NCT04747808
Study LL-BMT10001

A Phase 2a Study of Safety, Tolerability, and Efficacy of Drug-Delivering Contact Lens LL-BMT1 in Patients With Primary Open-Angle Glaucoma or Ocular Hypertension

Statistical Analysis Plan
Date: 11 February 2021

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Protocol details:

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Date:	21-DEC-2020

Author details:

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Author(s):	[redacted]

Review and Approval

The undersigned have approved this Statistical Analysis Plan for use in this study.

Trial Runners, LLC Approval:

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Biostatistician

Feb 12, 2021
Date

[redacted]
Project Manager

Feb 12, 2021
Date

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Data Manager

Feb 12, 2021
Date

MediPrint Ophthalmics, Inc. Approval:

[redacted]
Chief Operating Officer

Feb 12, 2021
Date

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GLOSSARY OF ABBREVIATIONS

Abbreviation	Meaning
AE	Adverse Event
BCVA	Best-corrected visual acuity
CLDEQ-8	Contact Lens Dry Eye Questionnaire-8
IOP	Intraocular Pressure
ITT	Intent-to-treat
mITT	Modified intent-to-treat
OHT	Ocular hypertension
POAG	Primary open-angle glaucoma-999
TEAE	Treatment-emergent adverse event

1 INTRODUCTION

This statistical analysis plan (SAP) provides a comprehensive and detailed description of analyses and reporting of data for LL-BMT1 study protocol LL-BMT10001. The purpose of the SAP is to ensure the credibility of the study findings by pre-specifying the statistical approaches to the analysis of study data prior to data base lock.

1.1 Changes from Protocol

Not applicable.

2 STUDY OBJECTIVES

2.1 Primary Objective

The primary objective of this study is to evaluate the safety of LL-BMT1 in patients with POAG or OHT.

2.2 Secondary Objective

The secondary objectives of this study are:

- To evaluate the safety and tolerability of LL-BMT1 in patients with POAG or OHT, and
- To evaluate efficacy by IOP-lowering effects of LL-BMT1 in patients with POAG or OHT.

3 STUDY DESIGN

This study is an open-label, phase 2a clinical study consisting of 5 patients at up to 2 sites within the United States, each with a treatment duration of 1 week. All patients will be assigned to the study intervention (LL-BMT1 lenses) and will wear then for 1 week.

3.1 Sample Size Considerations

Due to the exploratory nature of this study, no formal power sample size calculation has been performed. An empirical sample size of at least 5 evaluable patients is planned. Assuming a 10-20% drop-out non-evaluable rate, up to 7 patients (7 study eyes) will be consented to begin acclimation screening. Those who are consented but fail acclimation screening will be replaced until at least 5 patients successfully complete the acclimation screening. Five patients who pass acclimation screening will be enrolled as patients for study treatment.

3.2 Randomization

Not applicable, as all study subjects will be assigned to a single treatment, LL-BMT1 lenses.

3.3 Schedule of Evaluations and Analysis Visit Windows

The schedule of visits and procedures are provided in the study protocol, LL-BMT10001, version 1.2, section 1.3. The study consists of a screening period, 2 acclimation periods where the subject wears 2 sets of nonmedicated lens for 1 week each, 1 treatment week where the subject wears 1 set of LL-BMT1

lenses for 1 week, and a follow-up visit after lens removal. Visit days and windows are summarized in the table below:

Visit	Target Day of the Visit	Visit Windows (Days) for Analyses
Visit 1 - Screening	-45 to -14	< -14
Visit 2 – Acclimation	-14	-14
Visit 3 – Acclimation	-7	-7
Visit 4 – Acclimation	-6	-6
Visit 5 – Baseline	0	0
Visit 6 – LL-BMT1 Lens Insertion	1	1
Visit 7 – On-treatment	4	4
Visit 8 – End of treatment	7	7
Visit 9 – Follow-up	8	8
Visit 10 – Conditional Follow-up / End of study	9	9

4 ANALYSIS POPULATIONS

4.1 Intent-to-Treat Population

The intent-to-treat (ITT) population includes all patients who have LL-BMT1 lenses successfully inserted. This population of patients will be used to summarize protocol deviations.

4.2 Safety Population

The safety population includes all patients who have LL-BMT1 lenses successfully inserted.

5 STUDY VARIABLES/PARAMETERS

5.1 Primary Endpoints

The primary safety endpoint is the adverse event (AE) rate, defined to be 100 x [number of AEs / number of eyes exposed to treatment].

5.2 Secondary Endpoints

The secondary safety endpoints include the following:

- AEs
- Concomitant medications
- Heart rate and blood pressure
- BCVA
- IOP
- Biomicroscopy
- Conjunctival hyperemia
- Percent of patients with ≥ 5 mmHg increase from baseline in IOP at each visit
- Abnormal slit-lamp biomicroscopy findings at the Baseline, Day 1, and Day 7 Visits
- Contact lens protein deposits at the Day 7 Visit
- Change from Baseline in CLDEQ-8 results at the Day 7 Visit

The secondary efficacy endpoint will be the change from baseline in IOP at each visit.

6 STATISTICAL ANALYSIS METHODS

There are no formal study hypotheses to be tested in this study. Safety and efficacy endpoints will be summarized using frequency, mean, median, standard deviation, min and max for continuous variables, and frequency and percentage for categorical variables.

6.1 Subject Disposition

The number and percentage of subjects screened, enrolled, completed treatment, completed study, and within each population will be summarized.

Individual subject disposition data will be listed.

6.2 Protocol Deviations

The number and percentage of protocol deviations will be presented using the intent-to-treat population.

6.3 Missing Data and Imputation

No Imputation will be conducted for this study.

6.4 Demographics and Baseline Characteristics

Baseline and demographic assessments will be presented descriptively using the safety population. Mean, median, standard deviation, min and max will be used for continuous variables, while number and percentage will be used to describe categorical variables.

6.5 Prior and Concomitant Medications

Prior and concomitant medication will be coded using the World Health Organization Drug Dictionary (WHO DD), September 2020. The number and percentage of subjects who reported taking prior and/or concomitant medications will be summarized using the safety population.

Individual subject prior and concomitant medication data will be listed.

6.6 Medical History

The number and percentage of past and concurrent medical conditions will be summarized using the safety population.

Individual subject medical history data will be listed.

6.7 Primary Analysis

The primary safety analysis will be treatment-emergent adverse events, defined to be any AE with an onset date equal to or after the date of the first insertion of the study lens and during the treatment, using the safety population.

Pre-existing AEs, those identified after enrollment but before treatment with LL-BMT1, will be tabulated for all consented patients. The rate of adverse events will be defined as 100 x [number of AEs / number of eyes exposed to treatment].

6.8 Secondary Analysis

There will be both safety and efficacy assessments in the secondary analysis.

The secondary safety analysis will consist of identifying the following:

- Percent of patients with ≥ 5 mmHg increase from baseline in IOP at each visit
- "Abnormal" and "Severe" slit-lamp biomicroscopy findings at the Baseline, Day 1, and Day 7 Visits
- Contact lens protein deposits at the Day 7 Visit
- Change from Baseline in CLDEQ-8 results at the Day 7 Visit

The secondary efficacy analysis will consist of identifying the change from baseline in IOP at each visit. Study eyes only within the modified intent-to-treat population will be used for this part of the analysis.

7 INTERIM ANALYSIS

No interim analysis is planned for this study.

8 VERSION HISTORY LOG

Version	Date	Implemented Changes	Author
1.0	11-FEB-2021	First Approved Version	Lauren Mudd