EFFICACY AND SAFETY FOR DASATINIB IN EARLY CHRONIC PHASE CML PATIENTS WITH LATE SUBOPTIMAL RESPONSE TO FRONTLINE IMATINIB. PRELIMINARY RESULTS FROM DASAPOST STUDY

Valentin Garcia-Gutierrez , Beatriz Colom , Fermin Sanchez-Guijo , Rosa Ayala , Concha Boqué , Casado Luis Felipe , Isabel Montero , Blanca Xicoy , César Soto , Raquel de Paz , Anna Kreutzman , Cecilia Muñoz , Juan Luis Steegmann

Abstract: E1117 Type: Eposter Presentation

Background

The additional benefit of achieving major molecular response (MMR) in patients with Complete Cytogenetic Response (CCyR) response is still under debate, and therefore, patients with CCgR without MMR after 12 months of treatment are considered as a “warning” by European LeukemiaNet (ELN) recommendations. Several clinical trials have shown how patients treated with imatinib front line and classified as late warning responders can benefit from treatment changed to nilotinib in terms of improving molecular response. However, there are no data regarding to treatment change to dasatinib in this group of patients

Aims

To evaluate the efficacy and safety of treatment change to dasatinib in patients treated with imatinib first line with late suboptimal response (patients with CCyR without MMR after at least 18 months of treatment) by the ELN 09 recommendations

Methods

We are presenting preliminary results of the first 18 patients enrolled in the phase II DASAPOST study (NCT01802450). Main inclusion criteria were patients treated with late suboptimal response by the ELN09 (CCyR without MMR after 18 months of treatment). Previous treatment with imatinib 600mg (but not 800mg) was allowed. Median exposure to imatinib before dasatinib was 5.1 years (1.8-12.2). Sokal risk groups % (L/I/H) was 22.5%, 55% and 22.5%. Median age was 56 years (34-77). Primary end point was the achievement of MMR after 6 months of dasatinib. Secondary endpoints were to assess the efficacy of dasatinib in terms of depth and kinetics of molecular response, as well as the relationship of response with lymphocyte alterations. Responses evaluations were performed following indications of the ELN. All BCR-ABL/ABL (IS) measurements were centralized in an EUTOS laboratory.

Results

Clinical: Eighteen patients have been enrolled in the study. Median follow up at data cut-off was 262 days (21-380). Three out of 18 (16%) patients had discontinued dasatinib due to side effects (pancreatitis, pleural effusion and low grade, persistent side effects (fever, arthralgias, anemia and asthenia). 16/18 patients have been evaluated at 3 months, 12 at 6 months and 6 at 12 months. Cumulative incidences by ITT of MMR calculated by competing risks by 3 and 6 months were 50 and 83%. However, for patients who reached the 6 months assessment frequencies of MMR and MR4.5 were 85% and 42% respectively. No patient have lost CCyR while 1 patient in MR4.5 lost MMR. 1 patient had reduced dasatinib dose to 70mg due to congestive heart failure (patient achieved and maintained undetectable molecular response). Immunological: Lymphocyte counts were done before and after dasatinib intake at baseline, at 3 and 6 months, observing an increment of counts post intake in most patients. At baseline the median increase post intake was 1,79 fold (0,98-3,2). There was no significant association between this increment and MMR at 3M (MMR at 6 months was not studied, as most patients obtained this response at that timepoint)

Summary
Our study shows, for the first time to our knowledge, that in patients treated with Imatinib and late suboptimal (warning) responses, switch to Dasatinib induced MMR in 83% of the patients, although 16% discontinued treatment because of toxicity. No association was found between lymphocyte “mobilization” post intake and response. Dasatinib appears to have a good benefit/ risk ratio in this type of patients. More details on the immunologic studies will be provided