EXHANCE-3: A Phase III, 3-Month Study of Safety and Efficacy of an Exhalation Delivery System with Fluticasone (EDS-FLU) in Patients With Chronic Rhinosinusitis With (CRSwNP) and Without Nasal Polyps (CRSsNP)

BACKGROUND

- Chronic rhinosinusitis (CRS) with (CRSsNP) and without (CRSsNP) nasal polyps is a common and burdensome disease. The overall annual economic burden of CRS in the United States was estimated at $7.0 billion (direct and indirect costs) in 2014.1,2
- Defining symptoms include nasal congestion/disturbance, rhinorrhea (postnasal drip and runny nose), facial pain/pressure, and hypersensitivity to cold, wind, and air pollutants. The overall effect is an impairment of quality of life (QoL), which has been measured to be similar in magnitude to other serious diseases, such as cancer, CHF, and Parkinson’s disease.3

CRS is characterized by widespread nasal mucosal inflammation involving key anatomical structures, including the ostiomeatal complex (OMC), where the sinuses drain and ventilate, and where nasal polyps most commonly originate.3

- Intranasal corticosteroids (ICS) are recommended as standard of care in multiple treatment guidelines; however, conventional ICS sprays are relatively inefficient and ineffective in delivering topical acting drug to key disease sites beyond the nasal valve area (including the OMC), potentially reducing treatment benefit, and are associated with local treatment satisfaction.4

- EDS-FLU uses BreathPower® "B-Directional" delivery to optimize deposition of Fluticasone propionate to the entire nasal cavity, including key high and deep anatomical regions, such as the OMC (Figure 1).

- EDS has been shown to deposit drug deeper and more broadly in the nasal cavity (particularly superiorly) posteriorly, e.g., the OMC, with less drug delivery to the paranasal sinuses and sphenoid, compared with conventional nasal sprays.5,6 EDS-FLU aims to meaningfully improve outcomes by using an EDS to substantially modify delivery of local antiinflammatory drug, including to the OMC.

METHODS

- 12-week, open-label, multireiter, repeat endoscopy study.

- Eligible patients were ≥18 years of age, with CRSsNP or CRSsNP as determined by nasal endoscopy and ≥1 history of diagnosis of CRS within the past 12 weeks, and were currently experiencing ≥2 defining symptoms of CRS, of which had to be nasal congestion obstruction or rhinorrhea.

- Mean SNOT-22 scores improved dramatically, and similarly, in CRSsNP (23.7) and CRSsNP (24.4) patients by week 12. Importantly, this magnitude of improvement for extracranial clinical significance of a 0.9-point improvement and is comparable to that of previous extracranial studies in CRS patients.

- A similar relative magnitude of improvement was also observed for the SNOT-22 subscales, regardless of the presence of nasal polyps at baseline.

RESULTS

- Of 968 patients screened, and 706 patients were enrolled at 38 centers in the United States. Seven hundred five patients received study drug, of which 601 (85.2%) completed the study.

- Baseline characteristics are shown in Table 1. Patients with nasal polyps at study entry experienced an extensive reduction in polyp grade, and nearly 50% of patients experienced polyp elimination in at least 1 nostril (Figure 2).

- Among patients with baseline Lund-Kennedy edema scores 0, EDS-FLU treatment was associated with complete resolution of edema in 33.3% of CRSsNP and 54.8% of CRSsNP patients at week 12 (Figure 2).

- For CRSsNP, the percentage observed to have polyp elimination in at least 1 nostril (Grade 0; no polyps seen) by nasal endoscopy increased over the course of the study (Figure 5a). Among those completing 12 weeks of treatment, 44% of CRSsNP patients reported complete resolution of nasal polyps (at least 0.5 cm in diameter) at week 12 (Figure 5b).

- With nasal polyps at study entry achieved a large reduction in polyp grade, with a mean decrease in bilateral nasal polyp score of 0.8 and 1.3 at week 4 and week 12, respectively (Figure 5c). 63% of CRSsNP patients had >1 point improvement in polyp grade.

- Using standardized assessments of surgical eligibility, at end-of-study, the number of CRSsNP patients eligible for surgery decreased from 42.2% to 18.2%.

- Approximately 90% of patients reported that the EDS-FLU delivery device was somewhat or very easy to use. At week 4, the majority of patients reported much less/less drop out of the nose (67%) and drop down the throat (74%) with EDS-FLU compared to that of their most recent conventional INBID.

REFERENCES


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RESULTS

• EDS-FLU was well tolerated, with a safety profile similar to that reported with traditional intranasal steroids studied in patients with CRS for a similar duration.

• The most common AEs (5%) included infections and infestations (10.5%), epistaxis (all types 4.5%), tinnitus (nasal 2.3%), and headache (nasal 2.3%).

• Patients with nasal polyps at study entry experienced an extensive reduction in polyp grade, and nearly 50% of patients experienced polyp elimination in at least 1 nostril (Figure 2).

• Results of EDS-FLU reported improvement, and very few reporting worsening—a result reinforced by the large improvement measured by SNOT-22.

• The AEs reported were generally local in nature, tended to be mild in severity, and were largely transient. AEs did not increase in frequency or severity with increasing duration of exposure to study drug. One of the most common AEs was epistaxis.

• Improvement in symptoms, QoL, and objective signs of disease, including polyp grade, was likely due to the EDS-FLU delivery system's delivery superiorly and posteriorly throughout the nasal cavity, including the OMC, where polyps originate and stabilize.

• In patients with moderate to severe symptoms of CRS (with and without polyps) and frequent past use of conventional INBID sprays, EDS-FLU was well tolerated and produced significant improvements in symptoms and objective measures of disease, indicating the important role of superior/posterior drug delivery via EDS.