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MOLECULAR SCREENING OF TYROSINE KINASE INHIBITOR RESISTANCE IN TUNISIAN PATIENTS WITH CHRONIC MYELOID LEUKEMIA

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INTRODUCTION

Tyrosine kinase inhibitors (TKIs) have revolutionized the management of chronic myeloid leukemia (CML); a myeloproliferative neoplasm caused by the BCR-ABL1 fusion gene. However, resistance occurs and is possibly mediated by mutation within this fusion gene or independent mechanism, accounting for up to 20% of all clinically observed resistance.

AIM

This study was carried out to assess the most mutation in two genes; ABL (T315I) and ASXL1 (c.1934dupG), in Tunisian CML patients with imatinib resistance.

METHOD

An 8-year retrospective study was carried out in the Hospital University of Sfax, south of Tunisia (2016- 2023).

A total of twenty TKI-resistant CML patients were enrolled in this study.

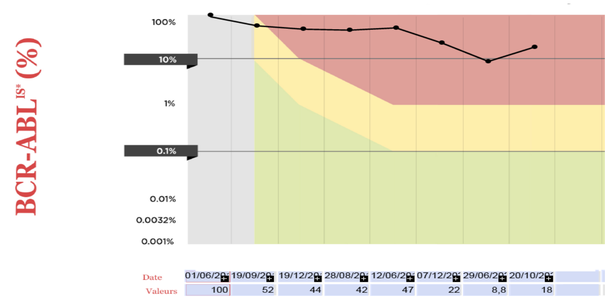
Quantitative assessment of the BCR-ABL transcript was performed using the Cepheid *Xpert BCR-ABL* ultra-assay.

According to the European Leukemia Net guidelines, molecular response and outcome were evaluated.

For molecular screening of the ASXL1 and ABL mutations, Sanger sequencing was performed using a high-fidelity DNA polymerase.

RESULTS

None of the CML patients have the T315I mutation or c.1934dupG of the ABL and ASXL1 genes, respectively.



Minimal residual disease in TKI- resistant CML patient

CONCLUSIONS

Our findings suggest that both mutations are uncommon in Tunisian CML-resistant patients. A comprehensive mutational analysis of other genes and epigenetic factors is mandatory to elucidate the molecular mechanisms that lead to kinase inhibitor resistance..

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