Treatment of Knee Osteoarthritis with Intra-Articular SM04690, in Development as a Potential DMOAD, Improved WOMAC A1 “Pain on Walking” – Results from a Phase 2 Study of a Wnt Pathway Inhibitor

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Background

SM04690 is an intra-articular (IA); small molecule, Wnt Pathway inhibitor, in development as a potential disease modifying knee OA drug (DMOAD).• Preclinical studies demonstrated inhibition of inflammation and cartilage degradation compared with vehicle.1
• A phase 2a study demonstrated improvements in WOMAC Pain, Function and radiographic medial joint space width (mJSW) compared with placebo (PBO) in clinically relevant subgroups at 52 weeks.2

WOMAC Question A1: “How much pain have you had when walking on a flat surface?” Major symptom of tibio-femoral OA and differentiates from patella-femoral OA.3,4 Multi-dimensional question incorporating pain and function scored 0-10 on visual-analog scale (VAS).

Results

A post-hoc analysis of responses to SM04690 measured by WOMAC A1 from this phase 2a study was performed.

Methods

Knee OA subjects met ACR criteria, Kellgren-Lawrence (KL) grades 2 or 3, pain 30-80 mm (0-100 mm VAS) in target (most painful) knee. Subjects received 2 mL IA SM04690 0.03 mg, 0.07 mg, 0.23 mg, or PBO. WOMAC Pain & Function scores collected at Weeks 0, 4, 13, 26, 39, and 52. Two clinically relevant subgroups were identified which demonstrated significant improvements compared with PBO for 0.07 mg group at 52 weeks: 1) Unilateral symptomatic (UNI; pre-specified) and 2) Unilateral symptomatic w/o widespread pain (UNI WP; post-hoc).

Conclusions

• In this post-hoc analysis of phase 2a data, in UNI WP- subgroup, SM04690 0.07 mg dose demonstrated the following responses at Week 26 persisting through Week 52:
  - Significant WOMAC A1 pain improvements compared with PBO, which mirrored changes seen in full composite WOMAC Pain and Function scores.
  - WOMAC A1 effect size was also similar to those demonstrated by WOMAC Pain and Function subcores at Week 52; therefore supporting the responsiveness of the A1 question.

  The improvements seen in pain and function suggested SM04690, a potential DMOAD, has a role in the treatment of signs and symptoms of knee OA.

References


All authors are employees, shareholders, or consultants of Samumed, LLC. Other disclosures are listed in the published abstract.

Poster #1364

Figure 1. WOMAC Function, Pain, and A1 Subscores Showed Similar Responses Over Time in UNI WP- Subjects

Table 1. Week 52 Effect Size: UNI WP- Subjects

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Difference</th>
<th>Mean Squared Error</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>WOMAC A1</td>
<td>-1.40</td>
<td>3.36</td>
<td>0.764</td>
</tr>
<tr>
<td>WOMAC Pain</td>
<td>-5.93</td>
<td>81.74</td>
<td>0.655</td>
</tr>
<tr>
<td>WOMAC Physical Function</td>
<td>-24.65</td>
<td>1061.00</td>
<td>0.757</td>
</tr>
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0.07 mg SM04690 vs. Placebo

Table 2. Week 52 Effect Size: UNI WP- Subjects

<table>
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Improved WOMAC A1 “Pain on Walking”

150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0.0 Time (weeks)

Results

Setting

1) Unilateral symptomatic (UNI; pre-specified) and 2) Unilateral symptomatic w/o widespread pain (UNI WP; post-hoc).

- 455 subjects were enrolled, mean age 60.3 ± 8.7 years, BMI 29.9 ± 4.6 kg/m², female 58.9%, KL 3,4 64.2%, UNI 36.0% and UNI WP- 28.1%.

- WOMAC A1, Pain and Function treatment effect from 0.07 mg dose in UNI WP- subgroup showed statistically significant improvement over PBO at Weeks 26, 39, and 52.

- WOMAC A1, Pain and Function effect sizes from 0.07 mg dose in UNI WP- subgroup were all numerically similar.

- WOMAC A1, Pain and Function effect sizes in UNI and UNI WP- showed statistically significant improvement over PBO at Weeks 26, 39, and 52.

- WOMAC Pain and Function scores collected at Weeks 0, 4, 13, 26, 39, and 52.

- WOMAC A1 response effect sizes in 0.07 mg dose group were compared to WOMAC Pain and Function effect sizes in UNI and UNI WP-.