3768 Switching to a Second Generation TKI in Chronic Myeloid Leukemia Patients with Late Suboptimal Response with Imatinib Obtained Better Molecular Responses That the "Watch and Wait" Approach. an Experience of a Multicenter Registry in Patients Outside Clinical Trials

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Introduction: Tyrosine kinase inhibitors (TKIs) have dramatically changed chronic myeloid leukemia prognostic. The European Leukemia Net guidelines are widely used for patients treated with TKIs. While strategies for patients with optimal response and failure after imatinib are clear, there are doubts about the best treatment option for patients with suboptimal response (SubR), specially for late SubR (patients with complete cytogenetic response (CCyR) but not mayor molecular response (MMR) after 18 months of treatment). Patients with MMR seem to have better outcomes than patients with CCyR but not MMR, but at this time, there are few data showing the benefits of treatment change in this group of patients.

Aims: To identify the benefits of treatment change in patients with late SubR, outside clinical trials, in the setting of a multicenter hospital-based registry.

Patients and methods: We have studied retrospectively a group of 488 CML chronic phase patients treated with imatinib as first TKI, identifying 96 patients (19%) with SubR criteria (following the ELN recommendations) after 18 months of treatment. These patients have been classified according to the strategy followed by their physician after SubR identification. Group 1 includes 65 patients (67%) continuing with imatinib (either initial dose or higher dose) and group 2 includes 31patients (33%) that were changed to second generation TKI (2GTKI: dasatinib or nilotinib). Sokal risk index was high in 17% and 9%; intermediate 44 % and 41%; and low in 39% and 50 % for group 1 and 2, respectively. 31% and 30% of patients had received interferon prior to imatinib. Molecular response was analyzed after 12 months of identifying late SubR (for group 1) or after switching to 2GTKI, for group 2.

Results: The use of 2G TKIs resulted in significant benefit to patients in terms of improving molecular responses. Complete molecular responses (CMR) and MMR rates were 3.8% vs 27% and 41.5% vs 69% for group 1 and 2 respectively (p=0.006). Time for the achievements the best molecular responses was significantly lower for patients receiving second generation TKI (4.1 vs 20.2 months, p=0.004). Probabilities of treatment failure, defined as loss of CCR, were also higher in patients remaining with imatinib (15.4% vs 5.7% (p=0.12). Progression free survival was 93.8% vs 97.2% (p=0.18) for group 1 and 2 respectively. Changing treatment for late SubR patients was also safe, and only 17% of patients needed to switch to another TKI due to intolerance.

Conclusions: In CML patients treated with Imatinib with late SubR, and outside clinical trials, switching to second generation TKI increased probabilities of achievement a deeper molecular response, with a good safety profile.

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