soho2023
ELEVENTH ANNUAL MEETING

ASSESSMENT OF *ASXL1* MUTATION IN TKI-RESISTANT CHRONIC MYELOID LEUKEMIA IN TUNISIAN PATIENTS: A PRELIMINARY STUDY

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INTRODUCTION

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm caused by the BCR-ABL1 fusion gene, which aberrantly activates ABL1 kinase and promotes the overproduction of leukemic cells. Although Tyrosine kinase inhibitors (TKIs) have revolutionized the treatment of CML, resistance occurs and possibly mediated by mutation in several genes independently to bcr-abl1 kinase mechanism.

Mutations in the additional sex combs-like 1 (*ASXL1*) gene are common and associated with worse clinical outcomes when detected in chronic phase CML (CP-CML)[1,2]. The most detected *ASXL1* mutation accounting for approximately half of somatic truncating mutations[3].

AIM

This study investigated the *ASXL1* mutation in TKI-resistant CML patients.

METHOD

A seven years retrospective study was carried out in the Hospital University of Sfax, south of Tunisia.

A total of 19 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 (ELN) based guidelines, molecular response and outcome were evaluated.

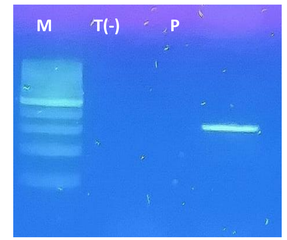
A Sanger sequencing was performed using a high-fidelity DNA polymerase.

RESULTS

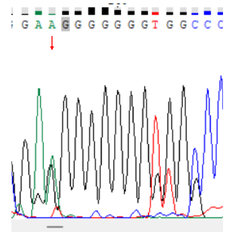
The median age was 55 years, the sex ratio M/F was 0,9.

Among patients failing a TKI; 14(73,6%) and 5 (26,4%) patients demonstrate primary and secondary resistance; respectively.

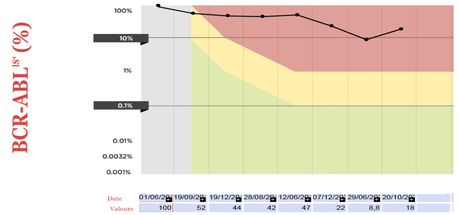
ASXL1 mutation was detected in a 52-year-old patient who is resistant to the second-generation TKI given as first-line therapy [Figures].



Revelation of the PCR product covering exon 13 of the *ASXL1* gene



Electrophoregram showing the *ASXL1* mutation:



Minimal residual disease in resistant patient with ASXL1 mutation:

CONCLUSIONS

To the best of my knowledge this is the first study that investigated ASXL1 mutation in Tunisian-resistant CML patients.

Despite the limit of our study, our finding highlights that truncating *ASXL1* mutation, may be a potential biomarker for predicting therapeutic efficacy and the treatment strategy of CML with ASXL1 mutation should be established.

Moreover, future studies need to comprehensively identify the landscape and clinical relevance of genetic and epigenetic alterations in CML, which can be used to develop novel therapeutic strategies.

REFERENCES

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