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Poster Session

ACUTE MYELOID LEUKEMIA - THERAPY, EXCLUDING TRANSPLANTATION POSTER II

Single-Agent Clofarabine Produces Durable Remissions in Patients with Acute Myelogenous Leukemia (AML) Who Are ≥ 70, Have Intermediate or Unfavorable Cytogenetics, Antecedent Hematological Disorders (AHD), or 2 or More Unfavorable Prognostic Factors.

Harry P Erba[1], Stefan Faderl, MD[2], David F. Claxton, M.D.[*,3], M. Arellano[*,4], Roger M Lyons[5], Tibor J. Kovacsovics, MD[6], Janice Gabrilove, MD[7], Stephen Eckert, Ph.D[*,8], Dirk Huebner, MD[9] and Hagop M. Kantarjian, MD[10]

[1] University of Michigan Health System, Ann Arbor, MI, USA,
[2] Leukemia, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA,
[3] Hematology-Oncology, Penn State Milton S. Hershey Medical Center, Hershey, PA, USA,
[4] Emory University, Atlanta, GA, USA,
[5] Cancer Care Centers South Texas/US Oncology, San Antonio, TX, USA,
[6] Ctr. for Hematological Malignancies, OHSU, Portland, OR, USA,
[7] Mount Sinai School of Medicine, New York, NY, USA,
[8] BioMedical Data Sciences & Informatics, Genzyme Corporation, San Antonio, TX, USA,
[9] Genzyme Corporation, Cambridge, MA, USA,
[10] Leukemia, MD Anderson Cancer Center, Houston, TX, USA

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Background: Outcomes in older patients with AML have not improved in several decades. Response rates decline and treatment related mortality increases with advancing age [Appelbaum, Blood 2006]. Older adults have a higher incidence of unfavorable prognostic factors, such as antecedent hematologic disorders (AHD) and unfavorable cytogenetics, and outcomes worsen with increasing numbers of unfavorable prognostic factors [Leith, 1997, *Blood*; Kantarjian, 2006, *Cancer*; Malfuson, 2008, *Haematologica*] Clofarabine has demonstrated remissions regardless of age, cytogenetics, AHD, or multiple unfavorable prognostic factors. We present data on durability of remission, 30 day mortality, and overall survival in prospectively defined subgroups from the CLASSIC II trial: age ≥ 70, intermediate or unfavorable cytogenetics, AHD, and in patients with 2 or more of these factors.

Methods: CLASSIC II was a single-arm, multi-center, Phase II, open-label, study of patients with previously untreated AML, ≥60 years old, and at least one unfavorable prognostic factor: age ≥70 years, AHD, Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 2, and/or intermediate/unfavorable risk myeloblast karyotype. Single-agent CLO was administered on days 1-5 at 30 mg/m^2 during induction and 20 mg/m^2 during re-induction/consolidation for a maximum of 6 cycles. Overall response rate (ORR) was defined as Complete Response (CR) plus Complete Response with incomplete platelet recovery (CRp). Duration of remission (DoR) was measured from the time the patient achieved remission until relapse or death, censored for alternative antileukemic treatment at date of therapy initiation. Disease-free survival (DFS) was measured from the time of remission until relapse or death, regardless of any alternative antileukemic treatment. Overall survival (OS) was measured from the first dose of CLO. These 3 time-to-event endpoints were analyzed using Kaplan-Meier methodology.

Results: 112 patients were evaluable for efficacy assessments. 78% had at least 2 unfavorable prognostic factors. ORR, CR, DoR, DFS, OS and 30 day mortality for each subgroup are presented in Table 1. In addition to the Table 1 analyses, we assessed results for specific combinations of prognostic factors. Patients with 2 unfavorable prognostic factors (n=45) had ORR of 51%, DoR 37 weeks (95% CI 17, NE) DFS 26 weeks (95% CI 12,41) and OS 37 weeks (95% CI 25, 53). Patients with 3 unfavorable factors (n=40) had OR 38% and OS 37 weeks (95% CI 16,57); DoR and DFS were not yet estimable (NE). 30 day mortality for patients with 1, 2 or 3 factors was 8%, 9%, and 10%, respectively. Patients ≥ 70 with intermediate or unfavorable karyotype (n= 25), had ORR 48% and CR 40%; in patients ≥ 70 with unfavorable karyotype (n=9) ORR and CR were 56%. Patients ≥ 70 with both AHD and unfavorable karyotype (n= 18), ORR was 33% and CR 22%. In patients ≥ 70 with AHD and intermediate karyotype (n=8), ORR and CR were 63%.

Table 1: **Efficacy Outcomes For AML Patients ≥ 70, AHD, Intermediate or Unfavorable Cytogenetics**

Endpoint	Patients ≥ 70 (n=69)	Patients w/AHD (n=41)	Patients w/Intermediate Cytogenetics (n=46)	Patients w/Unfavorable Cytogenetics (n=62)
ORR	39%	51%	54%	42%
CR	33%	39%	48%	32%
Median DoR	65 weeks (17, NE)	≥37 weeks* (37, NE)	65 weeks (65, NE)	41 (28, NE)
Estimated median DFS	51 weeks (17, NE)	51 weeks (26, NE)	65 weeks (17, NE)	34 weeks (23,51)
Estimated median OS	31 weeks (17, 55)	50 weeks (30, NE)	53 weeks (33, NE)	31 weeks (19, 48)
30-day mortality	13%	7%	11%	10%

* Median DoR for patients with AHD could not yet be estimated as <50% of the patients had an event (deathor recurrence)

Data presented for each group regardless of other risk factors

Conclusions: Clofarabine produces durable response rates with low 30 day mortality in patients ≥ 70, with AHD, intermediate or unfavorable cytogenetics, and 2 or more of these factors; ORR was consistent across these subgroups. Among patients ≥ 70, ORR was maintained in those who also had AHD and/or intermediate or unfavorable cytogenetics.

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Footnotes

* Asterisk with author names denotes non-ASH members.

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