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Mutational Analysis of JAK2V617F in Tunisian CML Patients with TKI-Resistance

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Abstract : Background:Chronicmyeloidleukemia (CML), a hematologicaldisease, ischaracterized by t (9; 22) and relatedoncogene BCR-ABL formation. Although Tyrosine kinase inhibitors (TKIs) have revolutionized the treatment of CML, resistanceoccurs and possibly médiates by mutation in severalgenesindependently of the bcr-abl1 kinase mechanism. it has been reportedthat JAK2V617F/BCR-ABL double positivitymaybe a potential marker of resistance in CML. Aims: This studywasinvestigated the JAK2V617F mutation in TKI-resistant CML patients. Methods: A retrospectivestudywasconducted in the Hospital University of Sfax, south of Tunisia, including all CML TKI-resistant patients. A Sanger sequencingwasperformedusing a high-fidelity DNA polymerase. Results:Nineresistant CP-CML patients wereenrolled in thisstudy. The JAK2V617F mutation wasdetectedin 3 patients with TKI resistance. Conclusion:Despite the limit of ourstudy, ourfinding highlights the high frequency of JAK2V617F/BCR-ABL double positivity as an important marker of resistance. So; the combination of JAK and TKI inhibitorsmightbe effective and potentiallybeguided by molecular monitoring of minimal residual disease1.

Keywords : chronic myeloid leukemia, tyrosine kinase inhibitors, resistance, JAK2V617F, BCR-ABL
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