

Saline-Based Placebo and Sham Injections Demonstrated Equivalent Improvements on Knee Osteoarthritis Symptoms in a Randomized Controlled Trial, Suggesting a Strong Contextual Response

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Does IA placebo show symptomatic benefit over dry needle?

- **Background**

- Placebo (PBO) arms from randomized controlled trials of injectable knee osteoarthritis (OA) therapies have shown robust patient-reported pain responses, raising the question “does a saline-based PBO injection provide therapeutic benefit?”

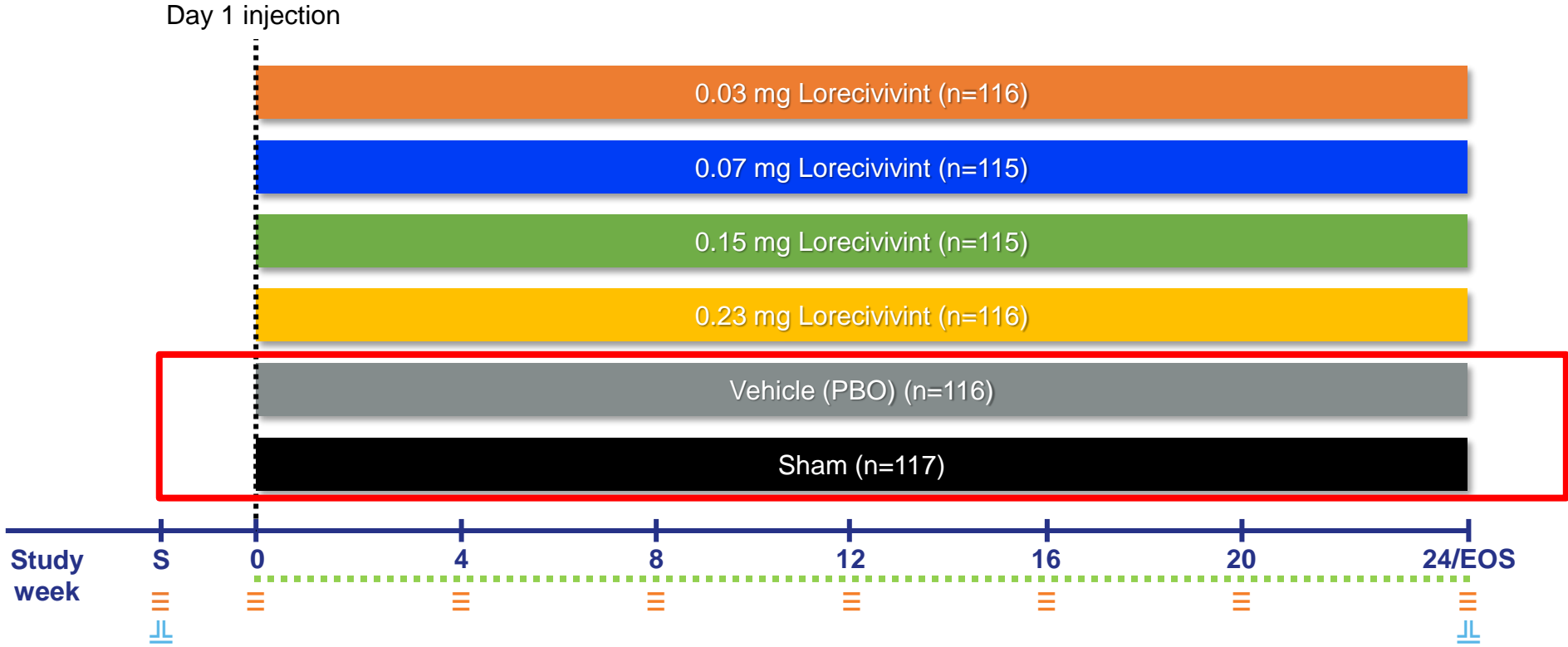
- **Hypothesis**

- There are no differences in treatment response between vehicle PBO and dry needle sham injections

- **Methods**

- In a prospective, randomized, 24-week Phase 2b study of lorecivivint (LOR; SM04690)
 - Effects of IA PBO were compared with sham injections
 - The potential impact of unblinding was also tested
 - Full study results of LOR, a potential disease-modifying knee OA drug, were presented previously

Lorecivivint Phase 2b study design



- ≡ **Clinical assessments:** Daily Pain NRS, WOMAC Function, WOMAC Pain, Patient Global Assessment, Physician Global Assessment, KOOS, KOOS-PS, daily NSAID
- ≡ **Imaging:** Knee X-ray
- ... **Safety assessments:** AEs, vital signs, physical exam, laboratory panels

Main study results

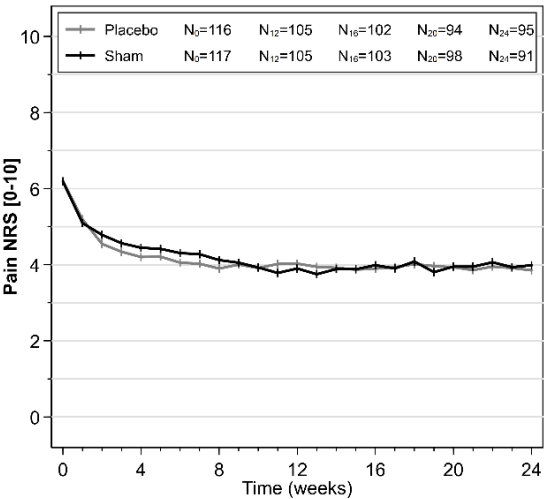
- Primary endpoints of Pain NRS, WOMAC Pain/Function, and PtGA were met for 0.23 mg and 0.07 mg LOR (Pain NRS only) compared with PBO at Week 24
- Incidence of adverse events was similar between groups
- PBO versus sham: N=233
 - 207 subjects [89%] completed the study

Subject Characteristics		
	PBO	Sham
n	116	117
Age at Consent (Years)*	60.1 (9.0)	59.0 (8.0)
BMI (kg/m ²)*	28.62 (4.29)	28.97 (3.84)
Female	63 (55.3)	72 (60.0)
Race		
<i>White</i>	89 (78.1)	86 (71.7)
<i>Black / AA</i>	16 (14.0)	27 (22.5)
<i>Asian</i>	6 (5.3)	3 (2.5)
Hispanic / Latino	16 (14.0)	24 (20.0)
KL 3	71 (62.3)	59 (49.2)

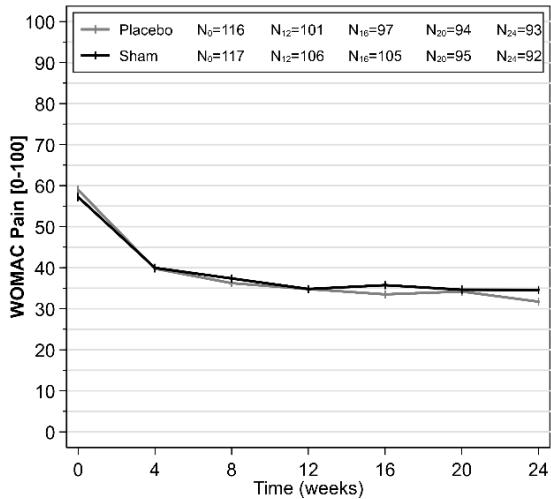
*Mean (SD) reported. Otherwise, n (%) reported.

No differences in PROs observed between PBO and sham

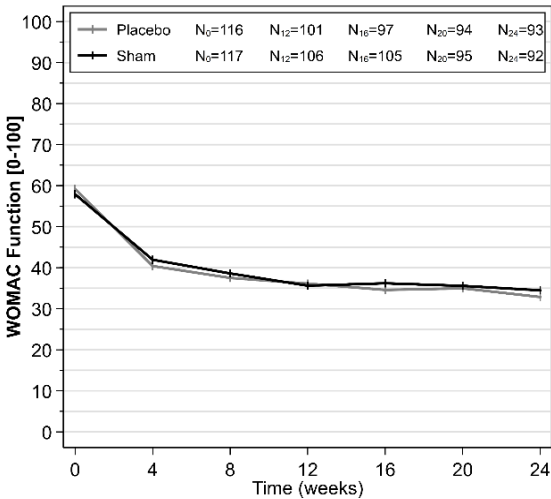
Pain NRS



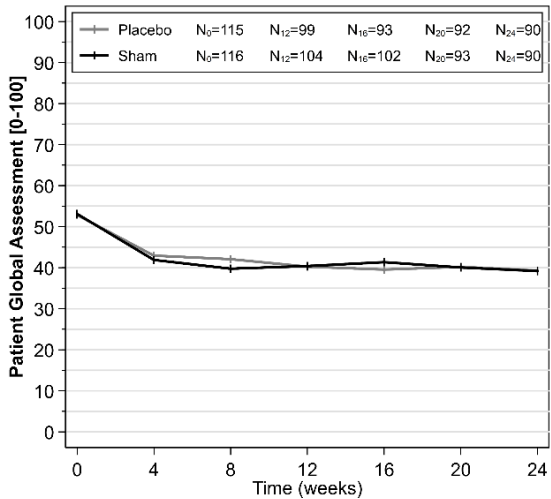
WOMAC Pain



WOMAC Function



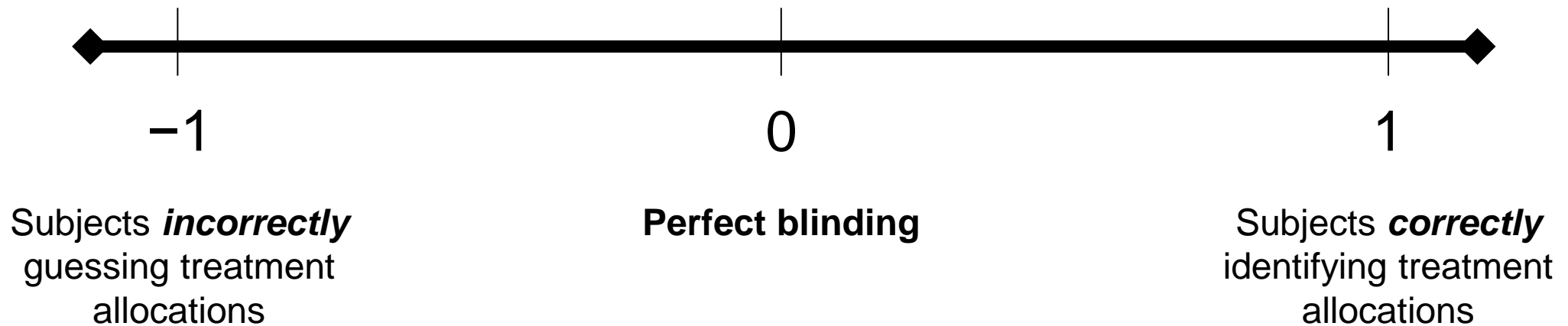
Patient Global Assessment



Observations over time depicting baseline-adjusted mean improvements in PROs of PBO compared with sham injections (FAS)

Bang's Blinding Index

- Immediately following injection and at Week 24, subjects were asked to identify which treatment (PBO, sham, or LOR) they thought they had received
 - Subject responses were compared using Bang's Blinding Index (BBI)
 - BBI scale is $-1 \leq 0 \leq 1$



No differences were detected between PBO and sham

Compared subjects' treatment identification accuracy using BBI

Visit	Planned Treatment	Subject Response				Total	Bang's BI ^a
		Lorecivivint	Vehicle	Sham	Don't Know		
Day 1	Lorecivivint	111	17	13	321	462	0.175
	Vehicle	23	2	4	87	116	-0.216
	Sham	29	7	3	78	117	-0.282
	Total	163	26	20	486	695	NA
Week 24	Lorecivivint	193	50	37	147	427	0.248
	Vehicle	47	16	7	32	102	-0.373
	Sham	43	13	11	38	105	-0.429
	Total	283	79	55	217	634	NA

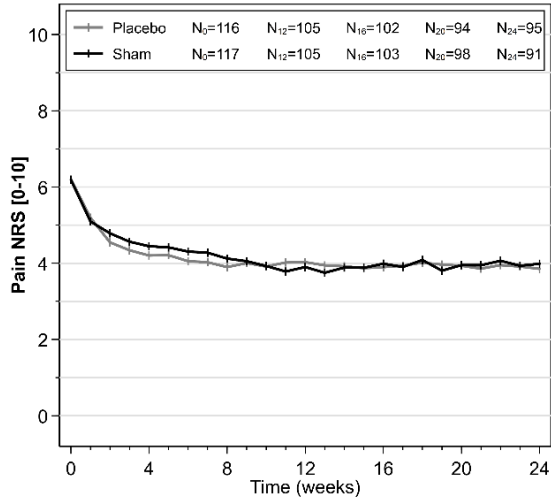
^a Bang's Blinding Index (BI) determines the percentage of unblinding that is beyond chance

- BI = -1 represents opposite guessing
- BI = 0 represents random guessing
- BI = 1 represents complete unblinding

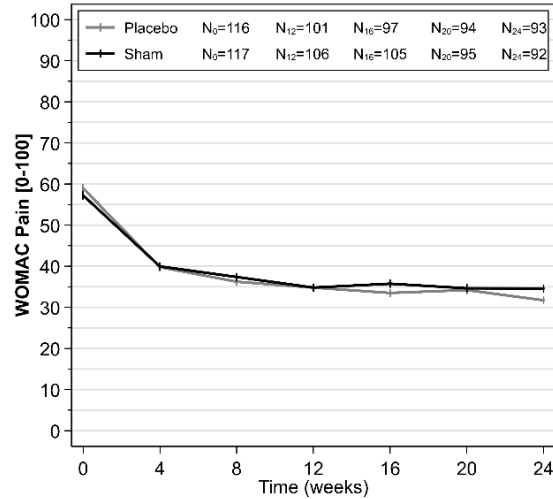
Subjects were unable to discern which treatment they received

IA PBO effects on PROs were “contextual,” not therapeutic

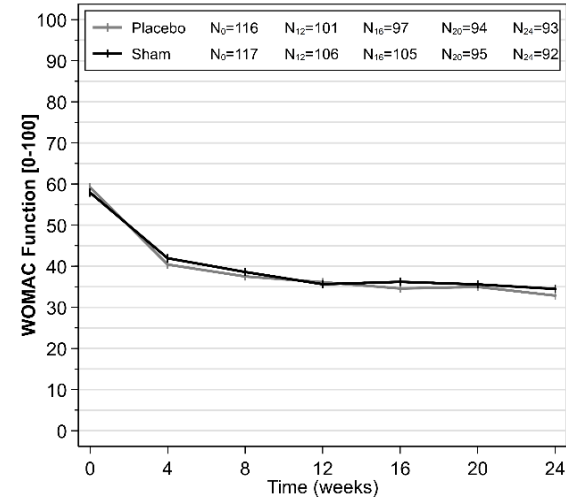
Pain NRS



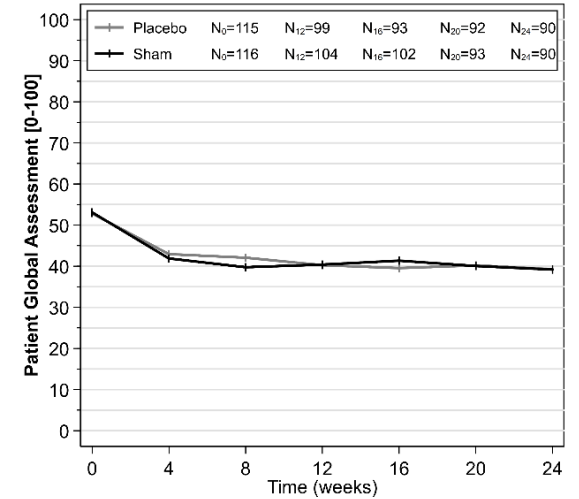
WOMAC Pain



WOMAC Function



Patient Global Assessment



- This is the first prospective comparison of IA PBO versus sham injections
- Observed PRO effects appeared to be “contextual,” resulting from the injection procedure rather than from therapeutic PBO effects
- To establish a true beneficial effect of an IA treatment for knee OA, results should establish improvements in PROs over PBO responses and not baseline

The background features a pattern of teal dotted lines that originate from a central point on the right side of the image and radiate outwards, creating a sunburst or starburst effect. The lines are thin and spaced out, filling the entire frame.

Thank you