## The tolerability issue of generic imatinib in patients with chronic myeloid leukemia *(Comment on Adi J. Klil-Drori et al., Haematologica 2019;104(7):e293)*

As imatinib becomes generic, physicians treating patients with chronic myeloid leukemia (CML) worldwide face doubts regarding the efficacy and toxicity of generics.[1] There are many studies, mostly retrospective in nature, from different countries with different outcomes.[2] Since generics differ from nation to nation, at least one of the possible reasons for these contradictory findings could be attributed to this fact. To date, all of the studies from Turkey show that both the efficacy and tolerability of generics are comparable to those of the original molecule.[3-7]

We have read with great interest the report of a study by Klil-Drori *et al*. from Canada, in which the authors compared generic and branded imatinib among patients with CML in chronic phase (CML-CP), focusing on non-persistence of treatment as the primary outcome.[8] They clearly showed that the duration of use of tyrosine kinase inhibitor (TKI) therapy in patients with CML-CP was significantly shorter among generic imatinib users than among those taking the branded originator, and intolerance was the main reason for this higher non-persistence.[8]

Although this report presents some very important findings, for our point of view, there are some aspects that need to be underlined. The authors stated within the text and in their *Online Supplementary Table S1* that some previous studies including ours[3,4] did not show the rates for TKI cessation due to intolerance among cases receiving generics. However, in the paper published in the *British Journal of Haematology*,[3] it was stated that there was no switch to second-generation TKI due to intolerance in patients taking generics, and only three patients receiving generics needed a dose reduction due to toxicity. Similarly, in the article published in *Clinical Lymphoma, Myeloma & Leukemia*,[4] in which we compared early molecular responses and long-term outcomes in patients taking generic imatinib or Glivec, nine patients out of a total of 43 cases receiving generics were switched to a second-generation TKI for any reason (failure or toxicity). Of these nine cases who had a TKI switch, seven did so because of treatment failure and the other two because of intolerance. In both of these studies, the percentages of patients who needed a switch to a second-generation TKI were similar for both generic and original imatinib, although the median durations of follow-up of Glivec users were significantly longer than those of generic imatinib users in both studies.[3,4]

TKI treatment can be associated with toxicities, which might result in temporary and/or permanent discontinuation of this therapy. Interruption of TKI therapy can also translate into less favourable outcomes. Since there is a growing number of studies among patients receiving generic imatinib from different countries with contradictory results, as the authors suggested, further comparative work on the tolerability of generics is still needed.

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### References

1. Eskazan AE, Ar MC, Soysal T. The efficacy and tolerability issue of generics of imatinib in the treatment of chronic myeloid leukemia: do generics really jeopardize patient safety? Leuk Lymphoma. 2015;56(4):1182-1183.
2. Soysal T, Eskazan AE, Ar MC. Generics in chronic myeloid leukemia: current arguments for and against and the established evidence. Expert Rev Hematol. 2014;7(6):697-699.
3. Eskazan AE, Ayer M, Kantarcioglu B, et al. First line treatment of chronic phase chronic myeloid leukaemia patients with the generic formulations of imatinib mesylate. Br J Haematol. 2014;167(1):139-141.
4. Eskazan AE, Sadri S, Keskin D, et al. Outcomes of chronic myeloid leukemia patients with early molecular response at 3 and 6 months: a comparative analysis of generic imatinib and Glivec. Clin Lymphoma Myeloma Leuk. 2017;17(12):804-811.
5. Eskazan AE, Elverdi T, Yalniz FF, et al. The efficacy of generic formulations of imatinib mesylate in the treatment of chronic myeloid leukemia. Leuk Lymphoma. 2014;55(12):2935-2937.
6. Malkan UY, Aksu S, Aktimur SH, et al. Generic imatinib mesylate is as effective as original Glivec in the clinical management of CML. UHOD. 2015;4:215-221.
7. Demirkan F, Sevindik OGG, Karaman A, et al. Comparing the efficacy of generic imatinib formulations with the original imatinib as the frontline tyrosine kinase inhibitor in chronic phase chronic myeloid leukemia. J Clin Oncol 2015; 33(Suppl):(e18024).
8. Klil-Drori AJ, Yin H, Azoulay L, et al. Persistence with generic imatinib for chronic myeloid leukemia: a matched cohort study. Haematologica. 2019;104(7):e293.