

Omalizumab reduced inhaled corticosteroid use and exacerbations in childhood allergic asthma

Milgrom H, Berger W, Nayak A, et al. *Treatment of childhood asthma with anti-immunoglobulin E antibody (omalizumab)*. *Pediatrics* 2001 Aug;108:e36.

QUESTION: In children with moderate to severe allergic asthma who require daily inhaled corticosteroid (ICS) treatment, is omalizumab (anti-immunoglobulin E [anti-IgE] antibody) more effective than placebo for reducing steroid use and asthma exacerbations?

Design

Randomised {allocation concealed*}†, blinded (clinicians, patients {outcome assessors, and statisticians}†),* placebo controlled trial with 34 weeks of follow up.

Setting

Research centres in 12 US states and in Washington, DC.

Patients

334 asthmatic patients who were 6 to 12 years of age (mean age 9 y, 69% boys) and whose asthma was well controlled with ICSs (beclomethasone dipropionate [BDP] and bronchodilator treatment) for ≥ 3 months before randomisation. Other inclusion criteria were allergic asthma for ≥ 1 year; positive skin prick test result to ≥ 1 of house dust mite, cockroach, dog, or cat; total serum IgE level between 30 and 1300 IU/ml; body weight < 90 kg; forced expiratory volume at 1 second (FEV₁) ≥ 60% of predicted normal; ≥ 12% increase in FEV₁ from baseline within 30 minutes of taking albuterol; and stable asthma. Exclusion criteria were previous treatment with omalizumab; sinusitis, respiratory tract infection, or lung disease within 1 month or systemic disease within 3 months of randomisation; abnormal findings on an electrocardiogram or a chest radiograph or abnormal laboratory values; or elevated serum IgE concentrations for reasons other than atopy. All patients were analysed for the stable steroid phase and the steroid reduction phase.

Intervention

Patients were allocated to subcutaneous omalizumab 150 or 300 mg every 4 weeks; omalizumab 225, 300, or 375 mg every 2 weeks (minimum dose 0.016 IU/ml per 4 wk) (n=225); or placebo (n=109). For 16 weeks, the baseline BDP dose was maintained; during the next 8 weeks, BDP was reduced stepwise to establish an effective minimum dose.

Main outcome measures

Reduction of BDP dose and asthma exacerbations.

Main results

More patients who received omalizumab reduced the BDP dose than did patients who received placebo (p=0.002) (table). Asthma exacerbations occurred in

fewer patients receiving omalizumab (p < 0.001) (table), and the mean number of exacerbations per patient was lower in omalizumab recipients (0.42 v 0.72, p < 0.001).

Conclusion

In children with moderate to severe allergic asthma requiring daily inhaled corticosteroids, omalizumab reduced corticosteroid use and asthma exacerbations.

*See glossary.

†Information provided by author.

COMMENTARY

The study by Milgrom *et al* is their second on the use of omalizumab (anti-IgE antibody) in the treatment of asthma and the third published in the previous 3 months that addresses treatment with anti-IgE in large, multicentre asthma studies. Concurrent studies by Busse *et al*¹ and Soler *et al*² included > 500 adult patients aged 12 to 75 years and used medium- to high-dose inhaled steroids (500 to 1200 µg/d of beclomethasone). They used a design similar to that of Milgrom *et al* and achieved similar results as regards to steroid reduction and decreases in exacerbations. These studies, along with an earlier publication by Milgrom *et al*,³ make a case for anti-IgE antibodies as adjunctive treatment for steroid-dependent patients with asthma.

The advantages of anti-IgE over conventional treatments include once or twice monthly subcutaneous injections and its tolerability with infrequent side effects. However, many questions remain. Although the association between asthma and elevated IgE is well established, the actual mechanism by which anti-IgE improves asthma is not known. Whether a role exists for anti-IgE in patients who do not have positive skin test results but who do have elevated IgE — as is commonly seen in asthma patients — is also unclear. The high placebo response role in these studies needs to be reconciled. Longer term studies (≥ 12 mo) must be done to establish whether anti-IgE has a lasting effect on steroid use, enabling it to be used either intermittently or not at all. Such studies must also determine whether anti-IgE can be used as an initial treatment for patients with mild asthma or whether a patient must be stabilised with corticosteroids before being treated with anti-IgE treatment.

Bruce Mazer, MD
Meakins Christie Laboratories,
Montréal, Québec, Canada

- 1 Busse W, Corren J, Lanier Q, et al. Omalizumab, anti-IgE recombinant humanized monoclonal antibody, for the treatment of severe allergic asthma. *J Allergy Clin Immunol* 2001;108:184–90.
- 2 Soler M, Matz J, Townley R, et al. The anti-IgE antibody omalizumab reduces exacerbations and steroid requirements in allergic asthmatics. *Eur Resp J* 2001;18:254–61.
- 3 Milgrom H, Fick RB Jr, Su JQ, et al. Treatment of allergic asthma with monoclonal anti IgE antibody. *N Engl J Med* 1999;341:1966–73.

Sources of funding:
Genentech, Inc. and
Novartis
Pharmaceuticals
Corporation.

For correspondence: Dr
H Milgrom, National
Jewish Medical and
Research Center, 1400
Jackson Street, Denver,
CO 80206, USA.
milgromh@njc.org.

Omalizumab v placebo for childhood allergic asthma‡

Outcomes	Omalizumab	Placebo	RBI (95% CI)	NNT (CI)
75% to 100% reduction in BDP dose at 34 weeks	65%	50%	32% (8 to 65)	7 (4 to 23)
RRR (CI)				
Asthma exacerbations at 12 weeks	18%	39%	53% (32 to 67)	5 (4 to 10)

‡BDP = beclomethasone dipropionate. Other abbreviations defined in glossary; RBI, RRR, NNT, and CI calculated from information provided by author.