Aim/Background: The emergence of ABL point mutations is the most frequent cause for imatinib resistance in chronic myelogenous leukemia (CML). The aim of the study is to investigate mutations of the BCR-ABL tyrosine kinase domain (TKD) during TKI treatment in CML.

Methods: Karyotyping and BCR-ABL TKD mutation screening are performed in 115 imatinib resistant CML patients who were on imatinib at the time of loss of hematologic response (HR), cytogenetic (CyR) or molecular response (MR). Imatinib – Resistance Mutation Analysis (Qualitative) were detected by Nested RTPCR and Sanger’s Sequencing. Out of 115 patients, 42 patients received escalated Imatinib, 38 Nilotinib and another 35 Dasatinib.

Results: In 115 BCR-ABL positive imatinib, nilotinib and dasatinib resistant patients, 11 different BCR-ABL TKD mutations were detected. The analysis revealed no mutations-51 patients, M351T-13 patients, G250E-11 patients, F317L-10 patients, M244V-5 patients, E255K-5 patients, V379I-5 patients, F359V-4 patients, H396R-4 patients, Y253F 4 patients, E355G - 3 patients, T315I-2 patients. The eleven novel mutations (F317L, G250E, M244V, F359V, T315I, E355G, H396R, V379I, E355G, T315I) conferring Imatinib resistance, 10 Nilotinib –resistant mutation (M244V, F359V, T315I, E355G, G250E) and 8 Dasatinib-resistant mutation (H396R, F317L, H396R, T315I, M351T) were seen in our patient population. T315I which confers resistance to all TKIs was detected only in 3/115 patients who demonstrate loss of response in our population.

Conclusions: As compared with other western studies the incidence of T315I mutation is very low in our study. In addition analysis of mutation patterns at baseline may help in stratifying patients for treatment. In our practice if nilotinib –resistant mutation was detected, dasatinib was preferred and if a dasatinib-resistant mutation was detected, nilotinib was preferred. We are planning for using Bosutinib, Panotinib and Omacetaxine (SC route) in third line therapy in Imatinib, dasatinib and nilotinib resistant different mutation positive chronic myeloid leukemia.

Disclosure: All authors have declared no conflicts of interest.