ERYTHROPOIETIN THERAPY OF MYELODYSPLASTIC SYNDROMES

To the Editor:

In a recently published study, Stein et al[1] report the use of pharmacologic doses of recombinant human erythropoietin (Epo) in the treatment of patients with myelodysplastic syndromes. In this study, as in previous studies,[2-4] Epo was administered intravenously as there was more information available on this at the time of the trial design. In their results and discussion, the investigators question whether subcutaneous dosing might be effective.

We performed a pilot study in six patients with myelodysplastic syndrome who were treated with escalating doses of subcutaneous recombinant human Epo (Chugai-Upjohn, Rosemont, IL). Details of the patients are shown in Table 1. After pretreatment assessment, patients were started on Epo at a dose of 100 U/kg subcutaneously three times per week. After 4 weeks the dose was escalated in nonresponders to 300 U/kg three times per week, and after a further 4 weeks to 600 U/kg three times per week. Patients were maintained on the latter dose for a total of 16 weeks; the total study duration per patient was 24 weeks. Bone marrow examinations were performed before and after therapy and Epo levels were measured both before therapy and after each dose escalation.[5]

As can be seen in the Table, one patient (no. 006) had a clear response to Epo. This individual's hemoglobin normalized completely and his dose had to be held periodically while at the highest level to allow his hemoglobin to fall back to the lower limit of normal. A second individual (no. 005) had a period in the middle of his highest-dose phase when he was transfusion free for approximately 7 weeks, but his overall transfusion requirement did not change. One patient (no. 001), while having no red blood cell response, did in fact have an increase in his platelet count from a level of approximately 1×10^9/L to 10×10^9/L, which held during the course of his treatment. His platelet count promptly fell

Table 1. Patient Characteristics

Patient No.	Age (yr)	Diagnosis	Cytogenetics	Epo Level (mU/mL)		RBC Response	Notes
				Pretherapy	24 h*		
001	64	RA	Abnormal	180	360	No	↑ Platelets
002	73	RA	Normal	150	220	NE	DVT wk 10
004	71	RAEB	Normal	4,360	4,090	No	
005	77	RA	Normal	2,100	—	No	
006	66	RA	Normal	200	780	Yes	
007	69	RA	Abnormal	1,910	—	NE	Removed for noncompliance

Abbreviations: RA, refractory anemia; RAEB, refractory anemia with excess blasts; NE, not evaluable; DVT, deep vein thrombosis; RBC, red blood cell.

*After first dose.

back to the lower level on cessation of therapy. While this increase was not great numerically, it was clinically significant and ameliorated his chronic epistaxis.

Finally, we note that one patient (no. 002) had a documented deep vein thrombosis while on the second week of his highest dose level and Epo was discontinued at that point. Whether this complication was related to Epo is not clear, but given the problems seen in renal patients this is something to be considered.

Overall, the response rate of 25% in the four patients who completed the trial was similar to that reported by Stein et al as well as in previous pilot studies.[1-4] The ability to administer Epo subcutaneously with some responses in this patient population will hopefully encourage others to proceed with larger trials using subcutaneous dosing in myelodysplastic patients.

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