

Accepted as an oral presentation at the Arthritis Foundation's Osteoarthritis Clinical Studies (OACS) Annual Conference 2020, December 8–10, 2020

Lorecivivint Injection Improved Responder Outcomes in Subjects with Knee Osteoarthritis: A Post Hoc Analysis from a Randomized Controlled Trial

Sarah Kennedy, PhD, Christopher J. Swearingen, PhD, Ismail Simsek, MD, Jeyanesh Tambiah, MD

Samumed, LLC, San Diego, CA

Teaser Summary: Lorecivivint, a novel intra-articular Wnt pathway modulator in development as a potential knee osteoarthritis treatment, improved the odds of subjects achieving clinical threshold responses over placebo.

Background: In knee osteoarthritis (OA) trials, discrete threshold responses may demonstrate the clinical relevance of improved patient-reported outcomes (PROs). In a 24-week trial, lorecivivint (LOR), an intra-articular (IA) drug in development as a potential knee OA treatment, showed statistically significant improvements in PROs over placebo. A post hoc analysis compared subject proportions reaching 30%, 50%, or 70% threshold improvements over baseline. The pivotal dose (0.07 mg) results are reported.

Methods: In a randomized trial, symptomatic knee OA subjects (Kellgren-Lawrence 2–3) received a single 2 mL IA knee injection of LOR (0.03, 0.07, 0.15, 0.23 mg) or placebo. Post hoc, subjects meeting 30%, 50%, or 70% improvements over baseline at Week 12 were determined for Pain Numeric Rating Scale (Pain NRS, [0–10]), WOMAC Pain, WOMAC Function, and Patient Global Assessment (PtGA, [0–100]). The odds ratios (OR [95% CI]) of achieving threshold improvements were calculated and compared between LOR and placebo.

Results: 635 (91.4%) subjects completed the trial. Pivotal dose 0.07 mg LOR significantly increased the odds of a 30% threshold improvement in Pain NRS (OR 2.47 [1.45, 4.19]; $P < 0.001$) and WOMAC Function (OR 1.86 [1.10, 3.12]; $P < 0.05$) and a 50% threshold improvement in WOMAC Pain (OR 1.79 [1.06, 3.03]; $P < 0.05$) and PtGA (OR 2.28 [1.25, 4.16]; $P < 0.01$) over placebo. Numerically, not statistically, more subjects achieved a 70% threshold improvement in all PROs.

Conclusion: A single IA 0.07 mg LOR injection significantly increased the odds of achieving 30% and 50% improvements in PROs over placebo. Pivotal trials are ongoing.

Significance/Clinical Relevance: Lorecivivint shows potential as a novel treatment that may provide meaningful clinical benefits for knee osteoarthritis subjects. Clinical trials are ongoing.