

[7025] Phase II study of single agent clofarabine in previously untreated older adult patients with acute myelogenous leukemia (AML) unlikely to benefit from standard induction chemotherapy.

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Background: Studies have identified a population of older AML patients unlikely to benefit from standard combination induction therapy ("7+3") based on adverse prognostic factors such as advanced age, poor performance status (PS), antecedent hematologic disorder (AHD), or intermediate/unfavorable risk karyotype. This study assessed the efficacy and safety of single agent clofarabine (CLO) in this population. Methods: Single arm, Phase II, open-label, 2-stage study; planned total enrollment of 109 patients. Eligible untreated AML patients included adults >60 years with >1 adverse prognostic factor: >70 years, AHD, PS 2, and/or intermediate/unfavorable risk karyotype. CLO given on days 1-5 as a 1-hr IV infusion: 30 mg/m<sup>2</sup> during induction and 20 mg/m<sup>2</sup> during re-induction/consolidation (6 cycles maximum). Primary endpoint was overall remission rate (ORR = CR + CRp). Preliminary Results: Enrollment completed with 116 patients. As of Aug 2007, safety data were available for 54 patients; efficacy data for 40 patients. Median age was 71 years. Baseline prognostic factors: 65% >70 years, 37% with AHD (13% yet unreported), 70% with intermediate/unfavorable risk karyotype (30% yet unreported), and 19% with PS 2. 30-day all-cause mortality was 13%. Drug related adverse events in >20% of patients: nausea (41%), vomiting (28%), diarrhea (26%), febrile neutropenia (24%), and rash (20%). Most treatment-related events were Grades 1-2. Treatment emergent Grade 3 febrile neutropenia occurred in 30% of patients. Treatment emergent Grade 4 neutropenia was reported in 33% of patients with baseline ANC values available. The ORR was 43% (95% CI: 27.0%, 59.1%): 40% CR (95% CI: 24.9%, 56.7%) plus 3% CRp (95% CI 0.1%, 13.2%). ORR by prognostic factor: 58% for unfavorable risk karyotype, 44% for intermediate risk karyotype; 44% for AHD; 32% for age >70, 67% for age <70; and 14% for PS 2. Conclusions: These interim data indicate that single agent CLO is active and well-tolerated in treatment-naïve, older AML patients with >1 adverse prognostic factor, especially unfavorable risk karyotype and/or AHD. Safety and efficacy results for all patients will be presented.

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