American Society of Clinical Oncology
2006 ASCO Annual Meeting
June 2-6, 2006, Atlanta, Georgia

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General Poster Session, Sat., June 3, 8:00 AM – 12:00 PM

[6579] Darbepoetin alfa for treating anemia in patients with low-risk myelodysplastic syndromes: Exploratory analysis of baseline predictors of response

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Patients (pts) with myelodysplastic syndromes (MDS) often develop anemia, resulting in fatigue and increased transfusions. The erythropoiesis-stimulating agents (ESAs) epoetin alfa and darbepoetin alfa (DA) can raise hemoglobin (Hb) levels in low-risk MDS pts. Baseline (BL) endogenous erythropoietin (eEPO) levels, transfusion history, and FAB sub-type can be predictive factors of response to ESAs (Hellström-Lindberg et al., 2003). Methods: This is an ongoing, fully enrolled (n = 209), phase 2, single-arm, 52-week (wk) study of DA 500 mcg every three weeks (Q3W) for treating anemia (Hb $\leq$ 11 g/dL) in low- or intermediate-risk MDS pts. A planned interim analysis was done after 13 wks (n = 189). The primary endpoint is the proportion of pts with an erythroid response by 13 wks. Other endpoints include change in Hb levels and in FACT-F score from BL. Results are stratified by whether pts received an ESA before enrollment: ESA-naïve (ESA-N) pts vs ESA-treated (ESA-T) pts. Exploratory analyses of the percentage of pts with an erythroid response adjusted by BL eEPO or FAB category were done. Results: Of 130 ESA-N pts, 52% were women, 86% were white, 58% had refractory anemia (RA), 34% had RA with ringed sideroblasts (RARS), 8% had RA with excess blasts (RAEB), and the mean (SD) age was 74.8 (10.1) years. The 59 ESA-T pts had similar demographics. A majority of ESA-N pts had an erythroid response, achieved a target Hb of 11 g/dL, and had a clinically significant rise in FACT-F score; ESA-N pts with lower BL eEPO levels were more likely to have a major erythroid response (Table). A major erythroid response was seen in 50% of pts with RA (n = 111), in 30% of pts with RARS (n = 64), and in 23% of pts with RAEB (n = 13). Of all 189 pts, 78% had an adverse event (AE), 1 had a serious treatment-related AE (hypertension), and none had thrombotic events. Conclusions: These interim results suggest that FAB sub-type and BL eEPO may affect response. Final 13-wk data from all enrolled pts (n = 209) will be shown.

Results After 13 Weeks of DA Treatment	ESA-naive pts, N = 130	Pts with prior ESA treatment, N = 59
Crude % pts transfusion dependent at screening*	2%	10%
Crude % (95% CL) pts with a major erythroid response	49% (40, 58)	24% (14, 37)
Crude % (95% CL) pts with a minor erythroid response	21% (14, 29)	20% (11, 33)
Crude % pts with BL eEPO < 100 mU/mL that had a major erythroid response	61% [n = 82]	25% [n = 40]
Crude % pts with BL eEPO $\geq$ 100 and $\leq$ 500 mU/mL that had a major erythroid response	29% [n = 28]	10% [n = 10]
Crude % pts with BL eEPO > 500 mU/mL that had a major erythroid response	9% [n = 11]	33% [n = 6]
Mean (SD) BL Hb, g/dL	9.8 (0.9) [n = 113]	9.9 (1.2) [n = 48]
Crude % (95% CL) pts who achieved target Hb of 11 g/dL	65% (56, 74) [n = 117]	40% (27, 53) [n = 55]
Mean (SD) change in FACT-F score at wk 13 from BL (available data)	6.2 (11.0) [n = 93]	1.8 (9.5) [n = 37]
*3 or more RBC transfusions in 3 weeks prior to screening		

Citation: *Journal of Clinical Oncology*, 2006 ASCO Annual Meeting Proceedings Part I. Vol 24, No. 18S (June 20 Supplement), 2006: 6579