

# The following abstracts were featured at the 2005 ASH Annual Meeting and contain the latest and most exciting developments in scientific research.

## [2524] Azacitidine Prolongs Survival and Time to AML Transformation in High-Risk Myelodysplastic Syndrome (MDS) Patients $\geq 65$ Years of Age.

Session Type: Poster Session 728-II

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The prognosis for patients with refractory anemia with excess blasts (RAEB) or RAEB in transformation (RAEB-T)  $\geq 65$  years of age has been poor. These high-risk patients are often not eligible for intensive induction/transplantation regimens or combination chemotherapies, leaving few treatment options besides supportive or palliative care. In the publication of the CALGB trial by Silverman et al (JCO 2002;20:2429), no age- and/or risk- related subgroup analyses for azacitidine (Vidaza®) were presented. To assess the treatment effect of azacitidine versus supportive care on survival and time to AML transformation in a homogeneous sample of high-risk patients with MDS, we performed a subgroup analysis on the 191 patients included in the CALGB trial. All patients with a baseline diagnosis of RAEB or RAEB-T who were  $\geq 65$  years of age were included in the comparative analysis, using intent-to-treat (ITT) principles based on randomization to azacitidine or supportive care. Efficacy was analyzed using three survival endpoints: overall survival, time to death or AML transformation, and time to AML transformation. In all, 31 azacitidine patients and 37 supportive care patients met the criteria for this high-risk subgroup analysis. No significant differences in demographics

or disease characteristics between the two groups were observed. For all three survival analyses, a statistically significant difference was observed for patients in the azacitidine group compared with those in the supportive care group. (Table) Median time to transformation to AML, in particular, was prolonged for 24 months in azacitidine patients compared with patients in the supportive care group. A sensitivity analysis of the overall survival results was conducted by performing 10 additional subgroup analyses based on ages  $\geq 60$  through  $\geq 70$  years in increments of one year with all overall survival results remaining significant ( $p < 0.05$ , except for 2 subgroup analyses based on ages  $\geq 60$  and  $\geq 66$  where both p-values were 0.051). The sensitivity results demonstrated robust patient benefit in the subgroup  $\geq 65$  years of age. The most common adverse event observed with azacitidine was myelosuppression, which decreased in frequency as therapy continued. Azacitidine provided clear treatment effect and patient benefit to this difficult-to-treat, high-risk group of RAEB and RAEB-T patients  $\geq 65$  years of age by significantly prolonging overall survival and time to AML transformation. *Abstract #2524 appears in Blood, Volume 106, issue 11, November 16, 2005*

### Time to Event Analysis

Clinical Outcome	Median 95% CI) in Months <sup>a</sup>			
	Azacitidine N = 31	Supportive Care <sup>b</sup> N = 37	Difference	P Value <sup>c</sup>
Overall Survival	19.5 (14.4 – 31.9)	14.0 (6.3 – 18.6)	5.5	0.04
AML Transformation	42.0 (19.1 – DNE <sup>d</sup> )	17.7 (12.0 – 23.5)	24.3	0.04
Death or AML Transformation	19.1 (12.1 – 22.9)	9.2 (4.3 – 14.2)	9.9	0.008

<sup>a</sup>Months are 28-day treatment cycles.

<sup>b</sup>The ITT supportive care arm included 20 crossover patients who received azacitidine.

<sup>c</sup>P-value are two-sided and exact from log-rank tests for equality of survival curves.

<sup>d</sup>DNE denotes does not exist.