(0.42%) was in minor molecular response (mMR), 11 patients (4,62%) in complete cytogenetic response (CCyR), 1 patient (0,42%) in partial cytogenetic response (PCyR), 1 patient (0,42%) in minor cytogenetic response (mCyR) and 12 patients (5,04%) were in complete hematological response (CHR).The 2 patients with MMR were both treated with imatinib as the patient with mMR. Among the 11 patients in CCyR, 10 were treated with imatinib and 1 with dasatinib. Of the 12 patients in CHR, 9 were under imatinib and 3 patients were treated with hydroxiurea. The T315I mutation was found in only one patient, diagnosed in 1998 who was in clinical and hematological relapse after several lines of treatment (interferon + Ara-C, imatinib, dasatinib). *Conclusions*. The T315I mutation was a very rare event in our patient population, despite a high proportion of patients who had a suboptimal response after TKI treatment. An explanation could be the fact that few of our patients were treated as first line therapy with TKIs; also, few patients were treated with high-dose TKIs. Therefore it is possible that there was not enough time and selective pressure for the emergence of the T315I mutation. Further follow-up of the patients treated as first line-therapy TKI may result in a higher rate of T315I detection. This aspect is of utmost importance as such CML patients may be the ones who will actually benefit from allogeneic stem cell transplantation.

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NILOTINIB (AMN107) CAN INDUCE COMPLETE CYTOGENETIC RESPONSES (CCYR) AND MOLECULAR RESPONSES IN PATIENTS (PTS) WITH CHRONIC MYELOID LEUKEMIA (CML) RESISTANT OR INTOLERANT TO IMATINIB MESYLATE (IM) . REPORT OF THE COMPASSIONATE USE PROGRAM (CUP)OF NILOTINIB IN MEXICO

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Background. Nilotinib, a potent and highly selective BCR-ABL inhibitor, has been approved in more than 50 countries including Mexico. Nilotinib is indicated for the treatment of Philadelphia chromosome-positive chronic myelogenous leukemia (Ph^+ CML) patients (pts) in chronic (CML-CP) or accelerated phase (CML-AP) resistant or intolerant to prior therapy including imatinib (IM). Before the approval of nilotinib by FDA or EMEA a CUP of nilotinib was initiated in Mexico. Aims: To evaluate the rates of cytogenetic and molecular responses to nilotinib in IM-resistant or -intolerant Ph^+ CML included in the CUP of nilotinib in Mexico. *Design and Methods*. The pts included in this program were adults pts with imatinib-resistant or intolerant CML-chronic phase (CP),-accelerated phase (AP), or -blast crisis (BC). IM resistance was considered if pts had failure to standard doses of IM or had loss of response and/or progression and were treated with higher doses of IM (600 mg/day or 800 mg/day) and did not respond to these dose escalation, IM intolerance/resistance was considered if pts with previous failure to standard doses of IM did not tolerate the dose escalation and needed a subsequent dose reduction.Physical examination, EKG, bone marrow aspiration, karyotyping and BCR-ABL mutation screening were performed in all pts before starting nilotinib. All pts signed an informed consent. Nilotinib was administered orally at a dose of 400 mg twice daily (BID). No dose escalation was allowed. All pts were monitored with karyotyping. Patients that achieved CCyR were evaluated with quantitative RT-PCR for molecular evaluation (Quest Diagnostics and Molecular MD) The results of CUP of nilotinib in Mexican patients are reported in this abstract including the cytogenetic, qRT-PCR and mutational analysis in a highly-resistant CML patient population. Results: Between October 2006 and June 2007, 47 pts were included in the nilotinib CUP in Mexico. The median age was 41.7 years (range 22-68) and 20 (44%) were men. Of the 47 pts, 28 (59.6%) had advanced phase CML which includes 7 (14.9%) blastic phase (BP) and 21 (44.7%) accelerated phase (AP) pts. 19/47 pts (40%) were in chronic phase (CP) of CML. Most patients were resistant to IM (86%) and 14% were IM-intolerant/resistant. The median duration since CML diagnosis was 74 months (range 14-183). The median duration of prior IM use was 27 months. All pts had been treated with hydroxyurea, interferon, and/or cytarabine prior to IM. At the time of starting nilotinib 17/47 pts (36.12%) had BCR-ABL mutations (P-loop mutations in 3 pts, IM binding mutations in 5 pts, catalytic domain mutations in 5 pts, and A-loop mutations in 4 pts). Only 3/47 pts (6.38%) had T315I mutation. The median duration of exposure to nilotinib was 403 days (range 19-840). Most pts tolerated nilotinib well. One patient developed long-term myelosupression. At the time of data cut-off (January 31th, 2009), 25 pts (53.2%) remain on therapy. Reasons for discontinuation of therapy were: a) lack of efficacy in 7/47 pts (14.9%) including 3 pts with T315I mutation; b) disease progression in 13/47 (27.5%); c) adverse events in 1/47 (2.1%); d) lost of follow-up in 1/47 (2.1%). The cytogenetic and molecular evaluation was performed after 12 and 18 months of treatment with nilotinib, respectively. The rate of overall hematological response (HR) was 79%. The major cytogenetic response (MCyR) according the phase of the disease were as follows: 57% in CP, 40% in AP and no MCyR was observed in BP. Of the 47 pts, 11 (23.4%) achieved CCyR (7 pts with CP-CML and 4 pts with AP-CML), five patients (10.63%) achieved molecular responses (3 pts with CP-CML and 2 pt with AP-CML) including 2 pts (4%) with complete molecular response (CMR) and 3 (6%) with major molecular response (MMR). *Conclusions*. Nilotinib showed efficacy in IM-resistant or -intolerant CML pts in Mexico regardless of the presence or absence of BCR-ABL mutations. Nilotinib induced complete cytogenetic and molecular responses in some of resistant CP and AP-CML patients.

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KINETICS OF BCR-ABL TRANSCRIPTS IN PATIENTS WITH CHRONIC PHASE CML (CML-CP) TREATED WITH IMATINIB MESYLATE (IM): A PREDICTOR OF RESPONSE AND PROGRESSION FREE SURVIVAL (PFS)

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Aims. To assess whether early kinetics of molecular response to IM therapy is a predictor of PFS, and sustained hematological and cytogenetic responses in newly diagnosed patients with CML-CP. *Design and Methods*. Ninety-five newly diagnosed Egyptian patients with CML-CP were treated with a daily oral dose of IM 400 mg unless otherwise indicated. Conventional karyotyping and fluorescent *in situ* hybridization (FISH) analysis were performed at diagnosis, every 6 months during the first 2 years of treatment, and then annually or as necessary during a median follow-up period (FUP) of 26 months (range 6-64 months). Molecular monitoring by real time quantitative polymerase chain reaction (RT-QPCR) was performed at diagnosis and at regular intervals every 3 months during the FUP. Mutational analysis of the ABL kinase domain was performed by allele-specific oligonucleotide PCR (ASO-PCR). *Results*. The study demonstrated that 98% of patients achieved a hematological response after three months of therapy with IM 400 mg/day. Fifty-nine of 95 patients (62%) showed a 2-log reduction of the BCR-ABL/ABL ratio at 6 months of IM therapy, of whom 49 patients (83%) achieved a complete cytogenetic response (CCyR) and 42 of 59 (71%) of patients achieved a major molecular response (MMR) at 12 months. BCR-ABL transcripts remained undetectable in 22 patients (37%) after 26 months of consecutive measurements and these patients remained in CCyR at the time of data cut-off. Among the 36 patients who did not achieve a 2-log reduction of the BCR-ABL/ABL ratio at 6 months, only 5 patients (15%) achieved a CCyR and MMR by 12 months. There was a statistically significant difference between both groups in the duration of cytogenetic and molecular responses ($p<0.0001$). Failure to achieve a 2-log reduction at 6 months of IM therapy correlated with a decreased rate of PFS at 2 years ($p<0.03$) and with the presence of ABL kinase domain mutations ($p<0.001$). All primary resistant cases (16/16, 100%) and 16/18 (89%) suboptimal IM responders failed to achieve a 2-log reduction of BCR-ABL transcripts after 6 months of IM treatment versus 2/59 (3%) of the optimally responding group ($P < .0001$). Among 15 patients (10 suboptimal responders and 5 with primary resistance), ABL kinase domain mutations were detected in 11/15 (73%) of these patients. *Conclusions*. The present data demonstrate the predictive value of an early molecular response to IM for patients with CML-CP. Less than a 2-log reduction in BCR-ABL transcripts at 6 months of IM treatment could