Dose response relationship of a timothy grass (*Phleum pratense*) pollen allergoid preparation

Hansen S; Tribanek M; Praechter C; Narkus A; Hahner D. Allergopharma GmbH & Co. KG, Reinbek, Germany

**Background**

We performed a double-blind, randomized, placebo and actively controlled study to investigate the dose response relationship of a high-dose hypoallergenic *Phleum pratense* pollen preparation (allergoid) for subcutaneous specific immunotherapy (SCIT) in patients suffering from allergic rhinoconjunctivitis +/- bronchial asthma. Intracutaneous testing (ICT) served as primary outcome measure for efficacy. Additional assessments were conducted in an environmental challenge chamber (ECC).

**Methods**

Adult patients (FAS; n = 98) with allergic rhinitis/rhinoconjunctivitis +/- bronchial asthma were randomized to 3 different doses of the investigational product (IMP), a *Phleum pratense* preparation: standard dose (n = 18), 3-fold lower (n = 20), or 3-fold higher (n = 18) than standard dose (strength A: 1,000 TU/ML, strength B: 10,000 TU/ML). The active comparator group (n = 22) was treated with a standard dose of commercial 6-grass allergoid. Twenty patients received placebo. All groups underwent 9 preseasonal injections (Figure 1). The primary efficacy endpoint was the change of swelling size (area in mm²) 6 hours after ICT injection between baseline and the end of the treatment period. In the ECC, rhinitis symptoms were assessed. Safety endpoints included adverse events, vital signs and laboratory parameters.

**Results**

All patients treated with either IMP or active comparator showed statistically significant ICT wheal size reductions after treatment (p < 0.001 for each comparison of one active treatment group to placebo) (Figure 2). The results of the ECC assessment were in accordance with these findings (Figure 3).

No serious adverse event occurred during treatments. At least 1 drug related mild systemic allergic reaction was observed in 1 patient (5.3 %) in the high dose group (decreased PEF), 2 patients (9.1 %) in the active comparator group (eyelid edema, peripheral edema), and 1 placebo patient (5.0 %) (decreased PEF).

**Conclusion**

Taking into account the study results, the standard dose (10,000 TU/ML) of the high-dose hypoallergenic *Phleum pratense* preparation shows the best benefit-risk-ratio and demonstrates comparable efficacy to the marketed dose of the 6-grass-pollen allergoid preparation.

---

**Table 1: Demographic characteristics of patients (FAS; n = 98)**

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Placebo (n = 20)</th>
<th>Low dose (n = 20)</th>
<th>Standard dose (n = 18)</th>
<th>High dose (n = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean (range)</td>
<td>32 (18-46)</td>
<td>30 (23-50)</td>
<td>35 (21-50)</td>
</tr>
<tr>
<td>Gender [n] male/female</td>
<td>9/11</td>
<td>9/12</td>
<td>13/5</td>
<td>7/11</td>
</tr>
<tr>
<td>Asthma status [n]</td>
<td>No asthma symptoms</td>
<td>16</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>Duration of allergy (years)</td>
<td>Mean (range)</td>
<td>13 (2-19)</td>
<td>9 (3-17)</td>
<td>10 (3-17)</td>
</tr>
</tbody>
</table>

**Figure 1: Treatment schedule**

**Figure 2: Intracutaneous test: Change in late phase reaction (LPR)**

**Figure 3: Environmental challenge chamber: Total nasal symptom score (TNSS) – Baseline vs. after treatment**