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Poster Session

ACUTE MYELOID LEUKEMIA - THERAPY, EXCLUDING TRANSPLANTATION

Clofarabine Produces Durable Remissions in Older Patients with AML with Unfavorable Prognostic Factors and Multiple Comorbidities.

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Abstract 4155

Background: Clofarabine has produced overall remission rates of 46% (38% complete remission, 8% complete remission with incomplete platelet recovery), manageable toxicity, and 30 and 60 day mortality of 10% and 16%, respectively, in patients ≥ 60 with acute myelogenous leukemia (AML) and at least one unfavorable prognostic factor: age ≥70 years, antecedent hematologic disorder (AHD), Eastern Cooperative Oncology Group (ECOG) performance status of 2, and/or intermediate/unfavorable risk myeloblast karyotype (*JCO* 2009; 27:371s, A.7062). Two indices of baseline comorbidity have been adapted for older patients with acute myelogenous leukemia (AML): the revised Charlson comorbidity index (CCI) classification (Etienne, 2007, *Cancer*) and the Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) (Sorror, 2005, *Blood;* Giles, 2007, *British Journal of Haematology*)). A post-hoc analysis was conducted to evaluate comorbid conditions based on the CCI and HCT-CI indices. Long-term efficacy data based on ≥ 12 month follow-up is presented for this patient population.

Methods: The CLASSIC II trial was a single-arm, multi-center, Phase II, open-label study of patients with previously untreated AML. Clofarabine 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. Primary endpoint was ORR (CR + CRp). Secondary efficacy endpoints included duration of remission (DoR), disease-free survival (DFS) and overall survival (OS). Baseline comorbidity was evaluated retrospectively using the revised CCI classification and the HCT-CI based on medical/surgical histories, concurrent conditions, baseline laboratory values, concomitant medications, and pretreatment physical examinations.

Results: Table 1 shows the number of patients with baseline comorbidities according to the revised CCI and the HCT-CI. By CCI, most patients enrolled in CLASSIC II had ≥1 comorbidities present at baseline; most common as follows: chronic pulmonary disease 24%, diabetes without complications 13%, prior myocardial infarction 13%, and heart failure 11%. By HCT-CI, the majority of patients also had ≥1 comorbidities, most common as follows: psychiatric disturbance (depression and anxiety for which treatment was administered) 37%, cardiac 35%, mild liver disease 25%, moderate pulmonary 24%, and diabetes 18%. By HCT-CI, 47% of all patients had at least 1 cardiac condition present prior to study treatment, including coronary artery

disease, congestive heart failure, myocardial infarction, or ejection fraction £50% in 35%; heart valve disease (except mitral valve prolapse) in 13%; and arrhythmia (atrial fibrillation or flutter, sick sinus syndrome, or ventricular arrhythmias) in 12%. With ≥ 12 month follow-up, the estimated DoR was 52 weeks (95% CI=33, 69 weeks) and DFS was 41 weeks (95% CI=26, 56 weeks). Estimated OS for all 112 patients was 40.7 weeks (95% CI=28.3, 52).

96% of patients experienced an adverse event (AE) considered related to clofarabine; only seven patients (6%) discontinued treatment due to an AE. The most common drug-related, non-laboratory AEs in ≥20% patients were nausea, febrile neutropenia, vomiting, diarrhea, rash, and fatigue. Febrile neutropenia was the most common Grade ≥3 AE.

Conclusions: By both the revised CCI and HCT-CI, the baseline health of the CLASSIC II patient population was comparable to or worse than that of older AML patients treated on other recent phase II studies of cytotoxic therapy. The treatment related mortality was low and clofarabine demonstrated durable remissions in a difficult-to-treat AML patient population with unfavorable prognostic factors.

Table 1 Number of Patients with Baseline Comorbidities According to the Revised CCI and the HCT-CI

CCI Score	Etienne[1] n (%)	CLASSIC II n (%)
0	83 (86)	45 (40)
1	16 (13)	43 (38)
2	19 (16)	12 (11)
3	3 (3)	10 (9)
4	0	1 (1)
≥5	1 (1)	1 (1)

HCT-CI Score	Giles[2] n (%)	CLASSIC II n (%)
0	39 (22)	4 (4)
1-2	54 (30)	55 (49)
≥3	84 (48)	53 (47)

[1] Based on 122 patients for Etienne and 112 patients for CLO243

[2] Based on 177 patients for Giles and 112 patients for CLO243

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Footnotes

* Asterisk with author names denotes non-ASH members.

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