The perspective of generic drugs in chronic myeloid leukemia

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Generic Imatinib

The potential impact of different crystal forms of Imatinib used in Gleevec (beta) vs. Generic Imatinib (alpha)

Bioequivalence in children

Different absorption due to gastrectomy and change in gastric acidity in patients with GIST
<table>
<thead>
<tr>
<th>Case reports</th>
<th>Population</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asfour, 2009</td>
<td>N-2, Egypt</td>
<td>CHR on Gleevec&lt;br&gt;Hematologic relaps with copy version</td>
</tr>
<tr>
<td>Goubran, 2009</td>
<td>N-1, Egypt</td>
<td>CHR on Gleevec&lt;br&gt;Hematologic relaps with IM-alpha crystal&lt;br&gt;CHR resumed with Gleevec</td>
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<tr>
<td>Chouffal, 2010</td>
<td>N-1, Morocco</td>
<td>CHR on hydroxyurea+INF&lt;br&gt;Hematologic relaps with IM-COPER&lt;br&gt;CHR resumed with Gleevec+hydroxyurea</td>
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## Imatinib copy - observational study

<table>
<thead>
<tr>
<th>Observational study</th>
<th>Populations</th>
<th>Details</th>
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<tbody>
<tr>
<td>Razmkhan 2009</td>
<td>N-30, Iran</td>
<td>90% CHR with Imatinib alpha crystal</td>
</tr>
<tr>
<td>Alwan et al 2011</td>
<td>N-126, Iraq</td>
<td>CHR on Gleevec 33% hematologic relapse with IM copy</td>
</tr>
<tr>
<td>Nair et al 2008</td>
<td>N-100, India</td>
<td>100% CHR at 9 months</td>
</tr>
<tr>
<td>Eddou et al 2011</td>
<td>N-26, Morocco</td>
<td>96% CHR at 3 months 77% MCgR at 18 months</td>
</tr>
<tr>
<td>Saavedra et all 2014</td>
<td>N-12, Colombia 8 switched 4 de novo</td>
<td>63% treatment failure (switched) 75% AE (switched) 100% resistence or suboptimal (de novo) 75% AE (de novo)</td>
</tr>
</tbody>
</table>
Comparison of CHR rates

- IRIS (18 months): 97%
- Nair (copy Imatinib, 9 months): 100%
- Eddou (copy Imatinib, 3 months): 96%
- Razmkhan (copy Imatinib, mean 28.8 months): 90%
Comparison of MCgR rates

IRIS (18 months) 87%
Eddou (copy Imatinib, 18 months) 77%
Comparison of MMR rates

- IRIS (24 months): 72%
- ENEStnd (12 months): 22%
- ENEStnd (36 months): 53%
- Nair et al (Imatinib copy, 6 months): 43%
- Eddou et al (Imatinib copy, 18 months): 8%
- Razmkhan et al (Imatinib copy, 28,8 months): 47%
Comparison of mean projected survival

IRIS Nair et al (Imatinib copy)

15.7 years

4.8 years
What is the situation like in Serbia?

- 2001 Glivec
- 2006 allowed on Health insurance
- January 2012 Generic Imatinib
- July 2012 Generic Imatinib in the positive list
What is the situation like in Serbia?

- The TKI drugs on the positive list in NHIF until June 2014:
  - Imatinib (Glivec, Anzovip, Imatinib Pharma Swiss, Alvotinib) as a 1st line therapy
  - Nilotinib (Tasigna) as a 2nd line therapy

- 220 patients were on Glivec until 2012 in Serbia
- 45 patients on Tasigna
During August and September 2012 all patients were switched from Glivec to Anzovip.

These are the results of using Anzovip after 18 months.

Two groups of patients were monitored:

- 55 CML patients on Glivec → Anzovip
- 15 newly diagnosed CML patients
Results

• 55 patients treated with branded Imatinib were switched to generic Imatinib

• 10 patients (18.1%) had lost complete cytogenetics response they already had, but without signs of biological illness transformation → they were switched to 2nd line therapy nilotinib
Results- de novo CML patients

- 15 newly diagnosed pts from september 2012 to april 2014
- 7 patients – median follow up 12 months (9-18 months)
- Median age 27 (19-60)
- Median duration of Imatinib generic 12 months (9-18 months)
- The patients belonged to intermediate and high Sokal risk group.
### Patients characteristics

<table>
<thead>
<tr>
<th>Patients</th>
<th>Sex</th>
<th>Age at diagnosis</th>
<th>Duration of Anzovip therapy (months)</th>
<th>Reason for switch to II line th</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>59</td>
<td>18</td>
<td>-</td>
<td>PCgR at CCgR, escalated dose II at 800 after 9 months, CCgR at 18 months</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>25</td>
<td>12</td>
<td>-</td>
<td>PCgR at 6m CCgR at 12 months</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>19</td>
<td>11</td>
<td>failure</td>
<td>Minor CgR at 6 months, 19% bcr/abl transcript at 9 months</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>60</td>
<td>10</td>
<td>Failure</td>
<td>No CgR at 6 months</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>27</td>
<td>9</td>
<td>intolerancy</td>
<td>PCgR at 6 months</td>
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<td>7</td>
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<td>56</td>
<td>12</td>
<td>-</td>
<td>CCgR at 12 months</td>
</tr>
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</table>
Results

- 42% CCgR in period of 12 months
- 57% switched to second generation of TKI
- 28.6% MMR in period of 12 months
- 57% switched to second generation of TKI
Instead of conclusion

- The safety and efficacy of the copy drug has not been established in randomized clinical trials.

- It is unknown whether patients, who responded to branded Imatinib and then switched to its copy versions, will tolerate the copy drug and maintain the previous response.

- Careful follow up of a selected patients several months after the switch to generic imatinib.

- Despite of the small number of patients our results in term of hematologic and cytogenetic response were close to the international series.
Thank You for Your attention!