Safety Profile to Date of the Novel, Intra-articular Agent Lorecivivint (LOR; SM04690), a CLK/DYRK1A Inhibitor That Modulates the Wnt Pathway, in Subjects with Knee Osteoarthritis

Ismail Simsek[1], Christopher J. Swearingen[1], Sarah Kennedy[1], Jeyanesh Tambiah[1], Yusuf Yazici[1], Nancy Lane[2], Marc Hochberg[3]
[1]Samumed, LLC, San Diego, CA; [2]University of California, Davis, CA; [3]University of Maryland, Baltimore, MD

Poster #1326

Background

- Safety concerns regarding osteoarthritis (OA) pharmacotherapy have led to treatment guideline revisions. These changes reinforce the unmet need for new OA therapies
- Lorecivivint (LOR), an intra-articular (IA) CLK/DYRK1A inhibitor that modulates the Wnt pathway[1,2], is currently in Phase 3 trials for treatment of knee OA
- The safety profile of LOR to date was evaluated through a pooled analysis of 3 completed placebo (PBO)-controlled trials (Phase 1, 2a, and 2b)[3-5]

Methods

- Safety data pooled from 3 randomized trials
  - NCT02095548 & NCT03122860 (24 weeks); NCT02536833 (52 weeks)
    - Subjects: Moderate to severe knee OA
    - Dosing: Single, 2mL, IA injection of 0.03 mg, 0.07 mg, 0.15 mg, or 0.23 mg LOR or control
- Subject groups compared: LOR-treated (any dose) and non-treated control (PBO/sham)
- Adverse events (AEs), serious AEs (SAEs), bone-health AEs categorized using MeDRA (Medical Dictionary for Regulatory Activities)

Results

Fig. 1. AE summary from total clinical trial population (N=1208)

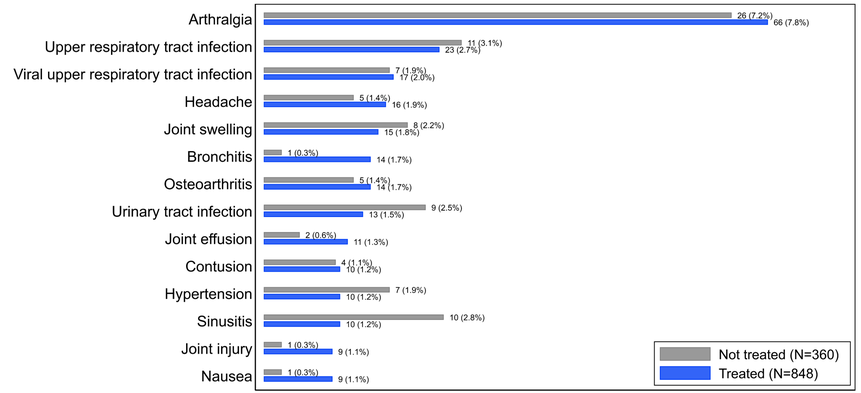
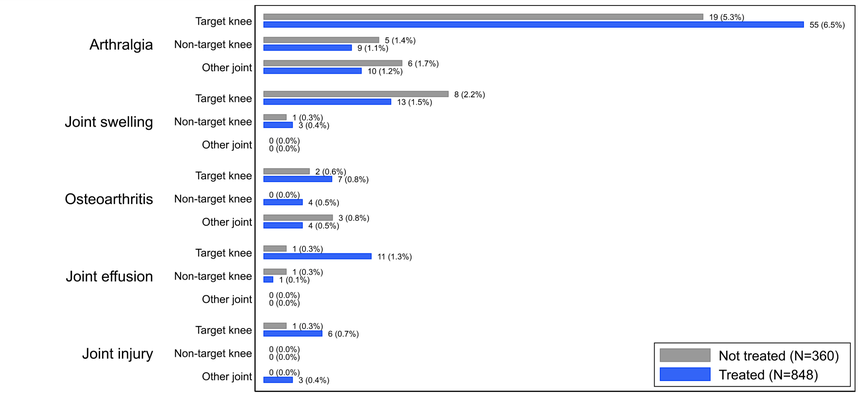


Fig. 2. Joint-related AE summary from total clinical trial population (N=1208)



- AE rates similar between LOR (350/848 [41.3%]) and control (138/360 [38.3%])
  - AEs >1% captured in **Fig. 1**
  - Arthralgia, defined as any exacerbation (increase in frequency, severity, or specificity) of an existing condition, was the most common AE in all subjects (LOR 7.8%, control 7.2%)
- SAE rates were 2.4% (20/848) in LOR subjects and 1.1% (4/360) in control subjects
  - All SAEs were deemed unrelated to LOR by investigators
- Target-knee arthralgia was the most common joint-specific AE (LOR 6.5%, control 5.3%) (**Fig. 2**)
- 16 bone-health-related AEs were seen in the development program
  - 9/848 (1.1%) LOR-treated subjects
  - 3/360 (0.8%) control subjects
  - 2 metabolic bone disorders in 2 subjects
    - Osteopenia/osteoporosis in 2 LOR-treated postmenopausal women
  - 14 fractures in 10 subjects
    - 7/846 (0.8%) LOR-treated subjects
    - 3/360 (0.8%) control subjects
  - All fractures were related to a trauma
    - 10/14 (71%) directly related to a fall
    - All fractures resolved without sequalae

Conclusions

- **In total exposure to date, IA LOR for the treatment of knee OA appeared to be safe and well tolerated**
- **In all categories, individual AEs were reported at comparable rates between groups**
- **No SAEs were deemed related to LOR by investigators**
- **Bone-health AE incidence rates between LOR and controls were similar**
- **These data support the continued evaluation of LOR as a treatment for knee OA**

References

1. Deshmukh V, et al. *Osteoarthritis Cartilage.* 2017.
2. Deshmukh V, et al. *Osteoarthritis Cartilage.* 2019.
3. https://clinicaltrials.gov (Identification No. NCT02095548).
4. https://clinicaltrials.gov (Identification No. NCT03122860).
5. https://clinicaltrials.gov (Identification No. NCT02536833).

All authors are employees, shareholders, or consultants of Samumed, LLC. Other disclosures are listed in the published abstract.

9381 Judicial Drive, San Diego, CA 92121
info@samumed.com