

Safety, Tolerability, and Pharmacokinetics of an Intra-articular Corticosteroid Injection Administered 7 Days Before or After Intra-articular Lorecivivint Injection into the Same Knee of Healthy Volunteers: An Open-Label, Parallel-Arm Study

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Disclosures

- A. Halseth, J. Tambiah, S. Kennedy, C. J. Swearingen, V. A. Lopez, I. Simsek, M. Fineman, Y. Yazici
 - Employed with and/or stockholders of Biosplice Therapeutics (formerly Samumed, LLC)

- Nancy E. Lane
 - Consultant for Biosplice Therapeutics, Amgen, Lilly, Pfizer
 - Speaker for Amgen

Disclaimer

- Lorecivivint (LOR; SM04690) is an investigational compound currently in clinical trials; LOR has not been approved by the US Food and Drug Administration (FDA), European Medicines Agency (EMA) or any other pharmaceutical regulatory authority, and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidate.
- While the complete mechanism of action (MOA) for LOR is unknown, further investigation is being conducted. All MOA information is based on non-clinical data and the relationship to clinical benefit is unknown.

Background

- First-line treatments for knee OA include intra-articular (IA) corticosteroid injections.
- Lorecivivint (LOR) is a novel IA CLK/DYRK inhibitor that modulates Wnt and inflammatory pathways.
- A single LOR (0.07 mg) injection appeared safe and effective in a knee OA clinical trial target population up to 12 months.¹⁻³
- No safety data exists regarding IA corticosteroid use in close time proximity to LOR.
 - LOR trials excluded IA corticosteroid use from 8-12 wks prior.
 - In practice LOR and corticosteroids could potentially be administered contemporaneously.
- This open-label, parallel-arm, healthy subject study assessed the potential for safety, tolerability, and pharmacokinetic (PK) interactions between LOR [0.07 mg] and triamcinolone acetonide (TCA) injections administered 7 days apart.

Methods

- Healthy subjects randomized to 1 of 2 treatment arms (TA) for right knee injection:
 - TA1 (TCA [40 mg] Day 1, LOR [0.07 mg] Day 8)
 - Plasma TCA assessed multiple times Days 1-15
 - Plasma LOR assessed on Day 8 (before and 8h after LOR injection)
 - TA2 (LOR [0.07 mg] Day 1, TCA [40 mg] Day 8)
 - Plasma LOR assessed multiple times Days 1-12
 - Plasma TCA assessed multiple times Day 8 (before and 12 h after TCA dosing) to Day 22
- TEAEs grouped by “Epoch” – injection-based subdivisions of the study timeline
 - Epoch 1 spanned from 1st to 2nd injection (Day 1 - Day 8)
 - Epoch 2 spanned from 2nd injection to end of study (Day 8 - EOS)

Results: Subject Characteristics

- 67 subjects screened, 41 enrolled and randomized
- N=40 subjects treated and completed (n=20 per TA)
 - Age 41.3 ± 7.2 years
 - BMI 27.8 ± 2.98 kg/m²
 - Female 40.0%
 - Majority white (80%) and Hispanic/Latino (100%)
- Subject characteristics similar between TA1 and TA2

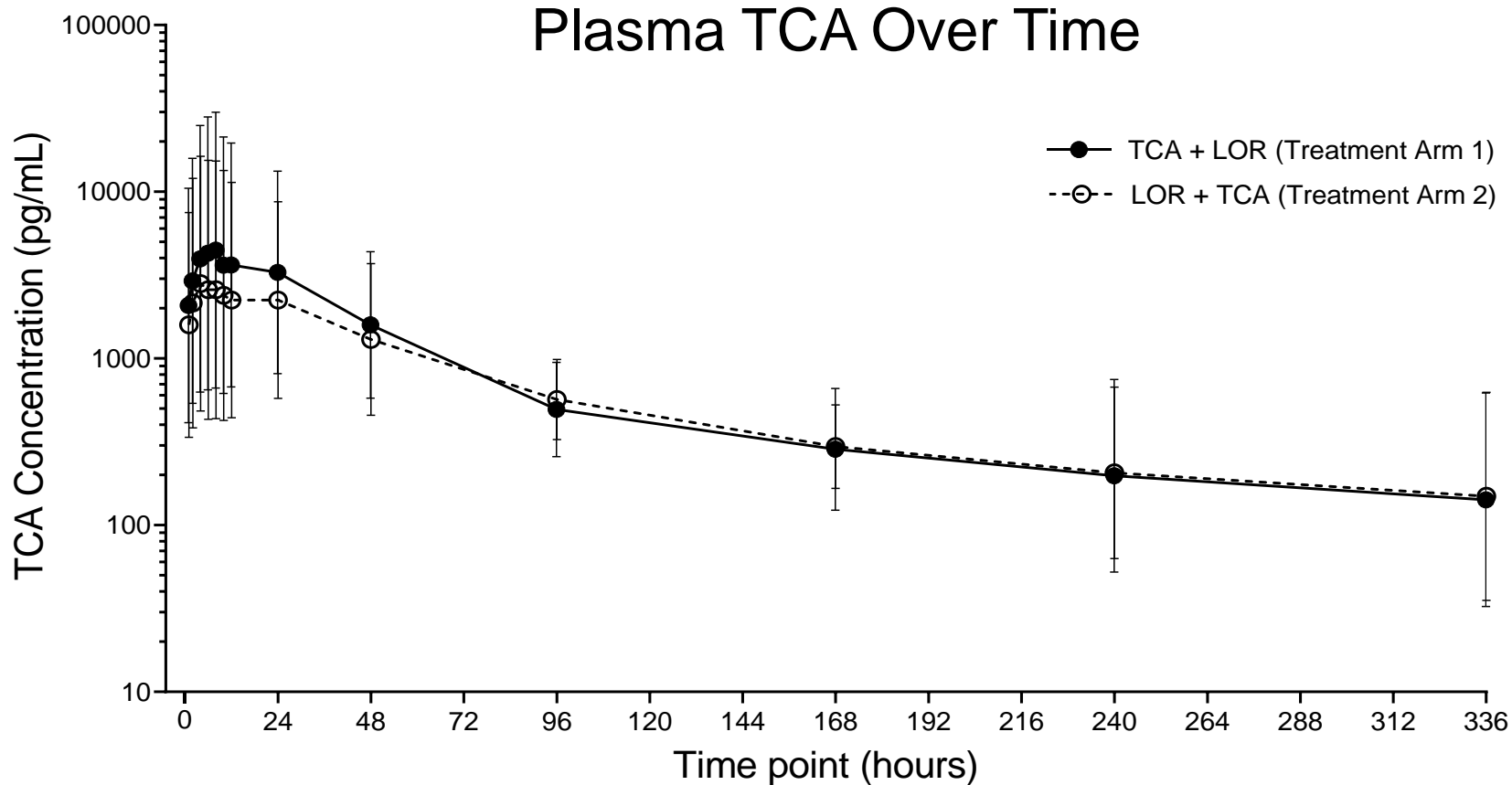
Results: Safety

- 18 TEAEs in 11 (27.5%) subjects
 - More TEAEs in TA1 Epoch 2 (TCA+LOR) but most appeared unrelated to the TCA/LOR combo
 - Incidence of related TEAEs and related TEAEs at injected knee were similar between TAs.
- 5 TEAEs in 4 (10%) subjects deemed “related/possibly related” to LOR injection*
 - All mild severity - headache or injection site pain/bruising
- No serious/severe TEAEs

Subdivision of study timeline (Period)	Treatment Arm 1		Treatment Arm 2	
	Period 1 (TCA—LOR)	Period 2 (LOR—EOS)	Period 1 (LOR—TCA)	Period 2 (TCA—EOS)
TEAEs [Events/N (%) subjects]	5 / 4 (20%)	8 / 3 (15%)	2 / 2 (10%)	3 / 3 (15%)
Inj. Site Bruising	4 / 4 (20%)	0 / 0	1 / 1 (5%)	2 / 2 (10%)
Inj. Site Pain	0 / 0	2 / 1 (5%)	0 / 0	0 / 0
Back Pain	1 / 1 (5%)	0 / 0	0 / 0	0 / 0
Flank Pain	0 / 0	1 / 1 (5%)	0 / 0	0 / 0
Musculoskeletal Discomfort	0 / 0	1 / 1 (5%)	0 / 0	0 / 0
Extremity Pain	0 / 0	1 / 1 (5%)	0 / 0	0 / 0
Headache	0 / 0	1 / 1 (5%)	1 / 1 (5%)	0 / 0
Hypersensitivity	0 / 0	0 / 0	0 / 0	1 / 1 (5%)
Skin Abrasion	0 / 0	1 / 1 (5%)	0 / 0	0 / 0
Adnexa Uteri Pain	0 / 0	1 / 1 (5%)	0 / 0	0 / 0

Results: Plasma Concentrations (PK) of LOR and TCA

- Plasma [LOR] below limit of quantification (0.1 ng/ml) in all subjects, at all time points



- No statistically significant differences in geometric mean [TCA] between arms

Discussion and Conclusions

- No safety signals observed in this healthy subject study.
- No quantifiable levels of LOR was detected in plasma in either treatment arm.
- LOR injection did not appear to alter peak exposure or PK characteristics of TCA when compared with TCA alone.
- Safety and PK data suggested no drug-drug interactions between LOR and TCA.
- IA administration of LOR and TCA within 1 week of each other appeared to pose no safety concerns.

Thank you

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