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Lorecivivint, a Potential Disease-Modifying Treatment for Knee Osteoarthritis: Factors Driving WOMAC Pain Subscore Changes - A Post Hoc Analysis of Phase 2b Data

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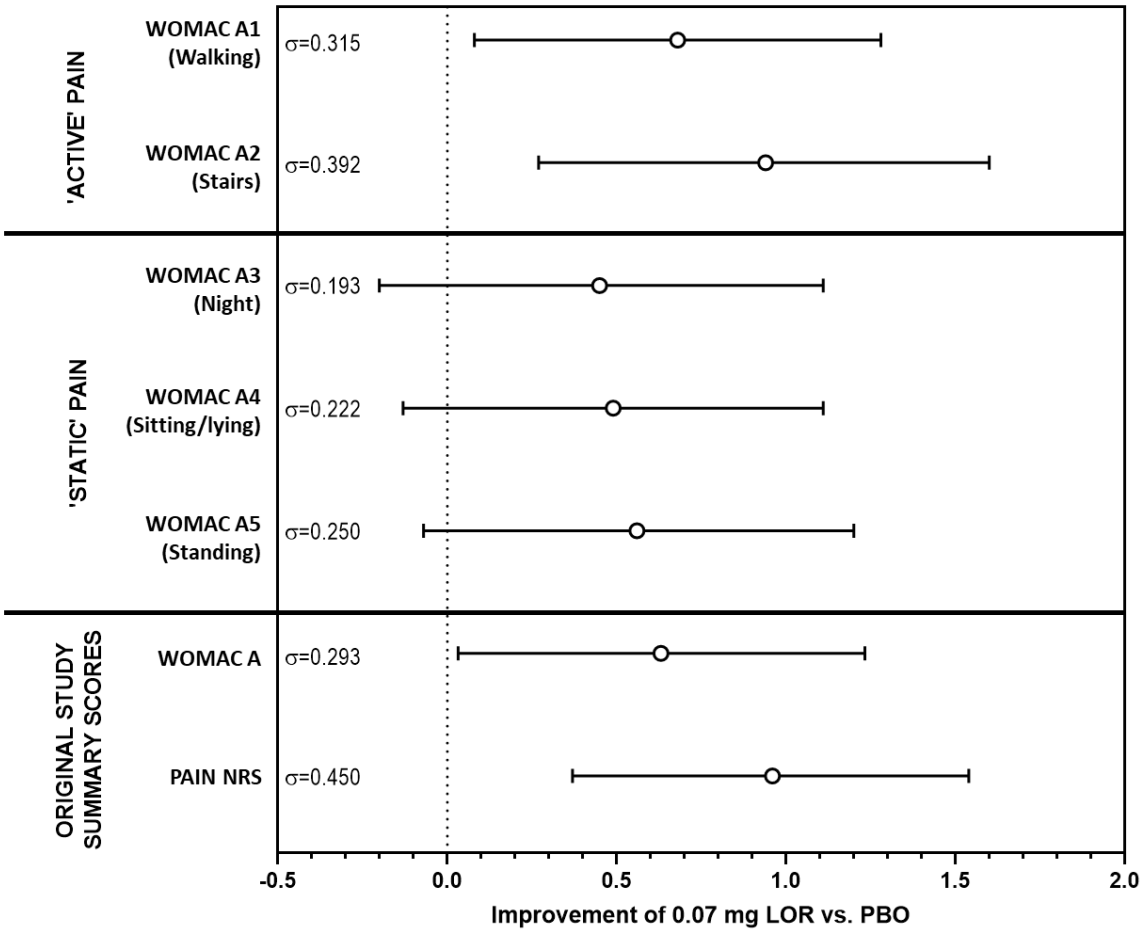
Background: Knee osteoarthritis (OA) is a heterogenous disease characterized by pain, functional loss, and deformity, which can confound patient-reported outcomes (PROs). The WOMAC Pain subscore addresses this variability by capturing "active" (A1–A2) and "static" (A3–A5) pain items. We hypothesize that measurement of "active" versus "static" pain dimensions may demonstrate differential effect sizes when assessing treatment benefit. Lorecivivint (LOR; SM04690), a small-molecule, intra-articular CLK/DYRK1A inhibitor, is in development as a potential disease-modifying treatment for knee OA. A post hoc analysis of a Phase 2b study of LOR was performed to examine PRO effect size (ES) changes.

Methods: Pain was assessed using the weekly average of daily Pain NRS and WOMAC Pain subscore. WOMAC Pain questions were analyzed as "active" (walking, stairs) and "static" (night, sitting/lying, standing) items. These questions from subjects treated with 0.07 mg LOR were compared with the primary 24-week study outcomes of mean Pain NRS and summed mean WOMAC Pain subscore at Week 12 in the Full Analysis Set. Baseline-adjusted analysis of covariance for A1–A5 scores was conducted on LOR-treated subjects versus placebo (PBO)-treated subjects.

Results: The primary study analysis (N=231, KL grade 3 63.2%) demonstrated efficacy of LOR versus PBO for Pain NRS and WOMAC A subscores (ES: 0.450 and 0.293, respectively). Each WOMAC A item had lower ES than Pain NRS at Week 12. Post hoc, LOR treatment versus PBO showed significant improvements in ES of A1 (ES=0.315, P=0.028) and A2 (ES=0.392, P=0.006). A3–A5 did not show statistical improvement for LOR versus PBO.

Conclusion: In this post hoc analysis, following LOR treatment, Pain NRS exhibited the greatest ES versus PBO. "Active" items demonstrated greater ES than "static" items and the full WOMAC Pain domain, providing support for the hypothesized dimensional constructs in knee OA pain assessment.

Figure: Effect sizes of 0.07 mg LOR versus PBO at Week 12.



All statistics are on a [0-10] scale