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ELEVENTH ANNUAL MEETING

CLONAL EVOLUTION ANALYSIS USING NGS PANEL IN A COHORT OF 3,025 PATIENTS WITH ACUTE MYELOID LEUKEMIA

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INTRODUCTION

Acute myeloid leukemia (AML) is a hematologic neoplasm diagnosed mainly in older patients, and the study of the mutational profile at diagnosis is important for prognostic and therapeutic purposes.

AIM

To analyze the differences in molecular alterations among diagnosis, refractoriness and relapse in patients with AML.

METHOD

- Laboratory data from the PETHEMA (Spanish Hematology Treatment Program) AML group.
- Patients diagnosed between 2017 and 2022 were included in the study; diagnostic, relapse, and primary refractory samples were analyzed, using a NGS panel with 26 common genes:

ASXL1	EZH2	MPL	TET2
CALR	FLT3	NPM1	TP53
CBL	IDH1	NRAS	U2AF1
CEBPA	IDH2	RUNX1	WT1
CSF3R	JAK2	SETBP1	ZRSR2
DNMT3A	KIT	SF3B1	
ETV6	KRAS	SRSF2	

- Variant allele frequency (VAF) changes were analyzed too.
- Statistics were performed using SPSS version 22 (IBM, Armonk, NY, USA) .
- The chi-square test and the Student's t-test were used.

RESULTS

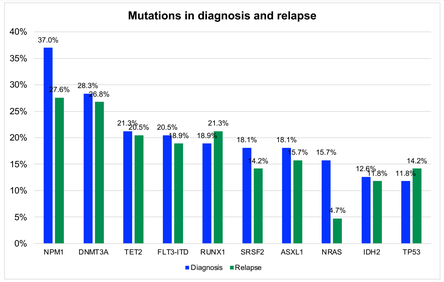
3,603 samples were registered during the study period: 3,025 diagnostic samples, 307 relapse samples, and 197 primary refractoriness samples; 74 samples correspond to other times of the disease.

Unpaired data were analyzed. The most frequent mutation at diagnosis, primary refractory and relapsed patients was *DNMT3A* (23.8%, 23.9% and 32.6%).

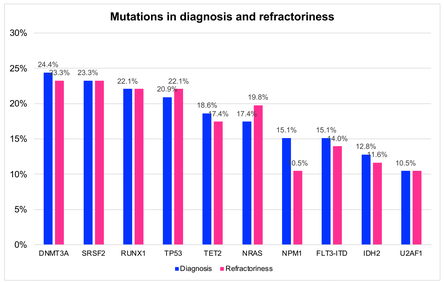
Comparing diagnosis and primary refractoriness, there were differences in *NPM1* (23.5% vs 11.7%, P<0.01), *RUNX1* (17.9% vs 23.9%, P=0.04), *SRSF2* (15.8% vs 21.3%, P=0.04), *IDH1* (9.9% vs 15.2%, P=0.02), *WT1* (5.1% vs 8.6%, P=0.03).

Comparing diagnosis and relapse, there were differences in *DNMT3A* (23.8% vs 32.6%, P<0.01), *RUNX1* (17.9% vs 23.1%, P=0.02), *TP53* (17.5% vs 10.4%, P<0.01), *NRAS* (15.8% vs 7.5%, P<0.01), *IDH1* (9.9% vs 15.0%, P<0.01), *KRAS* (7.9% vs 2.9%, P<0.01), *JAK2* (5.6% vs 2.9%, P=0.04), and *WT1* (5.1% vs 11.1%, P<0.01).

Paired diagnosis-primary refractoriness (57 patients) and diagnosis-relapse samples (97 patients) were studied. In diagnosis-relapse samples, there was a difference in *NRAS* mutation (15.7% vs 4.7%, P<0.01).

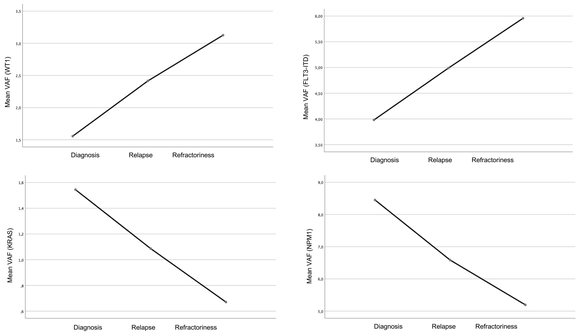


Paired samples: mutations in diagnosis and relapse.



Paired samples: mutations in diagnosis and refractoriness.

Comparing the mean VAF at diagnosis, relapse and refractoriness, the differences are significant with VAF decrease in *KRAS* and *NPM1* and increase in *WT1* and *FLT3-ITD*.



VAF differences in some genes (WT1, FLT3-ITD, KRAS, NPM1).

CONCLUSIONS

Clonal evolution studies can help to better understand the biology of AML and identify therapeutic targets in the most refractory alterations to conventional chemotherapy.

The study is limited because most samples are unpaired, and we do not distinguish between each mutated variant.

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