

Three patients (2 IM/HU, 1IM) were lost to follow-up. As prospectively designed, all available IM/HU patients (n=77) were analyzed together. According to the study protocol, patients from the CML IV study were to be added to obtain equal numbers for analysis. To arrive at a total of 77 IM patients, from study IV another 49 patients were selected by propensity score matching. The median age of the 154 patients was 55 years (range 18 – 82). The ELTS prognostic score was available for 141 patients and was high in 8 (5.7%), intermediate in 35 (24.8%) and low in 98 (69.5%), with no significant differences between treatment groups.

Results: The 5-year overall survival (OS) / progression-free survival (PFS) probabilities were 90.4 and 86.7% in the IM/HU and twice 84.9% in the IM arm (p=not significant). With IM/HU, the probabilities of complete cytogenetic response (CCR) at 6, 12, and 18 months were 54.3, 84.0, and 93.7%. In the IM arm, the corresponding numbers were 70.4, 84.9, and 83.3% (p=not significant). Primary endpoint was MMR rate at 18 months. There was no significant difference between IM/HU (65.8%) and IM (66.0%). At 6 months, MMR rates were 21.6 (IM/HU) vs 41.1% (p=0.0383) and at 12 months 41.9 (IM/HU) vs 58.9% (not significant). Time to event analyses of OS and PFS did not result in significant differences; neither did group comparisons between the probabilities of CCR and MMR. The median HU dose was 500mg (range 152-3000); the median IM dose was 400 mg (range 145-617mg) in both arms. The gross numbers of adverse events in general or of adverse events of grade 4 were not different between the two arms, but cumulative incidences showed an earlier occurrence in the IM/HU than in the IM arm (p= 0.0343, Gray test)

Summary/Conclusions: Compared to Imatinib only, the combination of Imatinib and HU resulted in a lower MMR rate at 6 months but a similar MMR rate at 18 months. Furthermore, IM/HU was associated with more early adverse events. There was no indication of a beneficial effect in the treatment of CML patients in 1st chronic phase using the combination of IM with HU.

PB1820

A MULTICENTER, OBSERVATIONAL, AMBISPECTIVE STUDY EVALUATING EFFICACY AND SAFETY OF GENERIC IMATINIB COMPARED TO GLEEVEC IN CHRONIC MYELOGENOUS LEUKEMIA IN CHRONIC PHASE - 3 MONTHS RESPONSE ANALYSIS

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Background: The efficacy of branded imatinib (Gleevec) in the first-line treatment of chronic myeloid leukemia (CML) has been demonstrated in several clinical studies. However, there are few consistent data in the literature on the efficacy and adverse effects of generic formulations of imatinib. In Brazil, CML patients have been treated in the national public health system with generic imatinib since June 2013.

Aims: The present study aims to evaluate the efficacy and safety of generic imatinib in the treatment of CML in comparison with the reference drug (Gleevec) in the first three months of imatinib treatment.

Methods: This is a multicenter, observational, ambispective, cohort-type study. The study was initiated in January 2015 with the intended participation of 17 Brazilian centers. In the prospective group, were selected chronic phase CML patients who started their first-line treatment with generic imatinib between January 2015 and October 2016, whereas retrospective group was treated with Gleevec between January 2010 and December 2011. All patients started imatinib less than six months from diagnosis. Study data were collected and managed using REDCap electronic data capture tools. Demographic data were collected at diagnosis: age, gender, Sokal, Hasford, EUTOS score, comorbidities, cytogenetics, BCR-ABL transcript type. The definition of the responses followed the European Leukemia Net 2013 criteria. Adverse events were assessed based on the Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0.3, 2010. Statistical analysis: SPSS version 21.0 was used applying the chi-square and t-test, when adequate. All analysis considered p-value <0.05 as significant.

Results: Ten centers have registered 177 patients in the retrospective group and 68 patients in the prospective group so far. For this preliminary analysis, response data from 132 patients were available (47 from prospective and 85 from the retrospective groups). The median age of patients was 54 years in the prospective group and 46 years in the retrospective group (P=0.12). Sokal score in prospective and retrospective groups, respectively: low risk 42%/52%; intermediate risk 42%/31% and high risk 45%/67% (P=0.48). There was no difference between the groups concerning gender, Hasford, EUTOS scores, ECOG, blood cell counts at diagnosis and before starting

imatinib and BCR-ABL transcripts. Regarding responses, there was no difference in the hematological, complete cytogenetic responses and rate of BCR-ABL transcripts >10% at three months. However, there was a higher rate of failure at three months according to the ELN 2013 criteria in the prospective group (14.9% versus 4.7% Gleevec group, P=0.04). There was no significant difference in grade 3 and 4 hematological and non-hematological toxicity, but there was one early death in the prospective group (acute peripheral arterial occlusion and renal failure). Four patients discontinued imatinib: one from Gleevec group (resistance) and three from the generic group due to intolerance (1) and resistance (2).

Summary/Conclusions: According to ELN-2013 criteria, there was a higher rate of failure in the prospective group (generic Imatinib) at three months, but no difference in toxicity. The register is ongoing; the confirmation of this data and the impact in prognosis will be evaluated in the long-term follow-up, after increasing the number of patients.

PB1821

COMPLEX ADDITIONAL CHROMOSOME ABERRATIONS IN PH-POSITIVE CELLS IMPACT ON CHRONIC MYELOID LEUKEMIA PATIENTS' SURVIVAL IN THE ERA OF TYROSINE KINASE INHIBITORS

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Background: Additional chromosomal aberrations (ACA) as marker of clonal evolution in chronic myeloid leukemia (CML) patients were previously noted in association with resistance to therapy. The presence of ACA have been associated with a worse prognosis for survival in the pre-TKI era. The ACA classification proposed earlier was based only on its frequencies. Whereas ACA's clinical impact had not yet been clearly established.

Aims: The aim of our study was to evaluate the long-term impact of the ACA presence in Ph-positive cells in CML patients on TKI treatment results.

Methods: 30 patients with ACA in Ph-positive cells treated in our center from 2005 to 2015 years were included in this study. Cytogenetic analyses of at least 20 Giemsa-banded bone marrow metaphases were interpreted per ISCN 2013. We analyzed overall survival (OS) and cumulative incidence of CML-related death on TKI treatment. Cox regression was used for multivariate survival analysis, that included next covariates: number of ACA, type of ACA, age, TKI type, CP or AP at diagnosis. OS was estimated by Kaplan-Meier method with log-rank test for comparison. Cumulative incidence of CML-related death was estimated into consideration the presents of competing risks (CML-unrelated death) using Gray's test for comparison between groups.

Results: Median follow-up period in ACA group (n=30) was 51 months (3-124). ACA at diagnosis were detected in 16 (53%) of 30 patients. Chronic phase CML at diagnosis was determined in 23 (77%) patients. Imatinib was used as first-line in 20 (67%) patients, 3 (10%) patients were initially treated with Nilotinib. Accelerated phase was defined in 7 (23%) patients. In that group treatment of 6 patients was started with Imatinib and Dasatinib was given initially for one patient. «Major-route» ACAs (trisomy 8, +der(22)t(9;22)(q34;q11), i(17)(q10), trisomy 19,) were detected in 16 (53%) of 30 patients. Complex aberrations (2 ACA and more) were revealed in 7 (23%) patients, 4 patients from this group had «major-route» ACA. 10-years OS in the whole ACA group was 67%, 10-years cumulative incidence of CML-related death was 23%. Number of ACA (p=0.03, HR=13.2) and age (p=0.03, HR=1.14) had statistical significance influence on survival by regression analysis. 10-years OS was 31% and 77% (p<0.05) in patients with complex ACA and single ACA respectively, 10-years cumulative incidence of CML-related death was 54% for patients with complex aberrations versus 10% for single ACA patients (p<0.05) (Figure 1).

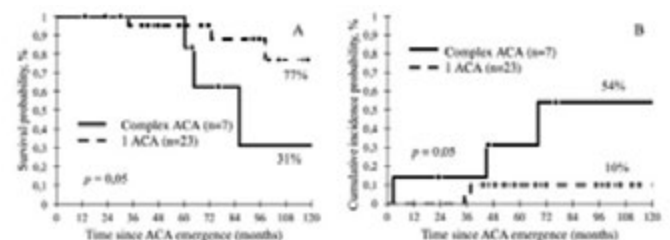


Figure 1. Overall survival (A) and cumulative incidence probability of death due to CML (B) in CML patients with complex ACA (n=30)

Figure 1.

Summary/Conclusions: Our results showed that TKI treated CML patients with complex ACAs have a higher risk of progression and death in comparison with single-ACA patients.