formoterol and once-daily budesonide in measures for asthma control, asthma symptoms, or HRQoL measures. Twice-daily versus once-daily budesonide/formoterol resulted in improved evening predose FEV_1, daytime rescue-medication use, rescue-medication–free days, and worsening asthma events. There were no differences in safety variables between the 3 treatment groups.

REVIEWER COMMENTS. This study was designed by scientists employed by a pharmaceutical company and conducted by a large group of clinicians. It adds to the data regarding safety of inhaled corticosteroid (ICS)/long-acting β_2 agonist (LABA) combinations in young children. In the twice-daily budesonide/formoterol group, the mean evening PEF and evening predose FEV_1 continued to increase during the study, which raises the question of whether the patients achieved true baseline status at the time of randomization. A longer run-in might have lead to different results in the comparisons between twice-daily and once-daily budesonide/formoterol. The authors warned that stepping-down from twice-daily budesonide/formoterol to once-daily dosing might lead to increased asthma symptoms without a change in safety profile but did not discuss potential long-term harm from ongoing unnecessary LABA/ICS use. Current product information and national asthma guidelines should continue to be followed regarding ICS/LABA use in children, but in individual patients for whom twice-daily dosing is not feasible, once-daily dosing (with careful monitoring) might be appropriate.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2011–2107MMM

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Use of Beclomethasone Dipropionate as Rescue Treatment for Children With Mild Persistent Asthma (TREXA): A Randomized, Double-Blind, Placebo-Controlled Trial

Martinez FD, Chinchilli VM, Morgan WJ, et al. *Lancet*. 2011;377(9766):650–657

PURPOSE OF THE STUDY. To determine the effectiveness of inhaled beclomethasone dipropionate when used as a rescue treatment for symptoms in children with mild persistent asthma.

STUDY POPULATION. Children and adolescents aged 5 to 18 years with well-controlled mild persistent asthma were enrolled from 5 clinical centers in a 44-week, randomized, double-blind, placebo-controlled trial.

METHODS. Participants who remained well controlled during the 4-week run-in period were stratified according to clinical center and age group and randomly assigned to 1 of 4 treatments: twice-daily beclomethasone with beclomethasone plus albuterol as rescue (combined group); twice-daily beclomethasone with placebo plus albuterol as rescue (daily beclomethasone group); twice-daily placebo with beclomethasone plus albuterol as rescue (rescue beclomethasone group); and twice-daily placebo with placebo plus albuterol as rescue (placebo group). Twice-daily treatment was 1 puff of beclomethasone (40 μg) or placebo, and rescue treatment for symptoms was 2 puffs of beclomethasone or placebo for every 2 puffs of albuterol (180 μg). The primary outcome, time to first exacerbation that required oral prednisone, and secondary outcome, linear growth, were analyzed according to intention to treat.

RESULTS. Of the 843 participants enrolled, 288 were assigned to a treatment group (combined, $n = 71$; daily, $n = 72$; rescue, $n = 71$; placebo, $n = 74$). Baseline characteristics were similar between included and excluded participants and among those in the 4 treatment groups. The frequency of exacerbations was lower in the combined (31% [95% confidence interval (CI): 21%–43%]; $P = .07$), daily (28% [95% CI: 18%–40%]; $P = .03$), and rescue (35% [95% CI: 24%–47%]; $P = .07$) groups compared with the placebo group (49% [95% CI: 37%–61%]). The frequency of treatment failure was 5.6% (95% CI: 1.6%–14%; $P = .012$) in the combined, 2.8% (95% CI: 0%–10%; $P = .009$) in the daily, and 8.5% (95% CI: 2%–15%; $P = .024$) in the rescue groups compared with 23% (95% CI: 14%–43%) in the placebo group. Compared with the placebo group, linear growth was 1.1 cm (SD: 0.3 cm) less in the combined and daily groups ($P < .0001$) but no different in the rescue group ($P = .26$).

CONCLUSIONS. Daily inhaled corticosteroids are the most effective treatment for children with mild persistent asthma. For children not taking a daily inhaled corticosteroid, inhaled beclomethasone used as a rescue medication with albuterol can lower the risk of exacerbations and treatment failures more effectively than albuterol alone but to a lesser extent than daily inhaled beclomethasone. Children with mild persistent asthma should not be treated with only rescue albuterol.

REVIEWER COMMENTS. This study differs from previous trials of inhaled corticosteroids during asthma exacerbations in that it evaluated the benefit of adding a low-dose inhaled corticosteroid as rescue medication whenever albuterol was needed for treatment of symptoms. The results confirm the relative effectiveness of low-dose daily inhaled corticosteroids, which remain the first-line maintenance therapy for children with mild persistent asthma. Compared with rescue albuterol alone, the results also suggest a possible benefit without increased risk of growth impairment from inhaled corticosteroids added as rescue medication for children not taking a daily inhaled steroid. Among children with well-controlled

mild persistent asthma, the ongoing need for and adherence to inhaled steroid controller therapy must be regularly assessed on an individual basis. These results might be useful when trying to balance the greater effectiveness and greater potential for adverse effects of daily inhaled steroid controller therapy in these patients.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2011–2107NNN

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Effectiveness of Omalizumab in Reducing Corticosteroid Burden in Patients With Moderate to Severe Persistent Allergic Asthma

Karpel J, Massanari M, Geba G, Fianifard F, Inhaber N, Zeldin R. *Ann Allergy Asthma Immunol.* 2010;105(6): 465–470

PURPOSE OF THE STUDY. To assess whether the addition of omalizumab to inhaled corticosteroid (ICS) therapy reduces the steroid burden during long-term treatment and improves clinical outcomes.

STUDY POPULATION. Patients ($N = 1071$) were aged 12 to 75 years with moderate-to-severe persistent allergic asthma that was inadequately controlled with ICSs. Eight percent of the patients were aged 12 to 18 years. All patients had confirmed allergic asthma, an immunoglobulin E (IgE) level between 30 and 700 IU/mL, and a baseline forced expiratory volume in 1 second (FEV_1) between 40% and 80%. Data were pooled from 1 US and 1 international randomized, double-blind placebo-controlled multicenter trial.

METHODS. After a 4- to 6-week ICS stabilization run-in period, patients were randomly assigned to receive omalizumab or placebo. The ICS steroid dose was held constant for the first 16 weeks of treatment and then tapered by 25% every 2 weeks as tolerated for a total of 12 weeks. Patients were then maintained for 24 weeks on continued randomized treatment as well as the lowest possible dose of ICSs established during the steroid-reduction period, and clinically appropriate dose adjustments of ICSs were permitted during this period. Measured outcomes included steroid burden (change from baseline ICS dose and number of oral corticosteroid [OCS] bursts) as well as clinical outcomes.

RESULTS. Baseline characteristics were similar between the 2 groups: patients used an average of 670 μg/day of inhaled beclomethasone and nearly 5 rescue puffs of albuterol daily, and their average IgE levels were in the 190s (IU/mL). At the end of the 3 study phases, there were statistically significant differences between the omalizumab and placebo groups in inhaled steroid dose (all $P < .001$) and number of OCS bursts (all $P < .001$). There were also significant reductions in frequency of exacerbations, improvements in FEV_1 and quality of life, and reduction in peripheral blood eosinophilia in those on omalizumab compared with those on placebo ($P < .001$).

CONCLUSIONS. Omalizumab use reduces corticosteroid burden and improves clinical outcomes in patients with moderate-to-severe persistent asthma.

REVIEWER COMMENTS. The results of this study add to a growing body of literature that substantiates the addition of omalizumab to the medical regimen of those with moderate-to-severe asthma. The high annual cost of this medication ($10 000–$30 000) and the need for supervised administration make it more suited to those who require frequent acute care for their asthma, frequent doses of oral steroids, or high-dose inhaled steroids. The study included a small but significant percentage of pediatric patients aged 12 to 17, for whom reduction in the amount of systemic steroid exposure is of arguably greater value. Ongoing studies are examining the safety of this medication in younger children.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2011–2107OOO

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Randomized Trial of Omalizumab (Anti-IgE) for Asthma in Inner-City Children

Busse WW, Morgan WJ, Gergen PJ, et al. *N Engl J Med.* 2011;364(11):1005–1015

PURPOSE OF THE STUDY. To evaluate the effectiveness of omalizumab in improving asthma control of inner-city children who are not adequately controlled on guideline-based therapy.

STUDY POPULATION. Inner-city children, adolescents, and young adults ($N = 419$) with persistent allergic asthma were included in this study. Eligible patients were required to have a physician's diagnosis of asthma or documentation of asthma symptoms for longer than 1 year before entry into the study and evidence of uncontrolled asthma. All patients had at least 1 positive skin-test result to a perennial allergen, weighed between 20 and 150 kg, and had a total serum immunoglobulin E (IgE) level between 30 and 1300 IU/mL.

METHODS. Participants ($n = 419$) were randomly assigned to receive subcutaneous injections of omalizumab or placebo every 2 or 4 weeks for a 60-week treatment period. Omalizumab doses were calculated on the basis of patient weight and total serum IgE level; the minimum monthly dose was 0.016 mg/kg body weight/IU IgE/mL. Routine clinic visits were scheduled every 3 months. Asthma-control assessment was based on Na-

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Pediatrics 2011;128;S131
DOI: 10.1542/peds.2011-2107NNN

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Pediatrics 2011;128;S131
DOI: 10.1542/peds.2011-2107NNN