Lorecivivint Injection for Knee Osteoarthritis Appeared Safe and Well Tolerated: Pooled Data from Three Randomized Controlled Trials

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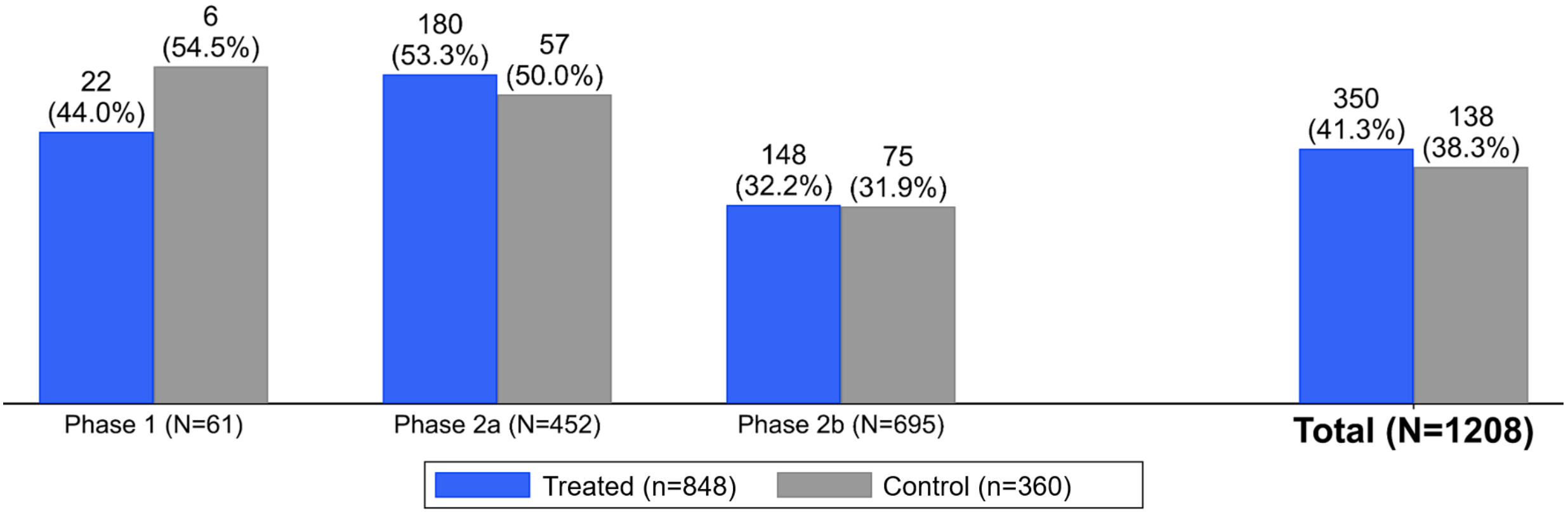
Background and methods

- Safety concerns regarding osteoarthritis (OA) pharmacotherapy have reinforced the unmet need for safe and effective OA therapies
- Lorecivivint (LOR; SM04690), an intra-articular (IA) CLK/DYRK1A inhibitor that modulates the Wnt pathway,[1,2] is in Phase 3 trials as a potential disease-modifying treatment for knee OA
- The safety profile of LOR to date was evaluated by a pooled analysis of 3 completed placebo-controlled trials (Phase 1, 2a, 2b)[3–5]

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. NCT02536833).
5. https://clinicaltrials.gov (Identification No. NCT03122860).

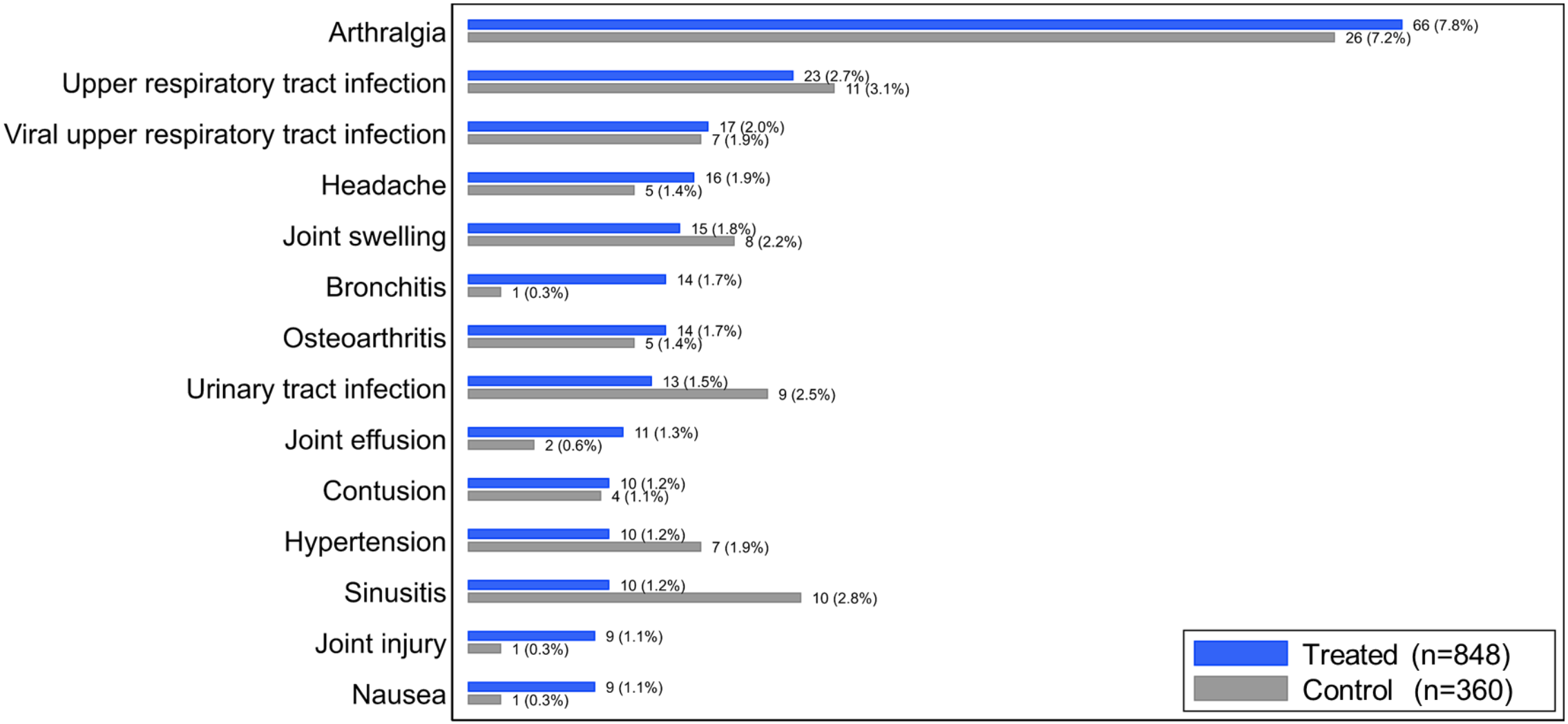
Incidence of AEs between treated and control subjects was consistent across studies and overall



All subjects received intra-articular procedures.

Integrated safety summary: AEs reported in >1% of treated subjects

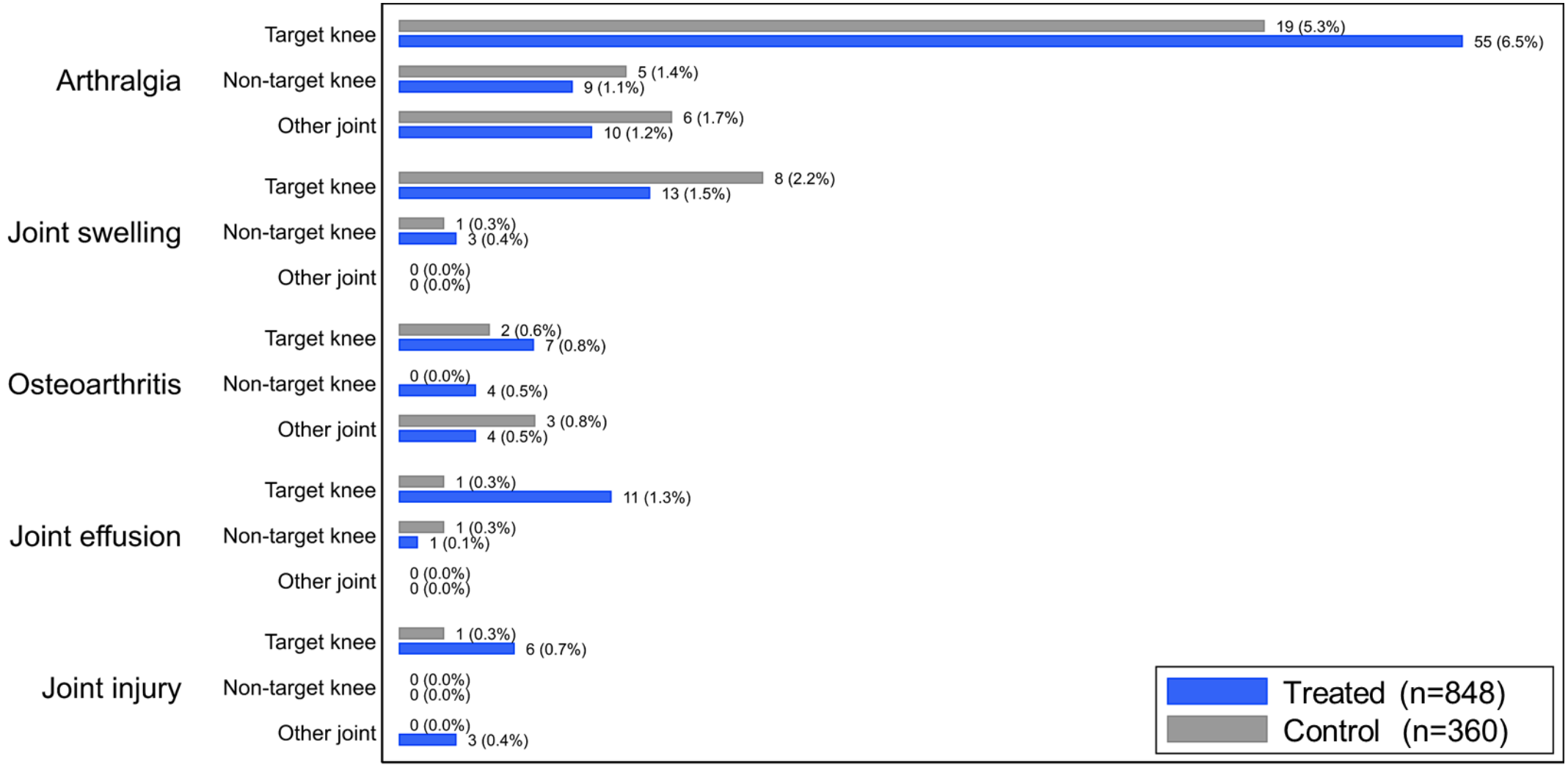
Total clinical trial population (N=1208)



Safety data from completed trials. All subjects received intra-articular injections.

Integrated safety summary: Joint-related AEs

Total clinical trial population (N=1208)



Safety data from completed trials. All subjects received intra-articular injections.

Serious adverse event summary

From Safety Review: 2018-10-23	Lorecivivint (LOR)				
	0.03 mg (n=234)	0.07 mg (n=235)	0.23 mg (n=226)	All LOR* (n=801)	Placebo (n=353)
Total SAEs (%)	**9 (3.8)**	**13 (5.6)**	**7 (3.1)**	**29 (3.5)**	**4 (1.1)**
Cardiac Disorders	**2 (0.8)**	**4 (1.6)**	0 (0.0)	**6 (0.7)**	**1 (0.3)**
Infections	**3 (1.2)**	**2 (0.8)**	**1 (0.4)**	**6 (0.7)**	0 (0.0)
Renal / Urinary Disorders	**1 (0.4)**	**1 (0.4)**	**1 (0.4)**	**3 (0.4)**	0 (0.0)
Vascular Disorders	**1 (0.4)**	**2 (0.8)**	0 (0.0)	**3 (0.4)**	0 (0.0)
Injury / Procedural Complications	0 (0.0)	0 (0.0)	**2 (0.8)**	**2 (0.2)**	**1 (0.3)**
Neoplasms	0 (0.0)	**1 (0.4)**	**1 (0.4)**	**2 (0.2)**	0 (0.0)
Reproductive System Disorders	0 (0.0)	**1 (0.4)**	**1 (0.4)**	**2 (0.2)**	0 (0.0)
Congenital / Genetic Disorders	0 (0.0)	**1 (0.4)**	0 (0.0)	**1 (0.1)**	0 (0.0)
Gastrointestinal Disorders	**1 (0.4)**	0 (0.0)	0 (0.0)	**1 (0.1)**	0 (0.0)
Hepatobiliary Disorders	0 (0.0)	**1 (0.4)**	0 (0.0)	**1 (0.1)**	0 (0.0)
General Disorders / Administration Site Condition	0 (0.0)	0 (0.0)	**1 (0.4)**	**1 (0.1)**	0 (0.0)
Nervous System Disorders	**1 (0.4)**	0 (0.0)	0 (0.0)	**1 (0.1)**	0 (0.0)
Musculoskeletal / Connective Tissue Disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (0.3)**
Respiratory Disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (0.3)**

There were no deaths. All SAEs were deemed unrelated to LOR by investigator.

*The 0.15 mg LOR dose group (n=106) had no SAEs.

Conclusions

- Based on AEs observed in completed trials (N=1208), IA LOR for the treatment of painful knee OA appeared to be safe and well tolerated
- Individual AEs were reported at comparable rates between treated and control subjects as well as among the various LOR dose groups
- No SAEs were deemed related to LOR by investigators
- Clinical development of LOR as a treatment for knee OA is ongoing

Thank you