PROCRIT® (epoetin alfa)
Once Every-Three-Weeks Dosing in Chronic Kidney Disease

SUMMARY

- In the PROCRIT for Maintenance Phase Treatment of Patients with Anemia due to Chronic Kidney Disease (PROMPT) study (N=519), hemoglobin (Hb) levels ≥11.0 g/dL were maintained in ~90% of patients receiving either epoetin alfa (EPO) 10,000 international units (IU) once weekly (QW) or 20,000 IU every 2 weeks (Q2W), and >75% of patients administered EPO 30,000 IU once every 3 weeks (Q3W) or 40,000 IU once every 4 weeks (Q4W). The most frequent adverse events (AEs) were hypertension (HTN), peripheral edema, urinary tract infection, and headache.[1]
- An additional prospective study[2] and post hoc analyses of PROMPT[3-5] have examined the efficacy and safety of EPO administered Q3W.
- Post hoc analyses of the PROMPT study[1] have been published.[3-5] In addition, Q3W EPO dosing in anemic chronic kidney disease (CKD) patients not on dialysis has also been evaluated in other retrospective studies and meta-analyses.[6-9]

CLINICAL DATA

The following studies evaluated the utilization of EPO as maintenance therapy administered at various extended dosing intervals, including up to Q3W and beyond.

Q3W Maintenance EPO

Provenzano et al (2005)[1] evaluated if extended EPO dosing schedules of up to Q4W were as effective as QW dosing in maintaining Hb levels ≥11 g/dL in CKD patients not on dialysis (N=519).

Study Design/Methods

- This was a prospective, randomized, open-label, multicenter, 16-week study.
- The PROMPT study included CKD patients (serum creatinine: 1.5-6.0 mg/dL for females, 2.0-6.0 mg/dL for males) receiving maintenance EPO for treatment of anemia for ≥2 months.
- Patients were randomized to receive 1 of 4 dosing regimens subcutaneously (SC) for up to 16 weeks: 10,000 IU SC QW; 20,000 IU SC Q2W; 30,000 IU SC Q3W; or 40,000 IU SC Q4W.
- Dose reductions were allowed during the study, but dose escalations were not.

Results

Patient Characteristics

- Mean±standard deviation (SD) baseline Hb and glomerular filtration rate (GFR) for all patients were 11.9±0.8 g/dL and 21.1±8.0 mL/min/1.73m^2, respectively.

Efficacy

- Of the 519 patients enrolled, 413 (79.6%) completed the 16-week study.
- The results of the study are presented in the Table: Study Results.

Study Results[1]

Epoetin Alfa	QW 10,000 IU	Q2W 20,000 IU	Q3W 30,000 IU	Q4W 40,000 IU
n=445[a]	108	114	114	104
Mean baseline Hb, g/dL (95% CI)	11.9 (11.7-12.0)	11.9 (11.8-12.0)	11.9 (11.8-12.1)	11.9 (11.8-12.0)
Mean final Hb, g/dL (95% CI)	12.2 (12.0-12.4)	11.9[b] (11.7-12.2)	11.2 (11.0-11.4)	11.4[b] (11.1-11.7)
% of patients maintaining Hb ≥11 g/dL	93.5	89.5	77.2	76.0

Abbreviations: CI, confidence interval; Hb, hemoglobin; IU, international units; QW, once weekly; Q2W, every 2 weeks; Q3W, every 3 weeks; Q4W, every 4 weeks.
[a]Five patients did not have a final Hb measurement and are not included in the above analysis.
[b]Significant 1-sided *P* value testing noninferiority from QW (defined as greater than -10% of the final mean Hb measurement of the QW group).

- Approximately 90% of patients administered EPO Q2W and >75% of patients administered EPO Q3W or Q4W maintained Hb levels ≥11 g/dL.
- Difference in mean final Hb between QW and both Q2W and Q4W met the criteria for noninferiority (*P*<0.001 and *P*=0.024, respectively) but did not meet criteria for noninferiority between Q3W and QW (-1.0 g/dL; *P*=0.084, 1-sided). The intent-to-treat analysis showed that all 3 groups were noninferior to the QW group.
- GFR remained stable during the 16-week maintenance phase in all dosing groups and 14 patients progressed to dialysis.

Safety

- The incidence of AEs was low and comparable across the study groups.
- The most frequent AEs reported by at least 5% of patients in any group included HTN (6.8%), peripheral edema (5.7%), urinary tract infection (4.3%), and headache (3.3%).
- Clinically significant AEs possibly related to vascular thrombosis were reported in 13 (2.5%) of patients.
- Sixteen (3.1%) of patients withdrew from the study due to AEs.

Petroff et al (2001)[2] evaluated various extended dosing frequencies of EPO in a community-based CKD clinic over a 1-year period (N=64).

Study Design/Methods

- This was a prospective study.
- All patients received QW EPO (100-150 IU/kg/week) until the target Hb (11-12 g/dL) was achieved.
- Depending on the response to QW dosing, patients were titrated to 1 of 4 EPO dosing intervals: QW, Q2W, Q3W, or Q4W.
- Anemia was defined as a Hb <10 g/dL.

Results

Patient Characteristics

- Diabetic nephropathy (43.8%) and hypertensive nephropathy (23.4%) were the most common causes of CKD.
- Mean Hb at baseline was 9.07 g/dL.

Efficacy

- Mean final Hb levels for patients who received EPO QW (n=10), Q2W (n=19), Q3W (n=7), and Q4W (n=28) were 10.27 g/dL, 11.10 g/dL, 11.71 g/dL, and 12.03 g/dL, respectively. These were significant increases from baseline Hb values of 9.73 g/dL, 9.71 g/dL, 9.72 g/dL, and 9.71 g/dL, respectively.
- Final Hb was significantly higher for the Q4W group compared with the other groups ($P<0.05$ in each case).
- Increasing dosing intervals correlated with decreasing monthly EPO requirements and higher Hb levels. Average monthly EPO dose was significantly lower for those receiving Q4W dosing compared with patients with the more frequent dosing intervals (17,542 IU vs 57,028 IU QW; 44,886 IU Q2W; 28,072 IU Q3W; $P<0.05$ in each case).

LITERATURE SEARCH

A literature search of MEDLINE®, Embase, BIOSIS Previews®, Derwent Drug File databases (and/or other resources, including internal/external databases) was conducted on 13 June 2024. To streamline this document and provide the most relevant information, only prospective studies have been summarized above. Post hoc analyses, retrospective studies, and meta-analyses have been cited in the Summary section.

REFERENCES

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