Microarray-based Measurement of Allergen-specific IgE-blocking IgG Reflects Clinical Efficacy of Vaccination with the Molecular Grass Pollen Vaccine BM32

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Abstract text

Text: Allergen-specific immunotherapy (AIT) is the most effective treatment for allergic diseases but is limited by side effects. We developed an AIT subunit vaccine platform using recombinant fusion proteins, combining the hepatitis B virus (HBV) surface antigen preS as an immunological carrier with hypoallergenic allergen-derived peptides. This platform induces allergen-specific IgG antibodies, which block IgE-mediated allergic inflammation. The recombinant grass pollen allergy vaccine BM32, based on this principle, has shown clinical efficacy in improving symptoms in grass pollen-allergic patients. This study aimed to identify an immunological marker for clinical improvement.

We analyzed sera from 68 patients in a double-blind, placebo-controlled AIT trial, where participants received three subcutaneous injections of aluminum-hydroxide-adsorbed BM32 (10, 20, or 40 µg of recombinant fusion proteins containing the major timothy grass pollen allergens Phl p 1, Phl p 2, Phl p 5, and Phl p 6) or placebo. The primary clinical endpoint was the difference in total nasal symptom score (TNSS) following grass pollen chamber exposure before treatment and 4 weeks after the last injection.

Since BM32 induces allergen-specific IgE-blocking antibodies, we assessed the ability of IgG in pre- and post-treatment sera to inhibit baseline IgE binding, measured by IgE-inhibition ELISA, basophil degranulation, and IgE inhibition to micro-arrayed allergens. BM32-treated patients developed allergen-specific IgG (mainly IgG1 and IgG4) in a dose-dependent manner (40 µg > 20 µg > 10 µg). The development of IgG correlated with clinical improvement. Patients treated with the 40 µg dose of BM32 showed the highest inhibition rates of allergen-specific IgE binding, correlating with improved clinical outcomes and a 2-5 fold greater ability to tolerate increasing amounts of allergens compared to placebo subjects as shown by basophil activation.

Our findings suggest that microarray-based measurement of IgE binding inhibition by blocking IgG is a simple, serological marker associated with clinical success in AIT.

Conflict of Interest statement

Do you have any conflict of interest to declare?: No

Affirmation

1. Consent to participate and present onsite: Yes

2. Consent to publication publication: Yes

3. Consent on treatment of contact details saved in this system: Yes