Prognostic Significance of Residual Disease Detected by Flow Cytometry in Acute Myeloid Leukemia with Normal Karyotype and Negative FLT3-ITD/ D835

Samiha Jaddaoui[1], Hanaa Bencharef[1], Sara Addakiri[1], Hind Dehbi[2], Mouna Lamchahab[3], Asmaa Quessar[3], Abdellah Madani[3], Bouchra Oukkache[1]

[1] Department of Hematology Laboratory, University Hospital Center, Hassan II University, Casablanca, Morocco
[2] Medical Genetics Laboratory of the Faculty of Medicine and Pharmacy, Hassan II University, Casablanca, Morocco
[3] Department of Haematology and Paediatric Oncology, Faculty of Medicine and Pharmacy, Hassan II University, Casablanca, Morocco

Abstract

MRD, LSC and FLT3 gene analysis are powerful prognostic factors for relapse that should be integrated routinely to guide our clinicians in risk stratification, especially in patients with normal karyotype.

Background

Complete remission in patients with AML is still cytomorphological, representing a highly heterogeneous state with a wide range of tumor burden and diverse clinical findings. [1,2]

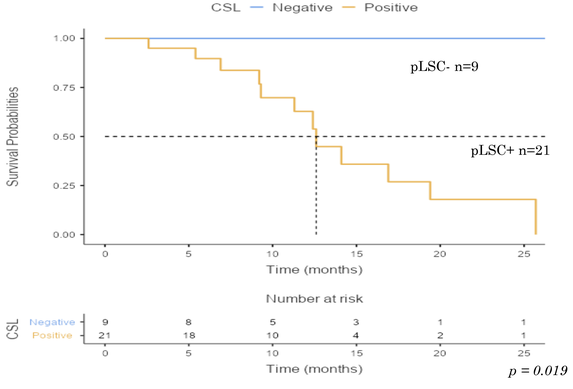


Figure 1. Prognostic Value of LSC Compartment Frequencies After Induction Treatment

Objective

Evaluate prognostic significance of residual disease detected by flow cytometry in acute myeloid leukemia with normal cytogenetics and negative FLT3-ITD/D835.

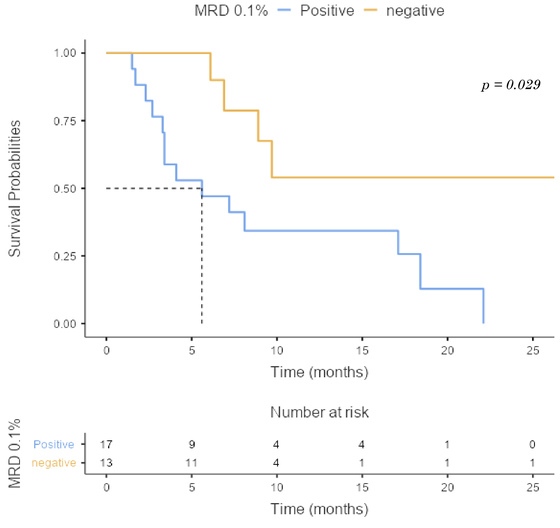


Figure 2. Prognostic value of MRD in all patients post-treatment induction

Materials & Methods

This is a prospective study, spanning a period of five years from January 2017 to December 2021. Our patients were followed for 25 months.

- We followed 54 adults patients diagnosed with AML according to the 2016 WHO criteria in the hematology and pediatric oncology department of the August 20 hospital in Casablanca, of which 30 of these patients achieved complete cytological remission after induction.
- Any patient presenting a therapeutic failure in post induction and salvage therapy was excluded from the study. After that, we selected patients with normal karyotype for *FLT3* gene mutational analysis.
- Quantification of MRD and leukemic stem cells (LSC) using a six-color Navios type flow cytometer and the cxp acquisition and analysis software. a large panel of monoclonal antibodies was used to determine leukemia associated immunophenotypes in most patients. molecular analysis of FLT3-ITD/D835 was performed by PCR/RFLP (Restriction fragment length polymorphism).

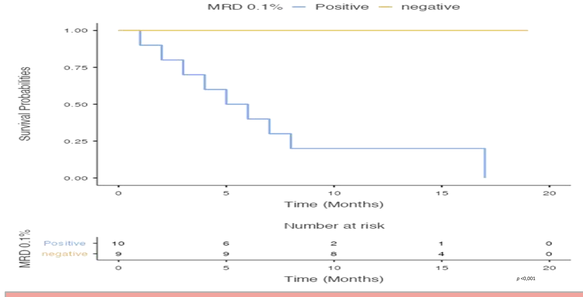


Figure 3. Relapse-free survival in patients with normal karyotype and FLT3 negative

Summary

The intermediate risk group was predominant with a rate of 83%, of which 67% (20/30) had a normal karyotype. MRD and LSC positivity in this group was predominant with considerable decrease in hematogon count frequency as a marker of good prognosis. non-mutated FLT3 gene in this group conferred a more improved RFS compared to that of the negative MRD in all our patients studied.

Discussion

Our study suggests that MRD shows prognostic relevance in AML patients with normal cytogenetics and FLT3 negative, and could lead to recommending HSC transplantation not only for patients with high-risk karyotype or FLT3-ITD positive, but also for those with favorable/intermediate prognosis and non-mutated FLT3 having a positive MRD. This option being able to provide a higher chance of prolonged relapse-free survival [3]

References

[1] R. P. Hasserjian, D. P. Steensma, T. A. Graubert, et B. L. Ebert, « Clonal hematopoiesis and measurable residual disease assessment in acute myeloid leukemia », *Blood*, vol. 135, nº 20, p. 1729-1738, mai 2020, doi: 10.1182/blood.2019004770.
[2] G. Roloff, C. Lai, C. Hourigan, et L. Dillon, « Technical Advances in the Measurement of Residual Disease in Acute Myeloid Leukemia », *J. Clin. Med.*, vol. 6, nº 9, p. 87, sept. 2017, doi: 10.3390/jcm6090087.
[3] L. Maurillo *et al.*, « Toward Optimization of Postremission Therapy for Residual Disease–Positive Patients With Acute Myeloid Leukemia », *J. Clin. Oncol.*, vol. 26, nº 30, p. 4944-4951, oct. 2008, doi: 10.1200/JCO.2007.15.9814.