Low-concentration Atropine for Myopia Prevention (LAMP-2) Study

Statistical Analysis Plan (SAP)

SAP Version: V1.0, 20 May 2019

1. Study objectives

To determine the effectiveness of 0.05% and 0.01% atropine compared with placebo in preventing the onset of myopia.

2. Outcomes

2.1. Primary outcomes

The primary outcomes will be the proportion of onset of myopia in each group (binary outcome) and the proportion of fast myopia progressor in each group (binary outcome).

2.2. Secondary outcomes

2.2.1. Change in spherical equivalent progression at each follow-up point (continuous outcome)

2.2.2. Change in axial length at each follow-up point (continuous outcome)

2.3. Exploratory outcomes

2.3.1. Time from randomization to occurrence of myopia (time-to-event outcome)

2.3.2. Changes in pupil size, accommodation, and visual acuity in each follow-up point (continuous outcome)

2.3.3. Visual function questionnaire scores (continuous outcome)

2.3.4. Side effects and adverse events (binary outcome)

3. Treatments

Trial arms:

0.05% Atropine group

0.01% Atropine group

Placebo

4. Analysis population

4.1. Full analysis population

The full analysis population will be referred to as the “intention-to-treat” population, as all participants with valid informed consent will be included based on the treatment they were/will be randomized, regardless of whether they lost to follow-up. The full analysis population will also be used to for the secondary and exploratory outcomes. In some analyses, data may need to be completed at specific time points, so only those populations with the available data will be included.

5. Data processing

5.1. Case report form

Case report forms will be used to record clinical data in the trial, and case report

forms will be in paper form. As original material, the CRF will not be changed at will. The relevant information of all patients participating in the trial will be recorded timely and truthfully.

5.2. Data management and cleaning

REDCap (Vanderbilt University, Nashville, TN, USA) will be used to build and manage the database. The data administrator will establish an electronic database according to the case report form. Data will be double entered into the database. To ensure data security, non-permitted personnel cannot access and modify the trial data. The data will be checked to ensure that there are no erroneous entries and changes will be made to the electronic data capture (EDC) database.

6. Statistical analysis

6.1. Analysis of primary outcomes

The primary outcomes will be two binary outcomes: proportion of onset of myopia and proportion of fast myopia progressor. The primary outcomes will be summarized by the number (%) of participants with events and incidence rates by treatment arms. The trend analysis for the different treatments will be calculated by logistic regression. The absolute difference among treatment groups will be compared using exact unconditional methods based on the Farrington-Manning score statistic.

The adjusted analyses will be carried out for the two primary outcomes to determine whether the results will be affected by the inclusion of covariates. The following covariates will be included in the adjusted analyses: baseline age, sex, baseline SE, outdoor time, near work, and parental myopia.

6.2. Analysis of secondary outcomes

The secondary outcomes will be the continuous outcomes, including changes in spherical equivalent and changes in axial length. We will use multiple linear regression model and generalized estimating equation to compare the changes among three treatment groups. The following covariates will be included in the analysis: age, sex, baseline SE/AL, outdoor time, near work, and parental myopia.

6.3. Analysis of exploratory outcomes

6.3.1. Analysis of time-to-event outcome

Survival curves will be plotted using the Kaplan-Meier method and compared the survival distributions among treatment groups using the log-rank test.

6.3.2. Analysis of continuous outcome

For the analysis for ocular biometrics, we will use generalized estimating equation to compare the changes among three treatment groups. Age and sex will be included in the analysis as the covariates.

For the analysis for questionnaire, we will use the analysis of variance (ANOVA) test

to compare the differences among three treatment groups.

6.3.3. Analysis of binary outcome

The binary outcome will be summarized by the number (%) of participants with event and rate by treatment arms. Pearson's Chi-square test will be used to compare the differences among three groups.