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RAPID ONSET OF EFFECTIVENESS WITH THREE ALTERNATIVE AZACITIDINE (AZA) DOSING REGIMENS IN PATIENTS (PTS) WITH MYELODYSPLASTIC SYNDROMES (MDS)

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Background. At a dosing schedule of 75 mg/m2/day SC for 7 consecutive days every 4 weeks, AZA is an effective and safe treatment for pts with MDS (JCO 2002;20:2429). An alternative dosing schedule that eliminates weekend dosing would be more convenient for pts and clinicians. Rapid onset of disease improvement is also important; the time to onset of hematologic improvement (HI) and red blood cell (RBC) transfusion independence (TI) in AZA-treated pts has not been formally studied. Aims. To assess the timing of HI or RBC TI using 3 alternative AZA dosing schedules that avoid weekend dosing. Methods. In this phase II, multicenter, open-label trial, pts with a diagnosis of FAB-defined RA, RARS, RAEB, RAEB-T, or CMMoL were randomized to 1 of 3 AZA alternative-dose regimens that were repeated every 4 weeks for 6 cycles: AZA 5-2-2 (75 mg/m2/day x 5 days, followed by 2 days no treatment, followed by 75 mg/m2/day x 2 days), AZA 5-2-5 (50 mg/m2/day x 5 days, followed by 2 days no treatment, followed by 50 mg/m2/day x 5 days) or AZA 5 (75 mg/m2/day x 5 days). Pts with ?56 days of treatment were evaluable for efficacy. Onset of HI and RBC TI in baseline transfusion-dependent pts, as defined by IWG 2000 criteria (Blood 2000;96:3671), was assessed by treatment cycle. Results. In all, 151 pts were randomized to AZA 5-2-2 (n=50), AZA 5-2-5 (n=51), or AZA 5 (n=50). Most pts were RA (43%) or RAEB (30%). Proportions of evaluable pts with HI (major + minor) were 44%, 52%, and 55% in the AZA 5-2-2, AZA 5-2-5, and AZA 5 groups, respectively, and onset of HI occurred within the first 2 treatment cycles for 82%, 58%, and 90% of pts, respectively (Table). Proportions of pts who achieved RBC TI after baseline dependence were 55%, 60%, and 63%, in the AZA 5-2-2, AZA 5-2-5, and AZA 5 groups, respectively, and onset of TI occurred within the first 2 cycles for 92%, 75%, and 75% of pts, respectively (Table 1). Onset of HI and TI continued to occur, however, during cycles 3 to 6. All three alternative dosing regimens were generally well tolerated with similar safety profiles to that seen with the approved AZA dosing schedule. Summary/conclusions. These data indicate the 3 alternative AZA dosing schedules are effective in the treatment of MDS. Moreover, these data demonstrate the rapid onset of action of AZA, with the majority of pts who achieve HI or RBC TI experiencing onset of effect within the first 2 treatment cycles. Although rapid onset of HI and TI occurred in the majority of pts, onset continued to be observed during later cycles.