AIC316-03-I-01

Summary of the Clinical Trial Protocol and Statistical Plan

A single-center, open-label, 2-period, fixed-sequence Phase 1 trial to evaluate the effect of esomeprazole on the pharmacokinetics of pritelivir

NCT number:	NCT05513625
Investigational drug:	Pritelivir
Sponsor:	AiCuris Anti-infective Cures AG
Address:	Friedrich-Ebert Str. 475 DE-42117 Wuppertal Germany
Finalization dates:	
Summary of the Clinical Trial Protocol and Statistical Plan, V1.0:	16Sep2022
Clinical Trial Protocol, V1.0:	04Jun2020
Safety Statistical Analysis Plan, V2.0:	21Jul2020
Pharmacokinetic Statistical Analysis Plan, V1.0:	01Jul2020

SUMMARY OF THE CLINICAL TRIAL PROTOCOL AND STATISTICAL PLAN

Name of Sponsor/Company:	AiCuris Anti-infective Cures GmbH
Title of the trial: A single-center, open-label, 2-period, fixed-sequence Phase 1 trial to evaluate the effect of esomeprazole on the pharmacokinetics of pritelivir	
Principal Investigator: Dr. Leela Vrishabhendra	
Trial center(s): Medpace Clinical Pharmacology 5355 Medpace Way, Cincinnati, Ohio 45227, USA	
Planned trial period: First Subject First Visit: Jul 2020 Last Subject Last Visit Sep 2020	Phase of development: Phase 1

Objectives:

- To investigate the effect of esomeprazole on the pharmacokinetics of pritelivir
- To investigate the pharmacokinetics of pritelivir metabolites AIC090015, AIC090105 and AIC090015-acylglucuronides
- To investigate the safety and tolerability of pritelivir

Trial design:

This will be a single-center, open-label, 2-period, fixed-sequence Phase 1 trial in 18 healthy adult male and female subjects (at least 7 subjects per sex). All subjects will receive treatment 1 (T1; single dose of 100 mg pritelivir will be administered on Day 1) in the first period, followed by treatment 2 (T2; single dose of 100 mg pritelivir will be administered on Day 1 and 40 mg esomeprazole will be administered qd from Day -3 to Day 1) in the second period. The wash-out period between pritelivir administrations in T1 and T2 is at least 4 weeks.

Number of subjects (planned):

18

Diagnosis and main criteria for inclusion:

Healthy adult male and female subjects (at least 7 subjects per sex) of any ethnic origin, aged 18 to 45 years inclusive.

Test product, dose and mode of administration:

Oral 100 mg pritelivir tablets

Oral 40 mg esomeprazole tablets (Nexium®)

Duration of treatment:

In Treatment Period 1:

Pritelivir: single dose of 100 mg on Day 1

In Treatment Period 2:

4 days

Esomeprazole: 40 mg qd from Day -3 to Day 1, inclusive

Pritelivir: single dose of 100 mg on Day 1

Reference therapy, dose and mode of administration, batch number(s):

Not applicable.

Criteria for evaluation:

Efficacy

Not applicable.

Pharmacokinetics

Primary variables:

- $AUC_{0-\infty}$, AUC_{0-last}, C_{max} of pritelivir in plasma

Secondary variables:

- t_{max}, t_{lag}, $t_{1/2z}$, CL/F, V_d /F, MRT of pritelivir in plasma
- $AUC_{0-\infty}$, AUC_{0-last}, C_{max}, t_{max}, t_{lag}, $t_{1/2z}$, MRT of metabolites AIC090015, AIC090105 and AIC090015-acyl glucuronides in plasma
- The ratio between each of the metabolites AIC090015, AIC090105 and AIC090015-acyl glucuronides versus pritelivir will be calculated for $AUC_{0-\infty}$, AUC_{0-last}

Pharmacokinetic profile will be determined in each period on Day 1 for 360 hours.

Pharmacogenomics/gene expression:

- Post-hoc analysis of alleles associated with altered drug metabolism/ disposition may be determined.

Safety

- Overall tolerability
- Nature, frequency, duration, severity and causality of adverse events
- Clinical laboratory parameters
- Vital signs (blood pressure, pulse rate)
- Standard 12-lead ECG

Statistical methods:

Pharmacokinetic data

The Pharmacokinetic Set (PKS) will include all subjects in the Safety Set (SS) with at least 1 plasma concentration time point for inclusion in the PK analysis. The PKS will be used for the PK analyses.

Descriptive statistics will be calculated for plasma concentrations of pritelivir and derived PK parameters. Statistics include sample size (n), mean, standard deviation (SD), %CV, geometric mean, median, minimum and maximum.

The relative bioavailability of pritelivir with respect to the primary variables $AUC_{0-\infty}$, AUC_{0-last} and C_{max} will be explored based on the log transformed data with an analysis of variance model with treatment (as fixed effect) and subject (as random effect). Point estimates (GMR) and 90% confidence intervals (90% CIs) will be computed for the ratio T2 (test) /T1 (reference) to evaluate the effect of esomeprazole on pritelivir PK under fasted conditions.

Safety data

Safety data analysis will be conducted on the Safety Set. Statistical analysis of the safety data will be limited to descriptive summaries.

The results of AE recording, vital signs, 12-lead ECGs, clinical laboratory investigations, and physical examinations will be listed by subject and analyzed by descriptive statistics as appropriate.

All adverse events will be coded according to the Medical Dictionary for Regulatory Activities (MedDRA). Incidences of treatment-emergent adverse events (TEAE) that began after the start of trial treatment (post-dose on Day 1 to End of trial examination) will be summarized at 3 levels: the overall subject level (occurrence of at least one TEAE), primary System Organ Class level, and preferred term level. All adverse events will be listed together with information on onset, duration, frequency, intensity, seriousness, relationship to IMP, outcome, and action taken.

Laboratory data will be presented in summary statistics of raw data and change from baseline values (mean, median, standard deviation, minimum, maximum), and by flagging values outside the reference range in data listings. Vital signs will be summarized presenting statistics of raw data and change from baseline values (mean, median, standard deviation, minimum and maximum).

ECG data will be summarized presenting statistics of raw data and change from baseline values (mean, median, standard deviation, minimum and maximum). In addition, 12-lead ECGs will be analyzed with a focus on the incidence and extent of QTc prolongation. QTc will be calculated according to Fridericia formula. Frequencies for classes of absolute values and differences from baseline will be provided according to the classifications defined by ICH-E14.

The World Health Organization Drug Dictionary (WHO-DD) will be used for coding of concomitant medications (except IMPs).