### BCR-ABL Kinase Point Mutations don’t Correlate with the Resistance of Chronic Myelocytic Leukemia (CML) to Imatinib Mesylate (IM); A Study on CML Patient Population in Qatar

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**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.

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

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**Vitamin D Status in Pregnant Women and their Babies in Qatar**

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**Back ground and Objectives:** Vitamin D deficiency is very common in pregnant women and the current guidelines for vitamin D intake during pregnancy of 200-400 IU has been challenged recently. We conducted this study to determine the prevalence of Vitamin D deficiency among pregnant women and to evaluate the safety weekly oral 50,000 IU vitamin D supplementation for the mother and the newborn.

**Setting and design:** prospective study, at Hamad Medical Corporation, outpatient unit and delivery room.

**Patients and Methods:** 97 pregnant women were recruited in their first trimester between December 2007 and March 2010. Weekly oral vitamin D 50,000 IU were prescribed after an initial testing for serum level of 25-hydroxyvitaminD, parathyroid hormone, calcium, phosphorus, total protein and albumin. Other multivitamins supplementations were allowed during pregnancy. The same tests were repeated at each trimester. Umbilical cords Vitamin D levels were determined at birth.

**Results:** Out of 97, 8 patients dropped out from the study for several reasons, and 19 patients had miscarriages.

Data were available for 97 women in the first trimester, 78 women in the second trimester and 61 women in the third trimester. The mean level of vitamin D in the first trimester and prior to starting vitamin D supplementation was 17.15ng/ml, 29.08ng/ml in the second trimester, 27.3 ng/ml in third trimester and 22.36 ng/ml in newborns. There were no toxic levels of vitamin D in any of the women at second or third trimester or in the newborns. The mean levels of vitamin D in the second and third trimester were not significantly different in the women who were taking multivitamin supplementation versus those who were not.

**Conclusion:** Weekly dose of 50,000 vitamin D during pregnancy is safe in our population, maintains acceptable vitamin D level during pregnancy and the newborns’ vitamin D level correlates with the mother’s levels.