To the Editor,

European LeukemiaNet (ELN) expert panel updated the 2006 CML management recommendations in Blood with minor modifications in Journal of Clinical Oncology. The most important criticism about this update is the preservation of the ambiguous concept “suboptimal response to imatinib”. This gray-zone concept has been generated without long-term follow-up data on imatinib and in the absence of second generation TKIs in 2006. Latest evidences indicated that the outcome of “imatinib-suboptimal responders” is very similar and as worse as “imatinib-failure patients”. Furthermore, in the Table 7, “Continue imatinib same dose; or test high dose imatinib...” was also recommended as a treatment for “imatinib-suboptimal responders”. High dose imatinib, which had inferior efficacy when compared to dasatinib and nilotinib, is not superior to standard dose imatinib too. Removal of the misleading concept “suboptimal response to imatinib” could also simplify Table 6 of the manuscript. Adherences of physicians and patients to previous ELN-CML recommendations are not so high. Simplification of recommendations may also increase the compliances and the response to treatment.

CML is a progressive disease and time is important. Even complete cytogenetic responders are not in the “safe heaven”. For instance; we followed a 51-year-old female patient admitted to our hospital with the complaints of fatigue and abdominal distension. Her hemoglobin was 9.4 g/dl, platelet count 914.000/mm³ and white blood cell count 152.800/mm³ with early myeloid cells in the peripheral blood smear. She had hepatosplenomegaly (7 cm and 15 cm below the right and left costal margins, respectively). The BCR-ABL fusion gene transcripts were detected in bone marrow aspiration by fluorescence in situ hybridization (FISH) and reverse-transcriptase polymerase chain reaction (RT-PCR). She was diagnosed as high-Sokal chronic phase CML. 800 mg daily imatinib for CML treatment was started. Since edema of the legs and face developed, imatinib dose was temporarily reduced to 400 mg with addition of furosemide 40 mg po two times a week. The drug dosage was again increased to 800 mg by resolution of edema after a month. She achieved complete cytogenetic remission (CCGR) after 3 months of imatinib. She remained in CCGR for one month until she developed a sudden blastic transformation after 7 months of diagnosis. She had hypercellular marrow with 90% myeloid blasts. Morphologic and immunophenotyping studies (CD7, CD13, CD22, CD34, CD117, HLA-DR positive) were consistent with myeloid blast crisis.
Simultaneous conventional and molecular cytogenetic (FISH) analysis of the bone marrow aspirate revealed the clonal evolution with 48,XX,+8,+19, t(9;22)(q34;q11.2)t and nucish 9q34(ABLx2) 22q11.2(BCRx2)/9q34(ABLx3)22q11.2(BCRx2) (BCRonABLx1)/9q34(ABLx2)22q11.2(BCRx2) (BCRonABLx1). Remission induction chemotherapy with idarubicin 12 mg/m² for 2 days and Ara-C 100 mg/m² for 5 days was given. She achieved hematologic remission and was taken to a maintenance therapy with Ara-C 10 mg/day sc plus imatinib 400 mg/day. One month later, leukemic relapse occurred. Further, cytogenetic and FISH analyses revealed the persistence of trisomy 8, trisomy 19 and Ph* chromosome and 93% of BCR-ABL fusion gene, respectively and T315I mutation. This unique case is another example of sudden blastic transformation even in “complete imatinib responders”.6

**START-B** trial showed that dasatinib 70 mg twice daily demonstrated high levels of hematologic and cytogenetic responses in patients with blastic phase of CML includes the full cohort of 157 patients.7,8 HR rates were higher in the MBP-CML cohort, whereas CyR rates were higher in the LBP-CML cohort. The MCyR rate actually exceeded the major HR in LBP-CML patients. All responses were obtained rapidly, and 81 and 47% of those patients who achieved a major HR, and 77 and 40% of those who achieved a MCyR remained progression free at the time of evaluation, for the MBP-CML and LBP-CML cohorts, respectively.6 Dasatinib, which is the only approved second generation TKI for blastic phase CML, may create the opportunity for patients with advanced phase CML disease and not eligible for transplant. It would be important to explore options such as dasatinib-based combinations to try to improve long-term outcome.

The expectations in the second generation TKI era of CML is high and all treatment recommendations should be established on the basis of long-term patient survival.

**REFERENCES**


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