Abstract: PB1781

Title: THE APPLICATION OF CF-DNA FOR NGS MRD STUDIES IN PATIENTS WITH LMA IMPROVES THE SENSITIVITY OF THE METHOD WITH RESPECT TO CTC.

Abstract Type: Publication Only

Session Title: Acute myeloid leukemia - Biology & Translational Research

Background:

The quantification of Minimal Residual Disease (MRD) has become a relevant marker as it can detect acute myeloid leukemia (AML) patients with a high risk of relapse. Although the reference MRD method in AML is to quantify tumor cells present in bone marrow (BM), the study of circulating tumor cells (CTC) in peripheral blood (PB) is also being incorporated into clinical protocols. However, cfDNA as an MRD biomarker in AML has not yet been validated.

Aims:

Evaluating the use of cfDNA by NGS test as a new method for MRD quantification in AML and comparing it application with the use of PB CTCs in disease monitoring

Methods:

This study included 37 patients with AML that received 3+7 or similar treatment schemes for fit patients and venetoclax, azacitidine based treatment for unfit patients. The mutational profile was defined by NGS (Ion Torrent System) at diagnosis using a panel of 42 genes involved in myeloid pathologies. Then, somatic mutations were selected and used for MRD monitoring on 116 liquid biopsy follow-up samples. MRD quantification was performed in the two main fractions, whole blood cells (WBC) and cfDNA as previously described (Onecha E. Haematologica 2019). The threshold for MRD positivity was set at 10^{-4}. An average of 66ng of cfDNA and 660ng of gDNA from WBC were used. In 20 patients, the results were compared with those obtained by multiparametric flow cytometry (MFC) in BM.

Results:

MRD evaluation by cfDNA in the overall series showed MRD positivity in 27 of the 37 cases analyzed, being negative for 10/37. When studying the correlation between CTCs and cfDNA in paired samples, a good correlation was observed with an R^2=0.924 (Figure 1A). However, an increased tumoral signal was observed in the cfDNA fraction. In addition for the 20 patients with MFC data available, 15 were positive. Of these 20 patients, by NGS, 12 were MRD positive.

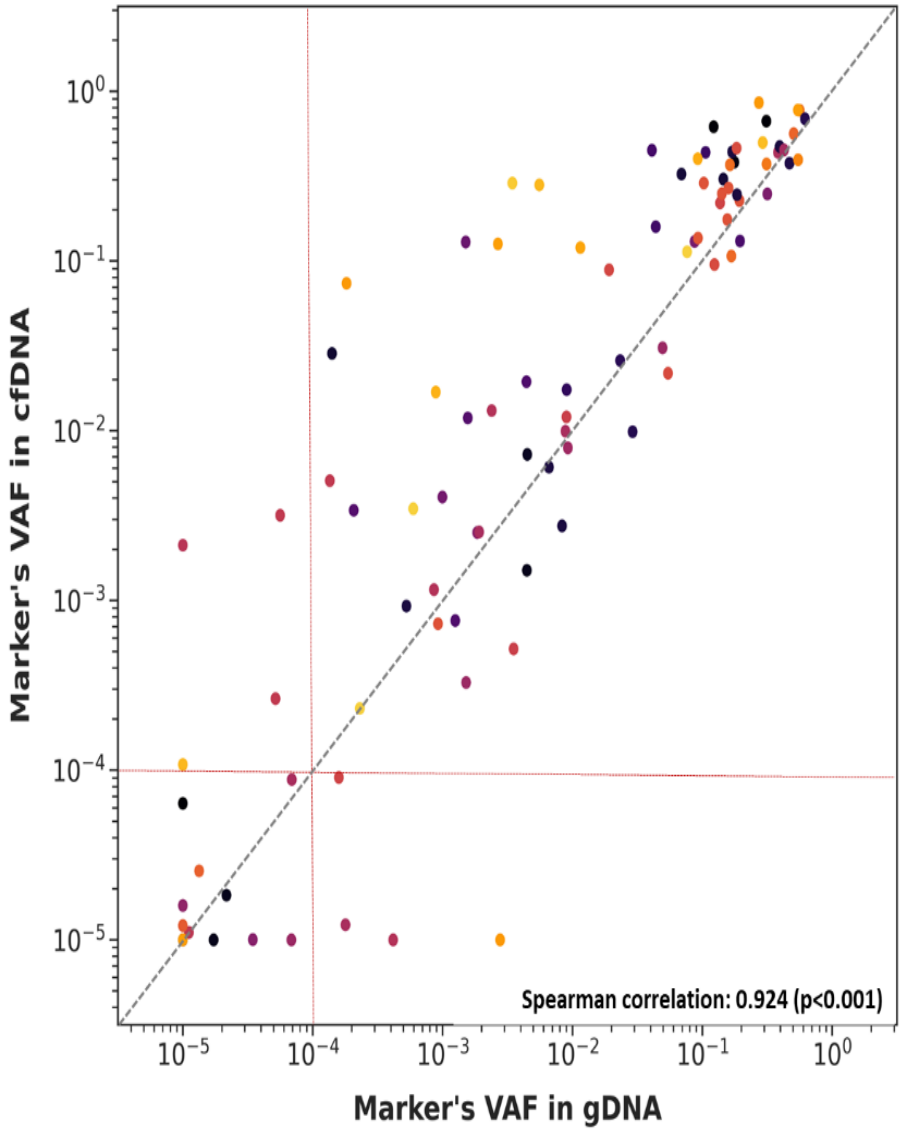
We showed one example with the following patient, three variants are detected at diagnosis in the BCOR, KRAS and RUNX1 genes. When MRD was quantified after the first treatment cycle, a positive MRD was observed. In cycle 7 of treatment, the MRD decreased by one logarithm, becoming negative in cycle 11, decreasing by 3 logarithms with respect to the first point studied. In the 3 variants studied, a good correlation was observed between the cfDNA and CTCs samples. The patient has not relapsed to date (Figure 1B).

Summary/Conclusion:

-A method for quantification of EMR by NGS has been optimised using liquid biopsy techniques in acute myeloid leukaemia.

-This method is applicable using CTCs (leukocyte DNA) as well as cfDNA (circulating DNA in plasma).

-A good correlation of the results of cfDNA and CTCs has been observed, with a predominance of cases with higher sensitivity in cfDNA.



Keywords: Acute myeloid leukemia, liquid biopsy, Minimal residual disease (MRD)