Imatinib Mesylate in Chronic Myeloid Leukemia

At this point of time Imatinib Mesylate does not need any introduction. It has some of the hallmarks of an ideal cancer drug; it is relatively specific, can be taken orally, and with few side effects. Available data suggest that overall survival is comparable, if not better than allogeneic stem cell transplant, which has considerably more toxicity and mortality[1]. However, it is costly and from some reports, the responses are durable only so long the drug is continued. It is currently recommended that the drug be continued lifelong[2]. Even so, targeted therapy appears to be the correct approach to cancer treatment and Imatinib will be the benchmark for future targeted therapies.

The IRIS trial randomized 1106 patients to either Imatinib or Interferon-cytarabine treatment. At the end of 5 years only 16 patients out of the 553 patients in the Interferon-Cytarabine treatment group have continued initial therapy[2]. Complete cytogenetic responses (CCR) in the Imatinib group were 69% by 12 months and 87% by 60 months. Patients achieving a complete or even a partial cytogenetic response were less likely to progress to advanced stages compared to those without a major cytogenetic response ($P<0.001$). In molecular terms, patients achieving more than 3 log molecular response at 18 months had 100% chance of progression free survival at 60 months. The estimated overall survival of patients on Imatinib therapy was 89% at 60 months.[2]

There is a paucity of data on Imatinib use in Indian patients.[3-4] In this issue, Jacob et al from Bangalore have presented their data on 100 patients.[5] Hematological responses appear to be comparable with western experience. However they have reported a complete cytogenetic response of 30% at 6 months and 38% at 12 months. They have speculated on the possible causes for poor cytogenetic response in their patients. Their patients were started on Imatinib within a median duration of three months after diagnosis. They noted the presence of blasts in peripheral blood of all patients and have suggested that this and other variables point towards a more advanced stage of disease than western patients. Perhaps their patients had disease for a much longer period prior to diagnosis

than suggested historically. Duration of disease prior to Imatinib along with pre-therapy peripheral blood blasts and cytogenetic response at 6 months is an important predictor of developing imatinib resistance.[6]

The authors discussed the possibility of adverse mutations at diagnosis that might contribute to the poor cytogenetic response. While this might be true, currently there is no evidence that mutations present prior to starting Imatinib are responsible for resistance. It is recommended to screen for mutations in selected patients who have suboptimal cytogenetic or molecular responses at 6 months and in those who have significant increases in BCR-ABL levels.[6] Alternative therapy with the newer tyrosine kinase inhibitors and allografting might then be considered.

Single institution data is unlikely to give a complete picture indicative of all Indian patients. Multi-center derived information will need a higher level of cooperation and sharing of data among institutions than what is presently prevalent. We will also need to establish quality control mechanisms among different laboratories if we hope to generate data which is internationally comparable.

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