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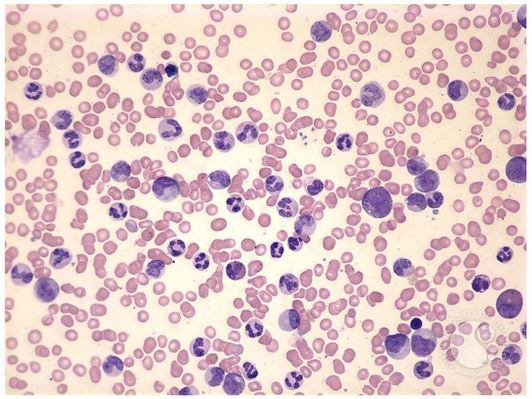
Challenges Navigating Therapies and Dosings in the Modern Era of TKIs in Low Resource Countries

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INTRODUCTION

A reciprocal translocation [t(9;22)(q34;q11.2)] that results in the fusion of ABL1 gene causes chronic myeloid leukemia (CML). Beginning in 2000, the prognosis and treatment dynamics for CML patients were altered by the accessibility and affordability of numerous BCR::ABL1 tyrosine kinase inhibitors (TKIs).



CASE PRESENTATION

A 71-year-old previously healthy lady presented for fatigue, and night sweats for the last two months with palpable splenomegaly. Laboratory tests showed normocytic anemia, leukocytosis 260,000/microL, 80% neutrophils, platelet count 680,000/microL. Peripheral smear compatible with CML confirmed by bone-marrow biopsy (chronic phase CML). PCR BCR-ABL: 75% IS stratified as high-risk group therefore she was started on Hydroxyurea for almost a month until access was obtained to Dasatinib 100 mg taken once daily. Three weeks later the patient improved clinically, however she developed severe thrombocytopenia 10,000/microL, therefore Dasatinib was stopped, and platelets recovered three weeks after. She was rechallenged with Dasatinib due to non-availability of different agent, had more profound and sustained thrombocytopenia, thus bone marrow was normal confirming the drug induced cause of thrombocytopenia. Since there was no available alternative dosing, Dasatinib 100 mg was given every other day for two weeks with similar thrombocytopenia. She was switched to Imatinib 400 mg with thrombocytopenia, attempt to decrease the dose resulted in maintained profoud thrombocytopenia and therefore imatinib was withheld due to bleed. Whenever TKIs were withheld, platelets count recovered. After two months of no available therapy, patient was started on Bosutinib 300 mg however severe fatigue and musculoskeletal debilitating pain occurred which resulted in decreasing the dose with thrombocytopenia of 30,000/microL. So, the dose decreased to 100 mg every other day with Eltrombopag which helped to keep her platelet count in an acceptable range. Surprisingly, she responded well with BCR-ABL 0.34% IS after two months of therapy.

CONCLUSION

Bosutinib trial in first line CML treatment (BFORE) used a reduced dose of bosutinib (400mg daily) and demonstrated superiority for MMR at 12 months, however lower doses of Bosutinib have not yet been found to show clinically significant result (<200mg). This case demonstrates that even a lower dose of Bosutinib can induce a molecular response in patients with CML.

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