2.0 Synopsis

<table>
<tr><td>Abbott Laboratories</td><td>Individual Study Table Referring to Part of Dossier:</td><td>(For National Authority Use Only)</td></tr>
<tr><td>Name of Study Drug:
Zemplar</td><td>Volume: NA</td><td>NA</td></tr>
<tr><td>Name of Active Ingredient:
Paricalcitol</td><td>Page: NA</td><td>NA</td></tr>
<tr><td colspan="3">Title of Study: Effectiveness and safety of a 6-month treatment with IV Zemplar® in patients on hemodialysis and with secondary hyperparathyroidism using iPTH/100 as initial dose.</td></tr>
<tr><td colspan="3">Investigator Coordinator:
Edmundo Alva, MD</td></tr>
<tr><td colspan="3">Study Site(s):
3 sites in Peru</td></tr>
<tr><td colspan="3">Publications: None</td></tr>
<tr><td colspan="2">Studied Period (Years): 2009-2010
First Subject First Visit: 26 Jun 2009
Last Subject Last Visit: 22 Sep 2010</td><td>Phase of Development: IV</td></tr>
<tr><td colspan="3">Objectives
Safety: To study the safety of IV Paricalcitol by analyzing the episodes of hypercalcemia, hyperphosphatemia, elevation in the Calcium X Phosphorus product and decrease of iPTH <150 pg/ml with a low initial dose regime.
Efficacy: To describe the proportion of patients treated with IV Paricalcitol who reach a 30% reduction in PTH levels and/or the therapeutic goal of iPTH between 150 and 300 pg/ml with a low initial dose regime (iPTH/100)</td></tr>
<tr><td colspan="3">Methodology: A total of 100 subjects with chronic kidney disease that require dialysis at least 3 times per week and fulfilling study eligibility criteria were enrolled at 3 sites. Study medication (iPTH/100) was administered during dialysis sessions. Efficacy and safety measurements were performed throughout the study. The follow up was every month for 3 months and the final visit was performed at 6 months.</td></tr>
<tr><td colspan="3">Number of Subjects (Planned and Analyzed): Planned: 120 screened subject / 100 enrolled subjects, Analyzed: 114 screened subject /100 enrolled subject.</td></tr>
<tr><td colspan="3">Diagnosis and Main Criteria for Inclusion: A subject will be eligible for study participation if he/she meets the following criteria:
1. Patients ≥18 years old with secondary hyperparathyroidism (PTH >300 pg/mL measured in the last 2 weeks).
2. Patients on hemodialysis who require starting therapy with IV Paricalcitol (de novo).
3. Patients attending 3 hemodialysis sessions per week.
4. Patients signing the informed consent approved by the Ethics Committee. If any individual is not capable of giving his/her consent, it can be obtained from a next of kin or from his/her legal representative, according to local laws and regulations.
5. The decision to initiate treatment is upon investigator and the decision to treat patients with IV paricalcitol must not be based on the inclusion of the patient in the study or any other way. The decision to treat a patient with IV paricalcitol will be taken prior to asking the patient to participate in the study.</td></tr>
<tr><td colspan="3">Test Product, Dose/Strength/Concentration, Mode of Administration and Lot Number: NA
Duration of Treatment: six months (24 weeks)</td></tr>
</table>

Reference Therapy, Dose/Strength/Concentration and Mode of Administration and Lot Number: Study drug was provided as prefilled syringes (5mcg paricalcitol in 1 ml) for IV administration during dialysis. The initial dose was calculated using the baseline iPTH/100 formula, the dose must be adjusted by 2-4 mcg until the patient reaches iPTH values between 150-300 pg/mL, once reached, a 20-25% reduction of the actual dose as maintenance is suggested. The product was stored at 25° C temperature (range 15 - 30 ºC) and in a safe and restricted access place.

Criteria for Evaluation

Efficacy: This was a prospective, multicenter study to describe the proportion of patients treated with IV Paricalcitol who reach a 30% reduction in PTH levels and/or the therapeutic goal of iPTH between 150 and 300 pg/ml with a low initial dose regime (iPTH/100) from the baseline to week 24. Response was evaluated by change in PTH levels compared with study entry, PTH at baseline, 4, 8, 12 and 24 weeks, as well as changes in individual PTH were analyzed descriptively.[CSR 9.5.3]

Pharmacokinetic: NA

Safety: Adverse Events, laboratory data, physical examinations and vital signs were assessed throughout the study.

Statistical Methods

Efficacy: The efficacy was performed on the set of patients who completed the 24 weeks of treatment with paricalcitol. Since this is not a confirmatory study, no per-protocol analysis is planned.

Pharmacokinetic: NA

Safety: The safety analysis was performed on the set of patients who received at least one injection of paricalcitol.

Summary/Conclusions

Efficacy Results: Efficacy evaluation of therapy was performed on the fifth visit (24 weeks). At the end of the study, 88 participants (100% of those who ended the follow up period) had complete data for the analysis of plasma iPTH values.

Eighty-five patients (96.59% from the total of patients who finished the study) reached a reduction of at least a 30% or a value of iPTH between 150-300 pg/mL during study period (up to week 24), while using paricalcitol.

The iPTH values decreased throughout the study, the initial iPTH mean decreased from 803.4 to 442.11 pg/ml (4 weeks, $p<0.05$) and to 322.38 pg/ml at 24 weeks, ($p<0.05$).

Pharmacokinetic Results: NA

Safety Results: 101 adverse events occurred during the study in 60 patients: 15 adverse events possibly related to the study drug, 58 adverse events probably related to the study drug, 1 adverse event probably not related to the study drug and 37 adverse events not related to the study drug. There were 22 serious adverse events, 3 of them were related to the study drug.

The most common adverse event was hypercalcemia (Ca>10.5 mg/dl) (37%). Hyperphosphatemia (P > 6.5 mg/dl)) was present in 30% of the cases.

Two deaths occurred during the study, both by acute respiratory insufficiency, one associated to community acquired pneumonia (not related to the study drug) and the other one to upper gastrointestinal hemorrhage (related to the study drug).

Conclusions: In conclusion, an initial paricalcitol dose calculated by using the formula PTH/100 is overall safe and effective in reducing iPTH values more than 30% from the baseline.