PR02-32-054 SYNOPSIS

NAME OF SPONSOR/COMPANY: Ortho Biotech Clinical Affairs, LLC NAME OF FINISHED PRODUCT: PROCRIT® NAME OF ACTIVE INGREDIENT(S): Epoetin alfa	INDIVIDUAL STUDY TABLE REFERRING TO PART OF THE DOSSIER Volume: Page:	(FOR NATIONAL AUTHORITY USE ONLY)

Protocol No.: PR02-32-054

Title of Study: An Open-Label Pilot Study to Assess Disability in Anemic Elderly Patients with Chronic Kidney Disease Receiving PROCRIT® (Epoetin alfa)

Principal Investigator: Not applicable

Publications (References): None

Study Initiation/Clinical Cutoff Dates: 07-Nov-2003 to 01-Sep-2005	**Phase of development:** 4

Objectives:

The primary objective of this study was to evaluate changes in disability in elderly patients (≥65 years of age) with chronic anemia (hemoglobin [Hb] <12.0 g/dL) due to chronic kidney disease (creatinine clearance >30 mL/min and <60 mL/min) receiving weekly (qw) subcutaneous (sc) PROCRIT® therapy.

The secondary objectives of this study were:

- to assess the effectiveness of qw sc PROCRIT dosing in achieving target Hb levels (≥13.0 to <14.0 g/dL) in elderly patients with anemia due to chronic kidney disease (CKD),
- to assess the effect of qw sc PROCRIT dosing on transfusion utilization in elderly patients with anemia due to CKD,
- to assess the safety of qw sc PROCRIT dosing in elderly patients with anemia due to CKD
- to evaluate the incidence of anti-erythropoietin antibodies (Ab) at Baseline, Week 9, and at end of study/early withdrawal in study patients who have received a minimum of 2 or more doses of PROCRIT over at least a 1-month period,
- to assess/evaluate change from baseline in Quality of Life (QoL) using the Medical Outcomes Study Short Form-36 (SF-36) in elderly patients with anemia due to CKD who are receiving qw PROCRIT dosing,
- to evaluate cognitive/executive function in elderly patients with anemia due to CKD who are receiving qw PROCRIT dosing.

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Methodology: This was a prospective, open-label, nonrandomized, multicenter pilot study. Assessments of physical disability, QoL, cognitive function, laboratory values, adverse events, vital signs, and transfusion information were obtained during the study. The assessments of physical disability included the 6-Minute Walk Test (6-MWT) and the Short Physical Performance Battery (SPPB) Summary Score. The QoL and cognitive function assessments included the SF-36 and the Trail Making Test (TMT), respectively.

Eligible patients with Hb levels <12.0 g/dL were enrolled and began treatment with qw sc PROCRIT at a starting dose of 5,000 units (Baseline/Week 1). The dose of PROCRIT was adjusted every 4 weeks until the target Hb level of 13.0 to 13.9 g/dL was achieved. If, after 4 weeks of dosing the Hb level was <13.0 g/dL, the qw PROCRIT dose was increased to the next dosing level. Dose increases were made according to fixed dose levels of 10,000, 20,000, and 40,000 U. No dose decreases were allowed until Week 3.

If at any time during the study the patient's Hb increased to ≥14.0 g/dL, PROCRIT dosing was to be temporarily withheld; Hb levels were monitored weekly. PROCRIT dosing was resumed when the patient's Hb level decreased to <13.0 g/dL; the PROCRIT dose was reduced by 25% of the patient's previous dose. Increases could then be considered at the next scheduled Dose Adjustment Evaluation (Weeks 5, 9, and 13).

In addition, if at any time during the study the patient's Hb level rose to >1.3 g/dL in a 2-week period, the PROCRIT dose was to have been reduced by 50% of the patient's previous dose. Increases could then be considered at the next scheduled Dose Adjustment Evaluation (Weeks 5, 9 and 13).

The total duration of this study was 20 weeks, a 16-week double-blind treatment phase and 4-week post-treatment follow-up phase. Patient screening was within 7 days prior to receiving the first dose of PROCRIT.

Number of Patients (planned and analyzed): This study was planned for an enrollment of approximately 30 patients. Thirteen patients were enrolled. No statistical analyses were performed.

Diagnosis and Main Criteria for Inclusion: Patients ≥65 years of age with chronic anemia (Hb <12.0 g/dL) due to moderate CKD (creatinine clearance of >30 mL/min and <60 mL/min) and not anticipated to receive dialysis within the next 4 months were eligible for enrollment.

Test Product, Dose and Mode of Administration, Batch Number: PROCRIT (Epoetin alfa) was formulated as a sterile, colorless, buffered solution containing 2.5 mg/mL human serum albumin. Each vial of PROCRIT contained approximately 1.1 mL of study drug in water for injection. Three formulations of PROCRIT were utilized:

- 10,000 U/mL Preservative-Free Vial: 1mL
- 20,000 U/mL Preserved Vial (containing 1% benzyl alcohol as the preservative)
- 40,000 U/mL, Preservative-Free Vial: 1mL

Batch Numbers: PROCRIT 10,000 u/mL vials Lot P008363; PROCRIT 20,000 U/mL vials Lot P008873, P009677, P010983, and P032913; PROCRIT 40,000 U/mL vials Lots P007983, P010967, P010968, P029309, P032441, and P032502.

Reference Therapy, Dose and Mode of Administration, Batch Number: Not applicable

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Criteria for Evaluation:

The study was terminated early due to slow enrollment after 13 patients had been enrolled. All patients who had received PROCRIT during the study were identified in the listings.

Efficacy

The primary efficacy outcome was the Minimal Clinically Meaningful Difference (MCMD) for the SPPB and the 6-MWT, which were used as surrogate markers of disability. The surrogate markers included the distance completed during the 6-MWT, the summary score from the SPPB, as well as the constituent variables of the SPPB (SPPB-Balance, SPPB-Gait, and SPPB-Chair Stand Test). The SPPB MCMD was defined as an increase in the SPPB summary score of 2 and the 6-MWT MCMD was defined as an increase of 50 meters in the 6-MWT.

The secondary efficacy outcomes were measured by Hb results, transfusion utilization, incidence of anti-erythropoietin (EPO) Ab, QoL assessment, cognitive/executive function assessment, and serum transferrin receptor levels. The study was terminated prematurely; therefore, only the primary efficacy data were summarized (i.e., descriptive statistics, listings).

Results for the secondary outcome data were listed (i.e., no summaries were performed).

Safety

Adverse events (AEs) were classified according to the product-specific Medical Dictionary for Regulatory Activities (MedDRA) dictionary version 8.0. All AEs were listed. Laboratory results were listed; change from baseline was not calculated. All vital sign results were listed; change from baseline was not calculated. All physical examination results for each body system were listed, as was the existence of a change compared to baseline for each body system identified on the physical examination case report form page.

Statistical Methods

This study was terminated prematurely due to slow enrollment; therefore, only an abbreviated examination of the efficacy and safety objectives was undertaken. Apart from descriptive summaries of selected demographic and baseline characteristics and selected efficacy assessments, no summary analyses were performed for this study. Efficacy and safety objectives were further examined using patient listings of study data. No formal assessments of change over time or formal statistical testing were undertaken.

SUMMARY – CONCLUSIONS

EFFICACY RESULTS: No formal statistical analysis of the data was performed. Thirteen patients were enrolled and 12 (92%) patients completed the study. Twelve of 13 (92%) patients achieved the target Hb levels (≥13.0 to <14.0 g/dL) and no patient required a transfusion during the course of this study. No anti-EPO antibody (Ab) levels were detected during the study.

SAFETY RESULTS: Nine of 12 (75%) patients reported at least one AE during the study. A total of 39 AEs were reported; 16 were mild, 19 were moderate, and 4 were severe, as determined by the investigator. One AE was considered by the investigator as definitely related to study drug (serum ferritin decreased), 1 AE was assessed as probably related (hypertension), and 1 AE was assessed as possibly-related (blood pressure inadequately controlled (2 occurrences in 1 patient). No deaths occurred during the course of this study. Two patients had at least one event considered by the investigator as drug related: Patient 005-502 had serum ferritin decreased, which was considered to be definitely related, and hypertension, which was considered possibly related to study drug. Patient 003-301 experienced uncontrolled blood pressure, which was considered by the investigator as possibly related to study drug. As expected for this study population of elderly patients with CKD, 5 of 13 (38%) patients had low Hb levels deemed clinically significant by the investigator and 4 of 13 (31%) of patients had high serum creatinine levels deemed clinically significant by the investigator. There were no AEs of loss of effect or pure red cell aplasia.

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CONCLUSIONS:

- Due to the early termination of the study and the limited number of patients enrolled, no conclusions about the efficacy of PROCRIT on changes in disability in elderly patients could be made.
- All 12 patients completing the study achieved the target Hb level of ≥13.0 to <14.0 g/dL level. No patient required a blood transfusion during the study.

No anti-EPO antibody levels were detected during the study.

- PROCRIT was generally safe and well tolerated. The incidence of AEs, clinical laboratory tests, vital signs, and other safety assessments suggested no clinically meaningful changes and findings were consistent with expected findings in this population of anemic elderly patients with CKD. There were no instances of PRCA or LOE.

Date of the report: 06 December 2006

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