# TEN YEARS OF TREATMENT WITH IMATINIB IN CML – ASSESSEMENT OF EFFICACITY, SAFETY PRIFILE AND PROGNOSTIC FACTORS OF RESPONSES AND SURVIVAL

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**Background**. Imatinib mesylate, a targeted inhibitor of the BCR-ABL tyrosine kinase, is the standard of care for chronic myeloid leukemia (CML). Imatinib has demonstrated a high level of efficacy and is associated with significant less toxicity than previously used therapies. Aims. To review the efficacy and safety of imatinib in patients with CML in chronic phase.

**Methods**. A retrospective review of patients in one department of hematology with a diagnosis of Ph/BCR-ABL positive CML and received imatinib. Criteria for treatment responses were according to the recommendations from the expert panel of European LeukemiaNet.

**Results**. From 15.02.2002 to 15.08.2012, 66 patients in CML-CP received imatinib were introduced in the study. The median age at diagnosis was 40 years old (range 13 to 79) with 51,5% men. Sokal score was 1,17 (0,45-13,38) with distribution (HR=30 IR=25 LR=11) and Hasford score 1025 (58-3231) with distribution (HR=14 IR=30 LR=22). All patients had positive karyotiping for Philadelphia chromosome.

**Treatment and outcome**. 22 (33%) patients received imatinib as upfront therapy, the others as second or third line treatment after hydroxiureea and/or interferon α, the mean time to initiate imatinib was 19 months (range 1-104). All the patients received a starting dose of 400 mg/day. Clinical assessment and laboratory investigations including cytogenetics studies were performed at regular intervals.

**Responses rate**. After starting imatinib, a CHR was achieved at 3 months by 87,5% patients. The CyR achieved was major in 62% (with 56% CCR), no CyR in 17 patients (25%). The molecular response was complete in 13 (20%) and major in 16 (24%) patients. Better cytogenetic and molecular responses were achieved by those with low and intermediary risc (Sokal) and those who were treated with upfront imatinib (74% vs 35% p 0.005) and those who received imatinib up to 24 months from diagnosis (72% vs 40% p 0,026). The doses were increased in 26 patients and an improved response was achieved in 17. Six patients were switched to Dasatinib and one to Nilotinib. Seven patients developed under imatinib additional cytogenetic anomalies : supplemental chromosome 8 (6), duplication of Ph1 (2), trisomy 17 and 19 (1).

**Survival data**. The median of follow-up was 69 months (range 18-180) and under imatinib was 52 months (range 3-126). Ten patients died : five of blastic transformation (44-104 months after diagnosis) four of septic shock and one of caschexia (in CMR). The Sokal score was a better predictor than Hasford's.

**Safety profile**. Adverse events were registered in 26 patients (40%). Nineten experienced hematological toxicities but grade 3 or 4, only in five, without future consequences. One patient experienced a secondary MDS, and seven an important edema or pleural effusion. **Conclusions**. The age at diagnosis in CML patients was decreasing during the last decades. Imatinib remains effective and well tolerated treatment for most of the patients, but there are still a significant number of patients who did not achieve a CyR. The responses and survival were not influenced by the previous treatments but the earlier introduction of imatinib is better. The Sokal score seems to have a better prognostic role.The survival is evidently improuved by TKI.