SYNOPSIS

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

Protocol No.: PR04-29-007

Title of Study: A Randomized, Open Label Study Assessing the Efficacy of Initiating PROCRIT® Dosing at Q2W vs. PROCRIT® Dosing at QW in Anemic HIV-infected Subjects

Publications: none

Investigators and Study Centers: 18 study centers in the United States.

First Subject Consent / Last Subject Completed: 05 January 2006 / 20 September 2006	**Phase of development:** 2

Objectives: The primary objective was to evaluate if initiating PROCRIT® every 2 weeks (Q2W) dosing was as effective as initiating PROCRIT® once weekly (QW) dosing in increasing hemoglobin (Hb) levels in anemic (< 12.0 g/dL) human immunodeficiency virus (HIV)-infected subjects.

The secondary objective was to assess the safety and tolerability of Q2W dosing and QW dosing.

Methodology: This was a 2-arm, randomized, open-label, multi-center study. The screening phase started 2 weeks prior to the first dose of PROCRIT® (Baseline/Day 1). HIV-infected subjects who had Hb levels of < 12.0 g/dL and were on stable antiretroviral (ARV) treatment regimens were screened for study eligibility. Subjects who satisfied eligibility criteria were randomly assigned in a 1:1 ratio to receive PROCRIT® 40,000 U subcutaneous (SC) injections either QW or Q2W. Hemoglobin levels were taken weekly for all subjects during the treatment phase of the study. The total duration of this study was 14 weeks, including a 2-week screening phase and a 12-week treatment phase.

Criteria for Evaluation:

The study was terminated early because of slow enrollment progress after 29 patients had been randomized. Thus, only abbreviated statistical summaries were generated and no statistical hypothesis testing was conducted.

Efficacy: The primary efficacy endpoint was the change in Hb from Baseline/Day 1 to the end of the study (Week 12). The secondary efficacy endpoints were the following: changes in Hb over time; the proportion of subjects reaching a Hb of > 13.0 g/dL; the time to the first Hb of > 13.0 g/dL; the proportion of subjects with < 0, 0 to < 1, 1 to < 2, 2 to < 3, and ≥ 3 g/dL of Hb increase; the proportion of subjects requiring dose escalation; the cumulative PROCRIT® dose from Baseline/Day 1 to the end of the study (Week 12); and the cumulative PROCRIT® dose from Baseline/Day 1 to the first Hb value of > 13.0 g/dL.

Safety: Safety endpoints included adverse events (AEs), clinical laboratory tests, vital signs, and physical examination findings.

Statistical Methods: Because the study was terminated early, an abbreviated examination of the efficacy and safety objectives was performed. All data were listed by subject. Descriptive statistics (n, mean, median, standard deviation, minimum, and maximum) were produced for demographics and baseline characteristics and selected safety and efficacy assessments, including Hb, PROCRIT® dosing, and AE data. No formal statistical comparisons were performed. Efficacy data were summarized for the modified intent-to-treat (mITT) and safety populations, and safety data were summarized for the safety population. The mITT population was defined as all randomized subjects who received at least 1 dose of study drug and had at least 1 post-randomization Hb measurement, and excluded subjects with Hb > 13.0 g/dL at baseline. The safety population included all randomized subjects who received at least 1 dose of study drug.

SUMMARY:

EFFICACY RESULTS: In the mITT population (excluding 2 subjects with Hb > 13.0 g/dL at baseline), mean Hb values at baseline were 11.4 g/dL in the QW group and 10.6 g/dL in the Q2W group. The mean change from baseline to Week 12 was similar in the QW (0.6 g/dL) and the Q2W group (0.9 g/dL). In the QW group, the mean Hb rapidly increased from 11.4 g/dL at baseline to 13.5 g/dL at Week 5, decreased to 12.1 g/dL at Week 9, and remained at that level until the end of the study. In the Q2W group, mean Hb levels increased steadily from

10.6 g/dL at baseline to a peak of 11.7 g/dL at Week 11.

The percentage of subjects reaching Hb > 13.0 g/dL was greater in the QW group (92%) than in the Q2W group (46%). In addition, subjects in the QW group tended to have larger maximum increases in Hb compared with the Q2W group. Of the 13 subjects in the QW group, 10 (77%) achieved ≥ 2 g/dL increases in Hb by Week 12, compared with 5 of 13 subjects (38%) in the Q2W group. All subjects in the QW group had increases in Hb during the study, while 2 subjects (15%) in the Q2W group had decreases in Hb during the study.

Six subjects (46%) in the Q2W group and 3 subjects (23%) in the QW group required dose escalation (to 60,000 U) during the study.

The mean cumulative dose was similar in the QW group (223,846 U) and in the Q2W group (214,615 U).

SAFETY RESULTS: There were no deaths, serious adverse events (SAEs), thrombotic vascular events (TVEs), or withdrawals due to AEs during the study. In the Q2W group, all AEs were considered not related to study drug. Three subjects in the QW group had possibly related AEs, including thrombocytopenia, myalgia, headache, and hypertension. The percentage of subjects with AEs was greater in the QW group (85%) than in the Q2W group (43%).

The most frequently reported events were infections and infestations (39% of subjects in the QW group and 21% in the Q2W group), gastrointestinal disorders (23% QW and 7% Q2W), and blood and lymphatic system disorders (15% QW and 7% Q2W).

CONCLUSIONS:

The study was terminated early because of slow enrollment progress, and insufficient numbers of subjects were enrolled to conduct meaningful statistical analyses. Based on the limited data available, the Hb increase at the end of the 12-week study period and the total cumulative PROCRIT® dose were similar in the two groups. In the Q2W group, fewer subjects exceeded an Hb level of > 13 g/dL and fewer subjects required dose reduction or a dose withheld.

Overall, PROCRIT® was well tolerated. There were no deaths, SAEs, TVEs, or withdrawals due to AEs reported during the study.

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