ORTHO BIOTECH

Abbreviated Clinical Study Synoptic Report

AN OPEN LABEL RANDOMIZED STUDY TO EVALUATE THE RESPONSE RATE OF PROCRIT® (Epoetin alfa) VERSUS NO/DELAYED PROCRIT TREATMENT IN PATIENTS WITH CANCER AND PERSISTENT CHEMOTHERAPY-INDUCED MYELOSUPPRESSION (ANEMIA)

Protocol PR03-27-063; Phase IIIb

(Epoetin alfa)

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DATE STUDY INITIATED:
7 June 2004

DATE STUDY CLOSED:
30 August 2005

Issue/Report Date: [7 JUNE 2006]
Department: ORTHO BIOTECH CLINICAL AFFAIRS
Document No.: EDMS-[XXXX-XXXXXXX]:2.0

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

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1. PROTOCOL TITLE

An Open Label Randomized Study To Evaluate The Response Rate Of PROCRIT® (Epoetin Alfa) Versus No/Delayed PROCRIT Treatment In Patients With Cancer And Persistent Chemotherapy-Induced Myelosuppression (Anemia)

2. OBJECTIVES

The primary objective of this study was to compare the efficacy of PROCRIT administered subcutaneously (sc) once every week (qw) vs. no PROCRIT treatment with regard to hematologic response in patients with cancer and persistent chemotherapy-induced myelosuppression (anemia).

The secondary objectives of the study were to assess the effect of the study treatment on transfusion administration for all patients, proportion of patients with two post baseline hemoglobin (Hb) values > 12 g/dL, mean final Hb, mean lowest Hb, proportion of patients with Hb level < 10 g/dL, and weekly Hb during the study for all patients. The effects of the study treatment on safety were also assessed.

Other endpoints included patient reported assessments of fatigue and work productivity, using the anemia and fatigue subscales of the FACT-An and the four attributes of the WPAI-SHP (percent work time missed, percent impairment while working, percent overall work impairment and percent activity impairment due to fatigue).

3. STUDY DESIGN

This was a randomized, open label, multi-center study. 252 patients who met all inclusion/exclusion criteria were to be randomized in a 2:1 ratio to receive either PROCRIT or no PROCRIT treatment. Patients were to be randomized to no PROCRIT treatment, (also referred to throughout this protocol as "No/Delayed PROCRIT treatment"), and if Hb level decreased to ≤ 10 g/dL, PROCRIT treatment would be started.

Patients were to start the Treatment Phase (Day 1, Week 1 visit) within 7-14 days after the last dose of Epoetin alfa received during the final chemotherapy cycle or, for patients who have not received prior Epoetin alfa, within 2 weeks after the first day of the final chemotherapy cycle. Treatment with PROCRIT was planned for a maximum of 12 weeks. Patients receiving PROCRIT were to followed weekly until 2 weeks after cessation of PROCRIT then every other week after that, for up to 13 weeks on study. For No/Delayed PROCRIT Treatment patients, initial visits with no treatment were to occur weekly for four weeks, then every other week after that while the Hb level remains > 10 g/dL, for up to 13 weeks on study.

Safety and efficacy evaluations were to be performed at specified intervals during the study. Hb, hematocrit (Hct) and blood pressure were to be monitored at each study visit. The FACT-An and WPAI-SHP were to be completed by patients at baseline and each scheduled visit thereafter until study completion or early withdrawal. Baseline assessment was to be performed within 3 days prior to the start of the study.

4. DOSAGE AND ADMINISTRATION

Patients were to be randomized in a 2:1 ratio to receive PROCRIT or no PROCRIT treatment as follows:

PROCRIT treatment group who received prior Epoetin alfa: The starting dose of PROCRIT was to be determined by the dose of Epoetin alfa received during chemotherapy and prior to randomization (i.e., 30,000 Units, 40,000 Units or 60,000 Units sc qw). Patients who received prior Epoetin alfa at a dose of 80,000 Units sc every two weeks will receive a starting dose of 40,000 Units weekly. The first dose must be given within 7-14 days after the last dose received during their final chemotherapy cycle.

PROCRIT treatment group who <u>did not</u> receive prior Epoetin alfa: The starting dose of PROCRIT was to be 40,000 Units sc weekly. The first dose was to be given within 2 weeks after the first day of the final chemotherapy cycle.

No/Delayed PROCRIT treatment group: Initial visits with no treatment were to be done weekly. If the Hb level remains > 10 g/dL for 4 consecutive weeks, the patient was to be followed every other week after that, for up to 13 weeks on study. If the Hb level decreased to ≤ 10 g/dL, PROCRIT was to be initiated at a dose of 40,000 Units sc weekly, with a weekly-follow-up schedule.

Transfusion of red blood cells was permitted during the study at the discretion of the investigator, according to the predefined transfusion trigger at each site.

During the study, all patients were to receive ferrous sulfate at a dose of 325 mg by mouth (po) once a day or an equivalent formulation as tolerated (unless there is a contraindication).

5. STUDY POPULATION

252 patients with non-myeloid malignancies and persistent chemotherapy-induced myelosuppression (anemia) (Hb ≥ 11 g/dL and ≤ 12 g/dL) were to enter this study. Patients treated with Epoetin alfa (30,000 Units, 40,000 Units or 60,000 Units sc qw) during chemotherapy were to have received weekly Epoetin alfa therapy with their chemotherapy for a minimum of 4 weeks, including 1 dose received during the final chemotherapy cycle. Patients treated with 80,000 Units of Epoetin alfa during chemotherapy were to have received at least 3 doses of Epoetin alfa every other week with their chemotherapy, including 1 dose received during the final chemotherapy cycle. **Only 2 patients were enrolled and randomized, one patient in each arm of the study.**

6. EFFICACY/PHARMACODYNAMIC/SAFETY RESULTS

This study terminated early due to low enrollment. Two patients enrolled, one into each arm of the study. A statistical analysis was not performed thus no statistical data or results were concluded. A formal safety analysis was not performed for the 2 patients enrolled in this study. Adverse events were

reported in the only patient treated with PROCRIT. All adverse events for this patient (mild diarrhea, mild vomiting, mild nasopharyngitis, mild skin irritation and moderate gastroesophageal reflux disease) resolved without sequelae. An adverse event of mild abdominal tenderness occurred for a duration of 1 day in one untreated patient. This AE was not related to PROCRIT and resolved without sequelae.

No Deaths were reported, nor were any Serious Adverse Events reported during the course of this trial.

7. CONCLUSIONS

This study terminated early due to low enrollment. Two patients enrolled, one into each arm of the study. Due to low enrollment, a statistical analysis was not performed thus no statistical data or results were concluded.

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