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Poster Session

MYELODYSPLASTIC SYNDROMES POSTER I

Randomized Phase II Study Evaluating the Efficacy and Safety of Romiplostim Treatment of Patients with Low or Intermediate Risk Myelodysplastic Syndrome (MDS) Receiving Lenalidomide.

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Poster Board I-796

Introduction: Romiplostim is a peptibody protein designed to increase platelet production by binding to and activating the thrombopoietin receptor. Low platelet counts in patients with myelodysplastic syndromes (MDS) may be due to the underlying disease or to treatment with disease-modifying agents, and platelet transfusions are often the only treatment for clinically significant thrombocytopenia (CST) or bleeding. This was a phase 2 multi-center, randomized, double-blind, placebo-controlled, dose-finding study that evaluated the effect of romiplostim on the incidence of clinically significant thrombocytopenic events (grade 3 or 4 thrombocytopenia and/or receipt of platelet transfusions) and the safety of romiplostim in patients with low or intermediate risk MDS receiving lenalidomide.

Patients and Methods: Patients who were ≥18 years old, had MDS by bone marrow exam and WHO criteria, had low or Intermediate-1 risk category MDS using the IPSS, and were planning to receive lenalidomide were eligible. Patients were randomized 1:1:1 into treatment groups receiving placebo, 500 µg romiplostim, or 750 µg romiplostim by weekly subcutaneous injections in combination with lenalidomide (one 10 mg capsule by mouth daily for each 28-day cycle). Treatments continued for a total of four cycles.

Results: The median age of the 39 randomized patients was 74 years (range, 39 to 90); 15 (39%) had platelet counts <50 x 10^9/L, and 7 (18%) had del(5q). We report trends due to baseline imbalances between treatment groups, likely due to the limited sample size. The overall incidence rates of CST appeared to be greater in the placebo group than either romiplostim group (Table). In contrast to the placebo patients, median platelet counts remained above 50 x 10^9/L in both the 500 µg and 750 µg romiplostim groups for the treatment period. The incidence of platelet transfusions appeared to be lower in the 500 µg romiplostim group, and the incidence of adverse events was comparable between all of the groups. No deaths were reported during the treatment period. Twelve patients (31%) discontinued the study. Disease progression to AML was reported in 1 patient in the romiplostim 500 µg group. The patient withdrew consent and discontinued the study. No

bone marrow was available to confirm AML by protocol-defined criteria. Fewer lenalidomide dose reductions and delays due to thrombocytopenia were seen in both of the romiplostim treated groups. The proportion of patients who achieved an MDS treatment response was 8%, 36% and 15% for the placebo, 500 µg romiplostim, and 750 µg romiplostim groups, respectively. MDS response rates appeared higher in the romiplostim group, regardless of baseline del(5q) status. Baseline imbalance between groups due to the small sample size limited our interpretation of the data.

Conclusions: Romiplostim appeared to be well-tolerated in low and intermediate risk MDS patients receiving lenalidomide. This preliminary information suggests that romiplostim may reduce the rate of clinically significant thrombocytopenic events in these patients while increasing platelet counts and decreasing the incidence of lenalidomide dose reductions and delays due to thrombocytopenia

	Treatment[a]		
	Placebo	Romiplostim	
		500 µg	750 µg
Baseline Demographics, n (%)	N=12	N=14	N=13
Platelets*			
$< 50 \times 10^9$/L	5 (42)	5 (36)	5 (39)
$\geq 50 \times 10^9$/L	6 (50)	8 (57)	8 (62)
IPSS Score*			
0	4 (33)	4 (29)	5 (39)
0.5	3 (25)	7 (50)	5 (39)
1.0	3 (25)	2 (14)	3 (23)
> 1.0	1 (8)	0	0
Efficacy Endpoints, n (%)			
Clinically Significant Thrombocytopenic Event	8 (67)	4 (29)	7 (54)
Platelet Transfusion	3 (25)	1 (7)	4 (31)
Lenalidomide Dose Reduction/Delay[b]	5 (42)	5 (36)	2 (15)
Overall MDS Response[c]	1 (8)	5 (36)	2 (15)
del(5q) Detected*	0/1 (0)	2/4 (50)	1/2 (50)
del(5q) not Detected*	1/10 (10)	3/9 (33)	1/11 (9)
Adverse events, n (%)	N=11	N=13	N=13
Any Adverse Event	10 (91)	13 (100)	13 (100)
Serious Adverse Events	6 (55)	5 (39)	4 (31)
Treatment-Related Serious Adverse Events	0	1 (8)	0
Deaths	0	0	0

[a] efficacy endpoints include all patients that were randomized; safety endpoints include all patients with at least one dose of romiplostim

[b] Any appropriate dose attenuation due to thrombocytopenia to occur during the treatment period was considered an event

[c] determined by the investigator based on modified MDS IWG guidelines

* Information not available for two ineligible patients

Disclosures: Lyons: *GlaxoSmithKline:* Consultancy, Speakers Bureau; *Johnson&Johnson:* Consultancy, Honoraria, Speakers Bureau; *Celgene:* Consultancy; *Amgen Inc.:* Consultancy, Honoraria, Research Funding, Speakers Bureau. **Off Label Use:** Use of romiplostim to treat Thrombocytopenia in MDS. **Larson:**

Amgen Inc.: Equity Ownership, Research Funding. **Liu:** *Amgen Inc.:* Honoraria, Research Funding. **Hu:** *Amgen Inc.:* Employment, Equity Ownership. **Franklin:** *Amgen Inc.:* Employment, Equity Ownership. **Berger:** *Amgen Inc.:* Employment, Equity Ownership.

Footnotes

* Asterisk with author names denotes non-ASH members.