose will be administered at the Week 8 visit, which will thus correspond to the End of Treatment (EoT) visit.

Post treatment Follow-up (44 weeks)

After completing the EoT visit, participants will enter a post-treatment follow-up period consisting of five visits at Week 8 + 1 day, Week 9, 16, 28 and 52 the latter being the End of Study visit. Following their study participation, participants will be further followed by their treating physician, if required, according to the local standard of care.

Figure 1-1 Study Design



1.2 Study reference documentation

Final study protocol (v04) is available at the time of finalization of Statistical Analysis Plan.

1.3 Study objectives and endpoints

Objective(s)	Endpoint(s)
Primary objective(s)	**Endpoint(s) for primary objective(s)**
• To assess the efficacy of q4w x 3 i.a. injections of LRX712 in restoring the morphometrics of articular cartilage in medial femoral condyle	• Change in medial femoral condyle cartilage volume in the index region measured by 7T MRI from baseline to week 28 in LRX712 vs. placebo – treated subjects
Secondary objective(s)	**Endpoint(s) for secondary objective(s)**
• To evaluate LRX712 and metabolite MAE344 pharmacokinetics in plasma and synovial fluid.	• PK parameters in plasma: Tmax, Cmax, Cmin in plasma (as per time-points defined in PK blood collection (see Protocol,Table 8-2). Synovial fluid: concentration at Day 1, Week 4, Week 8.

• To assess safety and local tolerability of multiple i.a. injections of LRX712.	• Vital signs (blood pressure, heart rate, temperature) as per assessment schedule. • Hematology, blood chemistry and urinalysis as per assessment schedule. • Local and Systemic Adverse Events. • ECG parameters (PR, QRS, heart rate, RR, QT, QTc) as per assessment schedule.
• To assess the efficacy of q4w x 3 i.a. injections of LRX712 in regenerating the articular hyaline cartilage in the medial femoral condyle.	• Change in articular cartilage [^{23}Na] content measured by 7T MRI from baseline to weeks 16, 28, and 52 in LRX712 vs. placebo-treated subjects
• To assess the efficacy of q4w x 3 i.a. injections of LRX712 in restoring the morphometrics of articular cartilage in the medial femoral condyle	• Change in medial femoral condyle cartilage morphometrics (volume and thickness) measured by 7T MRI from baseline to weeks 16, and 52 in LRX712 vs. placebo –treated subjects
Exploratory objective(s)	**Endpoint(s) for exploratory objective(s)**
CCI	


CCI

CCI

1.4 Primary estimand(s)

The primary clinical question of interest is: What is the effect of LRX712 treatment versus placebo on change from baseline at Week 28 in the medial femoral condyle cartilage volume in the index region in patients with mild/moderate knee OA?

The justification for the primary estimand is that it will capture the effect of the study drug under the research conditions versus placebo within the context of the protocol-specified guidelines for use of additional basic pain medication, and the use of rescue medications.

The primary estimand is described by the following attributes:

1. Population: participants suffering from symptomatic knee OA. Further details about the population are provided in Section 5 - Protocol.
2. Endpoint: efficacy is to be measured using the change from baseline to Week 28 of the double-blind study period in the medial femoral condyle cartilage volume in the index region.
3. Treatment of interest: the randomized treatments (the investigational treatment LRX712 or the control treatment) plus, if needed, intake of the allowed basic pain medication and the use of rescue medication. Further details about the investigational treatment and control treatment are provided in Section 6 - Protocol.
4. Identification of possible Intercurrent Events (ICEs):
   - At least one dose administration missed.

   These ICEs will be handled according to a hypothetical strategy, as if the ICE had not occurred (see Section 4.1.3 for details).
5. Summary measure: the difference between treatments in the mean changes from baseline to Week 28 of the double-blind study period in the medial femoral condyle cartilage volume in the index region .

1.5 First interpretable results (FIR)

First interpretable results (FIR) will be provided for this trial.

Study outputs required to be created at the time of the FIR will be highlighted in the TFL shells document and marked as “Key” in the Programming Deliverables Tracker (PDT) output list.

FIR will focus on the following analyses:

- Analysis populations (if needed)
- Participant disposition
- Demographics and baseline characteristics.
- Safety results:

    - Number and percentage of participants with adverse events by body system and preferred term with a breakdown by treatment.
- Pharmacokinetic results.
- Pharmacodynamic analyses.

2 Interim analysis

No formal interim analysis (IA) is planned for this study. However, IA for exploratory and program-wide purposes may be performed at the sponsor's discretion.

3 Statistical methods

3.1 Data analysis general information

The final analysis will be conducted on all subjects' data at the time that all subjects have the primary endpoint. Additional interim analyses may be conducted to support decision making concerning the current clinical study, the sponsor's clinical development projects in general, or in case of any safety concerns.

The analysis will be performed in-house by Novartis, and will be carried out using SAS software, version 9.4 or higher.

Any data analysis carried out independently by the investigator should be submitted to Novartis before publication or presentation.

3.2 General definitions

The term study drug or investigational treatment refers to LRX712 or Placebo, while the term investigational drug refers exclusively to LRX712.

Date of first administration of investigational drug

The date of last administration of investigational drug is defined as the last date when a nonzero dose of investigational drug is administered and recorded on dose administration (e)CRF. The date of last administration of investigational drug will also be referred as end of investigational drug or end of investigational treatment.

Study day

Study day 1 for all assessments is taken to be the start of investigational treatment.

The study day for all assessments will be calculated as follows:

1. If date of assessment occurred on or after the start of investigational treatment, then Study day = Date of assessment - Start of investigational treatment + 1.
2. If date of assessment occurred before the start of investigational treatment, then Study day = Date of assessment - Start of investigational treatment.

The study day will be displayed in the data listings. If an event starts before the reference start date, the study day displayed on the listing will be negative.

Baseline

For safety evaluations, the last available assessment on or before the date of start of investigational treatment is taken as "baseline" assessment. In case time of assessment and time of treatment start is captured, the last available assessment before the treatment start date/time is used for baseline.

For safety parameters (e.g. ECGs), where the study requires multiple replicates per time point, the average of these measurements would be calculated (if not already available in the database) before determining baseline.

In rare cases where multiple measurements meet the baseline definition, with no further flag or label that can identify the chronological order, then the following rule should be applied: If values are from central and local laboratories, the value from central assessment should be considered as baseline. If multiple values are from the same laboratory (local or central) or collected for ECGs or vital signs, then the last value should be considered as baseline.

If participants have no value as defined above, the baseline result will be missing.

For safety parameters other than ECG, scheduled pre-dose collections as well as unscheduled collections on Day 1 for which no time is available will be considered as pre-dose.

For ECG, study Day 1 scheduled pre-dose ECGs will be considered to have been obtained prior to start of investigational treatment if dosing time or ECG time is missing and used in the calculation of the baseline value. If a scheduled pre-dose measurement actually occurred post- dose, then the corresponding measurement will be treated and analyzed similar to an unscheduled post-dose measurement.

Regarding MRI, baseline is defined as the scan performed between Day -45 to -2.

On-treatment assessment/event

The overall observation period will be divided into three mutually exclusive segments:

1. ***pre-treatment period***: from day of participant's informed consent to before date of first administration of investigational treatment
2. ***on-treatment period***: from date of first administration of investigational treatment to *28* days after date of last administration of investigational treatment (including start and stop date)
3. ***post-treatment period***: starting at day 29 after last administration of investigational treatment.

Note: If dates are incomplete in a way that clear assignment to pre-, on-, post-treatment period cannot be made, then the respective data will be assigned to the on-treatment period.

Safety summaries (tables, figures) include only data from the on-treatment period with the exception of baseline data which will also be summarized where appropriate (e.g. change from baseline summaries). In particular, summary tables for adverse events (AEs) will summarize only on-treatment events, with a start date during the on-treatment period (***treatment-emergent*** AEs).

However, all safety data (including those from the post-treatment period) will be listed and those collected during the post-treatment period will be flagged.

3.3 Analysis sets

For all analysis sets, participants will be analyzed according to the study treatment(s) initially received.

The safety analysis set will include all participants that received any study drug (including the participants who received the 75 mg).

The PK analysis set will include all participants with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and with no protocol deviations that impact on PK data.

The PD analysis set will include all participants with available PD data and no protocol deviations with relevant impact on PD data.

The analysis sets and protocol deviation codes are related as follows:

Table 3-1 Protocol deviation codes and analysis sets

Category **Deviation code**	**Text description of deviation**	**Data exclusion**
Participants are excluded from PK analysis in case of these PDs: **INCL01:** Deviation from inclusion criterion 1 (Written informed consent must be obtained before any assessment is performed)		**Exclude participant from PK analysis set** Yes
Participants are excluded from PD analysis in case of these PDs: **INCL01:** Deviation from inclusion criterion 1 (Written informed consent must be obtained before any assessment is performed)		**Exclude participant from PD analysis set** Yes
Participants are excluded from all (safety) analysis in case of these PDs: **INCL01:** Deviation from inclusion criterion 1 (Written informed consent must be obtained before any assessment is performed)		**Exclude participant from all (safety) analysis sets.** Yes

If updates to this table are needed, an amendment to the SAP needs to be implemented prior to DBL.

3.4 Participant disposition, demographics and other baseline characteristics

3.4.1 Participant disposition

A summary disposition for all screened participants will be presented for each treatment. Screened participants include those who completed screening and were randomized, those who completed screening and were not randomized, and participants who did not complete the screening (with reasons for not completing screening).

Participant disposition data will be listed.

Screened participants not randomized will be listed.

3.4.2 Demographics and other baseline characteristics

All data for background and demographic variables will be listed by treatment and participant. Summary statistics will be provided by treatment for the Safety Analysis Set.

Categorical data will be presented as frequencies and percentages. For continuous data, mean, standard deviation, median, minimum, and maximum will be presented. For selected parameters, 25^{th} and 75^{th} percentile may be also presented.

Relevant medical history, current medical conditions, results of laboratory screens, drug tests and any other relevant information will be listed by treatment and participant.

3.5 Treatments (investigational treatment, rescue medication, concomitant therapies, compliance)

3.5.1 Investigational treatment / compliance

The Safety Analysis Set will be used for the analyses below.

Dose administration will be listed by treatment, date, and time. Prior, concomitant and post therapies, rescue and prohibited medications, as well as significant non-drug therapies prior to and after the start of the investigational treatment, will be listed and summarized using the WHO Anatomical Therapeutic Chemical (ATC) dictionary using the latest version available prior to clinical database lock, by preferred term, and treatment with a flag to differentiate those which started more than 29 days after the last investigational treatment.

4 Statistical methods for Pharmacodynamic (PD) parameters

All participants within the primary PD analysis set will be included in the PD data analysis, unless otherwise stated.

4.1 Primary objective

The primary objective of this study is to assess the efficacy of q4w x 3 i.a. injections of LRX712 in restoring the morphometrics of articular cartilage in the medial femoral condyle (MFC). To this end, a statistical analysis will be done to compare the change in medial femoral condyle cartilage volume in the index region measured by 7T MRI from baseline to week 28 in LRX712 vs. placebo –treated subjects.

Baseline refers to data collected at Screening for the imaging assessments (Day -45 to -2).

Medial femoral condyle is defined as sum of the International Cartilage Regeneration Society (ICRS) sub-regions MAC, MCC, and MPC. See Table 4-1.

Table 4-1 Regions/sub-regions based on the assessment method

Knee region	Cartilage region (ICRS)	Label (MRCHondralHealth)	Corresponding CCI region
Patellar sub-divided cartilage	LatSup	202	Lateral
	LatCent	203	
	LatInf	204	
	MedSup	206	Medial
	MedCent	207	
	MedInf	208	
Tibial sub-divided cartilage	MedAnt	222	Medial Anterior
	MedCent	224	Medial Central
	MedPost	226	Medial Posterior
	LatAnt	232	Lateral Anterior
	LatCent	234	Lateral Central
	LatPost	236	Lateral Posterior
Femoral sub-divided cartilage	MedAnt (MAC)	242	
	MedCent (MCC)	243	Medial Central
	MedPost (MPC)	244	Medial Posterior
	TrochLat (LT)	248	Lateral Trochlea
	TrochMed (MT)	249	Medial Trochlea
	TrochCent (CT)	250	
	LatAnt (LAC)	253	
	LatCent (LCC)	254	Lateral Central
	LatPost (LPC)	255	Lateral Posterior

4.1.1 Statistical model, assumptions and hypotheses

The primary efficacy variable, change from baseline in cartilage volume of the impacted compartment, will be analyzed using a mixed effect model for repeated measures (MMRM). The model will include baseline, treatment, time point, treatment by time points as fixed effects. An unstructured covariance will be assumed; if not possible, other appropriate covariance structures may be explored. Log-transformation of the dependent variable might be considered prior to the analysis.

Least squares means of the difference from baseline and the treatment difference will be reported together with coefficients of variation, two-sided 90% confidence intervals. Analysis of the primary endpoint will be done at Week 28 separately for the LRX712 15mg vs. Placebo and LRX712 25 mg vs. Placebo. No adjustment for multiplicity will be considered.

Three participants who completed dosing with 75 mg will be excluded from all model-based analyses.

4.1.2 Descriptive analyses

The change in cartilage volume will be listed by treatment, patient, and visit/time. Summary statistics will be provided by treatment and visit/time. Summary statistics will include mean (arithmetic), SD, median, minimum, maximum. Graphical methods (i.e., spaghetti plots and mean change from baseline, both in terms of % and absolute change from baseline) will be employed to show group and individual plots over time by treatment.

4.1.3 Handling of intercurrent events

All ICEs listed in Section 1.4 will be handled by a hypothetical strategy to estimate what the treatment effect would have been at Week 28 if all participants adhered to the initially randomized treatment through that time point. In the case of ICEs such as missing at least one dose administration the assessments collected post-ICE occurrence will not be evaluated for the purposes of the primary estimand. Although data post-ICEs are not required for the primary estimand, these assessments will be collected for estimation of secondary and/or supportive estimands.

Assessments collected post-ICE will be considered missing and implicitly imputed by the MMRM under the MAR assumption (i.e. assuming that participants with missing data would have efficacy outcomes like those of similar participants in their treatment who continue their randomized treatment). In case of an unexpectedly high number of discontinuations (in particular due to a similar reason) from the investigational treatment are observed, the assumptions underlying the strategy considered might be revised and modified as appropriate.

4.1.4 Handling of missing values/censoring/discontinuations

Some intermittently missing data may be expected due to participants occasionally missing a study visit while continuing with the randomized treatment. Such data will be implicitly imputed by the MMRM under the MAR assumption. Only participants with a baseline and at least one post-randomization measurement will be included in the primary analysis.

4.2 Secondary objectives

There are two secondary objective related to efficacy:

- To assess the efficacy of q4w x 3 i.a. injections of LRX712 in regenerating the articular hyaline cartilage composition in the medial femoral condyle
- To assess the efficacy of q4w x 3 i.a. injections of LRX712 in restoring the morphometrics of articular cartilage in the medial femoral condyle

Baseline is defined as scan performed between Day -45 to -2.

4.2.1 Statistical model, assumptions and hypotheses

Change in articular cartilage [^{23}Na] content from baseline to weeks 16, 28 and 52 in LRX712 vs. placebo-treated participants and change in the medial femoral condyle cartilage volume and thickness from baseline to week 16, 28 (thickness only) and 52 will also be determined using similar mixed effects model described in Section 4.1.1.

4.2.2 Descriptive analyses

The variables will be listed by treatment group, patient, and visit/time. Summary statistics will be provided by treatment group, and visit/time. Summary statistics will include mean (arithmetic), SD, median, minimum, maximum. Graphical methods will be employed to show group and individual plots over time by treatment.

4.2.3 Handling of intercurrent events

Same as for the primary analysis.

5 Safety analyses

All safety analyses will be based on the Safety set unless otherwise specified. Safety summaries include only on-treatment assessments (refer to Section 3.2); safety listings include all assessments with those more than 28 days after last investigational treatment flagged.

Safety assessments include AEs, laboratory data, vital signs, deaths and ECGs. All Section 16 safety listings are presented using the Safety Analysis Set, and Section 14 using Safety set unless otherwise specified. The Safety Analysis Set will be used for all safety summaries. Safety summaries include only on-treatment assessments (refer to Section 3.2), with a start date during the on-treatment period (treatment-emergent AEs).

For selected items, change from baseline summaries generated for laboratory values, ECG, vital signs may use data before start of investigational treatment for baseline calculations.

5.1 Adverse event (AEs)

All information obtained on adverse events will be displayed by treatment and participant.

The number (and percentage) of participants with treatment emergent adverse events (events started after the first dose of the study medication or events prior to start of the treatment but increased in severity based on the preferred term) will be summarized by treatment, primary system organ class and preferred term, and maximum severity.

Separate summaries will be provided for study medication related adverse events, death, serious adverse events, other significant adverse events leading to discontinuation.

A participant with multiple adverse events within a primary system organ class is only counted once towards the total of the primary system organ class.

If, for the same participant, several consecutive AEs (irrespective of start treatment causality, seriousness and severity) occurred with the same SOC and PT:

- A single occurrence will be counted if there is ≤ 1 day gap between the end date of the preceding AE and the start date of the consecutive AE.
- More than one occurrence will be counted if there is > 1 day gap between the end date of the preceding AE and the start date of the consecutive AE.

For occurrence, the presence of at least one SAE has to be checked in a block e.g. among AEs in a ≤ day gap block. If at least one SAE is occurring, then one occurrence is calculated for that SAE.

5.2 Deaths

All deaths will be listed using Safety Analysis Set and post-treatment deaths will be flagged. A separate listing of deaths prior to starting treatment will be provided for all screened participants.

5.3 Laboratory Data

All laboratory data will be listed by treatment, participant, and visit/time and if normal ranges are available abnormalities will be flagged. All laboratory data will be summarized by treatment, and visit/time. Shift tables using the low/normal/high/ (low and high) classification will be used to compare baseline to the worst on-treatment value.

5.4 Other Safety Data

5.4.1 ECG and cardiac imaging data

ECG data are summarized by treatment. The corresponding treatment for each ECG will be assigned as follows:

If ECG collection date/time is before dosing date/time on Day 1, no treatment will be assigned. While baseline does not have an assigned treatment, for the change from baseline summary tables, baseline will be summarized under each treatment to aid in the interpretation of the change from baseline summaries.

If ECG collection date/time is on or after dosing date/time on Day x but before the next dosing date/time (or before end of study if the next dosing date/time is not available) then treatment is the actual treatment received on Day x.

If ECG collection date/time is after the last dosing date/time + *30* days, no treatment will be assigned. If dosing time and/or ECG collection time is missing but the dates are the same, the ECG will be assigned to the actual treatment received on that day.

Data handling

When ECG triplicates are collected at any assessment, the average of the ECG parameters at that assessment will be used in the analyses.

Data analysis

12-lead ECGs including PR, QRS, QT, QTcF intervals and HR will be obtained for each participant during the study. ECG data will be read and interpreted.

The number and percentage of participants with notable ECG values will be presented.

- QT, QTcF
  - New value of > 450 and ≤ 480 ms
  - New value of > 480 and ≤ 500 ms
  - New value of > 500 ms
  - Increase from baseline of > 30 ms to ≤ 60 ms
  - Increase from baseline of > 60 ms
- HR
  - Increase from baseline >25% and to a value > 100 bpm
  - Decrease from baseline >25% and to a value < 50 bpm
- PR
  - Increase from baseline >25% and to a value > 200 ms
  - New value of > 200 ms
- QRS
  - Increase from baseline >25% and to a value > 110 ms
  - New values of QRS > 110 ms

A listing of all ECG assessments will be produced and notable values will be flagged.

ECG data will be summarized by presenting summary statistics of observed data and change from baseline by time point. The definition of baseline is provided in Section 3.2.

5.4.2 Vital signs

All vital signs data will be listed by treatment, participant, and visit, and if ranges available, abnormalities (and relevant orthostatic changes) will be flagged. Summary statistics will be provided by treatment and visit/time.

6 Pharmacokinetic endpoint(s)

LRX712 and MAE344 plasma as well as synovial concentration data will be listed by treatment, participant, and visit/sampling time point. Descriptive summary statistics will be provided by treatment and visit/sampling time point, including the frequency (n, %) of concentrations below the LLOQ and reported as zero. Samples collected outside the protocol defined time window will be listed but not included in the summary statistics.

Summary statistics will include mean (arithmetic and geometric), SD, CV (arithmetic and geometric), median, minimum, and maximum. Concentrations below LLOQ will be treated as zero in summary statistics and for plasma PK parameter calculations. Graphical summaries (including but not limited to, boxplots and mean plots with SD or geomean plots) may be provided by treatment and visit.

The following plasma pharmacokinetic parameters will be determined using the actual recorded sampling times and non-compartmental method(s) with Phoenix WinNonlin (Version 6.2 or higher): Cmax, Cmin and Tmax. PK values below the lower limit of quantification will be treated as "zero" in calculation of Cmax, Cmin and Tmax.

Plasma pharmacokinetic parameters will be listed by treatment and participant. Descriptive summary statistics will include mean (arithmetic and geometric), SD, and CV (arithmetic and geometric), median, minimum, and maximum. An exception to this is Tmax where median, minimum, and maximum will be presented.

All participants within the PK analysis set (PAS) will be included in the PK data analysis.

7 Sample size calculation

In the Proof of Concept (PoC) study CLNA043X2202 (EudraCT- number 2016-004052-30) a treatment different of 123 mm^3 change in medial femoral condyle cartilage morphometrics volume was observed at week 28 (Part A). Assuming a similar treatment effect and a standard deviation of 130 mm^3, 13 participants per arm will provide approximately 78% power to detect a statistically significant difference between LRX712 25 mg and placebo, or LRX712 15 mg and placebo at the two-sided 10% significance level. If necessary, sample size may be re-assessed at an interim analysis.

8 Change to protocol specified analyses

9 Reference

CCI

CCI [redacted]