ORTHO BIOTECH

Abbreviated Clinical Study Synoptic Report

EVALUATION OF DOSE CONVERSION FROM VARIABLE DOSING INTERVALS OF DARBEPOETIN ALFA TO VARIABLE DOSING INTERVALS OF EPOETIN ALFA (PROCRIT®) IN PATIENTS WITH THE ANEMIA OF CHRONIC KIDNEY DISEASE

Protocol PR02-06-044; Phase IV

(Epoetin alfa)

PRINCIPAL INVESTIGATOR:
Not applicable for this study

DATE STUDY INITIATED:
25 June 2003 First Patient Enrolled

DATE STUDY CLOSED:
10 September 2003 Last Patient Last Visit

Issue/Report Date: [TBD]
Department: ORTHO BIOTECH CLINICAL AFFAIRS

Compliance: The study described in this report was performed according to the principles of Good Clinical Practice (GCP).

1. PROTOCOL TITLE

Evaluation of Dose Conversion from Variable Dosing Intervals of Darbepoetin Alfa to Variable Dosing Intervals of Epoetin Alfa (PROCRIT®) in Patients with the Anemia of Chronic Kidney Disease

2. OBJECTIVES

The primary objective was to evaluate the proportion of patients that maintained hemoglobin levels at 10% of entry levels and/ or a range of 11-13g/dL for the duration of the study. The secondary objective was to evaluate safety in patients with chronic kidney disease (CKD).

3. STUDY DESIGN

This study was a prospective, non-randomized, open-label, multicenter study designed to address the hemoglobin stability after drug conversion to epoetin alfa in CKD patients previously receiving darbepoetin alfa therapy.

Approximately 180 CKD patients who were currently receiving darbepoetin alfa every two, three, or four weeks for a period of 3 months or more and who had a stable entry Hgb level of 12 $\pm$ 1 g/dL (range 11 to 13 g/dL) were eligible to participate.

A stable entry Hgb was defined as a Hgb within the range of 11 to 13 g/dL. Three (3) consecutive Hgb measurements, over the course of three months, must have been obtained prior to the study entry hemoglobin. To ensure stability, two (2) of the three (3) hemoglobin values must have been within 10% of the entry Hgb value. For example: Assume the study entry Hgb was 11.1g/dL. Two (2) out of three (3) Hgb values prior to the study entry must have been within the range of 10 and 12.2 g/dL for study eligibility.

4. DOSAGE AND ADMINISTRATION

Patients were to be given epoetin alfa (PROCRIT®) therapy every two, three or four weeks in accordance with the frequency of the previous administration of darbepoetin alfa.

- 20,000 IU of epoetin alfa (PROCRIT®) were to be administered subcutaneously every two (2) weeks for 24 weeks.
- 30,000 IU of epoetin alfa (PROCRIT®) were to be administered subcutaneously every three (3) weeks for 24 weeks.

- 40,000 IU of epoetin alfa (PROCRIT®) were to be administered subcutaneously every four (4) weeks for 24 weeks.

Darbepoetin Frequency	*PROCRIT® Frequency*	*PROCRIT® Dose*
Every Two Weeks	Every Two Weeks	20,000 IU
Every Three Weeks	Every Three Weeks	30,000 IU
Every Four Weeks	Every Four Weeks	40,000 IU

The study drug was supplied to sites as a 20,000 U/mL multi-dose, preserved vial for those patients who required 20,000 units, and as a 40,000 U/mL, single dose preservative free vial for those patients requiring 30,000 and 40,000 units. The amount per each injection was not to exceed 1.0 mL.

At any time, if the Hgb rose above 13.5 g/dL, epoetin alfa (PROCRIT®) therapy should have been held until the hemoglobin level was between 12.5-13.5 g/dL. Epoetin alfa (PROCRIT®) was then to have been resumed with a reduction in dose. This reduction was to have been 5000 IU below the most current dose. Also, the dose of epoetin alfa (PROCRIT®) was to be reduced by 5000 IU if the hemoglobin increase was > 1.5 g/dL in a 2-week period, >2.3 g/dL in a 3-week period, or >3g/dL in a 4-week period. If after holding the epoetin alfa (PROCRIT®) dose, the Hgb had decreased below 12.5g/dL., the patient was to be re-initiated at the epoetin alfa (PROCRIT®) dose used prior to the Hgb decrease.

If a patient's hemoglobin fell below 11 g/dL, the dose was to be increased by 5000 IU every 2, 3 or 4 weeks until the patient was within the targeted Hgb range of 11-13 g/dL. If Hgb values had decreased unexpectedly, the patient should have undergone a clinical evaluation, including but not limited to, stool guaiac testing, reticulocyte counts, evaluation of iron stores, Vitamin B12 and folate levels.

The maximal dose of epoetin alfa (PROCRIT®) allowed to maintain the target range was to be 30,000 IU every two (2) weeks, 40,000 IU every three (3) weeks, and 50,000 IU every four (4) weeks.

At the discretion of the physician, patients may have received either oral or parenteral (IV or IM) iron supplementation to attempt to achieve a target transferrin saturation of 25%.

5. STUDY POPULATION

Approximately 180 CKD patients who were receiving darbepoetin alfa every two, three, or four weeks for a period of 3 months or more and who had a stable entry hemoglobin of 12g/dL ± 1g/dL (11-13 g/dL) were eligible to participate. A stable entry hemoglobin was defined as hemoglobin within the range of 11-13g/dL. Three (3) consecutive hemoglobin measurements were to be obtained prior to the study entry hemoglobin. To ensure stability, two (2) of the three (3) hemoglobin values, over the course of three months, were required to be within 10% of the entry hemoglobin value.

Three patients were randomized of the 180 study patients planned, two of whom received at least one dose of study drug.

6. EFFICACY RESULTS

Due to poor enrollment, the sponsor terminated the study. Three subjects were randomized and two received at least one dose of study drug. No analysis of efficacy was performed.

7. SAFETY RESULTS

A formal safety analysis was not performed for the 3 randomized patients enrolled in this study. Case record forms were reviewed for adverse experiences and laboratory results. The two adverse events that occurred during this trial, urinary tract infection and hypoglycemia, were considered not related to study medication. One serious adverse event occurred during the trial. The patient was hospitalized due to unstable angina while being screened for eligibility to participate in this trial. The patient did not receive any study medication. The investigator assessed the event as not related to study medication. The patient recovered and was discharged from the hospital after two days.

No deaths were reported during the course of this trial.

8. CONCLUSIONS

This study terminated early due to low enrollment. Three patients were randomized. However, of the three randomized patients, only two patients were treated with at least one dose of study drug. A statistical analysis was not performed, nor were overall assessments of therapeutic results evaluated. No unexpected adverse events were observed.

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