SOHO ANNUAL MEETING 2024

TKI Resistance in Pakistani Patients With CML and Frequency of T315I Mutation in These TKI-Resistant Patients

U. Saleem MD, FCPS[1], M.A. Naveed MBBS, FCPS, PhD[2], H. Syndeed MBBs, FCPS[3] and K. Nawab Bsc MLT[2]

1. Nishtar Medical University, Multan, Pakistan
2. University of Health Sciences, Lahore
3. Aga Khan University, Lahore, Pakistan.

INTRODUCTION

Chronic myelogenous leukemia (CML) is one of the leading myeloproliferative neoplasms causing significant morbidity and mortality in patients suffering from this disease. Patients with CML usually have a high white blood cell count and often raised platelet count. The major underlying cause is a fusion gene that is known as BCR-ABL. This fusion gene leads to constitutional activity of tyrosine kinase inhibitors (TKIs). The paradigm of CML shifted after the development of TKIs, which led to improvement in terms of decreased mortality and increased quality of life in these patients; however, resistance to TKIs has emerged as a significant problem. T315I mutation has emerged as a very important cause of resistance to TKIs. Therefore, we planned this study to see the prevalence of resistance in patients with CML and T315I mutation in TKI-resistant patients.

AIM

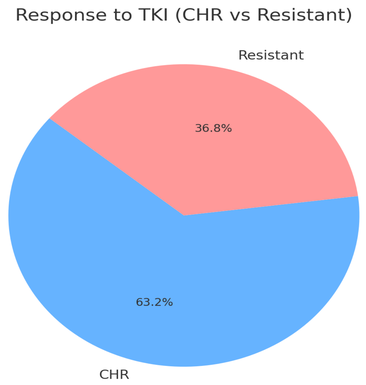
The study was conducted to determine the frequency of TKI resistance in Pakistani patients with CML along with T315I mutation in TKI-resistant patients.

METHODS

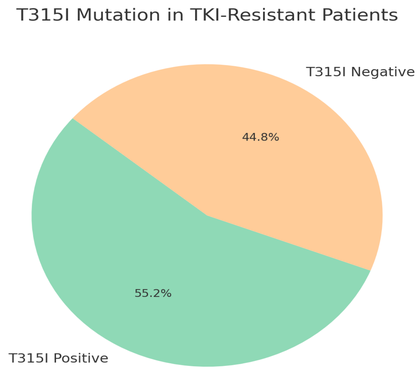
Study Design: Cross-sectional analytical study.
Setting: Mayo Hospital Lahore, Nishtar Medical University Multan, and University of Health Sciences.
Period: June 2022 to December 2023.
Material & Methods: We collected the samples by a non-probability consecutive sampling technique. Using this technique, we enrolled 190 newly diagnosed patients with CML. These patients were started on first-line TKIs and after 3 of their blood samples were analyzed for complete hematological response (CHR). All cases were labeled as resistant, in which CHR was not achieved as guided by Leukemia Net guidelines. Resistant cases were analyzed for T315I mutation by using PCR technique.

RESULTS

A total of 190 patients were enrolled in the study, comprising 118 males and 72 females. Among these patients, 63.16% of the patients showed response to TKI categorized as CHR, while 36.84% of the patients did not show CHR and were categorized as resistant to TKI. The TKI site mutation analysis for T315I mutation was positive for 39 patients (55.17%) out of a total 70 TKI-resistant patients (36.84% of all enrolled patients).



63.16% of patients showed response (CHR), while 36.84% were resistant.



55.17% of TKI-resistant patients tested positive for T315I mutation.

CONCLUSIONS

It was evident from our study that TKI resistance is common in Pakistani patients and a handful of patients showed T315I mutation in which poor response was documented.

REFERENCES

Majumdar A, Katara R, Mishra A, Gupta A, Sharma DK, Srivastava AK, Sharma S, Jaiswal A, Dixit M, Kumar V, Kumar S. A Retrospective Analysis of BCR-ABL1 Kinase Domain Mutations in the Frontline Drug Intolerant or Resistant Chronic Myeloid Leukemia Patients: An Indian Experience from a High-End Referral Laboratory. South Asian Journal of Cancer. 2022 Dec 31.

Akhilesh S, Ashish A, kumar Singh N, Kaur M, kumar Yadav A. BCR-ABL kinase domain mutations in CML patients, experience from a tertiary care center in North India. Leukemia Research Reports. 2024 Jan 1;21:100403.

Liu J, Yang H, Xu X, Yi S, Meng L. Mutations in the BCR-ABL1 kinase domain in patients with chronic myeloid leukaemia treated with TKIs or at diagnosis. Oncology letters. 2020 Aug 1;20(2):1071-6.

ACKNOWLEDGEMENTS

Oncology Departments of Mayo Hospital Lahore, Nishtar Medical University Lahore, University of Health Sciences Lahore

CONTACT INFORMATION

Email: dr.umera.saleem@gmail.com