Background: More than 45% of CML patients in Qatar resist the first line of treatment; Internationally, certain ABL mutations are the most common cause of IM resistance.

Objectives: To screen for BCR-ABL kinase mutations in CML patients treated in Qatar and to study if point mutations can be correlated with resistance to treatment.

Methods: Peripheral Blood (PB) and Bone Marrow (BM) samples were collected from 25 patients; total RNA was extracted and cDNA was produced via RT-PCR with special precautions to avoid amplification of wild type ABL and cover the whole ABL kinase domain.

Results: Over a period of three years, 39 PB and 30 BM samples from 25 patients receiving IM were studied for ABL mutations prior to treatment and at time of resistance.

For all 25 patients we noticed three nucleotide changes at A1258G, A1426G and A1739G of ABL (GenBank accession no. M14752). However, when we compared these changes with major SNP databases (NCBI, ENSEMBL), these changes were described by others as ancestral allele that does not convey any pathological changes.

Although, we found no evidence of ABL point mutations in patients at time of resistance, in one patient, who had complex cytogenetic abnormalities, we noticed a transient insertion of three nucleotides (AAG) at position 1432 which added an amino acid Lysine356 at time of resistance.

This patient was shifted to dasatinib and achieved major molecular response after three months of treatment.

Conclusions: Due to high rate of resistance of CML to IM, we tested our patients for BCR-ABL points mutations and could not reveal any of the described ABL domain mutations.

The significance of the insertion of the three nucleotides is still to be determined.

However, it must be kept in mind that direct sequencing has a limited sensitivity and might miss a low level mutation (less than 30% of the total ABL domain).

An alternative approach such as High Resolution Melting (HRM) technology accompanied with sequencing might be needed to detect and quantify low level mutations.