Lasofoxifene 0.25 mg Compared with Raloxifene 60 mg for Effects on Bone Mineral Density and Markers of Bone Turnover: Results from the Phase 3 Comparison of Raloxifene and Lasofoxifene (CORAL) Trial

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INTRODUCTION

• Lasofoxifene is a novel estrogen agonist/antagonist with potential advantages over current selective estrogen receptor modulators (SERMs).
• Studies in both animal and human models suggest that lasofoxifene may have a greater favorable overall estrogen agonist-agonist effect profile.
• In a Phase 2 study, lasofoxifene 0.25 mg and 1.0 mg were found to be effective in preventing vertebral and non-vertebral fractures, and responses in general were greater with lasofoxifene compared with raloxifene 60 mg.

STUDY DESIGN

• Multicenter, double-blind, randomized, placebo- and active-controlled Phase 3 study.
• Subjects: women aged 65-80 years, with a loss of BMD (LUMBAR T-score) of -1.0 or greater, with a baseline T-score < -1.0 on DXA scans and at least 3 years from last period.
• Participants were randomized to lasofoxifene 0.25 mg/day, raloxifene 60 mg/day, or matching placebo for 2 years.
• All were provided a daily supplement of 400 IU Vitamin D.

SUBJECT DEMOGRAPHICS & BASELINE CHARACTERISTICS

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean (SD)</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lasofoxifene 0.25 mg/day</td>
<td>179 (82.1)</td>
<td>61.8 (6.6)</td>
<td>61.3 (7.1)</td>
</tr>
<tr>
<td>Raloxifene 60 mg/day</td>
<td>179 (82.1)</td>
<td>61.8 (6.6)</td>
<td>61.3 (7.1)</td>
</tr>
<tr>
<td>Placebo</td>
<td>179 (82.1)</td>
<td>61.8 (6.6)</td>
<td>61.3 (7.1)</td>
</tr>
</tbody>
</table>

RESULTS

Lasofoxifene 0.25 mg/day was effective and superior to both raloxifene and placebo in preventing bone loss and reducing markers of bone turnover (\(C\)-telopeptide, \(N\)-telopeptide, osteocalcin, and bone-specific alkaline phosphatase). Superiority was observed in early Month 6 and was sustained over time. Lasofoxifene was also superior to placebo in all bone markers listed above.

CONCLUSIONS

• Lasofoxifene 0.25 mg/day was effective and superior to raloxifene in preventing bone loss and reducing markers of bone turnover, and in reducing bone turnover markers.
• These differences were seen as early as Month 6.
• Lasofoxifene also had a 1.5-fold greater likelihood of response compared to placebo.

REFERENCES