

EDITORIAL

Omalizumab for Atopic Dermatitis: Overtreatment or Lifesaver?

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Atopic dermatitis is a chronic inflammatory skin disease that affects 15% to 20% of children and 1% to 3% of adults worldwide.¹ Omalizumab, a medication administered by subcutaneous injection every 2 to 4 weeks, was approved for moderate-to-severe persistent asthma in patients aged 6 years or older by the US Food



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and Drug Administration in 2003.² Atopic dermatitis in children is often IgE mediated, and omalizumab is an anti-IgE medication that binds to human IgE and thus limits mast cell degranulation and inhibits the release of inflammatory mediators. Therefore, it makes logical sense that omalizumab could be efficacious in atopic dermatitis treatment.³ In this issue of *JAMA Pediatrics*, Chan et al⁴ conducted a 24-week double-blind, placebo-controlled randomized clinical trial to determine if omalizumab is effective in severe childhood atopic dermatitis. Their results suggested improved atopic dermatitis severity, as measured by the SCORAD (Scoring Atopic Dermatitis) index, and improved quality-of-life scores in the omalizumab group compared with the placebo group.⁴ Although the study by Chan et al⁴ suggested that omalizumab is efficacious for atopic dermatitis in children, more questions need to be answered before the drug can be used to treat atopic dermatitis in clinical practice. Specifically, this study questions whether omalizumab is cost-effective for atopic dermatitis. Cost-effectiveness analyses can help health care decision-makers choose between new and existing interventions as well as compare costs, benefits, and harms associated with each intervention.⁵ Although no cost-effectiveness analyses on omalizumab as a treatment for atopic dermatitis have been published to date, thinking through the associated costs, benefits, and harms can add perspective to the Chan et al study.⁴

First, what are the costs? Omalizumab is a costly intervention. Omalizumab is dosed according to IgE level and weight, and the wholesale acquisition cost of 150 mg of omalizumab is \$1106.36.⁶ Chan et al⁴ suggested that 1 reason their trial demonstrated a positive clinical outcome compared with results from previous studies is their use of higher doses of omalizumab. Chan et al⁴ stated that participants received higher doses than in previous studies, up to 1200 mg per month of omalizumab, which would cost \$8850 per month and \$106 210 per year. Although 1200 mg per month was reported as the upper bound of the doses in the study, these costs do not include fees related to administration; thus, the costs will be high even at lower doses. Nineteen studies have evaluated the cost-effectiveness of omalizumab for moderate-to-severe asthma, and approximately half of these studies concluded omalizumab was cost-effective.⁷ Some of the studies suggested omalizumab could be cost-effective with con-

siderable price discounts or medication targeted to specific severe subgroups.⁷ No studies have been conducted to establish the cost-effectiveness of omalizumab for atopic dermatitis, but with current pricing, omalizumab for this purpose may not be cost-effective. In general, asthma is a more severe disease than atopic dermatitis. Asthma was the cause of 383 000 deaths worldwide in 2015 according to the World Health Organization, compared with a slightly increased risk of death from other diseases in patients with atopic dermatitis.⁸ Multiple cost-effectiveness studies of asthma recommend reducing omalizumab costs to justify its use; the same argument could be made for omalizumab as a treatment for atopic dermatitis.

Atopic dermatitis is also expensive, with direct, indirect, and intangible costs estimated at \$5.3 billion in the United States in 2015.⁹ Direct costs include visits to the dermatologist or allergist, transportation to and from the appointment, prescription and over-the-counter medications, laboratory tests and procedures, and hospitalization. Indirect costs include impaired productivity of the patient and caregiver, which can include absenteeism (time taken off work because of atopic dermatitis); presenteeism (difficulty concentrating while at work or school); loss of employment; social burden causing embarrassment that may prevent individuals from going out; and the psychological burden from lack of sleep owing to pruritus, depression, anxiety, or other mental health conditions.⁹ The question that needs to be answered in future studies is whether these high costs of atopic dermatitis justify the costs of omalizumab. In addition, perhaps omalizumab is cost-effective in certain subgroups of individuals with severe atopic dermatitis. Atopic dermatitis is relatively common, but according to the 2007 National Survey of Children's Health, 67% of cases were mild and 26% were moderate¹⁰; thus, only a minority of patients with atopic dermatitis have severe disease. Defining the subgroup of individuals with severe atopic dermatitis who may be the most appropriate candidates for omalizumab will be important.

Second, what are the benefits? Identifying the benefits of omalizumab relies partly on evaluating the harms associated with atopic dermatitis, including its indirect costs. Assessing quality of life with atopic dermatitis is challenging, as currently no standardized measurements of the severity of this disease exist. The Chan et al⁴ trial demonstrated statistically significant improvement in the SCORAD index in the omalizumab group compared with the placebo group, but the SCORAD index is not recommended for use in clinical practice.¹¹ Nevertheless, quality of life appears to be poor with moderate-to-severe atopic dermatitis, which is associated with substantial decreases in health utility scores in the US population, even though most people with atopic dermatitis do not have substantial decreases in quality of life.¹²

Development of a standardized method for assessing atopic dermatitis severity would help in the identification of patients who may benefit from omalizumab and in monitoring their progress during treatment.

Third, what are the harms? After more than 15 years of clinical use, omalizumab appears to be generally safe. Nevertheless, adverse effects of omalizumab include anaphylaxis, which is reported to occur in 0.1% to 0.2% of patients; malignant neoplasms; and a constellation of symptoms such as fever, arthralgia, and exanthems.¹³ Additional adverse effects include injection-site reactions, with 45% of omalizumab-treated patients experiencing mild symptoms such as bruising, redness, or warmth, and 12% experiencing severe symptoms.¹³ Furthermore, current omalizumab treatment requires visits to a health care practitioner for injections every 2 to 4 weeks, which adds a logistical burden to the patient, parent, and health care system. Patient attitudes toward injection treatments for atopic dermatitis have not been studied extensively, but 1 study in Japan found that 46% of patients with moderate-to-severe atopic dermatitis opted for injections,¹⁴ and 53% opted out. The finding that fewer than half of the Japanese patients chose injection treatments suggests that patients may not choose omalizumab injections, which could have implications for adherence. Furthermore, this same study found that 77% of physicians opted for injection treatments for their patients with atopic dermatitis, suggesting that physicians have more favorable attitudes toward omalizumab injections; however, nearly a quarter of physicians still would not choose an injection.¹⁴

Understanding the existing medications for severe atopic dermatitis and their adverse effects can shed light on

the need for another medication alternative. Currently, moderate-to-severe atopic dermatitis sometimes requires continuous, long-term use of high-potency topical corticosteroids, oral corticosteroids, UV therapy, and systemic immunosuppressants, all of which have safety risks.¹⁵ Avoiding the long-term use of these medications in favor of omalizumab may have substantial advantages. Moreover, the results of the study by Chan et al⁴ may help the case for developing other forms of omalizumab delivery for atopic dermatitis. Currently, subcutaneous injection of omalizumab usually occurs in the clinic, but the introduction of self-injectable omalizumab may decrease the costs related to visiting the clinic and possibly increase adherence. In addition, developing an oral version of omalizumab may be valuable in the treatment of atopic dermatitis.

Chan et al⁴ conducted a rigorous randomized clinical trial that reported positive results for patients with severe atopic dermatitis, especially patients who are already taking systemic medications with substantial adverse effects, such as oral corticosteroids or systemic immunosuppressants. Even if the routine use of omalizumab for atopic dermatitis may not occur immediately, evaluating the efficacy of biological agents in treating atopic dermatitis will continue. Studies into the efficacy of dupilumab and other biological agents as atopic dermatitis therapy are ongoing as well.¹⁶ The critical next questions after establishing efficacy will likely center on whether omalizumab is cost-effective for atopic dermatitis. Specifically, which patients with atopic dermatitis should receive omalizumab given the high costs of this medication? Is using a \$100 000-per-year medication for an itchy condition an overtreatment or a lifesaver?

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