

Early Treatment of Cold Sores with Topical ME-609 decreases the frequency of ulcerative lesions:

A Randomized, Double-Blind, Placebo-Controlled, Patient Initiated Clinical Trial

BACKGROUND

- About 20% to 40% of the population experience recurrent outbreaks of herpes simplex labialis (or cold sores).
- The illness severity is generally mild, but it can be uncomfortable and can have certain social and psychologic consequences.

OBJECTIVE

- To determine the efficacy of ME-609 (Xerese, Xerclear) compared to topical acyclovir and placebo on prevention of new ulcers, reduction in healing time, and reduced size of lesions.

METHODS

- **Design:** Multicenter, double-blind, randomized, placebo-controlled trial. Duration: 17 months
- **Inclusion criteria:** Healthy individuals, 18 or older, with a history of recurrent (at least 3 episodes in the past year) herpes simplex labialis (HSL). In these episodes, the patients had to have experienced prodromal symptoms in at least 50% of episodes. At least 75% of the episodes needed to have progressed through the vesicle, ulcer, and crust stages.
- **Exclusion criteria:** Having skin conditions which could interfere with the assessment of the HSL episodes (such as eczema, psoriasis, or acne); known allergy to hydrocortisone, acyclovir, or any of the constituents in the vehicle
- **Primary outcome measure:** Prevention of ulcerative HSL lesions (frequency of patients with non-ulcerative episodes)
- **Secondary outcome measures:** Episode duration, time to complete healing, maximum lesion area (length X width), cumulative ulcerative lesion area, cumulative area for "all lesions," and duration of lesion tenderness
- 1443 patients initiated treatment with one of the following 5 times daily for 5 days:
 - 601 received ME-609 (5% acyclovir + 1% hydrocortisone) cream
 - 610 received 5% acyclovir cream
 - 232 received only the ME-609 vehicle (placebo)
- All treatment groups received follow-up daily for 5 days, then every other day until complete healing of lesion.
- Power was reported to be 90%.
- Data handling method was modified intention-to-treat.

RESULTS

- 1398 patients completed the study (582, 591, and 225 in ME-609, acyclovir, and placebo, respectively)

- **Primary outcome measure:** There were significantly more patients with non-ulcerative lesions in the ME-609 group (42%) than in the acyclovir (35%, $P=0.014$) and placebo groups (26%, $P < 0.0001$)
- **Secondary outcome measures:** The duration of recurrence was not significantly shorter in the ME-609 group than the acyclovir group (0.2 day difference, $P=0.365$, $CI= -0.578$ to 0.213) and was significantly shorter than the placebo (0.8 day difference, $P=0.008$, $CI= -1.299$ to -0.200). The time for ulcerative lesions to heal was significantly reduced by 1.4 days when ME-609 was compared with placebo ($P=0.002$, $CI= -2.285$ to -0.643) and not significantly reduced when ME-609 was compared with acyclovir (0.3 day difference, $P=0.297$, $CI= -0.901$ to -0.276). The overall disease burden calculated by total lesion area in the ME-609 group (78 mm^2) was significantly smaller than with the acyclovir (105 mm^2 , $P=0.014$) and placebo (155 mm^2 , $P < 0.0001$) groups.
- **Author's conclusion:** ME-609 significantly reduced the proportion of patients who had lesions which progressed to the ulcerative stage compared to topical acyclovir alone and placebo treatment.

STRENGTHS

- Primary and secondary outcome measures were clearly defined.
- The active control was appropriate.
- Unblinding was unlikely in this study.

LIMITATIONS

- Not stated how patients were recruited to participate in the study
- Not stated if the patients had received previous therapy for recurrent herpes simplex labialis
- Confidence intervals were not reported for all the outcomes
- Very large standard deviations (when reported) for outcomes

CONCLUSIONS

- ME-609 (Xerese) appears to have limited clinical benefit given its high cost.
 - Hydrocortisone 1% is currently available as a non-prescription product; therefore, it would be more cost effective for patients to simply use it along with the currently available acyclovir 5% cream.
- Further research is needed to determine the efficacy of ME-609 compared to other anti-virals, such as oral acyclovir or valacyclovir, in conjunction with a corticosteroid.

Reference: Hull, CM. et al. Early Treatment of Cold Sores with Topical ME-609 Decreases the Frequency of Ulcerative Lesions: A Randomized, Double-Blind, Placebo-Controlled, Patient-Initiated Clinical Trial. *J Am Acad Dermatol.* 2010 Sep 17. [Epub ahead of print]

Leesa Shine, PharmD Candidate
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