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Safety and efficacy of ragweed allergy immunotherapy tablets

Efficacy and tolerability of a novel ragweed allergen immunotherapy tablet in North American and European patients

Rationale

Three daily sublingual ragweed allergy immunotherapy tablet (AIT) doses were investigated to identify an effective therapeutic dose in ragweed allergic rhinoconjunctivitis subjects with/without asthma in North America and Europe.

Methods

Two trials were conducted. Trial 1 included 784 adults with ragweed pollen induced allergic rhinoconjunctivitis randomised 1:1:1:1 to daily ragweed AIT 1.5, 6 or 12 Amb a 1-U or placebo. Trial 2 included 565 adults with ragweed pollen induced ARC randomised 1:1:1 to daily ragweed AIT (6 Amb a 1-U, 12 Amb a 1-U) or placebo. Subjects were treated ~4 months before, throughout, and following ragweed season for a total of ~52 weeks. Symptoms and rescue medications were recorded in daily e-diaries. Efficacy endpoints included total combined daily symptom/medication score (TCS), daily symptom score (DSS) and daily medication score (DMS) during peak season. Safety was monitored through adverse event (AE) reporting and by an external data/safety monitoring committee.

Results

In both trials, the majority of subjects were multi-sensitised (78-85%) and 17-21% had asthma. In trial 1, the 12, 6 and 1.5 Amb a 1-U showed mean TCS improvement versus placebo of 24% (-2.0; p=0.0015), 19% (-1.6; p=0.0113), and 9% (-0.8; p=0.2192), respectively. DSS for 12 Amb a 1-U improved by 18% (-0.9, p=0.0118) versus placebo; 6 and 1.5 Amb a 1-U showed numerical improvement (9% and 5%). DMS improvement of 36% and 35% for 12 and 6 Amb a 1-U was significant (-1.10; p=0.0058 and -1.08; p=0.0053). Treatment effects were similar between continents. The majority of treatment related AEs were mild, local, application-site reactions with no observed difference between 12 and 6 Amb a 1-U or systemic allergic reactions. In trial 2, ragweed AIT 12 and 6 Amb a 1-U groups showed 26% and 21% improvement in TCS versus placebo with significant between-treatment score differences of -2.2 and -1.8 ($p<0.05$). DSS and DMS for 12 Amb a 1-U (17% and 45%) and 6 Amb a 1-U (14% and 34%) were superior versus placebo with significant between-treatment differences ($p<0.05$). Peak season efficacy was comparable to the entire season results. Most AEs were mild, local, application-site reactions with no reports of systemic allergic reactions. Both active doses demonstrated similar safety profiles.

Conclusions

Ragweed 12 Amb a 1-U AIT showed greatest efficacy, with 1.5 Amb a 1-U being ineffective. Treatment was well tolerated with no systemic allergic reactions. The dose of 12 Amb a 1-U AIT may present a novel treatment option for ragweed allergic rhinoconjunctivitis.