



Efficacy and Safety of Azacytidine in combination with fludarabine and high-dose cytarabine with G-CSF (FLAG) in Relapsed/Refractory Acute Myeloid Leukemia: A Nonrandomized, Open-Label, Phase II Study Shaima Al Aoun, Ibraheem Motabi, King Fahad Medical City



Background

Relapsed and refractory AML represent a clinical and therapeutic challenge to hematologist because of chemotherapy resistant disease and is associated with poor outcome. Allogeneic stem cell transplant (Allo-SCT) is the only potentially curative therapy for such patients and is only possible after achieving a second remission.

Objective

The primary objective of this study is to evaluate the overall response rate (ORR) of pretreatment with azacytidine followed by FLAG for the treatment of relapsed/refractory AML. The secondary objectives are the one year and overall survival, disease free survival, and to determine the global DNA methylation before and after the treatment with azacytidine and correlate it with treatment outcome.

Materials & Methods

- Patients with relapsed or refractory AML, ECOG performance status ≤ 2 , Patients must have preserved organ function.
- INTERVENTIONS:** Azacytidine was given at 75 mg/m² per day, for 5 days prior to the standard FLAG therapy.

Result

The CR/CRi with incomplete blood count recovery (CRi) rate was 53%. Of the 9 primary refractory patients, 5 (56%) achieved CR/CRi. Eight of 11 patients who achieved CR/CRi also attained minimal residual disease–negative status ($<1.0\%$ by flow cytometry), and 8 patients (73%) went for stem cell transplant. Of the 11 patients who achieved CR/CRi, 5 are still alive on the last follow-up.

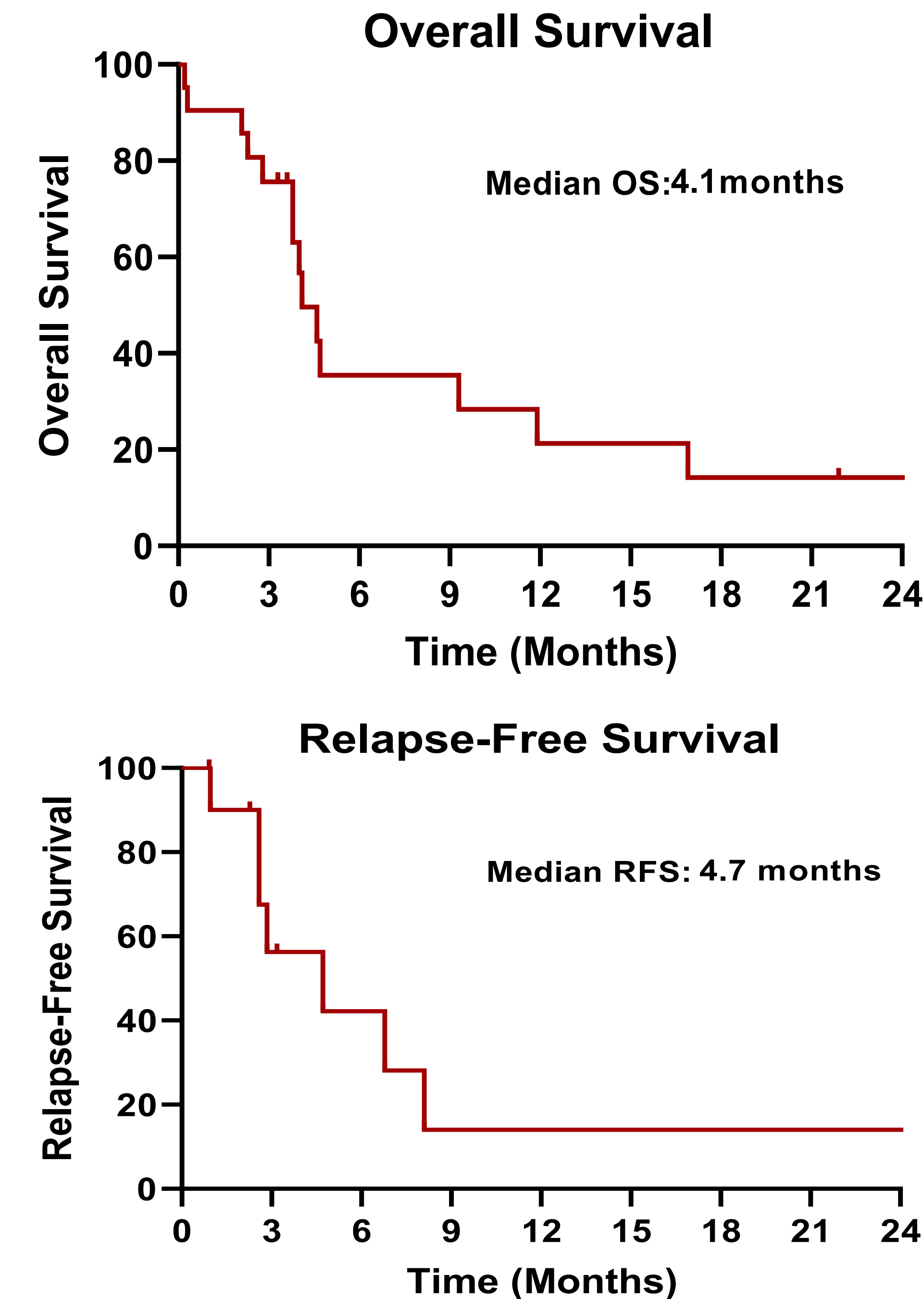


Figure1: Intention-to-Treat analysis of overall survival (panel A) and relapsed free-survival (panel B) for all relapse and refractory AML patient's population treated with Azacytidine in combination with fludarabine and high-dose cytarabine with G-CSF (FLAG).

Summary

AZA FLAG combination is safe and does not seem to have an added benefit in response rate or survival.

Discussion

In this phase II single-arm report of combination treatment, although with a limited number, the combination does not seem to have an added benefit in response rate or survival. The study is limited by the number of patients, the lack of compactor arm, and missing the detailed genetic and epigenetic signature examination. Further analysis into the global methylation and cell cycle, as well as mutational status, might identify biomarkers such as mutations in chromatin-modifying enzymes that predicted a better response with the addition of epigenetic treatment.

References

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