Intravenous and Subcutaneous Administration of Peginesatide and Epoetin in U.S. and Non-U.S. Patients on Dialysis

Sheila Doss-McQuitty[1], Hong Tang[2], Alex Yang[2], Min-jia Chen[2], Sandra Tong[2]

[1]Satellite Healthcare, San Jose, CA; [2]Affymax, Inc., Palo Alto, CA

BACKGROUND

- Lower ESA dose requirements have been reported with subcutaneous (SC) vs intravenous (IV) epoetin in patients on dialysis, but informal patient-survey data suggest that patients who have received drug by both routes prefer IV dosing.[1]
- Due to bundling, the added pressures to save costs may increase use of SC dosing for epoetin.
- Peginesatide is a synthetic, pegylated, peptide-based ESA recently approved in the U.S. for the once-monthly treatment of anemia due to CKD in adult patients on dialysis.
- Peginesatide demonstrated comparable safety and efficacy to epoetin in hemodialysis (HD) patients in two Phase 3 randomized, active-controlled, open-label, noninferiority trials (EMERALD 1,2).[2]

OBJECTIVE

- Prespecified analysis to compare IV and SC dosing of peginesatide and epoetin in HD patients.

METHODOLOGY

- Data were pooled from two Phase 3, randomized, active-controlled, open-label trials assessing the safety and efficacy of peginesatide once monthly compared with epoetin 1-3 times weekly in HD patients (EMERALD 1 and 2).
- For every 2 patients randomized to peginesatide, 1 patient was randomized to epoetin.
- Key inclusion criteria:
  - HD ≥3 months
  - IV or SC epoetin ≥8 weeks (stable dose ≥4 weeks) prior to randomization
  - Mean hemoglobin (Hb) ≥10.0 g/dL and ≤12.0 g/dL during screening
  - Transferrin saturation (TSAT) ≥20% and ferritin ≥100 ng/mL
- Patients received treatment for ≥52 weeks
  - Peginesatide starting dose based on total weekly epoetin dose during the last week of the screening period.
  - Doses titrated to maintain target Hb levels of 10-12 g/dL, consistent with dosing guidelines in effect when the studies were conducted.

METHODOLOGY (Cont.)

- The studies were conducted in the United States (EMERALD 1 and 2) and Europe (EMERALD 2).[2]
- Patients received study drug via the same administration route used during the last week of the screening period:
  - IV in EMERALD 1
  - IV or SC in EMERALD 2

RESULTS

- Baseline characteristics are shown in Table 1.

Table 1. Baseline Characteristics

	U.S. Patients		Non-U.S. Patients	
	Peginesatide (n = 853)	Epoetin (n = 436)	Peginesatide (n = 213)	Epoetin (n = 106)
Age, mean, y	58	58	58	59
Men, %	57	55	63	55
Race, %				
White	49	45	95	97
Black	46	48	3	1
Causes of CRF, %				
Pyelonephritis	0.2	0.5	16	24
Diabetes	43	46	15	11
Hypertension	37	34	13	8
>1 y on dialysis, %	90	89	79	76
TSAT,* %	30 (10.3)	29 (9.4)	33 (15.4)	34 (17.6)
Ferritin,* ng/mL	686 (348.3)	674 (363.6)	921 (738.1)	900 (580.4)
BMI,* kg/m^2	30 (7.7)	29 (7.5)	26 (5.2)	26 (4.8)

*Values are mean ±standard deviation.

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- Duration of patient exposure to study drug was similar in the peginesatide and epoetin groups, respectively:
  - 64 and 67 weeks in EMERALD 1
  - 64 and 63 weeks in EMERALD 2.

Table 2. Weight-Adjusted Doses of Peginesatide and Epoetin

Evaluation Period	Peginesatide		Epoetin	
	SC	IV	SC	IV
U.S. Patients, n	33	683	15	374
Median*	0.08	0.07	90	121
Interquartile range	0.03-0.14	0.04-0.12	46-207	67-222
Non-U.S. Patients, n	62	138	27	61
Median*	0.06	0.05	63	72
Interquartile range	0.04-0.10	0.03-0.08	32-99	43-99

*Median of the mean dose patients received during the evaluation period; units are mg/kg/injection for peginesatide and U/kg/wk for epoetin.

- Epoetin dosing was lower with SC than IV, whereas the same trend was not seen with peginesatide (Table 2). ESA dosing was higher for U.S. than non-U.S. patients.
- Despite this, similar Hb levels were achieved for SC and IV dosing during the evaluation period with peginesatide and epoetin:

U.S.

—Peginesatide: 11.3 g/dL (SC) and 11.1 g/dL (IV)
—Epoetin: 11.2 g/dL (SC) and 11.2 g/dL (IV)

Non-U.S.

—Peginesatide: 10.9 g/dL (SC) and 11.2 g/dL (IV)
—Epoetin: 10.8 g/dL (SC) and 10.9 g/dL (IV)

- TSAT and ferritin levels are shown in Table 3.

Table 3. TSAT and Ferritin During the Evaluation Period

	U.S. Patients		Non-U.S. Patients	
	Peginesatide	Epoetin	Peginesatide	Epoetin
No. of patients	662	343	178	83
TSAT,* %	35. 1 (13.5)	32.1 (13.0)	33.9 (16.7)	26.0 (12.6)
No. of patients	663	344	179	83
Ferritin,* ng/mL	676.0 (352.0)	738.4 (425.4)	756.3 (513.9)	723.5 (428.12)

*Values are mean ±standard deviation.

- Mean total IV iron through week 52 in the peginesatide and epoetin groups, respectively, was:
  - 2159 mg and 2413 mg (U.S.)
  - 2617 mg and 2604 mg (non-U.S.)

CONCLUSIONS/DISCUSSIONS

- Peginesatide doses were not lower with SC compared with IV administration in these patients.
- Epoetin doses were lower with SC compared with IV administration
- Although the analysis is limited by the relatively small patient numbers for SC dosing, the epoetin finding is consistent with the literature.[1]
- Despite similar Hb values in the range of 10-12 g/dL, IV and SC ESA doses in US patients were higher than in non-US patients, which may reflect differences in underlying comorbidities and iron use for these populations.
- Availability of once-monthly ESA with similar SC and IV dosing may provide another treatment option for dialysis patients with anemia due to CKD.

References: 1. Kaufman et al. NEJM 1998; 339:578-583. 2. Schiller et al. ASN 2010.

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