Zoledronic Acid (ZOL) Markedly Improves Bone Mineral Density (BMD) for Patients with Monoclonal Gammopathy of Undetermined Significance (MGUS) and Bone Loss

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Study Design

This open-label study was designed to evaluate the efficacy and safety of this dose and schedule of ZOL for MGUS patients with significant loss of bone.

Major Inclusion Criteria:
- ≥ 18 years of age
- Diagnosis of MGUS
- Osteopenia/Osteoporosis (T-score worse than -1) as verified by a DEXA scan

Major Exclusion Criteria:
- Prior use of oral bisphosphonates or fluorides for more than three months total within the last two years
- Prior use of intravenous bisphosphonates within the last two years
- Known secondary causes of osteopenia/osteoporosis other than MGUS (patients with concomitant postmenopausal osteopenia/osteoporosis were not excluded)
- Current systemic corticosteroid therapy of an equivalent of >10 mg of prednisone/d
- Disorders of the parathyroid or thyroid glands
- Known history of currently active malignancy
- Treatment with other agents known to affect osteoclastic activity
- Use of Selective Estrogen Receptor Modulators in the preceding three months
- KPS < 60 and/or life-expectancy < 3 months

Treatment Schema:
- ZOL at 4 mg was administered IV at 0, 6, and 12 months.

Objectives

The primary objective of this study is to:
- Determine the effect of ZOL on BMD of lumbar spine, utilizing Dual energy X-ray absorptiometry (DEXA) scan, among patients with MGUS with associated osteopenia/osteoporosis

World Health Organization established the definition of osteopenia and osteoporosis based on a comparison of BMD with the young adult reference mean. A BMD value of 1.0 to 2.5 standard deviations below the young adult reference mean is osteopenia. A BMD value of 2.5 standard deviations or more below the young adult mean confirms the diagnosis of osteoporosis.

The secondary objectives of this study are to:
- Determine the effect of ZOL on BMD of total hip
- Determine the effect of ZOL on skeletal fractures in MGUS patients with osteopenia/osteoporosis
- Determine the effect of ZOL on serum M-protein levels
- Determine the proportion of patients treated with ZOL that develop multiple myeloma or other related malignancies
- Determine the safety of the use of ZOL in the treatment of MGUS patients with osteopenia/osteoporosis

Results

Table 1 - Patient Demographics (n=54)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age (Range), Years</td>
<td>67 (50-91)</td>
</tr>
<tr>
<td>Male:Female</td>
<td>26:28</td>
</tr>
<tr>
<td>Mean Baseline L-spine T-score (Range)</td>
<td>-2.16 (-3.97 to -1.10)</td>
</tr>
<tr>
<td>Mean Baseline Hip T-score (Range)</td>
<td>-1.88 (-3.50 to -1.00)</td>
</tr>
<tr>
<td>Mean Baseline Serum M-Protein (Range), g/dl</td>
<td>0.9 (0.0 - 2.7)</td>
</tr>
</tbody>
</table>

No patient developed osteonecrosis of the jaw or a significant adverse renal event.

Summary

- One patient developed chronic lymphocytic leukemia while on study whereas no other patient showed progression to myeloma or a related B-cell disorder
- No patient developed osteonecrosis of the jaw or a significant adverse renatal event
- During the study, no patient developed a new fracture
- ZOL administered at 4 mg every 6 months significantly improves BMD for MGUS patients with bone loss (osteopenia/osteoporosis) safe and well-tolerated effective treatment to prevent the development of new fractures in this high risk population

Poster # 2760

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Table 2 - Patient Responses

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Δ L-Spine T-Score (Range), n=27</td>
<td>0.56 (-0.40 to 3.90)</td>
</tr>
<tr>
<td>Percent L-Spine Improvement (Range, P-value)</td>
<td>25.5% (-19.0% to +134%), P=0.0042</td>
</tr>
<tr>
<td>Mean Δ Hip T-Score (Range), n=28</td>
<td>0.27 (-0.60 to 2.00)</td>
</tr>
<tr>
<td>Percent Hip Improvement (Range, P-value)</td>
<td>14.4% (-54.5% to +163%), P=0.0046</td>
</tr>
<tr>
<td>Patients with New Fractures</td>
<td>0</td>
</tr>
<tr>
<td>Patients Progressing to Multiple Myeloma</td>
<td>0</td>
</tr>
</tbody>
</table>