Treatment of Knee Osteoarthritis with Intra-Articular SM04690, in Development as a Potential DMOAD, Improved Health-Related Quality of Life – Results from a Phase 2 Study of a Novel Wnt Pathway Inhibitor

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Poster #1366

Background

Short Form Survey (SF-36) is a measure of health-related quality of life (HRQoL)

- OA patients report significant loss of HRQoL.[1]
- SF-36 is a multi-dimensional instrument with 8 domains. It is validated for assessing health status outcomes in randomized controlled trials (RCTs) in OA patients.[2,3]

SM04690 is an intra-articular (IA), small molecule, Wnt Pathway inhibitor, in development as a potential disease modifying knee OA drug (DMOAD).

- In preclinical studies it inhibited inflammation and cartilage degradation compared with vehicle.[4]
- A phase 2a RCT demonstrated improvements in WOMAC Pain, Function and radiographic medial joint space width compared with placebo (PBO) in clinically relevant subgroups at 52 weeks.[4] SF-36 Week 52 results from this trial are presented here.

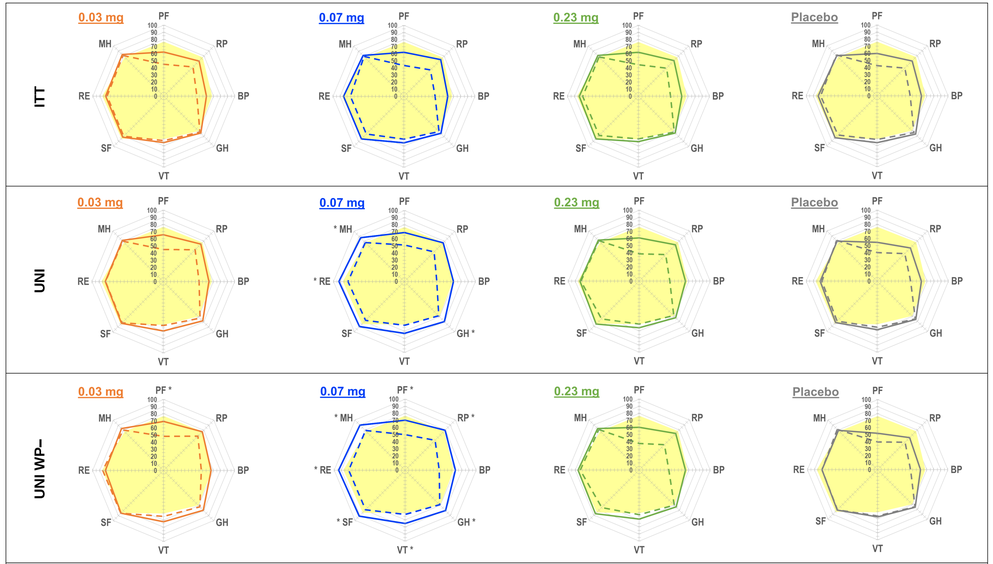
Methods

Subjects and study design

- Knee OA subjects (N=455) meeting ACR criteria, Kellgren-Lawrence (KL) grade 2 / 3, pain 30-80 mm (0-100 mm visual analog scale) in target knees were enrolled.
- Subjects were randomized to receive a single IA 2 mL, 0.03 mg, 0.07 mg, 0.23 mg SM04690, or PBO (phosphate buffered saline).
- Baseline-adjusted ANCOVA analyses were conducted in the intent-to-treat (ITT) population, with SF-36 improvements ≥ minimum clinically important differences (MCID - 5 points for domain scores; 2.5 points for summary component scores[5]) noted.
- Two subgroups were explored: 1) unilateral symptomatic (UNI) knee OA (pre-specified) and 2) unilateral symptomatic knee OA without widespread pain or comorbid symptoms (Widespread Pain Index ≤4 and Symptom Severity ≤2, post-hoc: UNI WP–).

Results

Figure 1. SF-36 Scores at 52 Weeks



Baseline (dash line) and Week 52 (solid line) scores over age and gender (AG) normative scores (yellow).

P<0.05 from baseline-adjusted ANCOVA compared with PBO;* **PF: Physical Functioning; **RP:** Role-Physical; **BP:** Bodily Pain; **GH:** General Health; **VT:** Vitality; **SF:** Social Functioning; **RE:** Role-Emotional; **MH:** Mental Health.

- 455 subjects enrolled, mean age 60.3 [±8.7], BMI 29.9 [±4.6] kg/m^2), female 58.9%, KL 3 64.2%, UNI 36.0% and UNI WP- 28.1%.
- 0.07 mg UNI subjects showed significant improvements ($p<0.05$) in 3 of 8 domains compared with PBO at 52 weeks and exceeded AG norms (Fig. 1).
- 0.07 mg UNI WP- subjects showed significant improvements in 7 of 8 domains and exceeded AG norms (Fig 1.)

Conclusions

- In this phase 2a trial at 52 weeks, IA SM04690 0.07 mg dose UNI and UNI WP- demonstrated:
  - Statistically significant and clinically meaningful HRQoL improvements compared with PBO
  - Improvements beyond age and gender normative scores
- Results supported a positive impact of SM04690 on HRQoL at 52 weeks in clinically relevant subgroups of knee OA subjects.
- These data, along with phase 2a clinical outcomes that showed improvements in pain and function, support further investigation of SM04690, as a potential DMOAD, for treatment of knee OA.

References

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