2. STUDY SUMMARY

Name of Sponsor/Company: Laboratorios Ojer Pharma S.L.	**Individual Study Table referring to Part ___ of Dossier** Volume: Page:	*(For authorities use only)*
Name of finished products: Lipovir® gel Zovirax® cream Acyclovir 5%		
Name of active ingredient: Acyclovir		

Title of Study:	An open-label study to investigate the local tolerability and acceptability of Lipovir® Gel (Acyclovir 5%) compared to Zovirax® Cream (Acyclovir 5%) on patients with Recurrent Herpes Labialis
Coordinating Investigator:	Ana Leblanc, MD aleblanc@blueclinical.pt
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Publications:	None.
Timelines of Clinical Part:	24FEB2018 (first enrolment) to 09AUG2018 (last completion).
Phase of Development:	Phase IV
Objectives:	<u>Primary Objective:</u> To evaluate the local tolerability and acceptability of Lipovir® Gel compared to Zovirax® Cream in patients with Recurrent Herpes Labialis (RHL), according to participants' self-report. <u>Secondary Objectives:</u> - To assess the time to healing of Lipovir® Gel compared to Zovirax® Cream in patients with RHL. - To evaluate the safety of Lipovir® Gel compared to Zovirax® Cream in patients with RHL.

Methodology:	Multicenter, randomized, active-controlled, parallel-group study in subjects with RHL. The study consisted of two visits: Visit 1 (screening/ baseline) and Visit 2 (end-of-study). At Visit 1, informed consent was obtained, and data on demographics and concomitant medication were recorded. After confirmation of eligibility, the subject was randomly assigned to treatment either with Lipovir® Gel or Zovirax® Cream. The products were applied in a thin layer, 5 times daily (approximately every 4 hours, avoiding sleep hours) until the lesion is healed, for a maximum of 10 days (i.e., 10 days is the maximal duration of the treatment period). Each participant was requested to complete a diary. On the diary, participants self-reported information on: i) herpetic lesion stage/evolution; ii) product use; iii) symptoms overall evolution; and iv) score of specific local symptoms that may be experienced by the subject because of his/her condition and/or product application. At Visit 2, the completed patient's diary was collected, and the participant was asked to answer questions about the product's acceptability. Adverse events (AEs) were monitored throughout the study.
Number of Subjects (Planned and Analyzed):	Planned: To enroll 60 subjects. Actual: Safety population and Intention-to-treat (ITT) population = 59 subjects (30 with Lipovir® and 29 with Zovirax®).
Diagnosis and Main Selection Criteria:	Male and non-pregnant female subjects with age ≥18 years with RHL and experiencing symptoms consistent with new episode of RHL were selected according to the inclusion and exclusion criteria.
Lipovir® Gel, Dose and Mode of Administration, Batch Number:	Name: Lipovir® Gel (acyclovir 5%) Dosage form/Route of administration: gel/topical Regimen: 5 times daily (every 4 hours, avoiding sleep hours) Batch no.: 170001 (expiry date: 31MAR2019)
Zovirax® cream, Dose and Mode of Administration, Batch Number:	Name: Zovirax® Cream (acyclovir 5%) Dosage form/Route of administration: gel/topical Regimen: 5 times daily (every 4 hours, avoiding sleep hours) Batch no.: C816075 (expiry date: 31JUL2019)
Duration of Treatment:	Up to a maximum of 10 days.
Criteria for Evaluation	
Primary Endpoints:	Product's local tolerability and product acceptability self-reported by the participant on a diary.
Secondary Endpoints:	Efficacy: Time to healing of the Herpes Labialis episode, as assessed by the participant. Safety: Incidence of adverse events (AEs).
Statistical Methods:	Descriptive statistics were calculated for all variables. Data were compared between treatment groups using Mann-Whitney U-tests. Survival curves for time-to-event data were estimated using

	the Kaplan-Meier method, and treatment groups were compared by the log-rank test. AEs were tabulated and summarized according to MedDRA system organ class (SOC) and preferred term (PT).
Summary – Conclusions	
Local Tolerability and Product Acceptability Results (Primary Endpoints):	The results showed lower severity scores with Lipovir® as compared with Zovirax®, with statistically significant differences for bleeding (p=0.042), burning (p<0.001), drying (p<0.001), itching (p<0.001), redness (p=0.004), swelling (p=0.015), and tingling (p=0.016). Similar scores between treatments were obtained for pain and stinging, as no statistical differences were found. The results also showed a statistically significant difference in favor of Lipovir® versus Zovirax®, regarding product's acceptability: "Spread well on the skin" (p=0.033), "Pleasant texture" (p=0.003), "Embarrassment social anxiety" (p=0.006), "Faster herpes healing" (p=0.039), "Less itching, burning and tingling" (p=0.010), "Comfort sensation" (p<0.001), "Refreshing sensation" (p<0.001), "Skin around herpes lesion less dehydrated than usual" (p=0.048), "Repairing effect" (p=0.026), and "Good tolerance" (p=0.006). Similar results between treatments were obtained for "Non-compliance due to aesthetic reasons" and "Smaller herpes lesion", as no statistical differences were found.
Efficacy Results (Secondary Endpoints):	Both products showed to be efficacious. However, a higher proportion of patients treated with Lipovir® ended the study with healed lesions, as compared with Zovirax® (93.3% versus 79.3%).
Safety Results (Secondary Endpoints):	During the study, no AEs were reported by subjects administered Lipovir® and one AE of moderate intensity was reported by one subject administered Zovirax®. There were no serious AEs or AEs leading to discontinuation.
Conclusion:	Overall, Lipovir® showed to have improved product's local tolerability and acceptability over Zovirax® and to be at least as efficacious as the last. Lipovir® Gel or Zovirax® Cream were both well tolerated in this study.
Date of Report:	29OCT2018