SAFETY OF THE 300IR AND 500IR DOSES OF A HOUSE DUST MITE ALLERGEN EXTRACTS SUBLINGUAL TABLET IN ADULTS WITH ALLERGIC RHINITIS

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ABSTRACT

Rationale: The efficacy of two doses (300IR and 500IR) of house dust mite (HDM) sublingual tablets was demonstrated in a randomized, DBPC study in patients with HDM-associated allergic rhinitis. Here we present the safety of this treatment.

Methods: Adults (18-50 years) with medically confirmed HDM-associated allergic rhinitis for at least one year were randomized to receive 300IR or 500IR HDM tablet or placebo once daily for one year and were followed for the subsequent year. Adverse events (AE) were monitored throughout the study and analyzed descriptively. All patients who received at least one dose of the investigational product were included in the safety set.

Results: 509 patients (300IR=170, 500IR=169, Placebo=170) were randomized and received at least one dose. 88% (300IR), 83% (500IR) and 80% (Placebo) reported at least one AE on treatment (TEAE). The most common TEAEs reported in the active groups were mild or moderate application site reactions i.e., oral pruritus (25-30% of patients), throat irritation (21-24%) and mouth edema (12-17%), which mostly occurred within the first month of treatment. Nine participants experienced serious TEAEs of which 4 were considered drug-related: pharyngeal edema (300IR), eczema (300IR), moderate respiratory distress related to a sublingual edema (500IR), and urticaria (Placebo); all recovered. Forty-two patients (300IR=17, 500IR=20, and Placebo=5) withdrew from the study due to a TEAE, most commonly pharyngeal edema, dyspepsia, nausea and mouth edema.

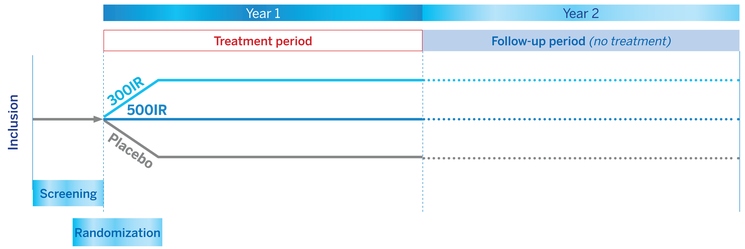
Conclusions: Treatment with HDM sublingual tablets at doses of 300IR and 500IR was associated with a favorable safety profile. There was no appreciable difference in tolerability between the tested doses.

METHODS

Randomized, double-blind, placebo-controlled, multi-center study conducted at 48 sites in 7 European countries

Design

- Patients received either 300IR, 500IR house dust mite (HDM) or placebo tablets once daily for one year and were followed for the subsequent year, post-treatment



Population

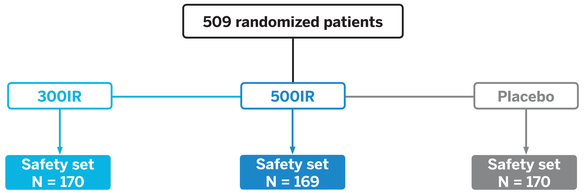
- Adults (18-50 years) with HDM-associated allergic rhinitis for at least one year
- Positive skin prick test for *Dermatophagoides pteronyssinus* or *Dermatophagoides farinae*
- *D. pteronyssinus*- or *D. farinae-specific* serum IgE ≥0.7 kU/L
- Baseline Average Rhinitis Total Symptom Score (ARTSS, scale 0–12) ≥5. The ARTSS is based on patient-recorded daily scores of 4 rhinitis symptoms (sneezing, rhinorrhea, nasal pruritus, and nasal congestion), each symptom evaluated on a scale from 0 (none) to 3 (severe)
- No asthma requiring treatment other than with inhaled beta-2 agonist

Data analysis

- Safety Set: All patients who received at least one dose of the investigational product
- Descriptive analysis of Treatment-Emergent Adverse Events (TEAEs)

RESULTS

Patient disposition

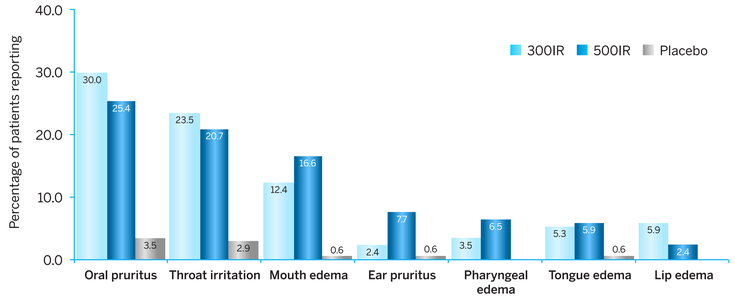


Overview of Treatment-Emergent Adverse Events

Patients with at least one:	300IR N = 170 n (%)	500IR N = 169 n (%)	Placebo N = 170 n (%)
TEAE	150 (88.2)	141 (83.4)	136 (80.0)
Drug-related TEAE	111 (65.3)	110 (65.1)	38 (22.4)
Serious TEAE	6 (3.5)	1 (0.6)	2 (1.2)
Serious drug-related TEAE	2 (1.2)	1 (0.6)	1 (0.6)
TEAE leading to withdrawal	17 (10.0)	20 (11.8)	5 (2.9)

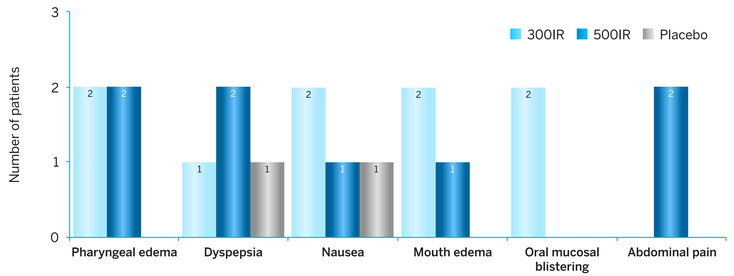
- The incidences of drug-related TEAEs were similar in the two active groups and lower in the placebo group
- Four serious drug-related TEAEs: severe pharyngeal edema on Day 11 (300IR), moderate eczema on Day 107 (300IR), moderate respiratory distress on Day 109 (500IR) and moderate urticaria on Day 37 (Placebo) – All resolved either spontaneously or with antihistamine and/or corticosteroids
- There were no deaths, no intensive care unit admissions, no reports of anaphylaxis, and no use of epinephrine

Most frequent adverse reactions (at least 5% of patients in any treatment group)



- The most common adverse reactions in the active groups were mild or moderate application site reactions (i.e., oral pruritus, throat irritation and mouth edema)
- These mostly occurred within the first month of treatment

Treatment-Emergent Adverse Events leading to study discontinuation (at least 2 patients)



- The most common TEAEs leading to study discontinuation were application site reactions: 14/17 patients (300IR), 11/20 patients (500IR) and 2/5 patients (Placebo)

Conclusions

Treatment with house dust mite sublingual tablets at doses of 300IR and 500IR was associated with a favorable safety profile. There was no appreciable difference in tolerability between the tested doses.

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