LP-310 Manuscript Supplementary Material

Safety and Efficacy of LP-10 Liposomal Tacrolimus in Oral Lichen Planus: A Multicenter Phase 2 Trial

Running title: **LP-10 Liposomal Tacrolimus for OLP: Phase 2 Trial**

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Date of submission (and revision/resubmission)

Supplementary information

Inclusion/exclusion criteria

Participants were included in the study if they fulfilled all the following criteria: 1. Provided written informed consent; 2. Male or female ≥ 18 years of age; 3. Oral biopsy performed within the last 10 years before the screening visit demonstrated oral lichen planus (OLP) and/or oral lichenoid mucositis in the absence of cancer or dysplasia; 4. Moderate OLP based on an OLP Investigator Global Assessment (IGA) score of ≥ 3 [1]; 5. OLP Pain or Sensitivity Numerical Rating Scale (NRS) score of ≥ 3; 6. Participants taking prescription oral steroid or rinse treatment(s) for their OLP symptoms at the time of the screening visit must have agreed to stop treatment for the duration of the trial and to undergo a 4-week washout period; 7. Willing and capable of understanding and complying with all requirements of the protocol, including proper completion of the self-administered questionnaires; 8.Willing to avoid live vaccines while enrolled in the trial; 9. Participants of child-bearing potential must have a negative pregnancy test and agree to undergo pregnancy testing at each study visit (unless patient has undergone a bilateral tubal ligation or hysterectomy and/or is post-menopausal as defined by the absence of menses for at least 12 months); 10. Participants of child-bearing potential and male participants with a female partner of child-bearing potential, agree to use a reliable method of contraception (condoms and/or oral contraceptives) for the duration of the trial and for 10 days thereafter.

Participants meeting any of the following criteria were excluded from enrollment in the study: 1. Hyperkalemia (potassium > 6.0 mmol/L); 2. Chronic kidney disease; 3. Long QT syndrome; 4. History of oral cavity or oropharyngeal cancers; 5. Active cancer, other than basal cell carcinoma; 6. Uncontrolled hypertension (i.e., > 145 mmHg systolic or > 95 mmHg diastolic); 7. Failed tacrolimus treatment for OLP in the past; 8. Was currently or had previously participated in another oral cavity therapeutic or device study within 3 months of screening and had not

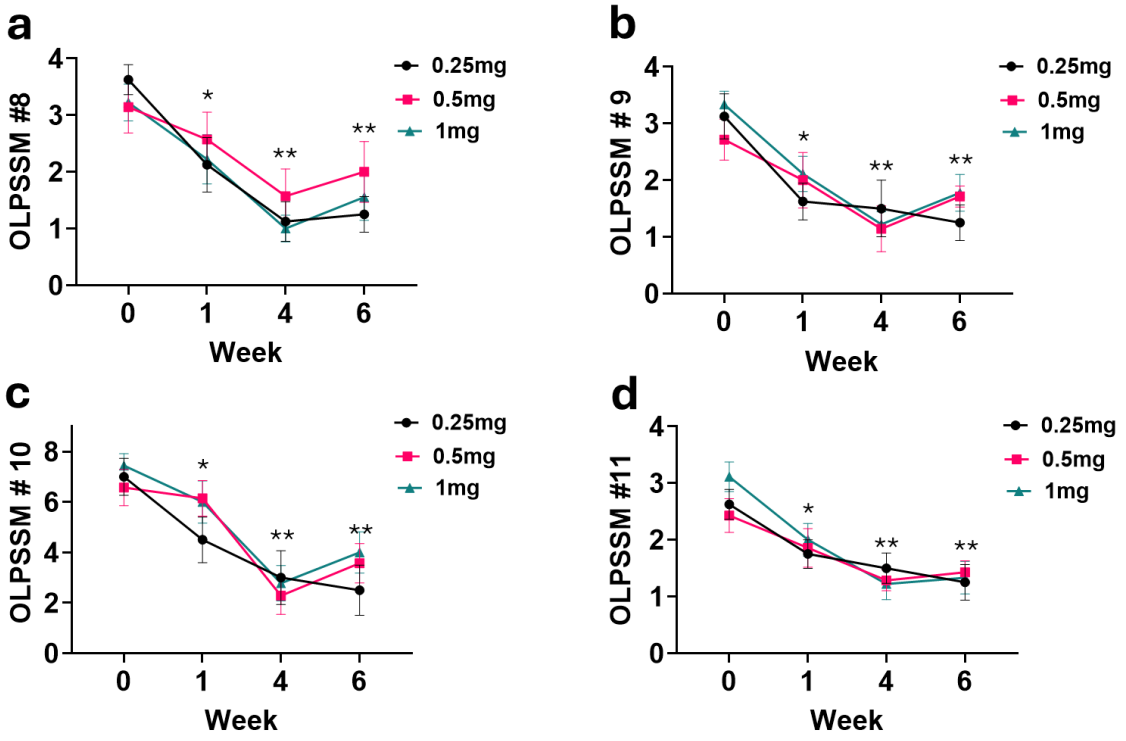
returned to baseline; 9. History of oral cavity infection (bacterial, viral, or fungal) within 3 months prior to screening; 10. Pregnant or lactating; 11. Active bleeding peptic ulcer disease; 12. Known allergy to liposomes and/or egg yolk and/or tacrolimus; 13. Evidence of renal impairment (creatinine > 2 × the upper limit of normal at Visit 1), hepatic impairment (aspartate aminotransferase [AST] or alanine aminotransferase [ALT] > 3 × the upper limit of normal at Visit 1), clinically significant cardiovascular, respiratory, or psychiatric diseases per investigator's judgment; 14. Currently taking magnesium and aluminum-hydroxide antacids or metoclopramide; 15. Currently taking aminoglycosides, ganciclovir, amphotericin B, cisplatin, nucleotide reverse transcriptase inhibitors, and protease inhibitors; 16. Presence of any clinically significant systemic disease or condition that in the opinion of the investigator would make the patient unsuitable for the study.

Supplementary Table 1. All treatment emergent adverse events considered related to treatment

List of all TEAEs considered related to treatment [n (%)]	**Group 1 N=8**	**Group 2 N=8**	**Group 3 N=11**	**Overall N=27**
Mild dry mouth	1 (12.5%) 1	1 (12.5%) 1	3 (27.3%) 3	5 (18.5%) 5
Mild oral dysaesthesia	2 (25.0%) 2	0	0	2 (7.4%) 2
Moderate oral dysaesthesia	0	0	1 (9.1%) 1	1 (3.7%) 1
Mild dyspepsia	0	0	2 (18.2%) 5	2 (7.4%) 5
Mild glossodynia	1 (12.5%) 1	0	1 (9.1%) 2	2 (7.4%) 3
Mild nausea	1 (12.5%) 1	0	1 (9.1%) 1	2 (7.4%) 2
Mild paraesthesia oral	2 (25.0%) 2	0	0	2 (7.4%) 2
Mild burning mouth syndrome	1 (12.5%) 1	0	0	1 (3.7%) 1
Mild gastroesophageal reflux disease	1 (12.5%) 1	0	0	1 (3.7%) 1
Mild hyperesthesia teeth	0	0	1 (9.1%) 1	1 (3.7%) 1

Mild hypoesthesia oral	1 (12.5%) 1	0	0	1 (3.7%) 1
Mild tongue dry	1 (12.5%) 1	0	0	1 (3.7%) 1
Mild tongue pruritus	1 (12.5%) 1	0	0	1 (3.7%) 1
Mild dysesthesia	0	2 (25.0%) 2	1 (9.1%) 1	3 (11.1%) 3
Mild dysgeusia	0	0	2 (18.2%) 2	2 (7.4%) 2
Mild taste disorder	1 (12.5%) 1	0	1 (9.1%) 1	2 (7.4%) 2
Mild ageusia	1 (12.5%) 1	0	0	1 (3.7%) 1
Mild headache	1 (12.5%) 2	0	0	1 (3.7%) 2
Mild migraine	1 (12.5%) 2	0	0	1 (3.7%) 2
Mild hypersensitivity	0	2 (25.0%) 2	0	2 (7.4%) 2
Mild food allergy	1 (12.5%) 1	0	0	1 (3.7%) 1
Mild oral allergy syndrome	1 (12.5%) 1	0	0	1 (3.7%) 1
Mild sensation of foreign body	0	1 (12.5%) 1	0	1 (3.7%) 1
Mild thirst	0	1 (12.5%) 1	0	1 (3.7%) 1
Moderate herpes simplex	1 (12.5%) 1	0	0	1 (3.7%) 1
Moderate oral fungal infection	0	0	1 (9.1%) 1	1 (3.7%) 1
Mild ALT increased	0	0	1 (9.1%) 1	1 (3.7%) 1
Moderate ALT increased	1 (12.5%) 1	0	0	1 (3.7%) 1
Mild AST increased	0	0	1 (9.1%) 1	1 (3.7%) 1
Mild eosinophil count increased	0	0	1 (9.1%) 1	1 (3.7%) 1
Mild dry throat	0	0	1 (9.1%) 1	1 (3.7%) 1
Mild throat irritation	1 (12.5%) 1	0	0	1 (3.7%) 1
Mild hyperchloremia	0	0	1 (9.1%) 1	1 (3.7%) 1
Mild hyperkalemia	0	0	1 (9.1%) 1	1 (3.7%) 1

ALT= alanine aminotransferase; AST= aspartate aminotransferase; TEAEs= treatment emergent adverse events



Supplementary Figure 1. Change in OLP symptom severity measure (OLPSSM) items 8 to 11 over the 4 weeks of treatment and two weeks of follow-up. Data are presented as mean ±SEM. a. OLPMMS #8: *<p<0.02; **p<0.0001, significant decline in OLPSSM #8 from baseline (week 0); b. OLPMMS #9-11: *<p<0.005; **p<0.0001, significant decline in OLPSSM #9-11 from baseline (week 0); Repeated measures ANOVA (Mixed-effects model) followed by Tukey's test vs Baseline (week 0).

Reference

1. Brennan MT, Bissonnette C, Lizano M, et al. New Investigator Global Assessment Scale in Lichen Planus: OLP IGA. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology* 2023; 135: e41. DOI: https://doi.org/10.1016/j.oooo.2022.09.025.