Omalizumab Improves Asthma-Related Quality of Life in Children With Allergic Asthma

Robert F. Lemanske, Jr, MD*; Anjuli Nayak, MD‡; Margaret McAlary, MS§; Francois Everhard, MS¶; Angel Fowler-Taylor, RPh§; and Niroo Gupta, MD, PhD§

ABSTRACT. Background and Objective. Omalizumab is a recombinant, humanized, monoclonal anti-immunoglobulin E (IgE) antibody, developed for the treatment of IgE-mediated diseases. In children with allergic asthma, it was shown to reduce the requirement for inhaled corticosteroids while protecting against disease exacerbation. Here we report the effects of treatment with omalizumab on asthma-related quality of life (AQoL) in children with allergic asthma.

Methods. This evaluation was part of a previously reported 28-week, randomized, double-blind, placebo-controlled study to assess the efficacy, safety, and tolerability of omalizumab (at least 0.016 mg/kg/IgE [IU/mL] per 4 weeks) in children with allergic asthma who were well controlled on daily treatment with inhaled corticosteroids. Dosage of beclomethasone dipropionate was kept constant for 16 weeks (steroid-stable phase), then reduced over 8 weeks to the minimum effective dose (steroid-reduction phase). This dose was then maintained for the final 4 weeks. The Pediatric Asthma Quality of Life Questionnaire (PAQLQ) was administered at baseline, week 16, and week 28.

Results. Baseline demographics, PAQLQ scores, and other data were comparable for the 2 treatment groups. At the end of the steroid-reduction phase, patients in the omalizumab group achieved clinically significant improvements in the “activities” and “symptoms” domain scores as well as overall AQoL compared with placebo. More patients in the omalizumab group achieved clinically relevant (≥0.5) changes in PAQLQ scores during the course of the study, and this difference was significant for activities and overall AQoL.

Conclusion. Omalizumab improves AQoL in children with allergic asthma. Pediatrics 2002;110(5). URL: http://www.pediatrics.org/cgi/content/full/110/5/e55; allergic asthma, IgE, omalizumab, children, quality of life, asthma.

ABBREVIATIONS. QoL, quality of life; PAQLQ, Pediatric Asthma Quality of Life Questionnaire; IgE, immunoglobulin E; AQoL, asthma-related quality of life; BDP, beclomethasone dipropionate.

Asthma can impair patient functioning not only in terms of symptoms, but also in terms of activity limitation, sleep impairment, and emotional functioning. Furthermore, patients with allergic asthma are often troubled by the concomitant symptoms of other atopic disorders, particularly allergic rhinitis. The traditional spirometric assessments (eg, forced expiratory volume in 1 second) do not measure the combined impact of these conditions on the patients’ quality of life (QoL). The frequency and severity of exacerbations and the number of times an asthma patient is hospitalized for serious exacerbations are other clinically relevant factors affecting QoL that are not recorded by purely spirometric assessments. Use of the validated Pediatric Asthma Quality of Life Questionnaire (PAQLQ) could provide a more sensitive and comprehensive approach to the assessment of asthma, incorporating all of these elements and providing a clearer picture of the individual patient’s overall disease status.

Nearly 90% of children with allergic diseases have positive skin tests to a common aeroallergen (eg, house dust mite, Alternaria, cockroach, cat, dog), indicating the presence of raised levels of circulating immunoglobulin E (IgE). Omalizumab (Xolair; Genentech, San Francisco, CA) is a recombinant humanized monoclonal anti-IgE antibody that forms complexes with circulating free IgE and prevents it from binding to high-affinity receptors on effector cells, thereby inhibiting allergen-induced activation.

It has been reported that subcutaneous treatment with omalizumab reduces the requirement for inhaled corticosteroids while protecting against disease exacerbation in a large placebo-controlled trial in children with moderate-to-severe allergic asthma. Here we report the findings of the effect of omalizumab on asthma-related quality of life (AQoL), which was evaluated during the latter clinical trial.

METHODS

Study Design and Patients

These QoL analyses were conducted as part of a multicenter, 28-week, randomized, double-blind, placebo-controlled study to assess the efficacy, safety, and tolerability of omalizumab in children with allergic asthma, whose asthma was well controlled with inhaled corticosteroids.

Briefly, the study enrolled male and female patients, aged 6 to 12 years, with a diagnosis of allergic asthma of at least 1 year in duration, with total serum IgE levels between 30 and 1300 IU/mL and a positive skin-prick test to at least 1 common aeroallergen...
OMALIZUMAB AND QUALITY OF LIFE IN CHILDREN

RESULTS

Demographics

Demographic information for the overall study population is shown in Table 1. A total of 334 patients were randomized in this study (225 for omalizumab, 109 for placebo). Gender, race, age, and clinical baseline measures, including mean PAQLQ domain and overall scores, were comparable between the treatment groups. Sixteen (7.1%) omalizumab and 12 (11.0%) placebo patients did not complete the study. Withdrawal of consent was the most frequent reason for premature study withdrawal in both the omalizumab (3.1%) and placebo (4.6%) groups. One patient in each treatment group discontinued participation, owing to lack of drug efficacy, and 1 patient in each group withdrew as a result of adverse events (urticaria in 1 omalizumab-treated patient, hip fracture in 1 placebo patient).

AQoL

Baseline PAQLQ scores reflected minimal impairment in AQoL. Both treatment groups showed modest improvements from baseline in PAQLQ scores during the course of the study. For within-treatment improvements, for both time periods (end of steroid-stable phase, end of study), omalizumab reached statistical significance for all domains (activities, emotions, symptoms) as well as for the overall score. Placebo reached statistical significance in the emotions domain at the end of both phases and statistical significance in the overall score only at the end of the steroid-stable phase.

For between-treatment improvements, omalizumab showed larger improvement over placebo in all domains at the end of the stable steroid phase, although the difference was not statistically significant for any domain. At the end of the study, however, omalizumab-treated patients experienced statistically significantly greater improvements from

<table>
<thead>
<tr>
<th>TABLE 1.</th>
<th>Summary of Demographics and Baseline Characteristics by Treatment (All Randomized Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Omalizumab</td>
</tr>
<tr>
<td></td>
<td>n = 225</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>158 (70.2)</td>
</tr>
<tr>
<td>Female</td>
<td>67 (29.8)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>168 (74.7)</td>
</tr>
<tr>
<td>Black</td>
<td>36 (16.9)</td>
</tr>
<tr>
<td>Other</td>
<td>19 (8.4)</td>
</tr>
<tr>
<td>Mean age, y (range)</td>
<td>9.4 (5–12)</td>
</tr>
<tr>
<td>Mean duration of asthma, y (range)</td>
<td>6.1 (1–12)</td>
</tr>
<tr>
<td>Mean BDP dose, µg/day (range)</td>
<td>284 (168–672)</td>
</tr>
<tr>
<td>Mean serum total IgE (range) (IU/mL)</td>
<td>348 (20–1269)</td>
</tr>
<tr>
<td>Mean FEV₁, % predicted (range)</td>
<td>84 (49–129)</td>
</tr>
<tr>
<td>Mean PAQLQ domain scores</td>
<td></td>
</tr>
<tr>
<td>Activities</td>
<td>4.9</td>
</tr>
<tr>
<td>Emotions</td>
<td>5.8</td>
</tr>
<tr>
<td>Symptoms</td>
<td>5.6</td>
</tr>
<tr>
<td>Overall score</td>
<td>5.5</td>
</tr>
</tbody>
</table>

FEV₁ indicates forced expiratory volume in 1 second.
baseline in the activities and symptoms domains as well as the overall score compared with placebo-treated patients (Fig 1). Likewise, at the end of the study, a greater proportion of patients in the omalizumab group achieved a clinically relevant improvement in the asthma-related QoL (defined as an increase >0.5 points) than in the placebo group, reaching statistical significance for the activities domain and the overall asthma-related QoL score (Fig 2). When considering a large improvement in AQoL (defined as an increase >1.5 points), the difference between the omalizumab-treated and placebo-treated groups was particularly marked for activities (23.3% vs 14.0%, respectively; \( P = .995 \)), symptoms domain (16.0% vs 9.3%, respectively; \( P = .1814 \)), and overall score (13.7% vs 8.1%, respectively; \( P = .2258 \)).

**DISCUSSION**

QoL assessment provides additional information that augments the traditional efficacy and safety data in clinical studies of asthma. In this study, we used the PAQLQ,\(^1\) a rigorous questionnaire that was specifically designed to be sensitive to small, within-subject changes in AQoL over time. One unique feature of the PAQLQ is that the patients themselves select 3 of the activity limitation items. This feature may enhance content validity and can help improve the relevance of the questionnaire in clinical practice. With this questionnaire an increase in domain or overall score of ≥0.5 points indicates a clinically relevant improvement in AQoL.\(^12\) This analytical approach allows a meaningful interpretation of the effect of therapeutic intervention on AQoL overall and in age-specific subgroups of children (7–17 years of age).\(^1\)

It has been reported that omalizumab reduces the requirement for corticosteroid therapy while protecting against disease exacerbation in children with allergic asthma.\(^11\) The present findings show that these changes are paralleled by significant improvements in AQoL. The lack of significant differences between treatments during the steroid-stable phase was not surprising, because the patients’ asthma was well controlled at baseline, and PAQLQ scores indicated
that they were relatively untroubled by their disease, leaving little room for improvement. At the end of the steroid-reduction phase, however, changes from baseline in “activities” and “symptoms” domain scores as well as overall AQoL were significantly higher for omalizumab than placebo. Furthermore, the percentage of patients achieving a clinically relevant improvement in overall AQoL was significantly higher in the omalizumab group than in the placebo group. The clinically relevant improvements in AQoL with omalizumab were achieved at the same time as a significant concomitant reduction in reliance on inhaled corticosteroids: the median dose reductions were 100% for children on omalizumab and 67% on placebo, and BDP was withdrawn completely in 55% of omalizumab-treated patients and 39% of the placebo group. This provides compelling evidence that omalizumab targets a cause of the underlying allergic disease. Although children in the placebo-treated group reduced their corticosteroid consumption, they also used more rescue medication in the steroid-reduction period than did children who received omalizumab. Hence, because these children may have relied heavily on rescue medication to control symptoms ordinarily controlled by corticosteroid therapy, the data would seem to report a high median reduction of steroid in this group.

This may also explain the positive response of placebo-treated patients in the quality of life variables.

CONCLUSION

The results of the present study indicate that omalizumab treatment is associated with clinically meaningful improvements in AQoL in children with allergic asthma. These AQoL improvements, in this already well-controlled patient population, parallel earlier findings of enhanced disease control, although there was a significant reduction in inhaled corticosteroid consumption during omalizumab therapy. The improvements in AQoL are also reflected in the finding that children treated with omalizumab had fewer school days missed as a result of their asthma during the double-blind treatment period (P = .04 vs placebo). Likewise, significantly fewer children treated with omalizumab experienced exacerbations during the steroid-reduction phase of the double-blind treatment period than those treated with placebo (P < .001 vs placebo). No children in the omalizumab-treated group were hospitalized; 5 children in the placebo-treated group required hospitalization for serious asthma exacerbations. With convenient subcutaneous administration every 2 or 4 weeks by their attending physician, treatment with omalizumab may overcome the potential for poor
compliance with anti-asthma therapy in children. Taken together, such findings confirm that omalizumab is a promising new agent for the treatment of allergic asthma.

ACKNOWLEDGMENTS

This study was supported by Novartis Pharma AG, Basel, Switzerland and Genentech, Inc, South San Francisco, California. In addition to the authors, the following investigators also contributed patient data: George Bensch, Allergy, Immunology and Asthma Medical Group; William Berger, Southern California Research Center; Jonathan Bernstein, Bernstein Clinical Research Center, Inc; Paul Chervinsky, New England Research Center; Albert Finn, Allergy and Asthma Centers of Charleston; Linda Ford, Nebraska Medical Research Institute; Stanley Galant, Clinical Trials of Orange County; Leon Greos, Colorado Allergy and Asthma Centers; Frank C. Hampel, Central Texas Health Research; Kevin Kelly, Medical College of Wisconsin; Phillip Korenblat, Clinical Research Center; Bobby Quentin Lanier, Lanier Education and Research Network; Michael Lawrence, Center of Clinical Research; Johnathan Matz, Atlantic Asthma and Allergy Center, Inc; Henry Milgrom, National Jewish Medical and Research Center; Nancy Ostrow, Allergy and Asthma Medical Group and Research Center; Bruce Prenner, Allergy Associates Medical Group, Inc; Paul Ratner, Sylvana Research; Michael Ruff, Pharmaceutical Research and Consult, Inc; Robert Schwartz, Allergy, Asthma and Immunology of Rochester Research Center; Nathan Segall, Clinical Research Atlanta; Robert Townley, Creighton University; Ita Tripathy, Clinical Research of the Ozarks, Inc; Martha White, Institute for Asthma and Allergy.

REFERENCES


http://www.pediatrics.org/cgi/content/full/110/5/e55
Omalizumab Improves Asthma-Related Quality of Life in Children With Allergic Asthma
Robert F. Lemanske, Jr, Anjuli Nayak, Margaret McAlary, Francois Everhard, Angel Fowler-Taylor and Niroo Gupta

*Pediatrics* 2002;110;e55
DOI: 10.1542/peds.110.5.e55

Updated Information & Services
including high resolution figures, can be found at:
/content/110/5/e55.full.html

References
This article cites 10 articles, 1 of which can be accessed free at:
/content/110/5/e55.full.html#ref-list-1

Citations
This article has been cited by 5 HighWire-hosted articles:
/content/110/5/e55.full.html#related-urls

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Pharmacology
/cgi/collection/pharmacology_sub

Therapeutics
/cgi/collection/therapeutics_sub

Asthma
/cgi/collection/asthma_sub

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
/site/misc/Permissions.xhtml

Reprints
Information about ordering reprints can be found online:
/site/misc/reprints.xhtml
Omalizumab Improves Asthma-Related Quality of Life in Children With Allergic Asthma

Robert F. Lemanske, Jr, Anjuli Nayak, Margaret McAlary, Francois Everhard, Angel Fowler-Taylor and Niroo Gupta

*Pediatrics* 2002;110;e55
DOI: 10.1542/peds.110.5.e55

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/110/5/e55.full.html