LYRA THERAPEUTICS

BEACON Study

Topline Results

LYR-220-2021-001 A Phase II, Patient-blinded, Two-part, Randomized, Parallel-group Trial to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of LYR-220 in Chronic Rhinosinusitis (CRS) Patients Who Have Had a Prior Ethmoidectomy

https://clinicaltrials.gov/study/NCT05035654

September 12, 2023

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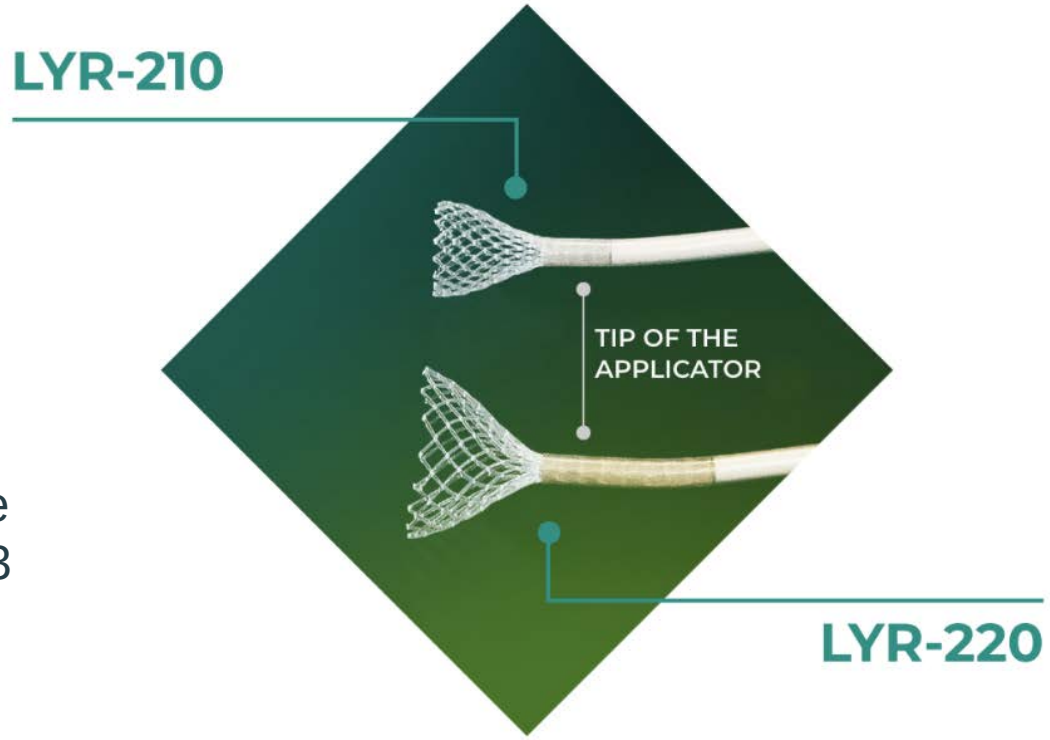
LYR-210 and LYR-220 are Designed to Address the Full Spectrum of CRS Patients

Topline results now available for the LYR-220 Phase 2 BEACON study

Candidate	CRS Patient Type	Phase 2	Phase 3
LYR-210 Long-acting Mometasone Furoate	Chronic Rhinosinusitis **Patients with Surgically-Naïve Anatomy** **ENLIGHTEN Phase 3 Program**		
LYR-220 Long-acting Mometasone Furoate	Chronic Rhinosinusitis **Patients with Post-Surgical Anatomy** **BEACON Phase 2 Trial**		

LYR-220 for CRS Patients who have Undergone Prior Sinus Surgery but have Persistent Symptoms

- LYR-220 is an enlarged version of LYR-210 to accommodate **post-surgical anatomy**
- LYR-220 is designed to provide **24 weeks** of mometasone furoate therapy directly to the site of disease
- LYR-220 dosage of mometasone furoate (7500 mcg) is the **same dose** being studied in the ongoing LYR-210 Phase 3 (ENLIGHTEN)



LYR-220 is being Developed to Address a Significant Proportion of the CRS Population

Current Treatments:

- **Medical Management**
  - Saline rinses, topical nasal steroids, oral steroids
- **Surgery**
  - ~400K sinus surgeries annually[1]

CRS in the United States Annually

~8M	CRS patients **treated**[2]
~4M	CRS patients **failing medical** management[3]
~1.4M	CRS patients **currently presenting to an ENT**[4]

40% of patients that present to an ENT have had a prior sinus surgery[5]

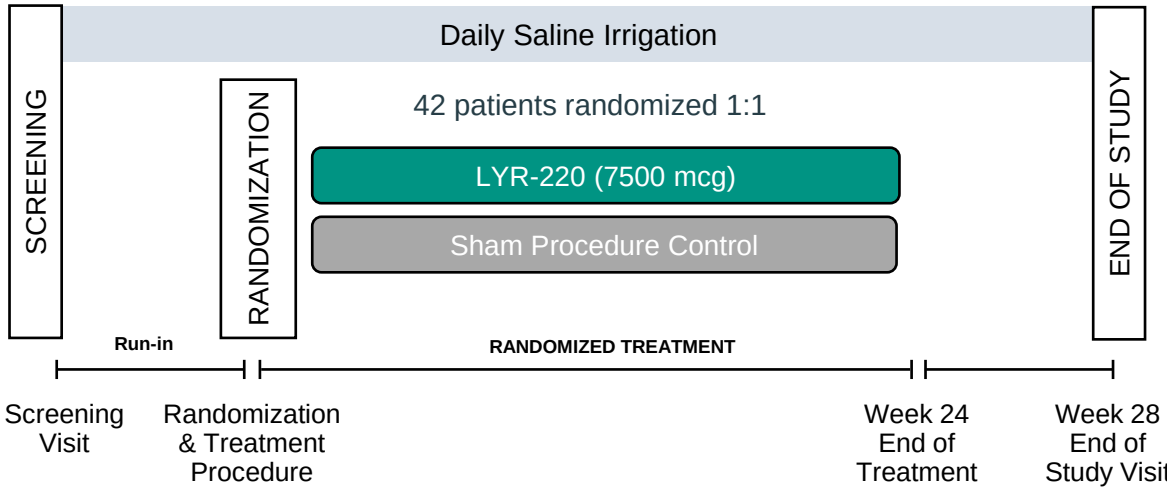
1) Biomedical Insights CRS Population Analysis, 1/2020 2)Jang et al. Otolaryngol Head Neck Surg, 2018; 3) Baguley et al. Int Forum Allergy Rhinol, 2014;4(7):525-32; 4) OM1 Real World Data Cloud (OM1, Inc, Boston, MA) 2015 – 4/2019. Analysis 9/2019 5) Biocom Consulting ENT Quantitative Market Research, 6/2019

BEACON: Phase 2 Clinical Study of LYR-220

- **CRS patients** who have had a prior bilateral ethmoidectomy
- Randomized, blinded, sham-controlled proof of concept study to assess safety and efficacy of LYR-220*
- **Safety endpoint:**
  - Serious adverse events
- **Key efficacy endpoints:**
  - 3 cardinal symptoms (3CS)** scores
  - SNOT-22 scores

*Preceded by feasibility phase to choose matrix design
**3 cardinal symptoms are defined as nasal blockage / obstruction, facial pain / pressure, and nasal discharge

BEACON Study Design

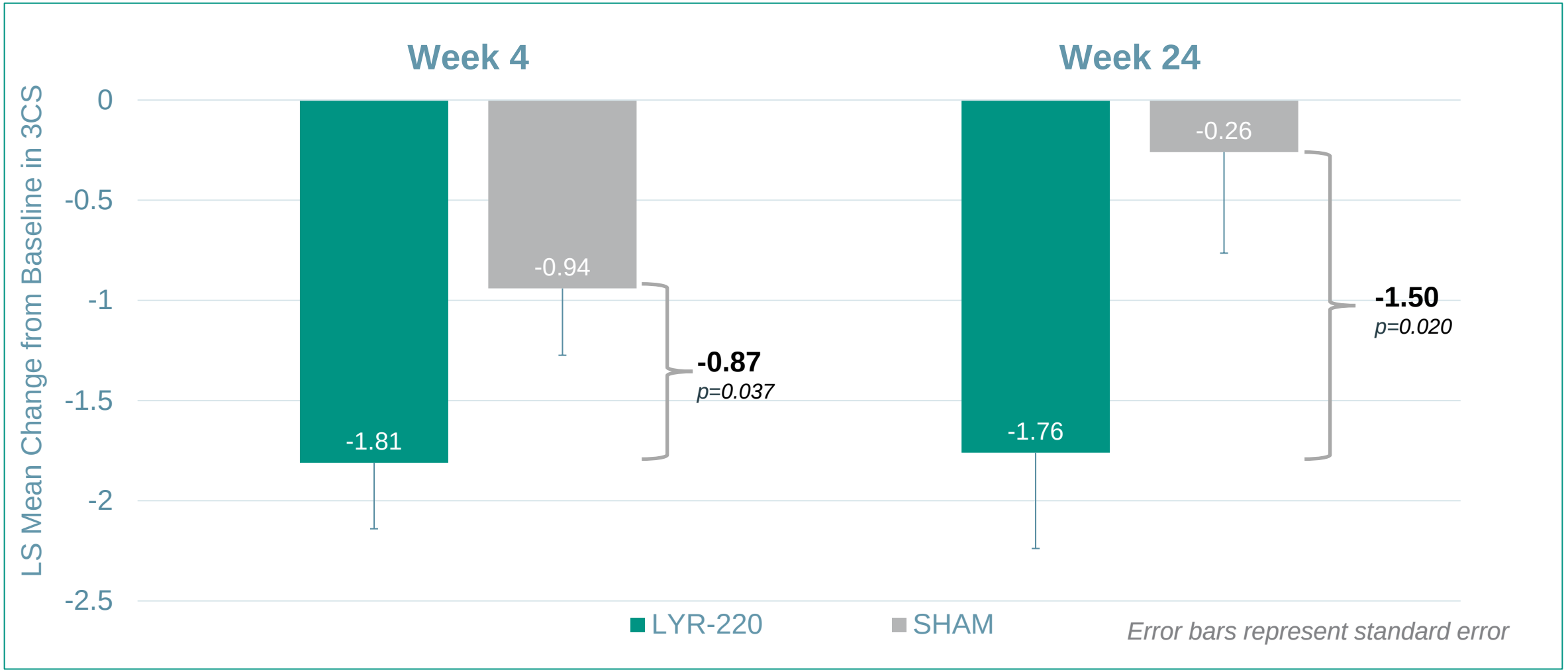


Note: Primary outcome measure was product-related serious adverse events

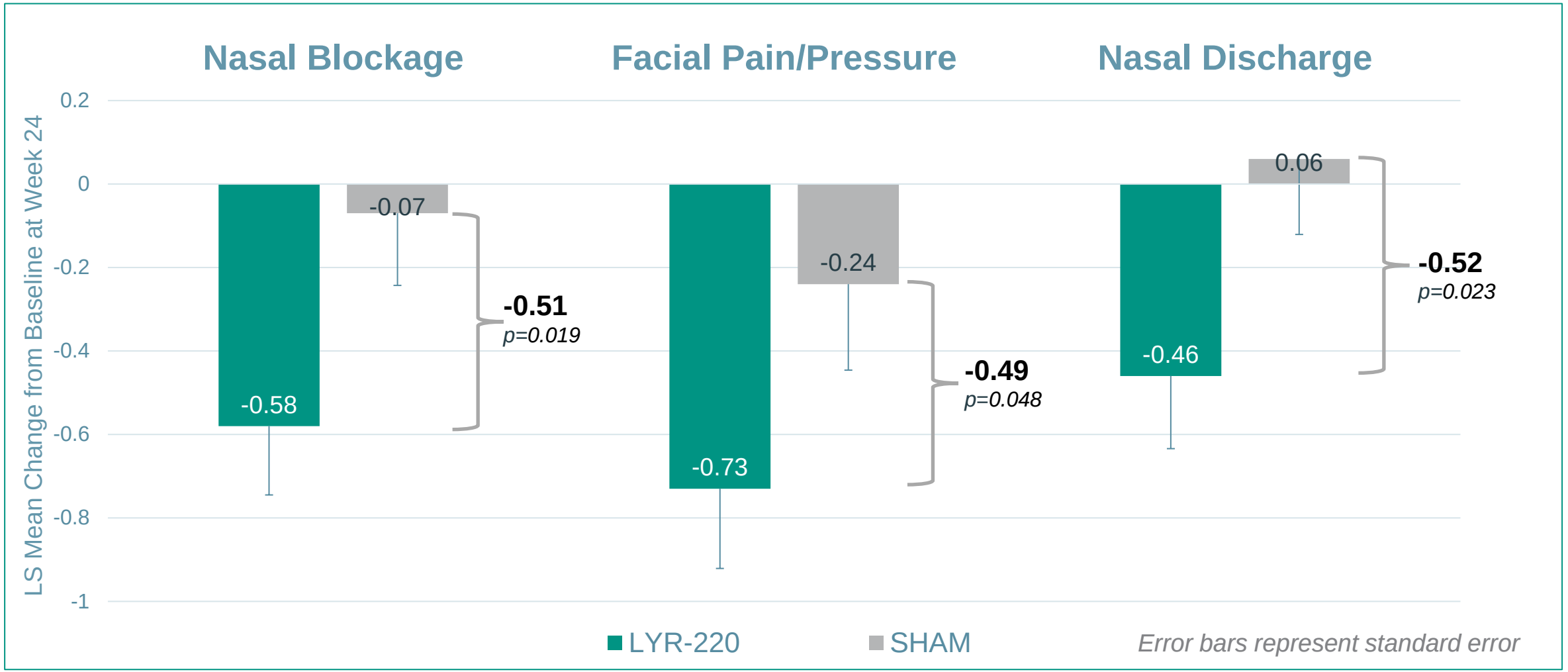
BEACON: Patient Demographics and Baseline Characteristics

	LYR-220 (n=21)	Sham (n=21)	Total (n=42)
Age in years (*mean, SD)*	48 (12.51)	55 (11.29)	**51 (12.35)**
Sex *(n, %)*			
Male	7 (33.3)	10 (47.6)	**17 (40.5)**
Female	14 (66.7)	11 (52.4)	**25 (59.5)**
Race *(n, %)*			
White	20 (95.2)	18 (85.7)	**38 (90.5)**
Black or African American	1 (4.8)	2 (9.5)	**3 (7.1)**
Baseline SNOT-22 Total Score (*mean, SD)*	56.1 (17.16)	50.0 (16.65)	**53.1 (16.9)**
Baseline 3CS Score (*mean, SD)*	6.4 (1.47)	6.8 (1.65)	**6.6 (1.56)**

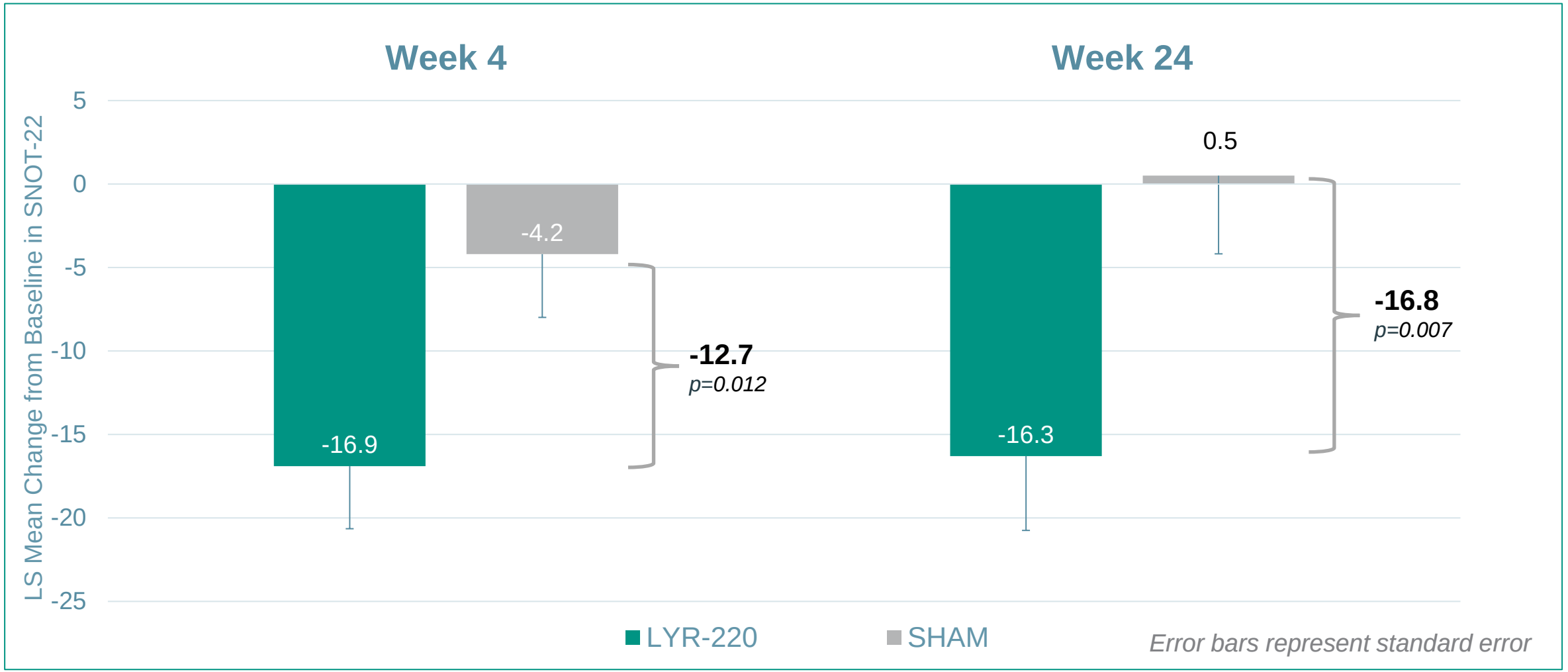
BEACON Efficacy Results:
Statistically Significant Improvement in 3CS Composite Score



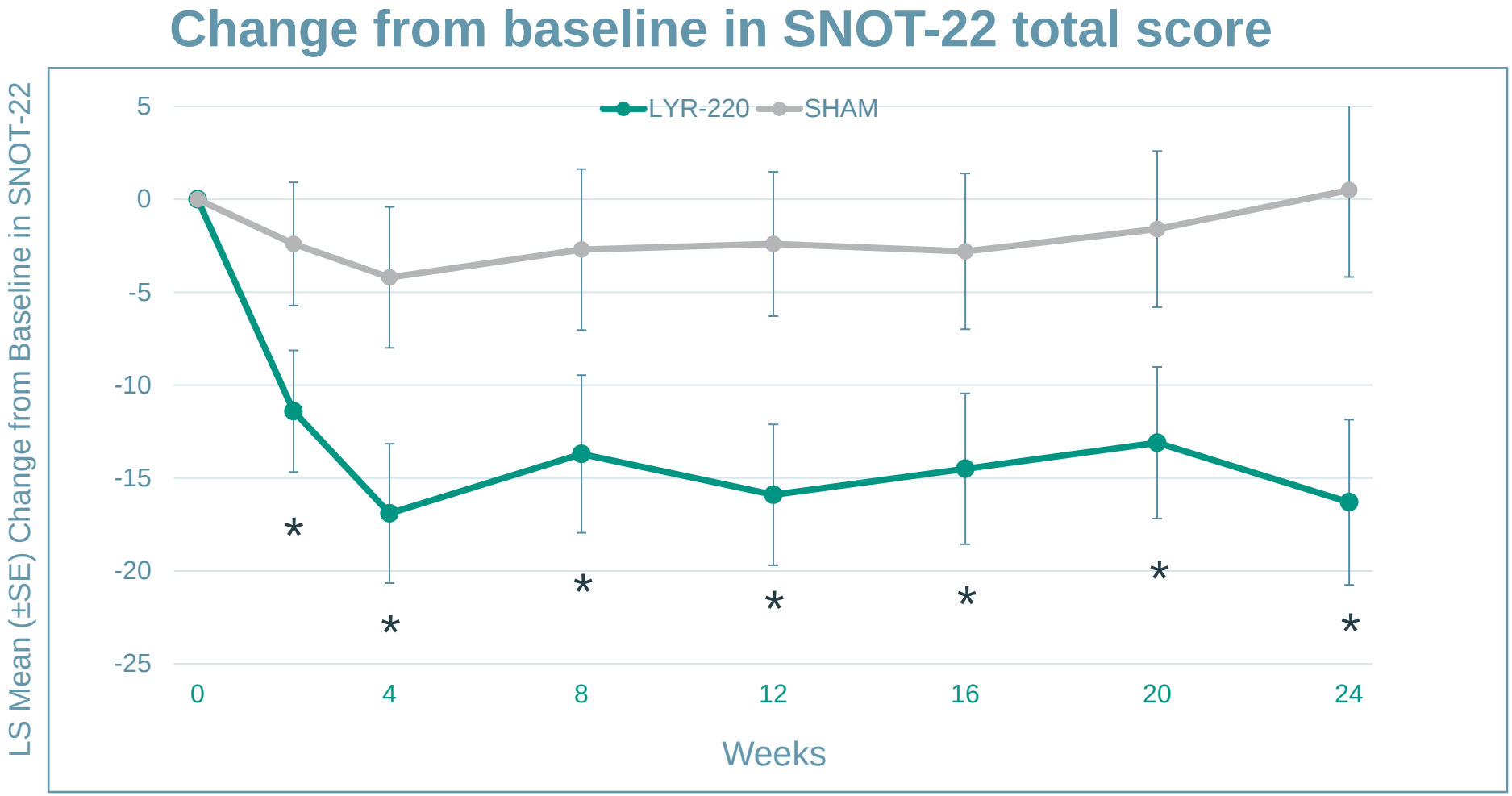
BEACON Efficacy Results:
Statistically Significant Improvements in Individual CS at Week 24



BEACON Efficacy Results:
Statistically Significant Improvement in SNOT-22 Score



BEACON Efficacy Results:
Early and Sustained Improvement in SNOT-22 Score



* p <0.05

BEACON Study Summary

No SAEs and statistically significant, clinically relevant improvements in key efficacy endpoints

- No serious adverse events observed. Most commonly observed adverse events included sinusitis, nasopharyngitis, bronchitis, and COVID-19
- Statistically significant improvement in a composite of the 3 cardinal symptoms of CRS (nasal obstruction, nasal discharge, facial pain/pressure) at week 24 (-1.50; p=0.02)
  - Statistically significant improvement for each individual cardinal symptom at week 24
- Statistically significant improvements in Sino-Nasal Outcome Test (SNOT-22) score compared to sham control at week 24 (-16.8; p=0.007)
- Statistically significant improvement in a composite of the 3 cardinal symptoms of CRS (nasal obstruction, nasal discharge, facial pain/pressure) as early as week 4 (-0.87; p=0.037)
- Statistically significant improvements in SNOT-22 were observed as early as week 2 (-9.0; p=0.031)
- Improvements in SNOT-22 were sustained throughout the study and clinically meaningful with almost twice the minimal clinically important difference observed at week 24 compared to sham (-16.8 points)

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