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Pulmonary Hypertension Is a Frequent Event in Patients with Chronic Myeloid Leukemia Treated with Tyrosine Kinase Inhibitors

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Pulmonary Hypertension Is a Frequent Event in Patients with Chronic Myeloid Leukemia Treated with Tyrosine Kinase Inhibitors

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Abstract
Tyrosine kinase inhibitors (TKIs) are the current standard of therapy for patients with chronic myeloid leukemia (CML). Data from earlier studies have suggested that tyrosine kinase inhibitors (TKIs) are associated with an increased risk of reversible pulmonary hypertension (PH). This study aims to further investigate the relationship between TKIs and PH. Methods: We conducted a retrospective analysis of 401 patients diagnosed with CML in chronic phase (CP) who were treated with TKIs (imatinib, dasatinib, or nilotinib) as initial therapy for CML and had a trans-ethnic echocardiographic (TEE) done at some point during the course of therapy. Results: PH was diagnosed in 40 (10%) patients on dasatinib, 6 (4.3%) on nilotinib and 4 (8%) on imatinib (P-value: 0.001). Conclusions: PH occurs in some patients with CML in chronic phase at baseline while others it appears during therapy with TKI.

Patients and Methods

- Chart review of patients with CML treated with TKIs at MDACC between 2000 and 2009.
- Excluded patients with CML in chronic phase (CP) enrolled in several studies using imatinib (800 mg orally daily), nilotinib (400 mg BID) or dasatinib (100mg orally daily) as frontline therapy who had at least one trans-ethnic echocardiogram (TEE) done at some point during the course of therapy.
- Among 390 patients, 10% (39) patients had PH.
- PH is seen more commonly in patients on dasatinib compared to imatinib or nilotinib.

Table 1. Patient’s Characteristics

<table>
<thead>
<tr>
<th>TKI</th>
<th>Median Age (y)</th>
<th>Median Hemoglobin (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imatinib</td>
<td>56 (30-82)</td>
<td>12.2 (6.2-14.1)</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>54 (19-80)</td>
<td>12.2 (6.2-14.1)</td>
</tr>
</tbody>
</table>

Table 2. TTE evidence of PH by TKI therapy

<table>
<thead>
<tr>
<th>TKI</th>
<th>Available</th>
<th>Elevated RVSP on TTE (%)</th>
<th>Possible secondary cause of elevated RVSP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imatinib</td>
<td>39</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>10</td>
<td>53</td>
<td>2</td>
</tr>
<tr>
<td>Nilotinib</td>
<td>14</td>
<td>63</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 3. Incidence of pleural effusion

<table>
<thead>
<tr>
<th>TKI</th>
<th>Used</th>
<th>PE and Concomitant RVSP</th>
<th>Patients with SOB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imatinib</td>
<td>3</td>
<td>4 (76%)</td>
<td>1</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>7</td>
<td>10 (70%)</td>
<td>4</td>
</tr>
<tr>
<td>Nilotinib</td>
<td>1</td>
<td>6 (17%)</td>
<td>0</td>
</tr>
</tbody>
</table>

References:

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