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

Jeyanesh Tambiah, MBBS, Sarah Kennedy, PhD, Christopher J. Swearingen, PhD, Yusuf Yazici, MD
Samumed, LLC, San Diego, CA

Disclosures

- **Jeyanesh Tambiah, MBBS**: Samumed employee and shareholder
- **Sarah Kennedy, PhD**: Samumed employee and shareholder
- **Christopher J. Swearingen, PhD**: Samumed employee and shareholder
- **Yusuf Yazici, MD**: Samumed employee and shareholder

Background

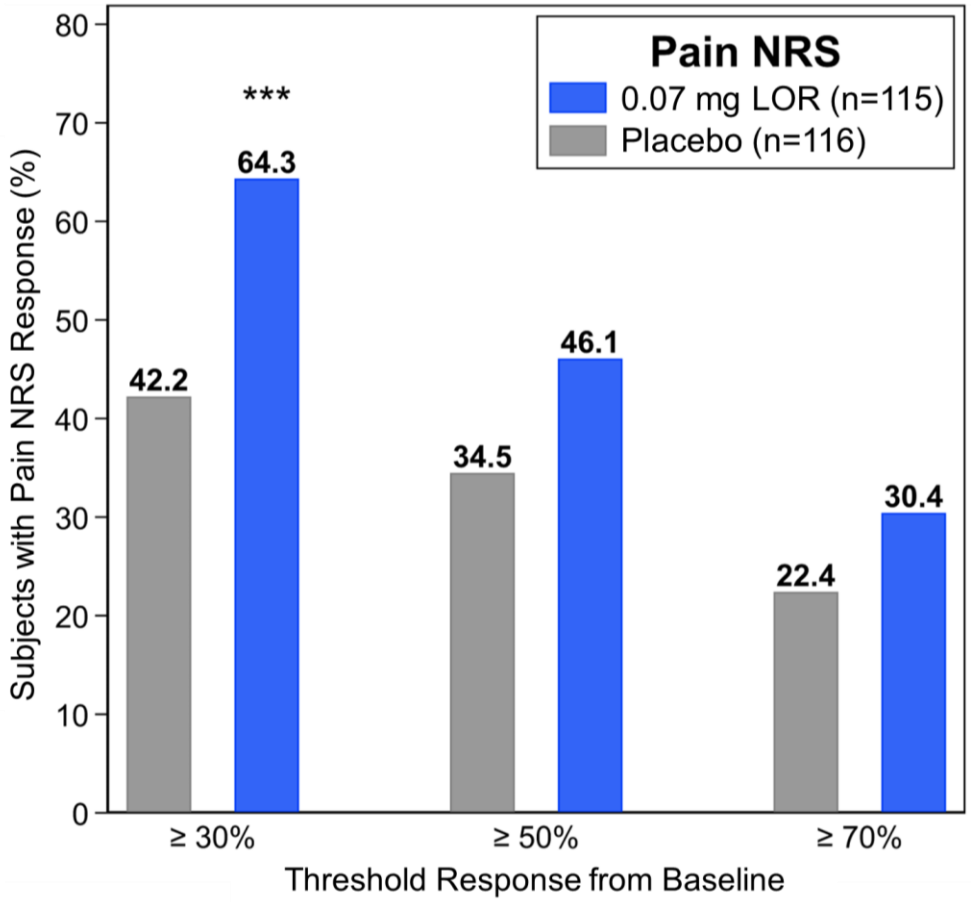
- Patient-reported outcomes (PROs) assess response to therapies, but are subject to high individual variability
- Evaluating discrete threshold responses can help identify how many subjects achieve clinically meaningful changes in PROs
- Lorecivivint (LOR; SM04690) is an intra-articular (IA) CLK/DYRK1A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

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).

0.07 mg LOR Phase 2b responder analysis at Week 12

Post hoc analysis

Pain NRS (FAS)



OR	95% CI
≥30%	
2.47***	[1.45, 4.19]
≥50%	
1.62	[0.96, 2.76]
≥70%	
1.51	[0.84, 2.73]

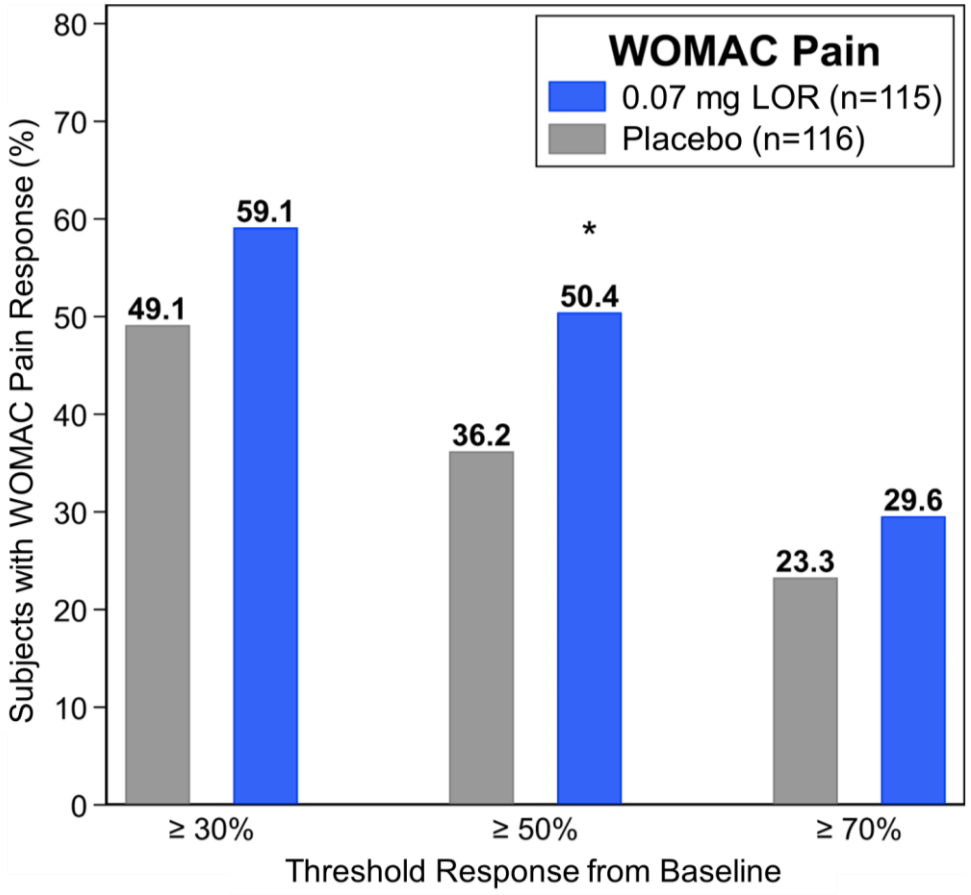
Logistic regression of LOR versus PBO using the Full Analysis Set (FAS, all subjects) and non-responder imputation.

*P<0.05, **P<0.01,***P<0.001; OR: Odds Ratio, CI: Confidence Interval

0.07 mg LOR Phase 2b responder analysis at Week 12

Post hoc analysis

WOMAC Pain (FAS)



	OR	95% CI
≥30%	1.50	[0.89, 2.52]
≥50%	1.79*	[1.06, 3.03]
≥70%	1.38	[0.77, 2.49]

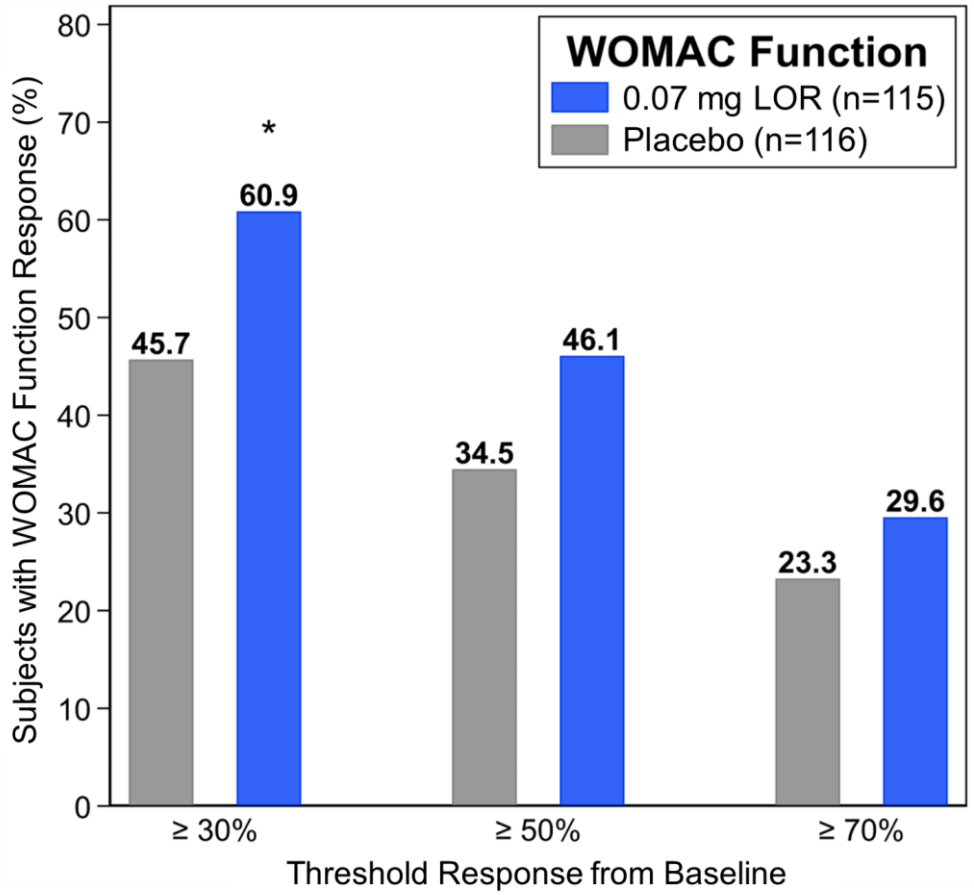
Logistic regression of LOR versus PBO using the Full Analysis Set (FAS, all subjects) and non-responder imputation.

*P<0.05, **P<0.01,***P<0.001; OR: Odds Ratio, CI: Confidence Interval

0.07 mg LOR Phase 2b responder analysis at Week 12

Post hoc analysis

WOMAC Function (FAS)



OR	95% CI
≥30%	
1.85*	[1.10, 3.12]
≥50%	
1.62	[0.96, 2.76]
≥70%	
1.38	[0.77, 2.49]

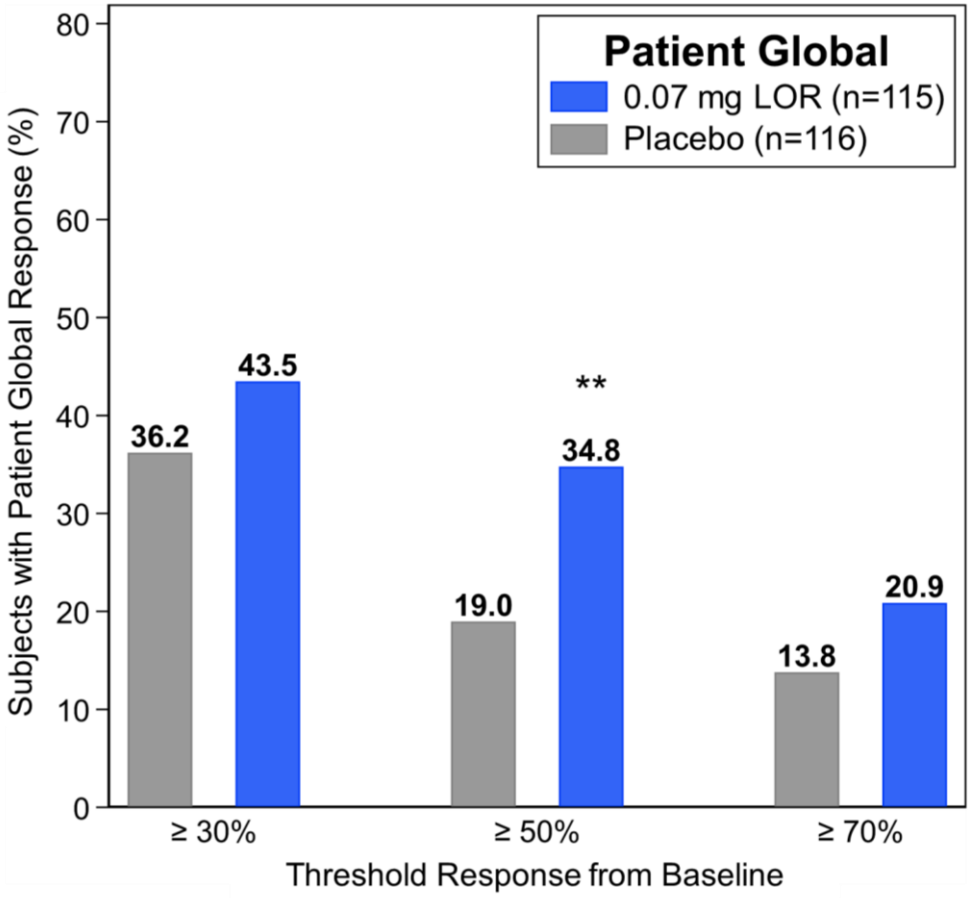
Logistic regression of LOR versus PBO using the Full Analysis Set (FAS, all subjects) and non-responder imputation.

*P<0.05, **P<0.01,***P<0.001; OR: Odds Ratio, CI: Confidence Interval

0.07 mg LOR Phase 2b responder analysis at Week 12

Post hoc analysis

Patient Global Assessment (FAS)



OR	95% CI
≥30%	
1.36	[0.80, 2.30]
≥50%	
2.28**	[1.25, 4.16]
≥70%	
1.65	[0.82, 3.30]

Logistic regression of LOR versus PBO using the Full Analysis Set (FAS, all subjects) and non-responder imputation.

*P<0.05, **P<0.01,***P<0.001; OR: Odds Ratio, CI: Confidence Interval

Conclusions

- This was a post hoc analysis of a Phase 2b trial of LOR in knee OA subjects
- Analysis of PROs at Week 12 showed that 0.07 mg LOR
  - Increased the proportions of subjects achieving 30%, 50%, or 70% threshold responses in PROs versus PBO
  - Significantly increased the odds of subjects achieving 30% and 50% threshold responses in specific pain and function PROs versus PBO

Thank you