ABSTRACTS

BCR-ABL KINASE DOMAIN MUTATION ANALYSIS IN CHRONIC MYELOID LEUKEMIA PATIENTS TREATED WITH TYROSINE KINASE INHIBITORS.

ALAMGIR KABIR

Professor of Hematology, Bangladesh Medical College Hospital, Dhanmondi, Dhaka, Bangladesh. E-mail: akabirk37@yahoo.com

Mutations in the Bcr-Abl kinase domain may cause, or contribute to, resistance to tyrosine kinase inhibitors (TKIs) in chronic myeloid leukemia patients. Over the last decade, intensive efforts have been spent in the characterization of the biologic and clinical significance of these mutations on one hand and in the development of novel inhibitors retaining efficacy against as many Bcr-Abl mutant forms as possible on the other hand. The knowledge of the Bcr-Abl KD mutation status is a valuable piece of information to be integrated in the decision algorithm aimed at tailoring the best therapeutic strategy for each of these patients: increasing imatinib dose, switching to the second-generation TKIs dasatinib or nilotinib, then to the third generation Bosutinib or ponatinib moving to allogeneic stem cell transplantation. BCR-ABL KD mutation analysis is not recommended in newly diagnosed chronic phase (CP) patients. Conversely, it can be performed in the rare cases who are in accelerated phase or blast crisis (BC) at the time of imatinib start. Mutation analysis is recommended both in case of failure and in case of suboptimal response to imatinib from a clinical standpoint, “failure” means that continuing a specific treatment is no longer appropriate because a favorable outcome is unlikely. Suboptimal response” means that the patient may still have a substantial long-term benefit from continuing a specific treatment, but the chances of an optimal outcome are reduced. During second-line dasatinib or nilotinib therapy in case of hematologic or cytogenetic failure BCR-ABL KD mutation analysis is recommended. In case of a T315I mutation, which is highly resistant to imatinib, dasatinib, and nilotinib, most appropriate alternative therapeutic option is ponatinib. In case of V299L, T315A, or F317L/V/I/C mutations, nilotinib is probably more effective than dasatinib. In case of Y253H, E255K/V, or F359V/C/I mutations, dasatinib is probably more effective than nilotinib. In case of any other mutation, dasatinib and nilotinib are likely to be similarly effective.

Keywords: BCR-ABL kinase domain mutation analysis, chronic myeloid leukemia , tyrosine kinase inhibitors.

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