Responder analysis for intracutaneous test (ICT) reactivity in a dose range finding (DRF) trial investigating a timothy grass (Phleum pratense) pollen allergoid preparation

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Background

Adult patients (FAS; n = 98) with allergic rhinitis/rhinoconjunctivitis +/- bronchial asthma (Table 1) 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). Response was defined as a reduction of 50 % in the primary efficacy endpoint: the change of swelling size (area in mm²) 6 hours after ICT injection between baseline and the end of the treatment period.

Methods

Outcome measures in clinical trials should clearly separate clinically relevant effects from only significant effects. Responder analyses provide an appropriate tool to prove if the magnitude of an effect reaches a well-defined threshold value to confirm clinically relevant efficacy. With this objective, we performed a responder analysis on the ICT reactivity of patients enrolled into a clinical trial investigating a high-dose hypoallergenic timothy grass (Phleum pratense) pollen preparation (allergoid).

Results

Patients treated with all doses of the Phleum pratense pollen allergoid and the active comparator showed clear and statistically significant responses (pairwise chi²-test p-value vs. placebo).

Response rates accounted for 73.3 % (p = 0.006) of patients in the high dose group, 83.3 % in the standard dose group (p = 0.001), 70.0 % in the low dose group (p = 0.006), and 85.7 % of patients in the active comparator group (p < 0.001). Whereas a response was observed for only 26.3 % of patients in the placebo group (Figure 2).

Conclusion

Using intracutaneous test reactivity in a dose range finding trial investigating different doses of a high-dose hypoallergenic Phleum pratense pollen preparation and a commercial 6-grass-pollen allergoid, a clear discrimination between actively treated (response rates 70.0 to 85.7 %) and placebo treated patients (response rate 26.3 %) was observed. This proved clinically relevant efficacy for the allergoid preparations at all doses investigated and demonstrates comparable efficacy between the marketed dose of the 6-grass-pollen allergoid and the standard dose of the Phleum pratense allergoid.