Immunotherapy With a Ragweed-Toll-Like Receptor 9 Agonist Vaccine for Allergic Rhinitis


PURPOSE OF THE STUDY. The conjugate compound of the ragweed antigen, Amba1, and an immunostimulatory DNA sequence containing a CpG motif is associated with a suppression of T-helper 2 cellular and cytokine responses via binding to toll-like receptor 9 (TLR9). This study investigated whether Amba1-immunostimulatory oligodeoxyribonucleotide conjugate (AIC) is a safe and effective immunotherapy for ragweed-sensitized patients.

STUDY POPULATION. A randomized, double-blind, placebo-controlled, phase 2 clinical trial in which 25 participants with a history of fall allergic rhinitis aged 23 to 60 years were assigned to receive a vaccine containing either AIC or placebo.

METHODS. Participants received a total of 6 weekly injections before the ragweed season. The primary clinical end point was the change in albumin level in nasal secretions assessed by a posttreatment nasal allergen challenge. Postchallenge rhinitis symptoms were also scored. Secondary clinical end points included the rhinitis visual analog score, daily nasal symptom diary score, use of relief medication, a rhinoconjunctivitis quality-of-life questionnaire, and skin-test sensitivity.

Immunologic evaluation included measuring Amba1- and ragweed-specific immunoglobulin (Ig) G and IgE and cytokine levels.

RESULTS. There was no affect on the primary end point with AIC treatment. However, during the 2 posttreatment ragweed seasons, subjects in the group that received AIC had better peak-season rhinitis visual analog scores, peak-season daily nasal-symptom diary scores, and midseason rhinoconjunctivitis quality-of-life scores. Those in the AIC group also had decreased peak-season use of relief medications and antihistamine and decongestant use in the second season posttherapy. AIC was associated with a rise in the Amba1-specific IgE level after treatment but was not associated with an increase in the Amba1-specific IgE level during either posttreatment ragweed season. There were no vaccine-associated serious adverse reactions.

CONCLUSIONS. AIC may have a potential therapeutic role in the treatment of ragweed-allergic individuals.

IgG-Blocking Antibodies Inhibit IgE-Mediated Anaphylaxis in Vivo Through Both Antigen Interception and FcγRIib Cross-linking


PURPOSE OF THE STUDY. It has been hypothesized that at least part of the mechanism of successful allergen immunotherapy is the induction of specific immunoglobulin (Ig) G that can “block” IgE-dependent responses by competitively preventing IgE binding and/or by signaling via inhibitory FcγRIib on basophils and mast cells, thereby downregulating FceRI-dependent signaling. In vivo evidence of this blocking function has been lacking. The authors of this study carefully addressed whether and how specific IgG can inhibit IgE-mediated anaphylaxis by using a murine model.

METHODS. The authors had previously established a model of anaphylaxis by immunizing BALB/c mice with goat antimouse IgD antibody (GoMD), which elicits a strong T-helper 2 response with high levels of IgE, IgG1, and mastocytosis. In this study they very cleverly modified the model by conjugating GoMD with the hapten trinitrophenyl to generate a trinitrophenyl-specific IgG and IgE response to allow for more detailed evaluation of the role of different antibody isotypes with the same epitope specificity. They used a number of tools including antibody blocking of FcγRs, FcγRIII-deficient knockout mice, and pharmacologic inhibition to discriminate between IgE- and IgG-dependent anaphylaxis. Assessment of anaphylaxis was by temperature drop and hemococoncentration. IgG-trinitrophenyl antibody complexes were measured by enzyme-linked immunosorbent assay (ELISA). In some experiments, interleukin 4 secretion was measured from whole blood by ELISA.

RESULTS. In immunized mice, the authors showed that IgE-dependent anaphylaxis is primarily inhibited by IgG preventing antigen-induced cross-linking of cell-associated IgE. In FcγRIII-deficient mice (ie, those capable of only IgE-dependent anaphylaxis), blockade of the FcγRIib inhibitory receptors did not exacerbate antigen-induced anaphylaxis, and IgG–antigen complexes could be detected in whole blood within 5 minutes of antigen administration. Furthermore, animals passively sensi-
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