A novel continuous topical steroid implant (LYR-210) reduces sinonasal type 2 inflammation and rhinologic symptoms in chronic rhinosinusitis

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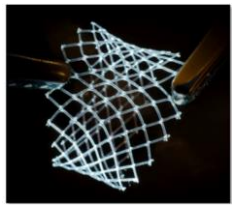
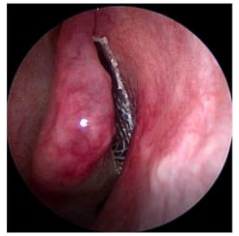
BACKGROUND:

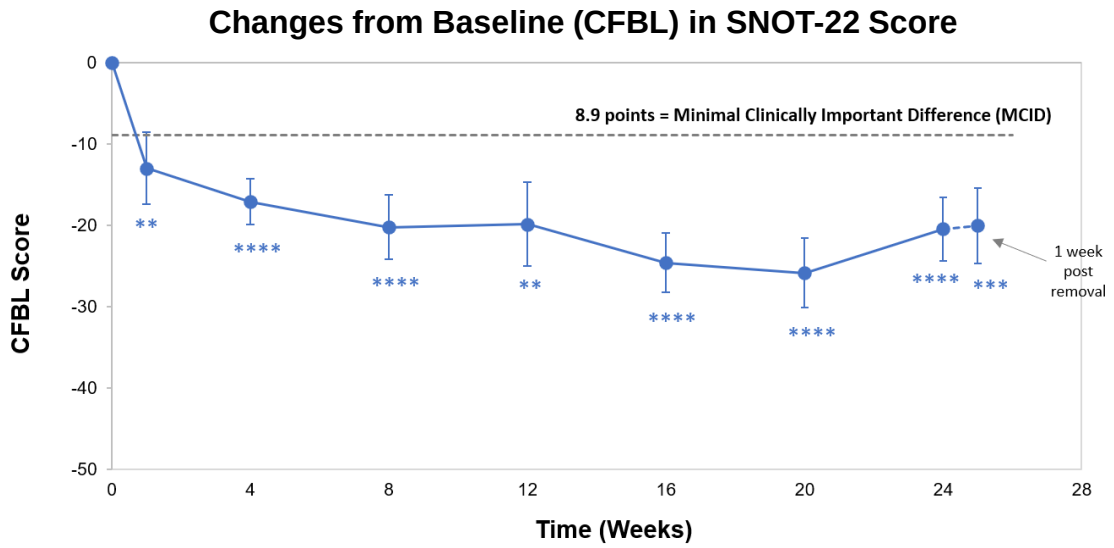
LYR-210 is a nasal drug delivery implant that gradually releases mometasone furoate to local tissues over 24 weeks. Patients with chronic rhinosinusitis (CRS) who received LYR-210 placed in the middle meatus showed promising clinical efficacy in a Phase I clinical study.

LYR-210



LYR-210 in the middle meatus





Douglas et al., Int Forum Allergy Rhinol. 2019

**P<0.01, ***P<0.001, ****P<0.0001 to baseline

OBJECTIVE:

This study evaluated how treatment with LYR-210 impacts type (T) 1, T2, and T3 inflammatory responses in CRS patients with and without polyps.

METHOD:

- **Nasal swabs and the 22-item Sino-nasal Outcome Test (SNOT-22) questionnaires were collected at baseline and at 4 and 12 weeks after LYR-210 placement in 20 CRS patients (CRSwNP (n=8), CRSsNP (n=12)) enrolled in a multicenter, open-label Phase I clinical trial.**
- **Protein markers for T1, T2 and T3 inflammation in nasal swabs were determined by Luminex.**
- **RNA markers were determined by quantitative RT-PCR in RNA samples that met quality and quantity criteria.**

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Sinonasal type 2 markers are suppressed by LYR-210

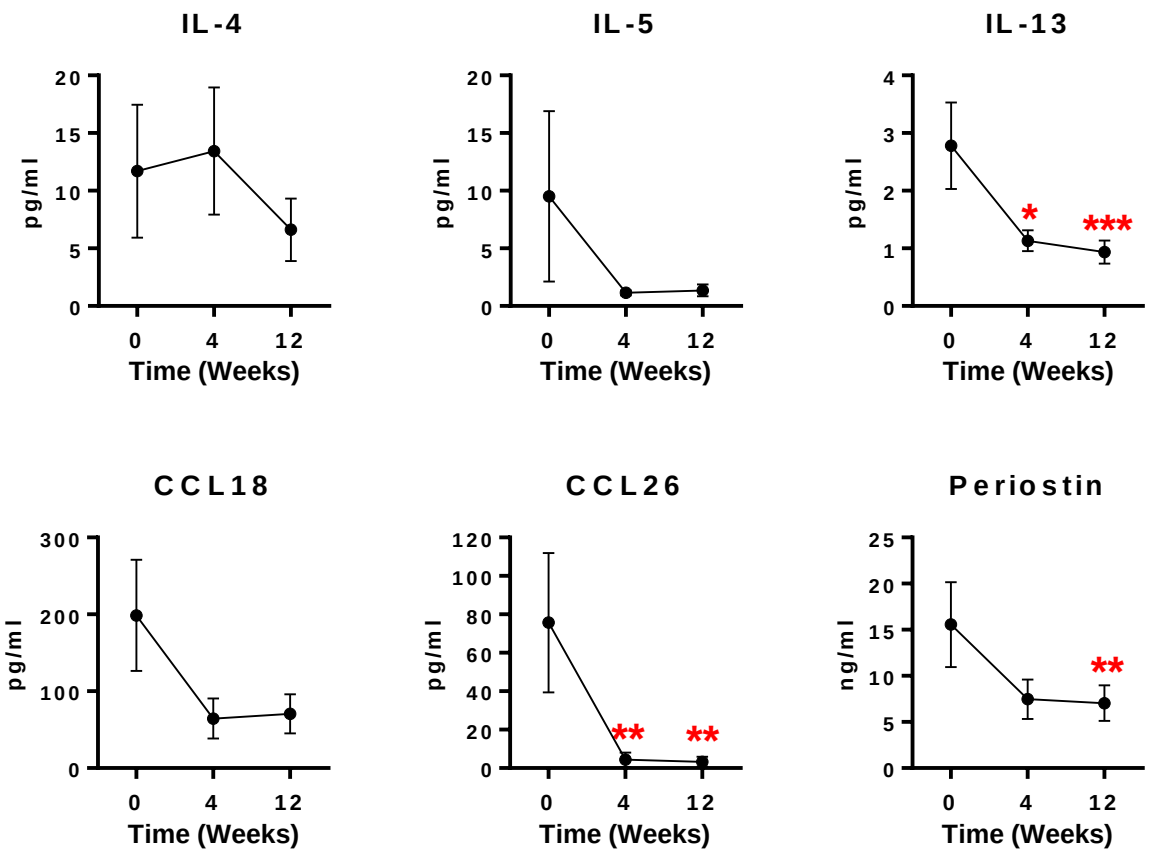

Figure 1. Sinonasal proteins of type 2 marker, IL-13, CCL26 and Periostin, were suppressed by LYR-210. Type 1 marker, IFN-γ, and type 3 markers, IL-17A and IL-23, were not affected by LYR-210 (data not shown).
Protein concentrations in nasal swabs at Baseline (week 0) (n=20), 4 weeks (n=18) and 12 weeks (n=20) were measured by Luminex kits. Results are shown as mean ± SEM. * p<0.05, ** p<0.01 and *** p<0.001 by the Wilcoxon matched-pairs signed rank test compared to baseline.

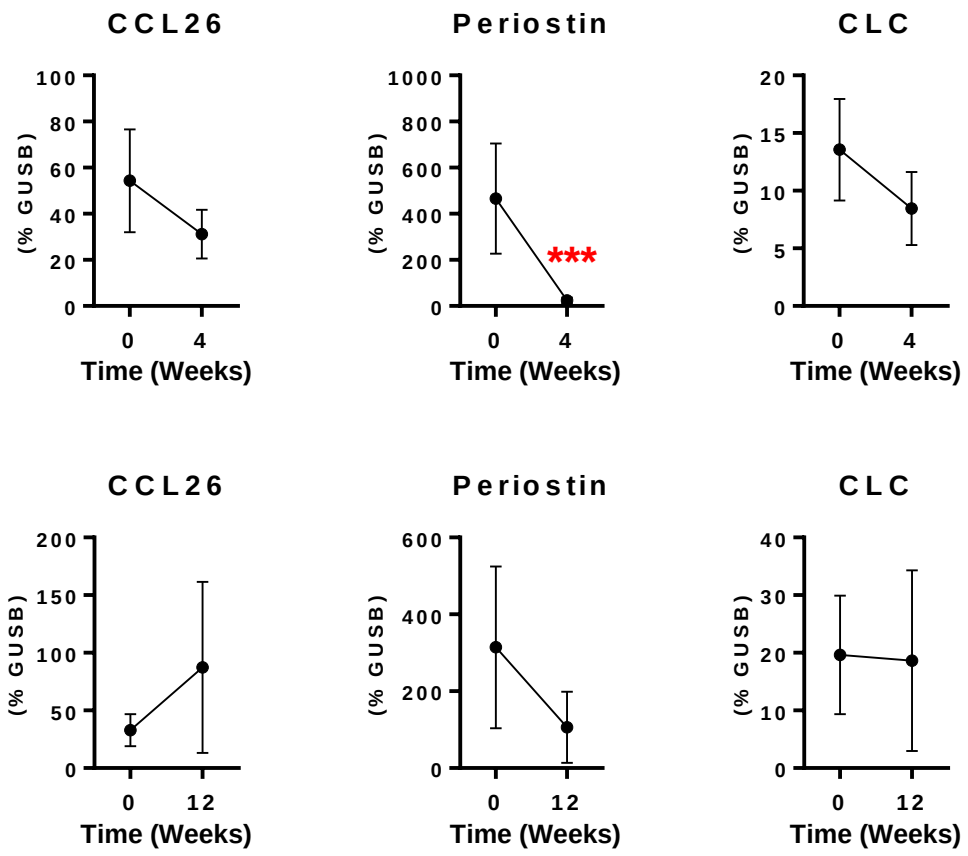

Figure 2. Sinonasal messenger RNAs of type 2 marker, CCL26, Periostin, and CLC, were suppressed by LYR-210. Type 1 markers, CXCL9 and CXCL10, were not affected by LYR-210 (data not shown).
Expression of mRNAs in nasal swabs at Baseline (week 0) (n=20), 4 weeks (n=11), and 12 weeks (n=9) were assessed by quantitative RT-PCR. Results show only paired samples at 4 weeks and 12 weeks that met RNA quality test. Gene expression levels are shown as % expression of a housekeeping gene, β-glucuronidase (GUSB). Results are shown as mean ± SEM. *** p<0.001 by the Wilcoxon matched-pairs signed rank test.

Potential correlation between baseline sinonasal type 2 markers and rhinologic symptom improvement following treatment by LYR-210

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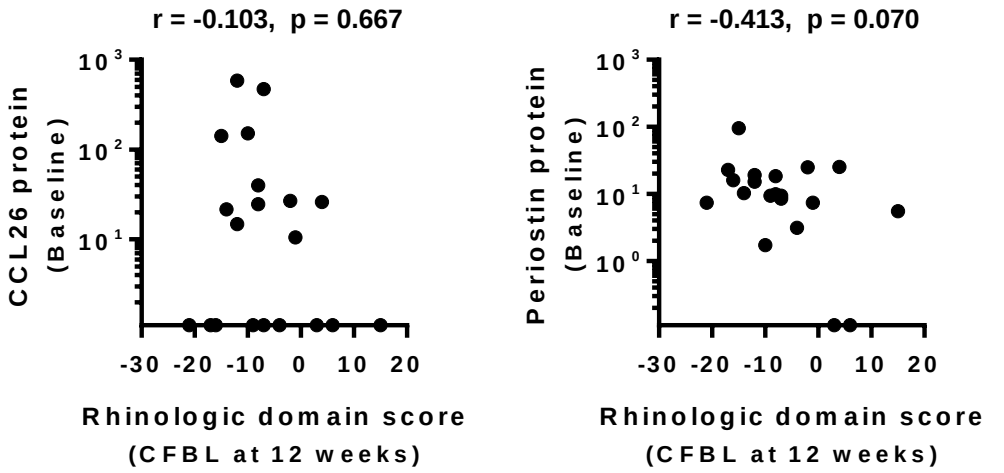
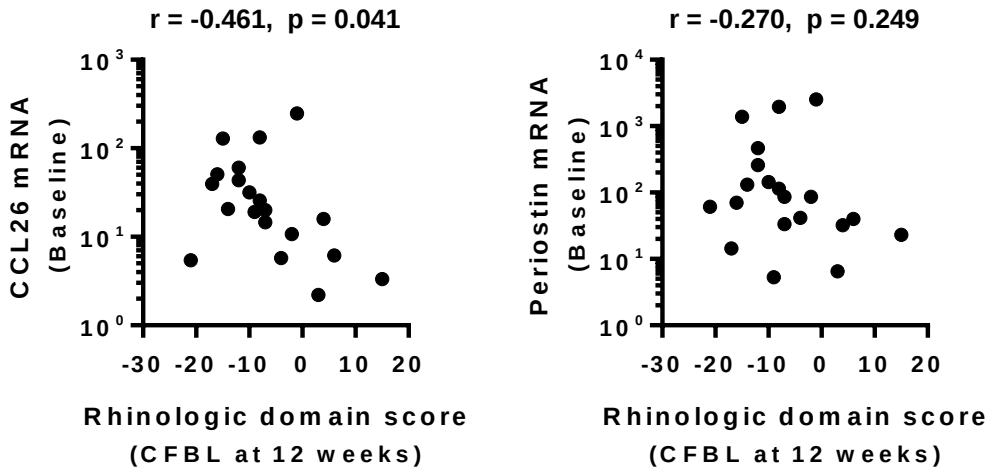
A. Protein



B. mRNA



CFBL: changes from baseline

Figure 3. Baseline expression of sinonasal protein (A) and mRNA (B) for type 2 markers might correlate with the reduction of rhinologic domain score following LYR-210 treatment. The concentrations of proteins in baseline nasal swabs were performed by Luminex kit (n=20) (A). The expressions of mRNAs in baseline nasal swabs were performed by quantitative RT-PCR (n=20) (B). Only makers which showed correlation with baseline symptom severity were reported. Gene expression levels are shown as % expression of a housekeeping gene, GUSB. The Spearman rank correlation was assessed by baseline expression of protein or mRNA and changes from baseline (CFBL) at 12 weeks in rhinologic domain scores from SNOT-22 (n=20).

SUMMARY AND CONCLUSIONS:

- **LYR-210 reduced sinonasal type 2 markers IL-13, CCL26, and Periostin in surgically naïve CRS patients with and without polyps.**
- **Sinonasal type 2 markers, CCL26 and Perostin, trended with rhinologic symptom improvement and may be a potential objective measure of response.**
- **Symptom improvement by LYR-210 may in part result from a reduction of sinonasal type 2 inflammation.**