APPEARANCE OF LYMPHOCYTOSIS DURING FIRST AND SECOND GENERATION OF TKI TREATMENT IN CML PATIENTS- RETROSPECTIVE STUDY OF THREE CASES

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Based on a study published by Mustjoki and associates, early onset of medullary lymphocytosis during Imatinib treatment is a very important prognostic factor of treatment response and is associated with cytogenetic response. Medullary lymphocytosis has been identified as a better predictor of CCR at 12 months and MMR at 18 months compared to standard factors. Thus, patients with failure or suboptimal response to Imatinib could be recognized even after 3 months of treatment (no lymphocytosis or CCR) and another generation of TKI should be considered.

A preliminary report of DASISION trial showed that CML patients on Dasatinib treatment have an early onset and higher incidence of lymphocytosis then patients on Imatinib treatment. The patients on Dasatinib treatment who developed lymphocytosis had higher rates of CCR and MMR at 12 months compared to those on Imatinib treatment or on Dasatinib arm without lymphocytosis.

In this study, we are presenting three patients who developed lymphocytosis at 34, 96 and 62 months after TKI treatment was started. Absolute count of lymphocytes was 4,95 x109/L, 8,023 x109/L and 4,56 x109/L. Two patients were on first generation of TKI treatment (Imatinib) and the third was on second generation of TKI treatment (Dasatinib). At lymphocytosis onset, two patients were in chronic phase and the third was in blastic phase.

The flow-cytometry exam of peripheral blood was performed in all cases at the time of lymphocytosis onset.

The results were: reactive lymphocytosis in one patient in MMR after Imatinib treatment and associated cirrhosis due to chronic HVC infection, lymphocytosis with NK cells in one patient with resistance to Dasatinib treatment and blastic phase of CML and B cell monoclonal lymphocytosis in one patient in MMR after Imatinib treatment and a previous history of renal carcinoma 5 months prior CML diagnosis.

After 6 months of B cell monoclonal lymphocytosis, the patient showed on whole body CT scan generalized lymph nodes and splenomegaly. Due to chronic lymphoproliferative disease progression (anaemia and thrombocytopenia due to massive haematopoiesis dislocation, reduced lymphocyte doubling time and adenopathies and splenomegaly progression), the patient received 2 cycles of R-CVP regimen. During all this time, the patient had no cytogenetic or molecular signs of CML.

The conclusion of this study is that the three CML patients on TKI treatment developed lymphocytosis during disease evolution and the aetiology of lymphocytosis was different in every case. We argue that more research should be conducted to better define the relationship between CML and lymphocytosis associated with TKI treatment.