Efficacy and Safety of a Pakistan-Manufactured Generic Imatinib in Newly Diagnosed Chronic-Phase Chronic Myeloid Leukemia: A Multicenter Phase IV Study

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Background. Imatinib remains the most widely used frontline TKI for chronic myeloid leukemia (CML) in low and middle-income countries, where access depends largely on generic preparations. Local efficacy data for Pakistan-manufactured generic imatinib are limited. We assessed the molecular response and tolerability of generic imatinib in newly diagnosed chronic-phase CML.

Methods. In this single-arm, open-label, multicenter Phase IV study, 101 adults with newly diagnosed Ph+/BCR-ABL1+ chronic-phase CML were enrolled at 7 Pakistani tertiary centers and treated with imatinib 400 mg orally once daily. Sokal score was calculated at diagnosis. The primary endpoint was rate of major molecular response (MMR; BCR-ABL1^{IS} ≤0.1%) at 12 months. BCR-ABL1^{IS} was quantified by RT-qPCR at baseline and at months 3, 6, and 12. Changes in transcript levels were tested with the Wilcoxon signed-rank statistic. We also estimated the annual out-of-pocket cost saving per patient versus Gleevec.

Results. Mean age was 43.6 ± 14.3 years, with an approximately equal male-to-female ratio. Sokal risk was low in 9.9%, intermediate in 40.6%, high in 18.8%, and unstratified in 30.7%. Eighty-one patients (80.2%) had an evaluable 12-month transcript. MMR at 12 months was achieved in 35 of 81 evaluable patients (43.2%; 34.7% of the intention-to-treat cohort). Median BCR-ABL1^{IS} fell from 55.0% at baseline to 5.21% at month 3, 1.87% at month 6, and 0.38% at month 12 (each $p<0.001$ versus baseline). Mean $\log_{10}$ reduction at 12 months was 2.14 ± 1.21. Applying ELN-2020 criteria at 12 months, 11.9% had BCR-ABL1^{IS} >1% (failure) and 16.8% were in the warning range. The drug was well tolerated, with grade 1–2 toxicities predominating: muscle cramps peaked at 14.9% in month 1 and declined to 4.0% by month 6; nausea or vomiting fell from 8.9% to 1.0%; thrombocytopenia from 5.0% to 1.0%. One patient discontinued for intolerance and one for primary resistance; three progressed to advanced phase. The estimated annual out-of-pocket saving per patient using Pakistan-manufactured imatinib versus branded imatinib was USD 7,295.

Conclusions. Pakistan-manufactured generic imatinib produced clinically meaningful, time-dependent molecular responses in newly diagnosed chronic-phase CML, with a tolerability profile consistent with branded imatinib. The 12-month MMR rate of 43.2% in evaluable patients supports its continued use as frontline therapy in resource-limited settings.