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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 therapy for patients with chronic myeloid leukemia (CML). Recent studies have shown that patients taking TKIs are at risk for developing pulmonary hypertension (PH). There have been some reports on the occurrence of reversible PH with dasatinib. We conducted a retrospective analysis in 401 patients diagnosed with CML in chronic phase who were treated with TKIs at MDACC between 2000 and 2009. Patients with CML in chronic phase treated with TKIs had a transbronchial echocardiogram (TTE) done at some point during the course of therapy. PH was diagnosed when patients had elevated right ventricular systolic pressure (RVSP); RVSP > 35 mmHg. Results
Of the patients who had elevated RVSP (suggesting PH), 13 patients had serial TTE during therapy (figure 1).

• 7 patients experienced worsening PH (receiving Dasatinib n=2, Nilotinib n=3).
• 3 of 3 patients with elevated RVSP at baseline normalized after starting treatment with nilotinib.
• Plural effusion was identified in 11 patients (55%) with elevated RVSP (Table 3).

Table 1. Patient’s Characteristics

<table>
<thead>
<tr>
<th>TKI</th>
<th>N</th>
<th>TTE Available</th>
<th>N</th>
<th>Elevated RVSP on TTE (%)</th>
<th>N</th>
<th>Possible secondary cause of elevated RVSP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imatinib</td>
<td>54</td>
<td>4 (8)</td>
<td>2 had ischemic CAD with low EF that worsened after starting TKI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dasatinib</td>
<td>19</td>
<td>10 (53)</td>
<td>2 had COPD, 1 had OSA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nilotinib</td>
<td>14</td>
<td>6 (43)</td>
<td>2 had OSA (with normal RVSP prior to starting TKI)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. TTE evidence of PH by therapy

Results
• 7 patients experienced worsening PH (receiving Dasatinib n=2, Nilotinib n=3).
• 3 of 3 patients with elevated RVSP at baseline normalized after starting treatment with nilotinib.
• Plural effusion was identified in 11 patients (55%) with elevated RVSP (Table 3).

Table 3. Incidence of pleural effusion

<table>
<thead>
<tr>
<th>TKI</th>
<th>N</th>
<th>Concomitant PE and/or SOB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imatinib</td>
<td>3</td>
<td>4 (76%)</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>7</td>
<td>10 (70%)</td>
</tr>
<tr>
<td>Nilotinib</td>
<td>1</td>
<td>6 of 17 (35%)</td>
</tr>
</tbody>
</table>

Conclusions
• PH occurs in some patients with CML in chronic phase at baseline while in others it appears during therapy with TKI.
• PH is seen less commonly in patients on imatinib compared to dasatinib or nilotinib.
• Concomitant pleural effusion and PH occurred more frequently in patients receiving dasatinib.
• Unclear whether there is a causal relationship between TKI and the development of PH.

References:

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