ORTHO BIOTECH

Clinical Study Synoptic Report

AN OPEN-LABEL EXTENSION (TO PROTOCOL EPOCKD2001) OF PROCRIT® (EPOETIN ALFA) MAINTENANCE THERAPY ADMINISTERED EVERY SIX WEEKS (Q6W) FOR THE TREATMENT OF ANEMIA OF CHRONIC KIDNEY DISEASE (CKD)

Protocol Addendum EPOCKD2001, CR003397 (Q6W arm); Phase IIIb

(Epoetin alfa)

PRINCIPAL INVESTIGATOR:
Multi-Center Study

DATE STUDY INITIATED:
16 August 2006 (First Subject Enrolled)

DATE STUDY CLOSED:
06 February 2007 (Last Subject Last Visit)

Issue/Report Date: 28 April 2008
Department: Centocor Ortho Biotech Services LLC

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

1. PROTOCOL TITLE

An Open Label Extension (To Protocol EPOCKD2001) of PROCRIT® (Epoetin Alfa) Maintenance Therapy Administered Every Six Weeks (Q6W) for the Treatment of Anemia of Chronic Kidney Disease (CKD)

2. OBJECTIVES

The primary objective of this open-label extension is to evaluate if PROCRIT® 40,000 U SC given every six weeks can maintain hemoglobin (Hb) within the range of 11-12 g/dL in subjects with anemia of CKD.

3. INVESTIGATOR(S)

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4. STUDY DESIGN

This was an open-label, single arm, multicenter extension of the Main Protocol EPOCKD2001 in pre-dialysis subjects with anemia of CKD.

Up to sixty (60) subjects with CKD who had completed the Main Protocol and had an entry Hb level between 11-12 g/dL were eligible to participate in this open-label extension.

This open-label extension had a Screening Phase of up to one week, an open-label Treatment Phase of 12 weeks, and a Post-treatment Follow-Up phase of 6 weeks.

Screening procedures for this open-label extension were to be completed at the Week 17/Completion Visit in the Main Protocol EPOCKD2001.

Subjects were evaluated for eligibility during the Screening Phase. During the Treatment Phase, Hb was to be measured weekly and all subjects were to receive a first dose of PROCRIT® 40,000 U SC (Week 18). A second dose of PROCRIT® 40,000 U SC was to be administered six weeks after the first dose (Week 24). A third and final dose of PROCRIT® 40,000 U SC was to be administered six weeks after the second dose (Week 30). Subjects were to

receive a maximum of 3 doses. A six-week follow-up period was required after administration of the third dose.

Hematology, serum chemistry, and iron status were to be assessed at intervals throughout the open-label extension. The number of units of blood transfused, pre-transfusion Hb level, and the reasons for transfusion were to be collected. Clinical laboratory results, vital signs, and the incidence and severity of adverse events were to be monitored during the open-label extension.

5. DOSAGE AND ADMINISTRATION

PROCRIT® was to be administered by a healthcare professional.

The starting dosage of PROCRIT® 40,000 IU SC was to be administered at Baseline/Week 18. A second PROCRIT® dose 40,000 IU SC was to be administered 6 weeks after the first dose (Week 24). Similarly, a third PROCRIT® dose 40,000 IU SC was to be administered 6 weeks after the second dose (Week 30). Subjects were to receive a maximum of 3 doses. A six-week follow-up period was required following administration of the third dose.

If, at the time of the second or third dosing visits the subject's Hb was > 12 g/dL or the rate of rise during the preceding one or two consecutive weeks was > 1 g/dL, the dose was to be reduced as follows:

- 40,000 Units SC Q6W to 30,000 Units SC Q6W
- 30,000 Units SC Q6W to 20,000 Units SC Q6W

Dosing was not to be increased during the open-label extension. If Hb fell below 10 g/dL at any time or the subject required transfusion, the subject was to be withdrawn from the open-label extension.

6. STUDY POPULATION

6.1. Planned Population

Sixty (60) subjects who participated and completed study EPOCKD2001 (Main Protocol) were potentially eligible to enter this open-label extension.

Subjects who had a Hb value between 11-12 g/dL 4 weeks after last Q4W injection, or 2 weeks after last Q2W injection, or one week after last QW

injection according to the Main Protocol were eligible to enter the open-label extension if they met the other inclusion-exclusion criteria.

Subjects should have been $\geq$ 18 years of age and have had a GFR between 15 and 90 mL/minute/1.73m^2. Subjects would not have been eligible if they were receiving or scheduled to receive dialysis, immunosuppressive drugs, or had congestive heart failure (NYHA Class IV) at entry into the open-label extension. Subjects with a history of or current diagnosis of active blood dyscrasias, hematological disorders, liver disease, seizures, and thrombovascular events (TVEs) were to be excluded. Subjects with iron deficiency or overload, uncontrolled hypertension (HTN) or who had been unresponsive to previous erythropoietic therapy were also to be excluded from the open-label extension.

6.2. Actual Population

Four subjects were randomized to the open label extension; one from the 20,000 IU Q2W arm, two from the 20,000 IU Q4W arm, and one from the 40,000 IU Q4W arm of the Main Protocol. This extension was initiated toward the completion of the main protocol when few subjects remained in the trial. Low enrollment resulted from this limited pool of subjects. Of the 4 subjects enrolled, 3 completed and 1 discontinued (Subject 515-106) the extension study.

7. EFFICACY/PHARMACODYNAMIC RESULTS

Due to the small number of enrolled subjects, a formal efficacy analysis was not performed. Hemoglobin results for all subjects are included in Appendix 1.3, Listing 5.

8. SAFETY RESULTS

8.1. Adverse Events

Adverse Events were reported in all 4 study subjects. No adverse events were considered to be related to PROCRIT. No adverse events led to early withdrawal from the study. Note – Subject 515-106 experienced GI bleeding and was withdrawn from the study. However, the reason for withdrawal was due to receiving a transfusion. Adverse event listings for all subjects are included in Appendix 1.3, Listings 6 and 15-17.

8.2. Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

No deaths were reported during the course of this trial. Subject 515-106 experienced a Serious Adverse Event (SAE) of Gastrointestinal Bleeding. The subject received two transfusions of packed red blood cells over the course of two days while hospitalized, and recovered without sequelae. This SAE was not considered to be related to PROCRIT. A full narrative on this subject appears in Appendix 1.4. No other significant adverse events were reported.

8.3. Clinical Laboratory Evaluation

There were no clinically significant changes in laboratory evaluations. Laboratory testing results are included in Appendix 1.3, Listing 19.

8.4. Other Safety Observations

There were no clinically significant changes in vital signs during the study period. Vital signs are listed in Appendix 1.3, Listing 12.

No doses of study drug were held due to a rise of Hb > 1 g/dL within 2 weeks. Nor were any doses of study drug held for Hb > 12 g/dL.

9. CONCLUSIONS

Due to the small number of subjects enrolled, no conclusions could be drawn.

10. REFERENCES

Please refer to Main Protocol for references.

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