Early Molecular Response in East African Ph+ CML Patients. Do we need an African Prognosis Score?

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Background
Philadelphia chromosome positive (Ph+) Chronic Myeloid Leukaemia (CML) is a haematologic malignancy and belongs to the group of myeloproliferative diseases. The annual incidence of CML in Europe ranges between 0.7 – 1.0/100,000 with a median age at diagnosis of 57-60 years [1]. Data from the US display an incidence rate of 1.6/100,000 and WHO suggests that no association with race or ethnicity seems to exist [2]. However, due to lack of reliable data, incidence rate for LIC remain an estimation [2], but taking the existing data for extrapolation, the worldwide annual incidence would be above 100,000. It is known that African patients are younger at time of diagnosis with an average of 39,5 years [3] and genetic varieties have been found by Koffi et al. [4]. Poor prognosis and adverse treatment outcome were related to additional chromosomal abnormalities and complex aberrations. Furthermore, the prognostic indices were not conclusive with treatment outcome. Studies on early molecular response under Imatinib treatment has not been published in East Africa yet. We present preliminary data from our study in Northern Tanzania.

Methods
All new diagnosed Ph+ CML patients were included and FBC, EUTOS Score and clinical investigations were performed. 3 months after Imatinib treatment, bcr-abl/abl ratio was obtained using real time PCR and clinical remission was documented.

Results
18 patients were evaluated for early MR and haematologic response. The age range were between 4 and 60 years (mean age 37.7), WBC at diagnosis between 78 and 499/nl (mean 311/nl), all patients had splenomegaly, 11 patients had hepatomegaly, 16 were in chronic phase and 1 in accelerated phase. 12 patients obtained complete hematologic response, favourable early molecular response (fMR) (bcr-ab-/abl <10%) in 7 patients. No correlation was found between EUTOS score or WBC count and fMR, but hepatomegaly was positively correlated with non-fMR (p=0.04911).

Discussion
This is the first study investigating early MR in Ph+ CML patients in East Africa. Despite the small number of patients, a trend towards fewer early MR as described in different ethnic group was found. Furthermore, hepatomegaly seems to be strongly associated with non-fMR. The same finding was reported 2008 from the Ivory Coast [5] and it was suggested to develop an “African CML prognostic score” that includes hepatomegaly. The “IMA-Fail” Score from Serbia [6] takes hepatomegaly also into account. Our results support these findings for the East African population. More patient data are needed to confirm our findings and further genetic testing of those with non-favourable response are necessary to understand the low response rate.

References
4. Koffi KG et al. Advances in Hematology; 2010

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<table>
<thead>
<tr>
<th>Characteristic of patients</th>
<th>CHR = complete hematologic response, fMR = favourable early molecular response</th>
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<tr>
<td>female-male ratio</td>
<td>1 : 2</td>
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<tr>
<td>average age</td>
<td>38 years</td>
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<tr>
<td>average WBC at time of Dx</td>
<td>311/nL</td>
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<tr>
<td>hepatomegaly at time of Dx</td>
<td>n=11 (61,1%)</td>
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<td>CHR at 3 months</td>
<td>n=12 (66,6%)</td>
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<tr>
<td>bcr/abl ration &lt;10% at 3 months</td>
<td>n=7 (38,9%)</td>
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CHR = complete hematologic response, fMR = favourable early molecular response