

# THE NOVEL, INTRA-ARTICULAR CLK/DYRK1A INHIBITOR LORECIVIVINT (LOR; SM04690), WHICH MODULATES THE WNT PATHWAY, IMPROVED RESPONDER OUTCOMES IN SUBJECTS WITH KNEE OSTEOARTHRITIS: A POST HOC ANALYSIS FROM A PHASE 2B TRIAL

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## Background

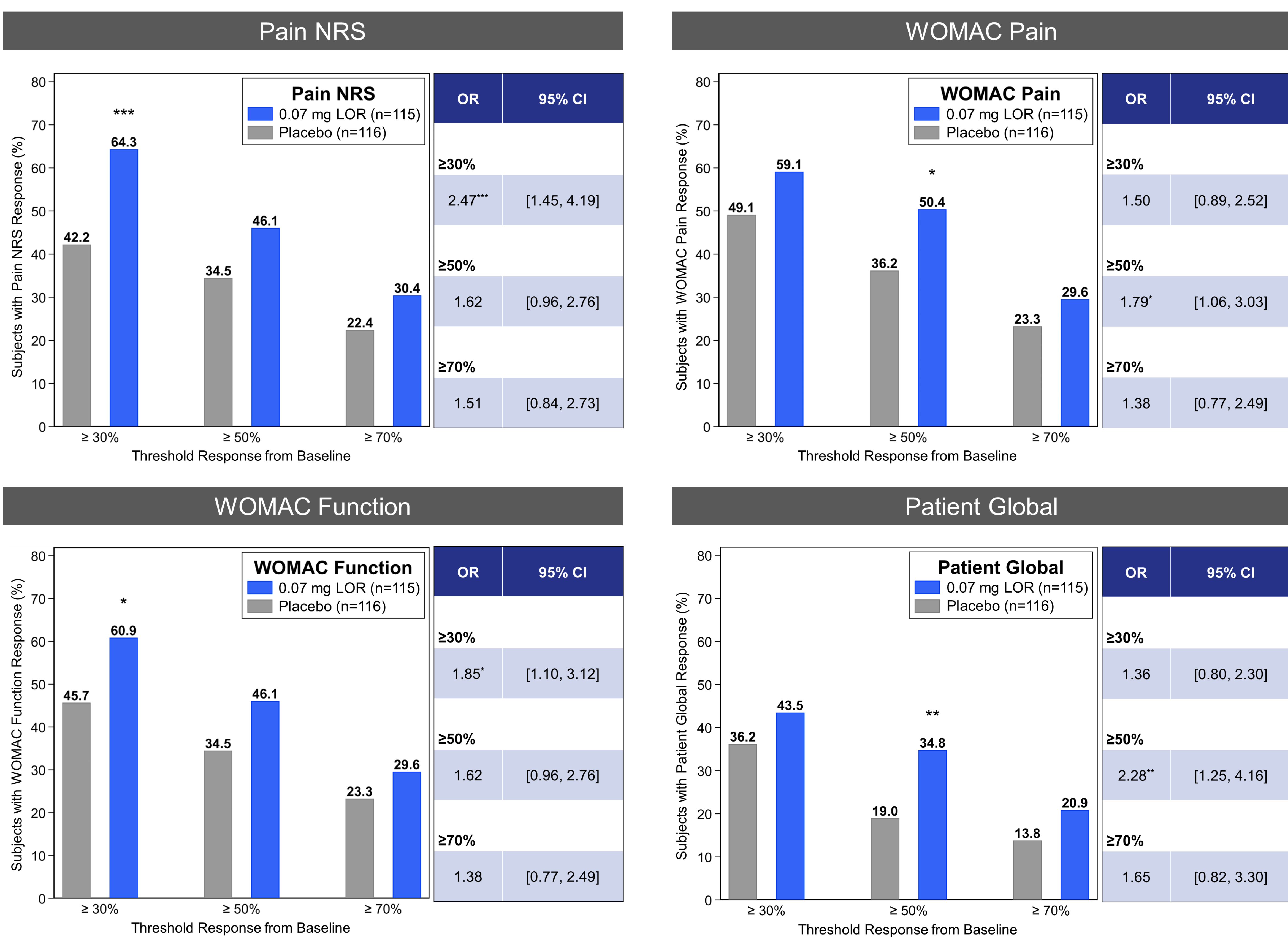
- Patient-reported outcomes (PROs) assess response to therapies, but are subject to high individual variability
- Evaluating discrete threshold responses can help identify how many subjects achieve clinically meaningful changes in PROs
- Lorecivivint (LOR; SM04690), an intra-articular (IA) CLK/DYRK1A inhibitor that modulates the Wnt pathway,<sup>1</sup> demonstrated improved PRO scores versus PBO in a 24-week Phase 2b knee osteoarthritis (OA) trial.<sup>2,3</sup> The primary objective was to identify potentially effective doses of LOR; results for the Phase 3-selected 0.07 mg dose are shown
- This post hoc analysis of these data presents the PRO results as  $\geq 30\%$ , 50%, or 70% threshold responses over baseline at Week 12

## Results

- 635 subjects (91.4%) completed the study: Mean age  $59.0 \pm 8.5$  years, BMI  $29.0 \pm 4.0$  kg/m<sup>2</sup>, female 58.4%, KL grade 3 57.3%
- Treatment with 0.07 mg LOR versus PBO at Week 12 (Figure) led to
  - Significantly increased odds of achieving a  $\geq 30\%$  threshold response in Pain NRS and WOMAC Function
  - Significantly increased odds of achieving a  $\geq 50\%$  threshold response in WOMAC Pain and PtGA
  - Improved numerical (but not statistically significant) odds of achieving a  $\geq 70\%$  threshold response

## Results

Figure. PRO responder analyses at Week 12



Logistic regression of LOR versus placebo using the Full Analysis Set (all subjects) and non-responder imputation; \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ ; OR: Odds Ratio, CI: Confidence Interval

## Conclusions

- IA 0.07 mg LOR increased the proportions of subjects achieving 30%, 50%, or 70% threshold responses in PROs versus PBO
- LOR significantly increased the odds of subjects achieving 30% and 50% threshold responses in specific pain and function PROs versus PBO
- These effects were observed in all analyzed PROs at Week 12

## Methods

- Knee OA subjects were randomized: KL grade 2–3, target knee Pain Numeric Rating Scale (NRS [0–10]) scores  $\geq 4$  and  $\leq 8$ , contralateral knee NRS  $< 4$
- Dosing: Single 2 mL IA injection of 0.03 mg, 0.07 mg, 0.15 mg, 0.23 mg LOR, or placebo (PBO; vehicle) at baseline
- PRO endpoints: Change from baseline in weekly average of daily target knee Pain NRS [0–10], WOMAC Pain [0–100], WOMAC Function [0–100], and Patient Global Assessment (PtGA) [0–100]
- Post hoc: Percent of subjects achieving 30%, 50%, or 70% threshold responses over baseline. Odds ratios (95% CI) of achieving each were calculated using non-responder imputation

## References

1. Deshmukh V, et al. *Osteoarthritis Cartilage*. 2019.
2. Yazici Y, et al. *Arthritis Rheumatol*. 2017; 69 (suppl 10).
3. Yazici Y, et al. *Arthritis Rheumatol*. 2018; 70 (suppl 10).

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