Otsuka Pharmaceutical Development & Commercialization, Inc.

Investigational New Drug

Tolvaptan (OPC-41061)

Protocol No. 156-12-298
IND No. 072975
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A Phase 3b, Two-part, Multicenter, One Year Randomized, Double-blind, Placebo-controlled Trial of the Safety, Pharmacokinetics, Tolerability, and Efficacy of Tolvaptan followed by a Two Year Open-label Extension in Children and Adolescent Subjects with Autosomal Dominant Polycystic Kidney Disease (ADPKD)

Statistical Analysis Plan

Version 1.0: 05 Feb 2020
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Amendment 2: 29 Jul 2020

Protocol 156-12-298

Table of Contents

Protocol 156-12-298

1 Introduction

This statistical analysis plan (SAP) documents the statistical methodology and data analysis algorithms and conventions to be applied for statistical analysis and reporting of efficacy, safety, and pharmacodynamic data of Trial 156-12-298. All amendments to the protocol are taken into consideration in developing this SAP.

2 Trial Objectives

The primary objective is to evaluate the long term safety effects of treatment with tolvaptan in a pediatric and adolescent Autosomal Dominant Polycystic Kidney Disease (ADPKD) population.

The secondary objective is to assess the pharmacodynamics (PD), pharmacokinetics (PK), and efficacy of tolvaptan in children and adolescent subjects with ADPKD.

3 Trial Design

3.1 Type/Design of Trial

The trial will comprise 2 phases as described below:

Phase A is a randomized, double-blind, placebo-controlled phase to compare tolvaptan with placebo. The duration of treatment is 12 months. It is open to subjects between the ages of 4 and 17 years, inclusive. Subjects between the ages of 12 and 17 years will be stratified by age and gender. When these stratified cohorts have been closed, enrollment for the trial will end (Figure 3.1-1). Additionally, subjects aged 4 to 11 years may be eligible for participation following discussion with the medical monitor.

Qualified subjects who complete Phase A may continue into Phase B. A qualified subject is defined as one who is willing to continue in the trial and who does not have any AEs that would require investigational medicinal product (IMP) discontinuation.

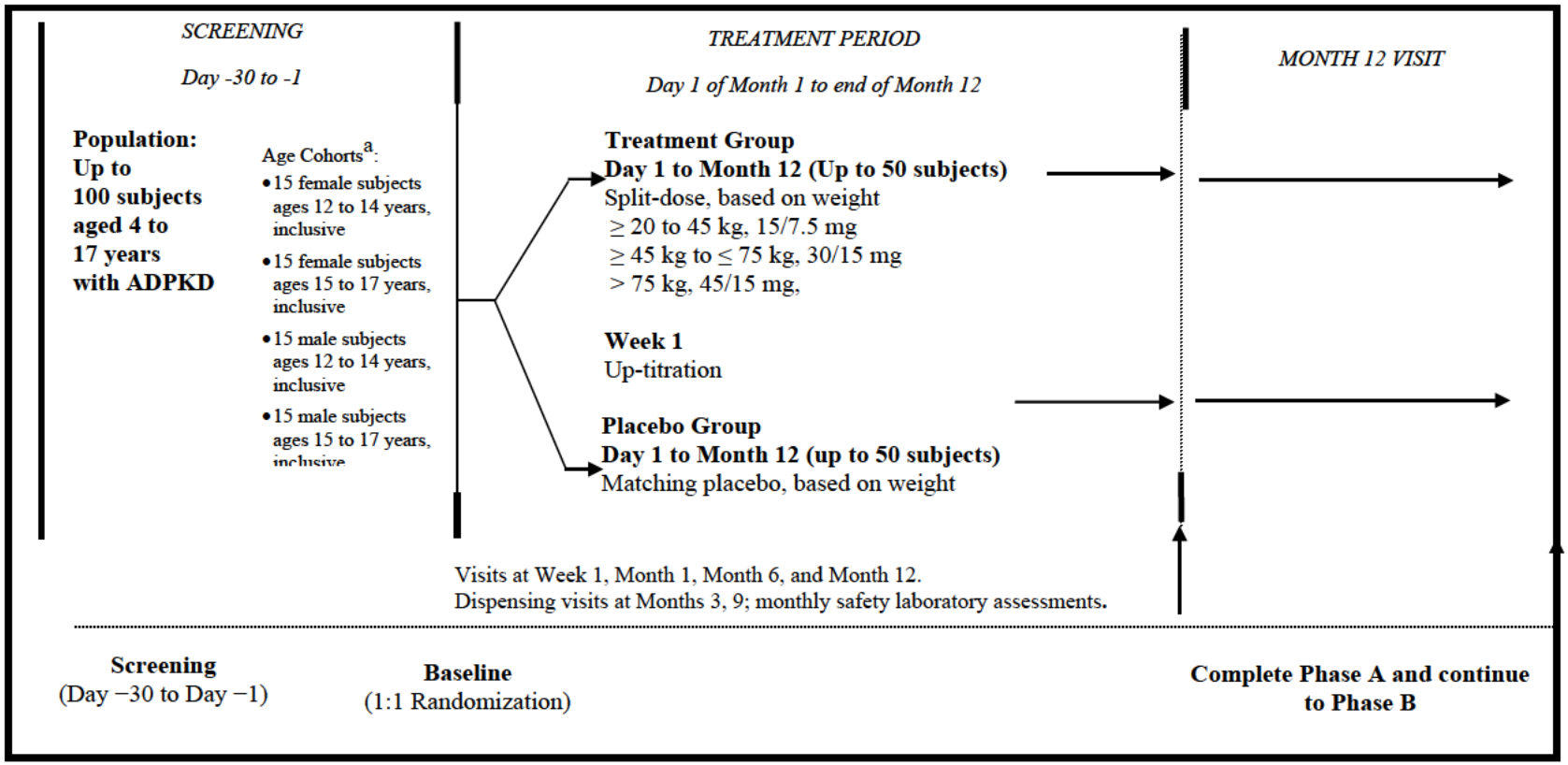
Phase B is an open-label phase during which subjects who have completed Phase A of the trial will receive treatment with tolvaptan for 24 months (Figure 3.1-2).

When all subjects in Phase A have either completed the Month 12 visit or early terminated from the trial, a snapshot of the data will be taken. At that time, the snapshot will be unblinded, and results analyzed and reported in an interim clinical study report

(CSR) to provide early information on safety. The protocol may be amended to further ensure continuing safety and tolerability measures are in place.

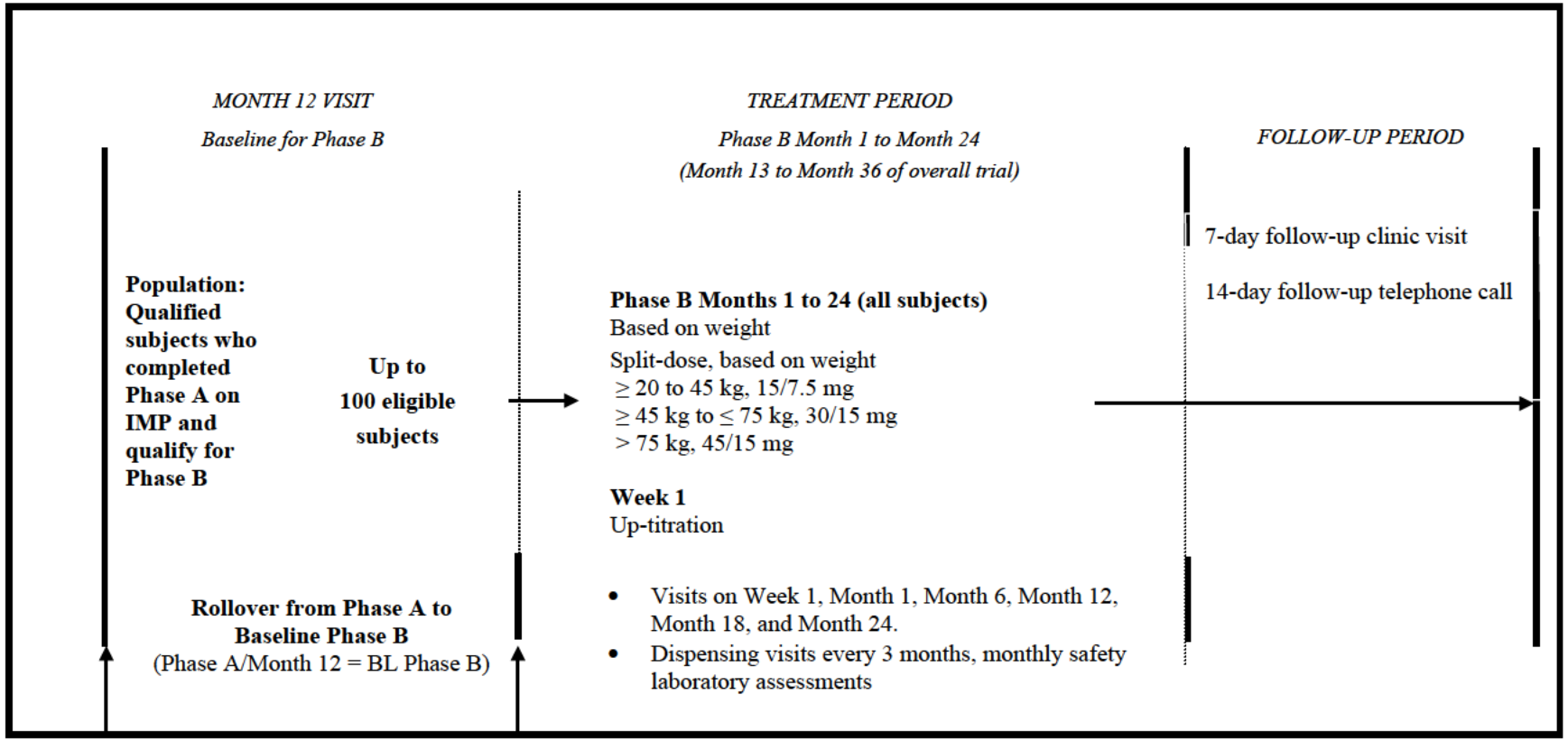
When all subjects in Phase B either complete the Month 24 visit, or the last ongoing subject terminates early, the database will be locked, and a final CSR will be provided to the regulatory authorities.

Figure 3.1-1 Trial Design Schematic Phase A, Randomized, Double-blind



[a]Subjects between the ages of 4 and 11 are eligible for the trial but are not included in the age cohorts.

Figure 3.1-2 Trial Design Schematic Phase B, Open-Label



3.2 Trial Treatments

Tolvaptan will be provided as 7.5, 15, and 30 mg spray-dried, immediate-release tablets with matching placebo. Tolvaptan will be administered as a split-dose, with the first dose taken upon awakening and the second dose taken approximately 8 hours later.

3.2.1 Treatment in Phase A

Subjects will be randomized to receive IMP defined as either active tolvaptan or matching placebo for 12 months. Starting doses will be based on weight as denoted below in Table 3.2.1-1.

After 1 week, subjects who have tolerated their initial dose will up-titrate once from their starting dose (Table 3.2.1-2). Subjects may down-titrate at any time during the trial, however subjects will be asked to stay on the highest tolerable dose (by weight group) if possible (Table 3.2.1-3).

It is recommended that each dose be administered with 240 mL of water, as part of the goal to maintain proper hydration status; the total 240 mL can be consumed over a 1-hour period following dosing. Water intake will be recorded for all in-clinic dosing.

Table 3.2.1-1 Starting Tolvaptan Dose

Body Weight	Time	Split-dose[a]
≥ 20 kg to < 45 kg	Upon awakening / 8 hours later	15/7.5 mg TLV or matching placebo
≥ 45 kg to ≤ 75 kg	Upon awakening / 8 hours later	30/15 mg TLV or matching placebo
> 75 kg	Upon awakening / 8 hours later	45/15 mg TLV or matching placebo

TLV = tolvaptan.

[a] Split-dosing will be twice daily dosing with the larger dose taken upon awakening and the smaller dose taken approximately 8 hours later.

Doses may be titrated down dependent upon subject tolerability.

Table 3.2.1-2 Up-titration Steps

Current Dose	Up-titrated Dose	Body Weight
15/7.5 mg TLV or matching placebo	30/15 mg	≥ 20 kg to < 45 kg
30/15 mg TLV or matching placebo	45/15 mg	≥ 45 kg to ≤ 75 kg
45/15 mg TLV or matching placebo	60/30 mg	> 75 kg

Protocol 156-12-298

Table 3.2.1-3 Down-titration Steps

Current Dose	Down-titrated Dose
7.5 mg once daily upon awakening	Subject to be withdrawn from IMP
7.5/7.5 mg	7.5 mg once daily upon awakening
15/7.5 mg	7.5/7.5 mg
22.5/15 mg	15/7.5 mg
30/15 mg	22.5/15 mg
45/15 mg	30/15 mg
60/30 mg	45/15 mg

Subjects should attempt to complete 7 days of dosing between down-titration steps to provide the best opportunity for a subject to be given their maximally tolerated dose.

3.2.1.1 Dosing for Dense PK and PD Sampling

A subset of 20 subjects, half on tolvaptan and half on placebo, in the 12 to 17 year old age group will have dense PK sampling after at least 1 month on IMP. The blind will be maintained by utilizing the Interactive response system (IXRS) to determine how many subjects on tolvaptan or placebo have been assessed and closing a group when 10 subjects have completed. The doses that the subjects will be given will be from their currently prescribed IMP. The morning dose will be administered at approximately 8:00 AM in the fasting state (no food within 8 hours prior to dosing or within 2 hours postdosing), the afternoon dose 8 hours later, and with dinner served at least 2 hours postdose. Each dose will be administered with 240 mL still, room temperature water; the total 240 mL can be consumed over a 1-hour period following dosing.

3.2.2 Treatment in Phase B

Subjects who have completed Phase A on treatment and continue in Phase B will receive open-label tolvaptan for up to 24 months. In order to preserve the blind in Phase A, subjects will be started at a dose based on their current body weight (see Table 3.2.1-1) and after 1 week, they will be asked to up-titrate once from their starting dose. Subjects who wish to lower their dose secondary to tolerance will have their doses adjusted as necessary.

3.3 Trial Population

The target trial population will be at least 60 male and female subjects aged 12 to 17 years (inclusive), with a diagnosis of ADPKD as defined by the presence of family history and/or genetic criteria AND who have at least 10 renal cysts, each of which measures at least 0.5 cm confirmed upon magnetic resonance imaging (MRI) inspection. In accordance with the PIP requirements, the trial will also allow subjects aged 4 to 11 years who meet criteria for entry to be enrolled concurrently during the recruitment

period for the target population. It is expected that the trial may enroll approximately 100 subjects.

Subjects who are MRI-naive or under the age of 12 should have at least 4 cysts that are at least 1 cm in size confirmed by ultrasound prior to MRI inspection.

Treatment groups for the required population will be stratified by age and gender in the following age cohorts:

- Female subjects ages 12 to 14 years, inclusive
- Female subjects ages 15 to 17 years, inclusive
- Male subjects ages 12 to 14 years, inclusive
- Male subjects ages 15 to 17 years, inclusive

When > 15 subjects are enrolled in an age cohort, new screening for that age cohort will be closed; subjects concurrently in screening for that age cohort may be enrolled if they meet inclusion/exclusion criteria. When the last subject in the final age cohort for the required population has been achieved, enrollment in the trial will cease.

The trial is also open to children between the ages of 4 to 11 years (inclusive) with ADPKD, who meet the above criteria and who, in the opinion of the investigator, would benefit from treatment. Subjects, aged 4 to 11 years (inclusive), must have an ultrasound to assess renal cysts.

Qualified subjects who complete Phase A are eligible to participate in Phase B.

4 Sample Size

A sample size of at least 60 subjects from 12 to 17 years of age inclusive is proposed for the Phase A of this trial. It is expected that the trial may enroll approximately 100 subjects in total. Since the data collected will be summarized using descriptive statistics and not aimed at testing a specific hypothesis, no formal power calculations are undertaken.

5 Statistical Analysis Datasets

5.1 Analysis Datasets

The following analysis sets are defined for the efficacy and safety analysis in this trial.

Randomized: It consists of all subjects who were randomized in the trial.

Protocol 156-12-298

Full Analysis Set (FAS) for Phase A consists of all subjects who have been randomized to a treatment group, received at least 1 dose of the IMP, have both a Phase A baseline and at least 1 post-baseline efficacy evaluation. They will be analyzed according to the treatment group to which they were randomized. FAS for Phase B consists of all subjects wo enrolled to Phase B, received at least 1 dose of the IMP, have both a baseline and at least 1 post-baseline efficacy evaluation in Phase B. The FAS, which is based on intent-to-treat principle, will be the primary analysis set for efficacy analyses on the primary/key secondary endpoints and other secondary endpoints.

Safety Analysis Set (SAS): It consists of all subjects who were administered at least 1 dose of IMP. The safety dataset will be used for safety analyses. The safety datasets for each phase are defined as:

I. Phase A Safety Set: All subjects who randomized and receive at least one dose of IMP in Phase A.
II. Phase B Safety Set: All subjects who are enrolled into Phase B and receive at least one dose of IMP in Phase B.

5.2 Handling of Missing Data

All safety/efficacy data will be summarized for observed (non-missing) values only. Missing data will be mitigated by encouraging subjects who withdrew from treatment to return for their remaining visits for collection of assessments as noted in the Schedule of Assessments, Table 3.7-1 for Phase A and Table 3.7-2 for Phase B, in protocol.

6 Trial Conduct

In general, analyses methods stated in Section 6 to Section 9 will apply to Phase A and Phase B unless otherwise specified. In the final CSR, Phase A and Phase B will be reported separately unless otherwise specified.

6.1 Subject Disposition

The number of subjects who have been randomized, the number of subjects who are treated, and the number of subjects who discontinue from the trial, together with the reasons for discontinuation taken from the case report form (CRF) status page will be provided.

6.2 Treatment Compliance

Treatment compliance will be calculated by dividing the total dosage taken by the total dosage the subjects are scheduled to take during the treatment phase based on the Study Medication panel of CRF.

6.3 Prior and Concomitant Medications

Use of concomitant medications prior to the start of trial medication will be summarized by number and percentage of users by treatment group.

Concomitant medications used post-baseline will be summarized in two categories of time interval: during the trial medication period and after the trial medication period. In each case, the use of concomitant medications will be summarized by number and percentage of users by treatment group.

6.4 Protocol Deviations

Major protocol deviations data will be summarized by type of deviations (eg, deviations in entry criteria, dosing, randomization, concomitant medication, procedural, etc) by center and treatment group. In addition, a subject listing will be provided describing the deviations for each subject.

7 Demographic and Baseline Characteristics

Demographic characteristics and medical history at screening will be summarized by descriptive statistics, eg, proportion, mean, median, SD, minimum and maximum values.

Baseline characteristics will be summarized for Treatment Phase A and Treatment Phase B, respectively.

For the Randomized Sample, baseline disease evaluation will be summarized by treatment group and overall with the mean, median, range and standard deviation presented.

8 Primary and Secondary/ Exploratory Endpoints Analyses

8.1 Primary Endpoint Analysis

The co-primary endpoints for the trial are the change from Phase A baseline in spot urine osmolality (premorning dose) and specific gravity (premorning dose) to Week 1.

Two variables will be derived for the co-primary outcomes:

- Change from Phase A baseline in spot urine osmolality (premorning dose) to Week 1
- Change from Phase A baseline in specific gravity (premorning dose) to Week 1

Descriptive statistics will be presented on the co-primary endpoints by treatment group, respectively.

Baseline measurements of co-primary efficacy variables are defined as their last measurements prior to the first dose of trial medication in Phase A.

8.2 Key Secondary Endpoint Analysis

The key secondary endpoint is the percent change from Phase A baseline in height-adjusted total kidney volume (htTKV) as measured at 12 months.

Descriptive statistics will be presented on the key secondary endpoint by treatment group.

Baseline measurements of key secondary efficacy variable is defined as its last measurement prior to the first dose of trial medication in Phase A.

8.3 Other Secondary Endpoints Analyses

Other secondary efficacy endpoints include:

- 24-hour fluid balance prior to Week 1.
- Change from baseline in renal function (eGFR by Schwartz formula) at each clinic visit (Week 1, Month 1, Month 6, and Month 12 in Phase A).
- Change from baseline in renal function (eGFR by Schwartz formula) at each clinic visit (Week 1, Month 1, Month 6, Month 12, Month18, and Month 24 in Phase B).
- Percent change in htTKV as measured by MRI from Phase B baseline to Phase B Month 12.
- Percent change in htTKV as measured by MRI from Phase B baseline to Phase B Month 24.
- Pharmacodynamic (PD) endpoints of urine volume (including 24-hour fluid volume), fluid intake and fluid balance, sodium, creatinine, and free water clearance during dense PK sampling (after at least 1 Month on IMP).
- Proportions of each Tanner Stage by gender and age compared to normative populations at baseline, 6 months, and 12 months during the placebo-controlled phase (Phase A), and every 6 months during the open-label extension phase (Phase B).
- Changes from baseline percentiles for height and weight by gender and age at baseline, 6 months, and 12 months during the placebo-controlled phase (Phase A), and every 6 months during the open-label extension phase (Phase B).
- Safety variables (changes from baseline in creatinine, vital signs, laboratory values including liver function tests [LFTs], rate of aquaretic AEs) in placebo and tolvaptan.

For all of the secondary endpoints in Phase A, descriptive statistics by visit will be presented by treatment group. For the secondary endpoints in Phase B, descriptive

statistics will be presented by previous Phase A treatment group (Tolvaptan and placebo) and pooled.

The formula for eGFR by Schwartz[1] is:

eGFR = 0.413 × height [cm] /serum creatinine [mg/dL]

To account for the hemodynamic effects of Tolvaptan, the analysis for change of eGFR in Phase A will be provided using week 1 as baseline as supplemental analysis.

8.4 Subgroup Analyses

Subgroup analyses on the primary and key secondary endpoints will be performed to examine the differences in treatment response based on Phase A baseline status (eg, gender, age stratum). Subgroups for age, sex, and tanner staging are defined as the following:

- Age: <12, 12-14, 15-17 years old
- Sex: male, female
- Tanner staging: <5, 5

Subgroup analyses for 12-17 years old will be provided as supplemental analysis.

[redacted]

[redacted]

Protocol 156-12-298

9 Safety Analyses

In general, Phase A baseline measurements of safety variables are defined as their last measurements prior to the randomization for the safety population. Phase B baseline measurements of safety variables are defined as the last measurements prior to the first dose of IMP in Phase B. Safety analysis will be conducted based on the safety population, defined in Section 5.1. Standard safety variables to be analyzed include AEs, change from baseline in creatinine, vital signs, laboratory values including liver function tests (LFTs), and rate of aquaretic AEs. In general, descriptive statistics will be provided for Phase A safety variables and Phase B safety variables as well.

Subgroup analysis of key safety endpoints by age cutoff (<12 years vs. ≥ 12 years) will be summarized.

9.1 Extent of Exposure

A subject's duration of exposure is defined as the trial medication end date - trial medication start date + 1 in each phase. Duration of exposure will be summarized by

treatment group in Phase A and by previous Phase A treatment group (Tolvaptan and placebo) and pooled in Phase B.

9.2 Adverse Events

All adverse events (AE) will be coded by MedDRA System Organ Class (SOC) and Preferred Term (PT). A treatment-emergent AE (TEAE) is defined as an AE which starts after start of trial medication), or an AE continues from baseline of the specific phase and becomes serious, worsening, trial drug-related or results in death, discontinuation, interruption or reduction of trial medication during this phase. The incidences of the following treatment-emergent adverse events (TEAEs) will be summarized by treatment groups:

- TEAEs by severity
- Potentially drug-related TEAEs
- TEAEs with an outcome of death
- Serious TEAEs
- Discontinuations due to TEAEs

Incidences of AEs above will be tabulated by treatment for Phase A safety dataset and Phase B safety dataset, respectively.

9.3 Clinical Laboratory Data

Summary statistics for changes from baseline in the clinical laboratory measurements will be provided for the safety population. Potentially clinically significant results in laboratory tests identified using prospectively defined criteria will also be summarized.

According to the Food and Drug Administration (FDA) Guidance[2], laboratory measurements that signal the potential for drug-induced liver injury (DILI) will be reported. An incidence table and a listing will be provided for subjects who meet one or combinations of the following criteria:

1) ALT (alanine transaminase) or AST (aspartate transaminase) ≥ 3x upper limit of normal (ULN) (or baseline value for subjects with abnormal baseline)
2) Increase in bilirubin ≥ 2x ULN (or baseline value for subjects with abnormal baseline)

9.4 Vital Sign Data

Summary statistics for changes from baseline in vital signs and potentially clinically significant results in vital signs will be summarized for the safety population. For a subject with repeat measures in either vital signs or lab tests at a visit, the last repeat will be used in the by visit summary. However, for outlier analysis (such as clinically significant abnormalities), data from all visits, no matter they are from the original visits, repeats, or unscheduled visits, will be included.

9.5 Physical Examination Data

By-patient listings will be provided for physical examination.

9.6 Electrocardiogram Data

Electrocardiogram (ECG) data will not be summarized since ECG data will be collected at the screening visit only.

10 Pharmacodynamic Analyses

Urinary excretions will be determined as urine concentration × urine volume; missing values will not be imputed. If urine concentration or volume is missing for any interval, the 0 to 24 hour values will not be determined. Urine volumes of zero, and consequently non reportable urine concentration, are not considered as missing data; values of 0 will be reported for volume and excretion.

Free water clearance will be determined as urine excretion rate − osmolar clearance.

Osmolar, sodium, and creatinine clearances will be determined by standard methods with average serum concentration determined by averaging the concentrations at the beginning and end of the urine collection interval. If urine volume for a collection interval is 0, then the clearance value for that interval and the following interval will be determined by using the average value of the 3 serum concentrations, the urine volume of the second interval and the total time of the 2 collection intervals (eg, 2 to 4 hour collection has urine volume of 0 mL). Clearance for the 2 to 4 and 4 to 8 hour intervals will be determined using serum concentrations at 2, 4, and 8 hours, the urine volume from 4 to 8 hour interval and total collection time of 6 hours (8 minus 2).

Values of urine osmolality will be summarized with descriptive statistics by total daily dose (all placebos grouped together) and collection interval. Sodium and creatinine urine concentrations will only be listed.

Values of excretions (osmoles, sodium, and creatinine) and clearances (free water, sodium, and creatinine) will be summarized with descriptive statistics by total daily dose (all placebos grouped together), collection interval, and 0 to 24 hours.

Serum concentrations (osmolality, sodium, and creatinine) and change from predose will be summarized with descriptive statistics by total daily dose (all placebos grouped together), analyte, and time point.

11 Interim Analysis

No interim analysis is planned before all randomized subjects either complete the Month 12 visit or early terminate in Phase A, the double-blind, placebo-controlled portion of this protocol. A snapshot of the database will be taken after all subjects in Phase A have completed or early terminated, these data will be unblinded, and an interim CSR will be written to provide early information on safety.

12 Monitoring of Safety Data

12.1 Independent Data Monitoring Committee

An independent data monitoring committee (IDMC) will be established for this trial. This committee will meet on a regular basis to ensure the safe and ethical treatment of trial subjects, ensure the scientific integrity of the trial, and to ensure the trial is conducted within the bounds of ethical medical practice. It may make recommendations to the sponsor and trial steering committee to amend or terminate the trial based on grounds of safety, futility, or greater than expected efficacy as defined by the accepted statistical practices and procedures to be detailed in their charter. The specific duties of the IDMC will be detailed in a separate IDMC charter document.

12.2 Hepatic Adjudication Committee

A hepatic adjudication committee (HAC) has been convened for the purpose of oversight of hepatic events. The HAC will independently determine probable cause(s) of any hepatic event occurring during the trial and will communicate with the IDMC that oversees the trial.

13 References

1 Schwartz G, Munoz A, Schneider M, Mak R, Kaskel F, Warady B et al. New equations to estimate GFR in children with CKD. J Am Soc Nephrol. 2009;20(3):629-37.

2 Guidance for Industry, Drug-Induced Liver Injury: Premarketing Clinical Evaluation. US Department of Health and Human Services, Food and Drug Administration, and Center for Drug Evaluation and Research (CDER), July 2009.

Protocol 156-12-298

14 Appendices

Appendix 1: Criteria of Potentially Clinically Significant Laboratory Test Abnormalities

Laboratory Test Abnormalities due to Test Value Increase

Test	Abnormality	Test Result Grade				
		0	1	2	3	4
APTT (sec)	Increase	ULN	>ULN - 1.5xULN	>1.5xULN - 2xULN	>2xULN	
ALT (SGPT) (IU/L)	Increase	ULN	>ULN - 3xULN	>3xULN - 5xULN	>5xULN - 20xULN	>20xULN
AST (SGOT) (IU/L)	Increase	ULN	>ULN - 3xULN	>3xULN - 5xULN	>5xULN - 20xULN	>20xULN
Bilirubin, Total (mg/dL)	Increase	ULN	>ULN - 2xULN	>2xULN - 3xULN	>3xULN - 10xULN	>10xULN
Creatinine (mg/dL)	Increase	B*	>B – 1.5xB	>1.5 x B – 3 x B	> 3 x B – 6 x B	> 6 x B
Eosinophils, Absolute (Thous/µL)	Increase	≤0.65	>0.65-1.5	>1.5-5	>5	
Glucose (mg/dL)	Increase	≤115	>115-160	>160-250	>250-500	>500
Hemoglobin (g/dL)	Increase	ULN	>ULN-20	>20-21	>21-22.5	>22.5
Potassium (mEq/L)	Increase	ULN	>ULN-5.5	>5.5-6	>6-7	>7
INR	Increase	ULN	>ULN - 1.5xULN	>1.5xULN - 2xULN	>2xULN	
Sodium (mg/dL)	Increase	<145	146 - 150	151 - 155	156 - 160	>160
Triglycerides (mg/dL)	Increase	ULN	>ULN - 2.5xULN	>2.5xULN - 5xULN	>5xULN - 6xULN	>6xULN
Urea Nitrogen (mg/dL)	Increase	≤22	>22-26	>26-31	>31	
White Blood Count (Thous/µL)	Increase	≤10.799	>10.799-15	>15-20	>20-25	>25

*B= Baseline

Laboratory Test Abnormalities due to Test Value Decrease

Test	Abnormality	Test Result Grade				
		-4	-3	-2	-1	0
Glucose (mg/dL)	Decrease	<30	30-<40	40-<55	55-<65	≥65
Hemoglobin (g/dL)	Decrease	<6.5	6.5-<8	8-<10	10-<LLN	LLN
Lymphocytes, Absolute (Thous/µL)	Decrease	<0.2	0.2-<0.5	0.5-<0.8	0.8-<LLN	LLN
Neutrophils, Absolute (Thous/µL)	Decrease	<0.5	0.5-<1	1-<1.5	1.5-<LLN	LLN
Platelet Count	Decrease	<25	25-<50	50-<75	75-<LLN	LLN

Protocol 156-12-298

Test	Abnormality	Test Result Grade				
		-4	**-3**	**-2**	**-1**	**0**
(Thous/µL)						
Potassium (mEq/L)	Decrease	<2.5	2.5-<3		3-<LLN	LLN
Sodium (mg/dL)	Decrease	<120	120-124	125-129	130-135	≥136
White Blood Count (Thous/µL)	Decrease	<1	1-<1.5	1.5-<2.5	2.5-<3.501	≥3.501

Protocol 156-12-298

Appendix 2: Criteria of Potentially Clinically Significant Vital Sign Abnormalities

Test Parameters	Unit	Age	Criteria (meet either one will count)	
			Limit	Change from baseline
Heart Rate	bpm	4 - 14 Years	<= 50 >= 140	Decrease >= 15 Increase >= 15
		15 Years and older	<=50 >= 120	Decrease >= 15 Increase >= 15
SBP, Sitting	mmHg	4 – 12 Years	<=70 >= 130	Decrease >= 20 Increase>=20
		13 – 17 Years	<= 120 >= 144	Decrease >= 20 Increase>=20
DBP, Sitting	mmHg	4 – 12 Years	<= 50 >= 86	Decrease >= 15 Increase>=15
		13 – 17 Years	<= 80 >= 92	Decrease >= 15 Increase>=15

Protocol 156-12-298

Appendix 3: Document History

Dates/Author	Description of Updates	Version	Document Updates
05 Feb 2020 [redacted]	NA	1.0	Original Version (Approved prior to Phase A's database lock on 21 Feb 2020)

30 Nov 2021 [redacted]	[redacted]	2.0	Updated Version (Prior to final database lock)

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