Post-authorisation safety study of the SQ tree sublingual immunotherapy tablet in real-life practice across Europe

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Introduction

- In northern and central Europe, birch pollen and other birch homologous species are one of the most common causes of allergic rhinitis and/or conjunctivitis (ARC).[1,2,3]
- The SQ tree sublingual immunotherapy (SLIT)-tablet is an allergy immunotherapy (AIT) authorised for treatment of moderate-to-severe ARC induced by tree pollen of the birch homologous group in adults.[4]
- In two phase III clinical trials, treatment-related adverse events most frequently reported were mild-to-moderate oral pruritus and throat irritation as local reactions related to the sublingual administration.[5,6]

Objectives

- The aim of this study was to conduct a post-authorisation safety study across Europe to investigate the real-world safety and tolerability of the SQ tree SLIT-tablet during the first 4-6 months of routine treatment.

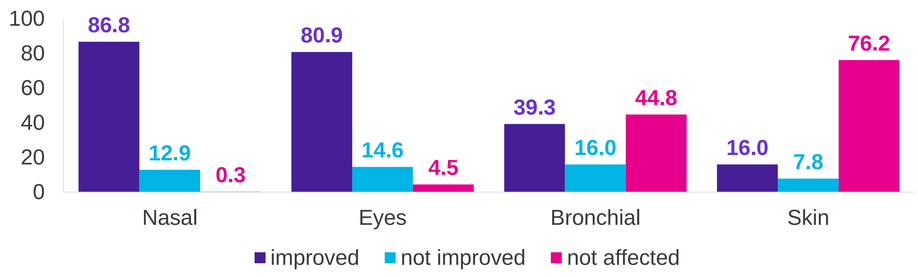
Methods

- A prospective, non-interventional, multicenter, open-label, multinational post-authorisation safety study was conducted in outpatient centers across 6 European countries (Denmark, Germany, Finland, The Netherlands, Norway, and Sweden) between March 2020 and June 2022.
- Eligible patients were adults (aged 18-65 years) with moderate-to-severe birch pollen-induced ARC and diagnosed by clinical history and a positive test for sensitisation to tree pollen allergens (skin prick test and/or specific immunoglobulin E (IgE)) and without contraindications to treatment with the SQ tree SLIT-tablet according to the Summary of Product Characteristics (SmPC).[4]
- Data were collected in an electronic case report form (eCRF) at treatment initiation and during up to 3 follow-up visits in an interval of 1-3 months on medical history, allergy symptoms, concomitant medication, and adverse events (AEs)/adverse drug reactions (ADRs).
- AEs/ADRs were categorised by seriousness, severity (mild, moderate, severe), and causality (possibly related, unlikely). ADRs were further classified into local, non-local, and systemic (potential anaphylactic reactions).
- Patients were stratified by clinical manifestations: ARC, ARC + allergic asthma (AA), ARC + pollen food syndrome (PFS), ARC+AA+PFS, ARC + atopic dermatitis (AD) (±AA±PFS).
- AEs and ADRs were coded according to the Medical Dictionary for Regulatory Activities (MedDRA, version 22.0 or higher) as System Organ Classes (SOCs) and Preferred Terms (PTs).
- Data were summarised by descriptive statistics. No formal sample size calculation and statistical tests were performed.
- Frequencies of ADRs were compared with those listed in the SmPC.
- The study was registered in the European Union Electronic Register of Post-authorisation Studies (EUPAS31470), approved by national authorities according to country-specific laws, and reviewed by responsible national ethics committees. The patients' written informed consent was obtained.

Results

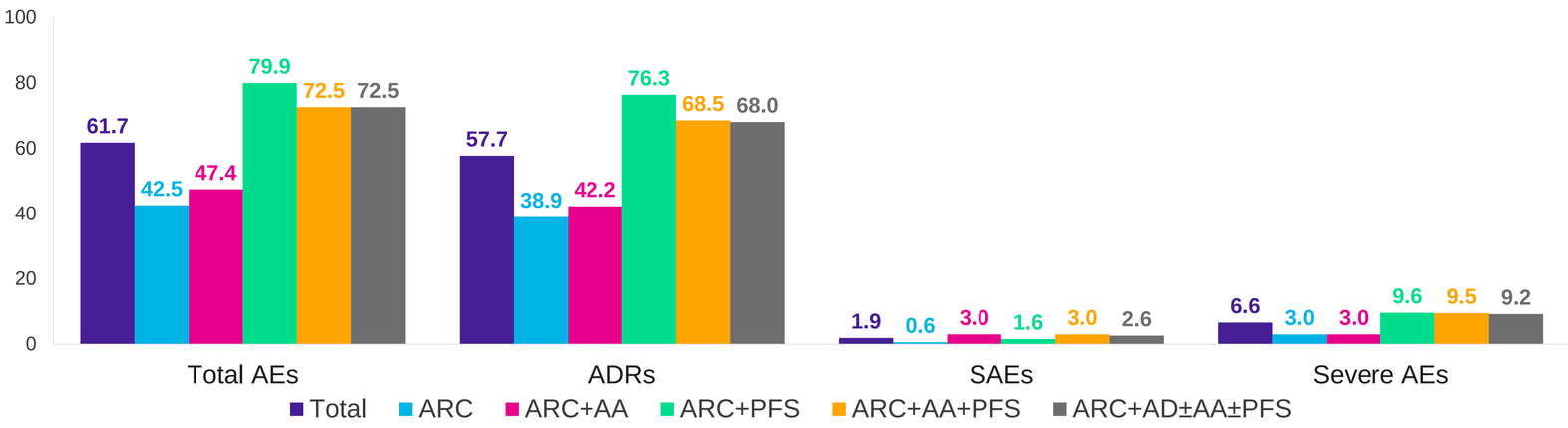
- Data from 1,069 adult patients with moderate-to-severe ARC induced by tree pollen of the birch homologous group from 112 sites in 6 countries (The Netherlands: 46 sites, Germany: 35, Denmark: 11, Norway: 11, Sweden: 7, Finland: 2) were analysed (treatment initiation at visit 1). 1,021 patients completed follow-up visit 2, 948 patients visit 3, and 816 patients visit 4.
- 10 to 20 patients per site were included (Germany: 409, The Netherlands: 312, Norway: 144, Sweden: 113, Denmark: 78, Finland: 13). Mean age was 37.5 years (median: 36) and 53.7% of patients were female.
- Mean duration of treatment with SQ tree SLIT-tablet during the entire study period was 5.4 months.
- Patients were stratified into 5 subgroups according to clinical manifestations: ARC only in 31.1% of patients, ARC+PFS in 23.3%, ARC+AA+PFS in 18.7%, ARC+AD (±AA±PFS) in 14.3%, and ARC+AA in 12.6%.
- At baseline (last season), moderate to severe nasal symptoms were reported in 95.5% of patients, eye symptoms in 77.9%, bronchial symptoms in 25.6%, and skin symptoms in 8.8%.

Figure 1. Change in symptoms at last visit vs. baseline



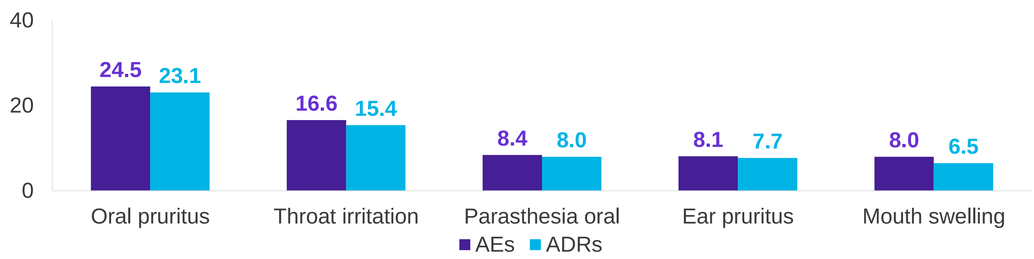
- In most patients, allergy symptoms improved (no symptoms/ symptoms decreased) at the individual last visit compared to baseline (**Figure 1**).
- Overall, AEs were reported in 46.7% of patients (ADRs: 45.9%) at first administration, and in 61.7% (57.7%) during the entire course of treatment.
- Severity of all ADRs was mild in 50.2% of patients, moderate in 19.8%, and severe in 4.7%; 0.7% of ADRs were classified as serious (dyspnoea in 3 cases, angioedema, worsening of asthma, constipation, and moderate oral mucosal swelling in one case each).
- Patients with ARC+PFS were most frequently affected by AEs/ADRs followed by patients with ARC+AA+PFS, and patients with ARC+AD±AA±PFS (**Figure 2**).

Figure 2. AEs stratified by clinical manifestations



- Most frequent AEs/ADRs in the entire course of treatment were MedDRA PTs *oral pruritus*, *throat irritation*, and *paresthesia oral* (**Figure 3**).

Figure 3. Most frequent PTs of AEs/ADRs



- Tolerability was rated as ‘very good’ or ‘good’ by the physicians in 85.6% of patients.
- At the end of the study, treatment was continued by 83.8% of patients.

Conclusions

- The large sample size of >1,000 patients in this NIS PASS provides a representative picture of the safety and tolerability during initiation and early treatment with the SQ tree SLIT-tablet.
- The SQ tree SLIT-tablet was found to be safe and well tolerated in real-life with no new safety risks identified.

References

1. Lorenz AR, Lüttkopf D, May S, Scheurer S, Vieths S. The principle of homologous groups in regulatory affairs of allergen products--a proposal. Int Arch Allergy Immunol. 2009;148(1):1-17. https://doi.org/10.1159/000151243.
2. Kleine-Tebbe J, Zuberbier T, Werfel T, et al. Is allergy immunotherapy with birch sufficient to treat patients allergic to pollen of tree species of the birch homologous group? Allergy. 2020;75(6):1327-1336. https://doi.org/10.1111/all.14130.
3. Gadermaier E, Flicker S, Aberer W, et al. Analysis of the antibody responses induced by subcutaneous injection immunotherapy with birch and Fagales pollen extracts adsorbed onto aluminum hydroxide. Int Arch Allergy Immunol. 2010;151(1):17-27. https://doi.org/10.1159/000232567.
4. ITULAZAX® Summary of Product Characteristics. ALK, 2019.
5. Biedermann T, Couroux P, Greve TM, Mäkelä M. Safety of the standardized quality tree sublingual immunotherapy tablet: pooled safety analysis of clinical trials. Allergy. 2021;76(12):3733-3742.https://doi.org/10.1111/all.14882.
6. Gappa M, Gagnon R, Horak F, Cichocka-Jarosz E, Dalgaard T, Hargreaves K, Mikler J, Emeryk A, Hansen KS, Pfaar O. The SQ tree sublingual immunotherapy tablet is effective and well tolerated in children-A pivotal phase III trial. Allergy. 2024 Nov 4. doi: 10.1111/all.16363.
7. Pfaar O, Wolf H, Reiber R, Knulst A, Sidenius K, Mäkelä MJ, Steinsvåg S, Janson C, van der Zwan L, Uss E, Arvidsson P, Borchert K, Himmelhaus H, Wüstenberg E. Treatment with the SQ tree sublingual immunotherapy tablet is safe and well tolerated in real-life. Clin Transl Allergy. 2024 Jul;14(7):e12373. doi: 10.1002/clt2.12373.

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