Evaluation of the use of antiretroviral regimens containing Raltegravir for prophylaxis of mother-to-child-transmission of HIV infection in pregnant women presenting with detectable viral load after 28 weeks of gestation: a pilot study

Statistical analysis plan

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Plan for Statistical Summaries and Analyses

General Considerations

All statistical summaries and analysis will be provided for the intent-to-treat population, defined as all patients who are randomized to treatment. Summaries and analyses of the baseline data and efficacy data will also be provided for the efficacy-evaluable population, defined as patients who meet the inclusion/exclusion criteria, take at least 80% doses of study medication, and complete the Week 6 (or termination) visit.

With the exception of the analysis of the primary efficacy endpoint, percentage of responders for the intent-to-treat population, missing data will not be estimated or carried forward in any statistical analyses.

All comparisons of the treatment groups will be performed using two-sided tests at a 0.05 level of significance (= 0.05). The null hypothesis for all analyses is that there is no difference between the treatment groups.

All summaries, statistical analyses, and individual patient data listings described below will be provided in separate appendices. Separate listings will be provided for each of the treatment groups in the intent-to-treat population as well as for the group of patients not randomized.

Disposition of Patients

Summaries of the number of patients randomized, the number of those completing the study, and the incidence of protocol violations will be provided for each treatment group.

The number (%) of patients with protocol violations that might affect endpoints of the study will be based on review of the database. This assessment will be made prior to determination of treatment assignment for all patients in the database.

Demographic and Disease Characteristics

The statistical analyses described below will be completed for:

the intent-to-treat patient population the efficacy-evaluable population

Demographic Characteristics

The following table identifies the demographic and disease characteristics used to determine the comparability of the treatment groups and the methods used to analyze them.

Table 1: Variables Assessed to Determine Comparability

Variable	Method of Analysis
Gestational Age at randomization	One-way ANOVA/KW
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Baseline VL	One-way ANOVA/KW
Baseline CD4	One-way ANOVA/KW

Efficacy Endpoints

The statistical analyses described below will be completed for:

the intent-to-treat patient population the efficacy-evaluable population

The primary efficacy endpoint is the number (%) of patients achieving the primary endopoint (HIV-1 RNA Viral Load <50 copies/ml) at the Week 6 (or termination) visit.

Patients will be counted as non-responders if they are missing Week 6 (or termination). The Raltegravir treatment group will be compared to SOC group with respect to percentage of responders using a Chi-square test. Two-sided 95% confidence intervals for the percentage of responders will be calculated for each treatment group.

The following table identifies the secondary efficacy endpoints and the methods used to analyze them.

Table 2 - Variables Assessed to Evaluate the main endpoints

Frequency of Adverse events (mother and newborns)	Chi-square test
Time to reach VL below 50 copies	One-way ANOVA/KW
% MTCT (HIV, HTLV)	Chi-square test

For each of these variables, the Raltegravir treatment group will be compared to the SOC group.

Safety Endpoints

The summaries and statistical analyses of the safety endpoints will be completed for the intent-to-treat population. The incidence of at least one Grade III or IV adverse event will be the primary safety endpoint of the study. The treatment groups will be compared with respect to the percentage of patients with at least one Grade III or IV adverse event using a Chi-square test.

Summaries of the number (%) of subjects in each treatment group with at least one adverse event, classified according to preferred term and body system, will also be provided for:

- drug-related adverse events
- serious adverse events

Secondary safety endpoints are the incidence of adverse events classified according to preferred term and body system, clinically significant laboratory test results, and changes in vital signs. The treatment groups will be compared with respect to the percentage of patients with clinically significant laboratory test results at the Week 2, 4, 5, or 6 Visits using Chi-square tests. Summaries of the physical examination data, vital signs (actual value and change from baseline), and laboratory data (actual value and change from baseline) at each visit will be provided.

Power/Sample Size:

Since this is a pilot study, power considerations does not apply.