Imatinib in the Early Chronic Phase

Richard Larson
Management of Chronic Myeloid Leukemia in Early Chronic Phase with Imatinib Mesylate (Glivec; Gleevec)

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The IRIS Study: International Randomized Study of Interferon + Ara-C vs STI571* in Chronic Myeloid Leukemia

*Imatinib / Glivec / Gleevec

Hahn et al. J Clin Oncol June 1, 2003
Hughes et al. New England J Medicine October 9, 2003
Druker et al. 5 Year update, in preparation
## Patient characteristics

1106 early chronic phase CML patients, enrolled from July 2000 – January 2001

<table>
<thead>
<tr>
<th>Median time from Diagnosis</th>
<th>2 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median)</td>
<td>51 years</td>
</tr>
</tbody>
</table>

### Sokal risk group

<table>
<thead>
<tr>
<th>Sokal risk group</th>
<th>Median Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (n=391)</td>
<td>46</td>
</tr>
<tr>
<td>Intermediate (n=228)</td>
<td>52</td>
</tr>
<tr>
<td>High (n=158)</td>
<td>51</td>
</tr>
<tr>
<td>Unknown (n=329)</td>
<td>49</td>
</tr>
</tbody>
</table>
Study Design, Current Patient Status, and Mean Follow-up (through Dec 2005)

Randomize

Imatinib
n = 553

IFN-\(\alpha\) + Ara-C
n = 553

Crossover

n = 397; 46 months
n = 263; 36 months
n = 0
n = 18

Reasons for Cross-over

- Lack of response: 18%
- Loss of response / increase in WBC: 14%
- Intolerance of treatment: 26%
- Reluctance to continue IFN: 7%
Current Daily Dose of Imatinib for the 397 Patients Still on First-line Imatinib

- 300 mg  9%
- 400 mg  81%
- 600 mg  6%
- 800 mg  4%

- Mean daily dose over entire treatment course is 382 +/- 50 mg.
Cumulative Best Response at 12 and 54 months on First-line Imatinib

- CHR: 96% (98%)
- MCyR: 85% (92%)
- CCyR: 69% (86%)

% responding over Months since randomization to Imatinib
Event-free Survival and Survival Without AP/BC on First-line Imatinib

Progression events:
- 6.5% AP/BC
- 4.7% loss of MCyR
- 2.5% loss of CHR
- 1.4% CML-unrelated deaths

Estimated rate at 54 months (with 95%CI)
- PFS: 84% (80-87)
- Survival without AP/BC: 93% (90-96)
Survival Without AP/BC by level of CyR at 12 months on First-line Imatinib

Response at 12 months

Estimated rate at 54 months

<table>
<thead>
<tr>
<th>Level of CyR</th>
<th>n</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCyR</td>
<td>350</td>
<td>97%</td>
</tr>
<tr>
<td>PCyR</td>
<td>86</td>
<td>95%</td>
</tr>
<tr>
<td>No MCyR</td>
<td>73</td>
<td>81%</td>
</tr>
</tbody>
</table>

\{ p<0.001 \}

\{ p=0.20 \}
Survival Without AP/BC by Molecular Response at 12 months on First-line Imatinib

- CCyR with \( \geq 3 \) log red: \( n = 136 \), 100%
- CCyR with <3 log red: \( n = 94 \), 95%
- No CCyR: \( n = 138 \), 89%

Estimated rate at 54 months:

- CCyR with \( \geq 3 \) log red: \( p < 0.001 \)
- CCyR with <3 log red: \( p = 0.007 \)
### Annual Progression Events on First-line Imatinib

(minimum of 4 years of follow-up)

<table>
<thead>
<tr>
<th>Year</th>
<th>Events*</th>
<th>AP/BC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>3.4%</td>
<td>1.5%</td>
</tr>
<tr>
<td>2nd</td>
<td>7.5%</td>
<td>2.8%</td>
</tr>
<tr>
<td>3rd</td>
<td>4.8%</td>
<td>1.6%</td>
</tr>
<tr>
<td>4th</td>
<td>1.5%</td>
<td>0.9%</td>
</tr>
</tbody>
</table>

* All deaths plus loss of response including AP/BC
Estimated Log reduction of *BCR-ABL* at 4 years by Sokal score (in %)

J Goldman et al, ASH 2005
# Grade 3-4 Toxicity to First-line Imatinib

<table>
<thead>
<tr>
<th>Hematologic / Liver</th>
<th>Overall toxicity (n=551)</th>
<th>Onset after 36 months (n=427)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>16.7</td>
<td>2.3</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>9.8</td>
<td>1.2</td>
</tr>
<tr>
<td>Anemia</td>
<td>4.7</td>
<td>0.9</td>
</tr>
<tr>
<td>Elevated liver enzymes</td>
<td>5.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Other drug-related AEs</td>
<td>16.5</td>
<td>2.6</td>
</tr>
</tbody>
</table>
Evolving Concepts in the Management of Chronic Myeloid Leukemia

Recommendations from an Expert Panel on Behalf of the European LeukemiaNet