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Tolerability and hematologic improvement assessed using three alternative dosing schedules of azacitidine in patients with myelodysplastic syndromes.

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Abstract: Background: At a dosing schedule of 75 mg/m2/day SC for 7 days every 4 weeks, azacitidine is an effective and safe treatment (Tx) for patients (pts) with myelodysplastic syndromes (MDS) (JCO 2002; 20:2429). An alternative dosing schedule that eliminates the need for weekend dosing would be more convenient to pts and clinicians. Methods: In this phase II, multicenter, open-label trial, pts with MDS were randomized to 1 of 3 regimens that were repeated every 4 weeks: AZA 5-2-2 (75 mg/m2/day × 5 days, followed by 2 days no Tx, followed by 75 mg/m2/day × 2 days), AZA 5-2-5 (50 mg/m2/day × 5 days, followed by 2 days no Tx, followed by 50 mg/m2/day × 5 days) or AZA 5 (75 mg/m2/day × 5 days). To determine if response/improvement according to International Working Group criteria (Blood 2000; 96:3671) can be maintained after 6 cycles, the study was amended to include a 12-month maintenance comparing AZA 5 every 4 weeks with AZA 5 every 6 weeks. Results: As of Nov. 30, 2006, 138 pts have been randomized to AZA 5-2-2 (n=46), AZA 5-2-5 (n=47) and AZA 5 (n=45). Most pts are RA (43%) or RAEB (30%), based on FAB classification. Of 104 pts who have received =2 cycles of Tx, hematologic improvement (major or minor in at least 1 cell line) occurred in 63% (65) of the patients (Table). Of these pts, 14% had a bi-lineage (AZA 5-2-2: 11%, AZA 5-2-5: 10%, AZA 5: 22%) and 6% had a tri-lineage AZA 5-2-2: 6%, AZA 5-2-5: 7%, AZA 5: 5%) response (based on any improvement). Ongoing pts in the study include AZA 5-2-2: 41% (19/46), AZA 5-2-5: 47% (22/47), and AZA 5: 58% (26/45). No treatment-related mortality has been reported. Most Tx-related grade 3 or 4 events were hematological (AZA 5-2-2: 39%, AZA 5-2-5: 24%, AZA 5: 16%). Updated data, including several pts who have completed at least 6 cycles maintenance, will be available at the time of the meeting. Conclusions: These data indicate that the 3 alternative azacitidine dosing schedules are safe, effective, and similar in efficacy with the FDA-approved regimen.

	AZA 5-2-2 (N=36)[a]		AZA 5-2-5 (N=31)[a]		AZA 5 (N=37)[a]	
Hematologic Improvement	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Hematologic Improvement [b]	19 (53)	40-72	22 (71)	53-86	24 (65)	49-80
Erythroid - Major	15 (42)	26-59	15 (48)	29-65	16 (43)	29-62
Erythroid - Minor	2 (6)	1-17	3 (10)	2-25	2 (5)	1-18
Platelet - Major	8 (22)	15-45	7 (23)	12-43	7 (19)	7-34
Platelet - Minor	0	0-9	0	0-11	3 (8)	2-21
Neutrophil - Major	3 (8)	4-27	4 (13)	4-29	7 (19)	8-34
Neutrophil - Minor	0	0-9	0	0-11	1 (3)	0-14

[a]Patients with at least 56 days on azacitidine; [b]Patients were counted once in the improvement total