Impact of LYR-210 Corticosteroid Matrices on the Incidence of Acute Exacerbations of Chronic Rhinosinusitis in Patients From the LANTERN Randomized Controlled Study

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Introduction

- Chronic rhinosinusitis (CRS) is an inflammatory disease of the sinonasal cavity with a substantial impact on quality of life.[1,2]
- Irrespective of CRS symptom severity, acute exacerbations of CRS (AECRS), defined as an aggravation of CRS symptoms, can result in lost productivity and decreased general health-related quality of life.[1,3-5]
- Approximately 25% of patients with CRS experience at least 1 episode of acute exacerbations in 12 months.[3-5]
- AECRS is often attributed to bacterial infection and routinely treated with antibiotics; however, frequent use of antibiotics can lead to drug resistance and, occasionally, allergic responses.[4,6]
- Effective treatment of CRS can decrease the frequency of AECRS episodes, as measured by reduced use of systemic rescue medication.[5]
- While the frequency of AECRS has been identified as an independent predictor of quality of life, appropriate medical management of baseline CRS can reduce the frequency of AECRS.[13]
- While topical steroids are the mainstay treatment for CRS, intranasal corticosteroids are suboptimal due to their limited ability to reach inflammation deep within the sinonasal passages, rapid clearance rates, and poor patient compliance.[1,4,7-11]
- LYR-210 is an implantable corticosteroid matrix with self-expanding properties that allow it to conform to the middle meatus.[12]
- LYR-210 is designed to continuously deliver up to 24 weeks of mometasone furoate to inflamed sinonasal tissue in surgically naive patients with CRS.[12]
- In LANTERN, a dose-ranging phase 2 study, LYR-210 (7500 µg) demonstrated safety and statistically significant efficacy improvements compared to control at week 24 in nasal blockage, facial pain/pressure, and nasal discharge (ClinicalTrials.gov Identifier: NCT04041609).[12]
- Here, we present results on the incidence of AECRS, a prespecified exploratory endpoint from the LANTERN study.

Methods and Materials

- **LANTERN**, a phase 2, multicenter, blinded, randomized, controlled, dose-ranging study, enrolled surgically naive adult patients with CRS who failed previous medical management and had not undergone functional endoscopic sinus surgery.[12]
- **Inclusion criteria** included patients aged ≥18 years with at least 2 of the 4 cardinal symptoms (4CS) of CRS: nasal blockage, facial pain/pressure, nasal discharge, and loss of smell for a minimum of 12 weeks and a baseline average 4CS composite score over the preceding 7 days of ≥7 on a 0 to 12 scale.[12]
- Patients were randomized (1:1:1) to sham procedure control or bilateral in-office administration of LYR-210 (2500 µg) or LYR-210 (7500 µg) into the middle meatus.[12] (**Figure 1**)
- Percentages of patients experiencing AECRS, defined as a sudden worsening of symptoms resulting in the treating physician reporting an escalation of treatment, were assessed at weeks 4, 8, 12, 16, 20, and 24.
- The number and proportion of patients experiencing AECRS, along with 2-sided 90% confidence intervals (CIs) vs control, were determined.
- Analyses were conducted on the intention-to-treat population, which included all patients who underwent a successful study treatment procedure and had at least 1 post-randomization efficacy assessment.[12]

Results

- Sixty-seven symptomatic adult patients with CRS who failed previous medical management were enrolled and received bilateral administration of LYR-210 (7500 µg) (n = 21) or LYR-210 (2500 µg) (n = 23) or sham-procedure control (n = 23).[12] (**Figure 1**)

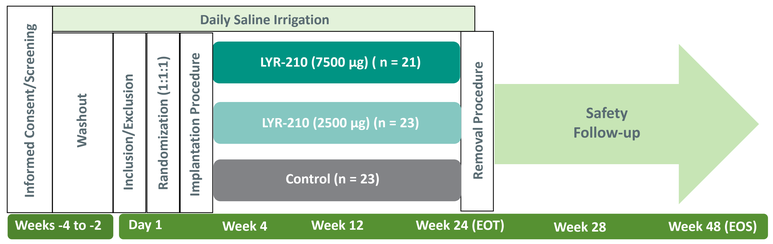

Figure 1. LANTERN Study Design.
EOT: end of treatment, EOS: end of study.

- Patients had moderate to severe disease based on the 22-item Sinonasal Outcome Test (SNOT-22) and composite 7-day average scores of the 4CS of CRS.12
- **Table 1** shows the mean number of antibiotic treatments that patients in each of the treatment arms had in the past year and the last 10 years.

Table 1. Antibiotic Treatment History.

Antibiotic Treatment	Control (n=23)	LYR-210 (2500 µg) (n = 23)	LYR-210 (7500 µg) (n = 21)	Total (n = 67)
No. of treatments in the past year, mean (SD)	1.6 (1.41)	1.4 (1.34)	0.8 (0.75)	1.2 (1.20)
No. of treatments in the past 10 years, mean (SD)	8.6 (6.50)	6.5 (6.86)	4.9 (5.79)	6.4 (6.38)

- LYR-210 demonstrated dose-dependent improvement in AECRS with LYR-210 (7500 µg)–treated patients experiencing fewer AECRS compared to LYR-210 (2500 µg)–treated patients and the control group. (**Figure 2**)
- The first incidence of AECRS in the control group occurred by week 4, compared to week 20 for the LYR-210 (7500 µg) group. (**Figure 2**)
- Fewer AECRS occurred in the LYR-210 (7500 µg) group compared to the control group during the 24-week treatment period. (**Figure 2**).
  - 30.4% of patients in the control group experienced an AECRS by week 24 compared to 9.5% of LYR-210 (7500 µg)–treated patients [90% CI: -0.4, -0.019] and 21.7% of LYR-210 (2500 µg)–treated patients [90% CI: -0.3, 0.13].

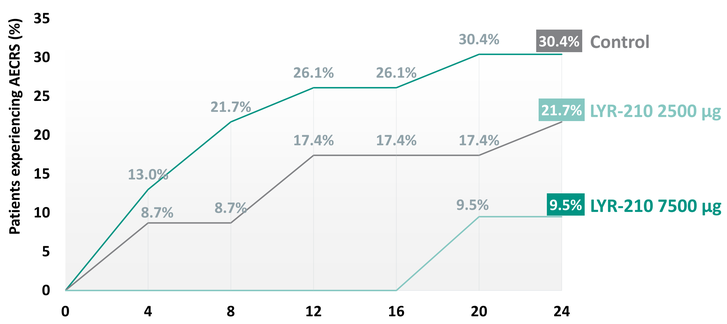

Figure 2. Percentage of Patients Experiencing AECRS.
Data are presented as cumulative n (%).

Results

- Compared to the control group, patients treated with LYR-210 had a dose-dependent reduction in AECRS. (**Figure 3**)

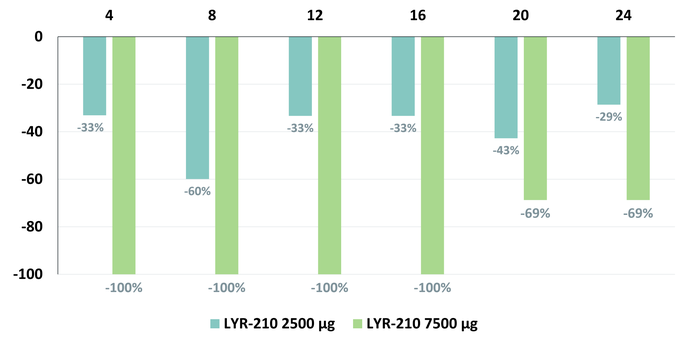

Figure 3. Percentage Reduction in AECRS in Patients Treated with LYR-210 Compared to the Control Group.
AECRS: acute exacerbation of chronic rhinosinusitis.

Conclusions

- In this analysis of the LANTERN study, there was a reduction in the occurrence of AECRS in the LYR-210 (7500 µg) group compared to the control group during the 24-week treatment period.
- The incidence of AECRS is being studied further in the pivotal phase 3 trials of LYR-210 (ENLIGHTEN I (ClinicalTrials.gov Identifier: NCT05219968) and ENLIGHTEN II (ClinicalTrials.gov Identifier: NCT05295459)). [14,15]
- LYR-210 may be a promising new long-acting treatment that addresses a significant unmet need for patients with CRS.[12]

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