# 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

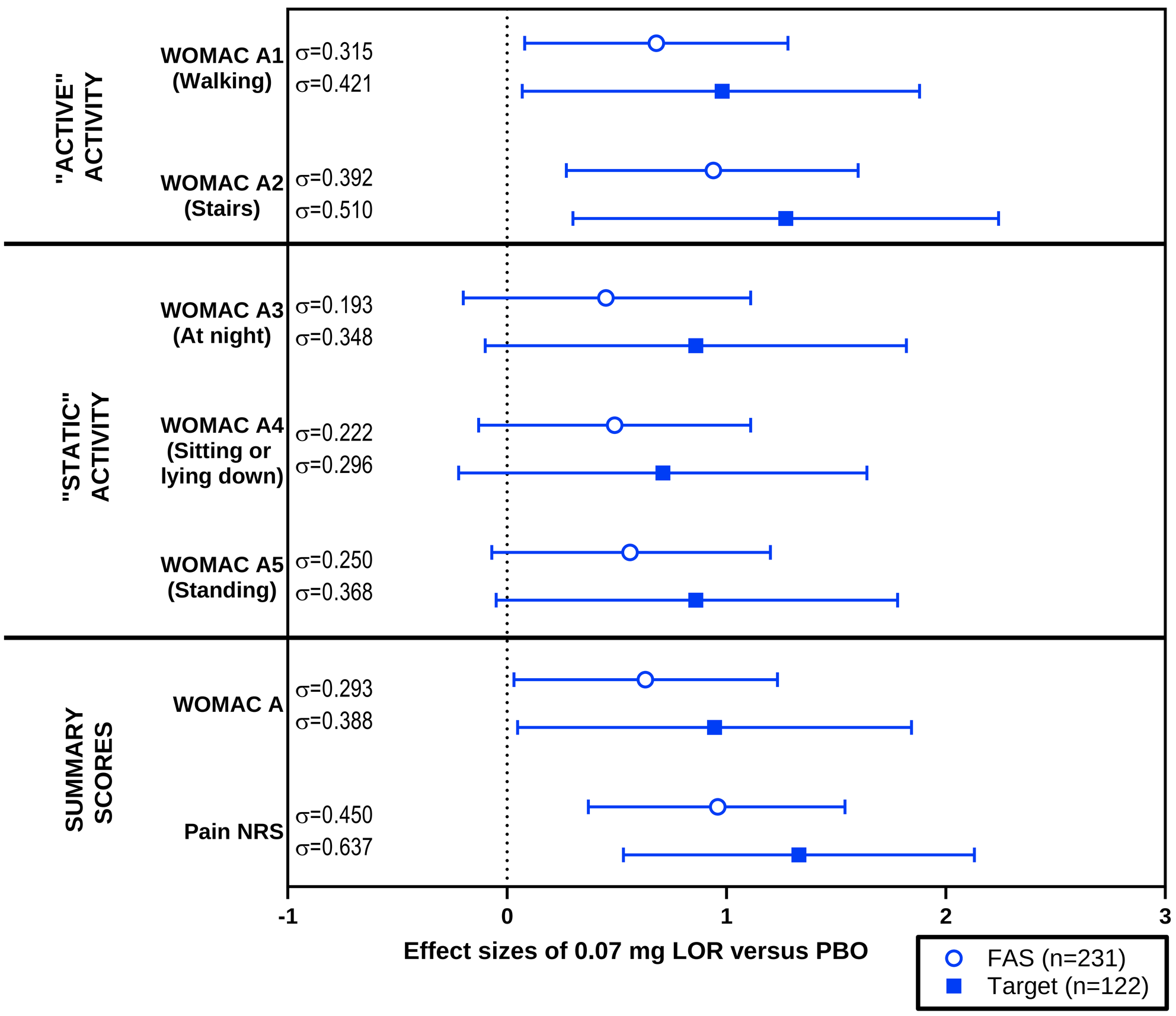
- Studies have suggested that some dimensions of knee OA pain are associated with activities corresponding to structural findings (e.g., pain when walking on a flat surface and tibiofemoral joint OA),[1] whereas other dimensions are driven by more centralized pain mechanisms[2]
- We hypothesized that Pain Numeric Rating Scale (NRS) and WOMAC Pain subscore "active" and "static" items demonstrate differential effect sizes in response to different treatment mechanisms, reflecting effects on different drivers of knee OA pain
- Lorecivivint (LOR; SM04690), a small-molecule, intra-articular CLK/DYRK1A inhibitor that modulates the Wnt pathway, is in development as a potential disease-modifying treatment for knee OA[3–7]; as such, LOR may differentially affect structure- and pain-associated PROs
- A post hoc analysis of a Phase 2b study of 0.07 mg LOR was performed to assess descriptive trends between the effect sizes of individual PROs in the Full Analysis Set (FAS) and a potential target population

## Conclusions

- **This post hoc analysis of knee OA subjects treated with 0.07 mg LOR suggested that**
  - **Pain NRS exhibited the greatest effect size of tested PROs for LOR compared with PBO**
  - **For all scores, effect sizes were enhanced in a target population of subjects with mJSW [2–4] mm without widespread (comorbid) pain compared with the FAS**
  - **Effect sizes observed with WOMAC Pain subscore "active" items may reflect associations between changes in the structural pathology of knee OA and assessments of PROs**
  - **Prospective comparisons of individual WOMAC Pain subscore items corresponding to mechanisms of potential treatments may be warranted in future studies**

## Results

**Figure. Effect sizes of 0.07 mg LOR versus PBO for the FAS and target population at Week 12**




σ: Difference in effect size between LOR and PBO; Point estimates of change with 95% CI; Target: mJSW [2–4] mm without widespread pain

## Methods

- 231 subjects (mean age 60.0 [±8.8] years, BMI 28.9 [±4.0] kg/m$^2$, female 56.3%, KL grade 3 63.2%) were included in this analysis
- Pain was assessed using the weekly average of daily Pain NRS [0–10] and WOMAC Pain subscore. Pain NRS intensity (Choose one number that best describes your average pain in your Left Knee in the last 24 hours) and WOMAC items A1–A5 (How much pain have you had "when walking on a flat surface?" [A1], "when going up or down stairs?" [A2], "at night in bed?" [A3], "while sitting or lying down?" [A4], and "while standing?" [A5]) were individually analyzed for subjects treated with a single intra-articular injection of 0.07 mg LOR (pivotal trial dose) and compared with the primary study outcomes of mean Pain NRS and summed mean WOMAC Pain subscore at Week 12. Questions A1–A2 were "active" items and A3–A5 were "static" items
- A baseline-adjusted analysis of covariance for WOMAC A1–A5 scores was conducted on LOR-treated subjects compared with placebo (PBO)-treated subjects in 1) the Full Analysis Set (FAS) of all dosed subjects and 2) a target population of subjects with medial joint space width (mJSW) [2–4] mm without widespread pain (Widespread Pain Index [WPI] ≤4, Symptom Severity Score Question 2 ≤2)

**References: 1)** Chan KK, et al. *PLOS ONE.* 2014. **2)** Bihlet AR, et al. *BMC Musculoskelet Disord.* 2018. **3)** Deshmukh V, et al. *Osteoarthritis and Cartilage*. 2017. **4)** Deshmukh V, et al. *Osteoarthritis and Cartilage*. 2019. **5)** Yazici Y, et al. *Osteoarthritis and Cartilage*. 2017. **6)** Yazici Y, et al. *World Congress on Osteoporosis, Osteoarthritis, and Musculoskeletal Diseases.* 2018. **7)** Yazici Y, et al. *Arthritis Rheumato*l. 2018; 70 (suppl 10).

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