One-Year Open-Label (OL) Comparison of Sitaxentan to Bosentan in Treatment of Pulmonary Arterial Hypertension (PAH) Related to Systemic Sclerosis (SSc)

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Abstract

Background: PAH is a leading cause of mortality and late disease morbidity in SSc and other CTDs. Short-term (1–12 week) randomized controlled trials (RCTs) in PAH studies (which included SSc) have provided significant insights into disease pathogenesis, functional status, hemodynamics, and quality of life in response to a variety of agents. Long-term controlled experiences are lacking, thus data on clinically important measures such as survival and estimates of time to clinical worsening are by necessity derived from OL observational series.

Objectives: We examined multiple outcomes in patients with PAH related to SSc who were participants in a one-year OL observational study of sitaxentan and bosentan.

Methods: Sitaxentan is an orally bioavailable selective antagonist of the endothelin (ET) type B receptor. An active metabolite of sitaxentan 100 mg and 50 mg with placebo, an open-label bosentan (nonselective endothelin antagonist) arm was also included for observational comparisons only. The 18-week follow-up was studied by a one-year OL study with sitaxentan 100 mg or bosentan (STRIDE-2X). We report here post hoc subanalyses in those patients with diagnoses of SSc (n=49) treated with the recommended doses of each agent: sitaxentan 100 mg (n = 29) or bosentan 125 mg (n=20).

Results: The two treatment groups appeared comparable in terms of gender, age, WHO functional class, hemodynamics, and time walk distance prior to treatment initiation (321 m sitaxentan vs 304 m bosentan). Table 1.

<table>
<thead>
<tr>
<th>Outcome at 1 Year</th>
<th>Sitaxentan</th>
<th>Bosentan</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>SAEs</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>ENA</td>
<td>16%</td>
<td>8%</td>
</tr>
<tr>
<td>AEs</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>Without clinical worsening</td>
<td>8%</td>
<td>8%</td>
</tr>
</tbody>
</table>

Discussion

Conclusion: Sitaxentan was well tolerated. Sitaxentan was as efficacious as bosentan when compared with patients treated with bosentan. Sitaxentan was well tolerated.

References