GC by inhaler alone or inhaler in combination with other routes. Nearly two-thirds of the children had asthma, and another 15% had asthma plus another condition being treated with GC. Almost one-third of the children were treated with ICS alone. The most commonly used ICS was fluticasone, with most children receiving doses of ~500 μg/day.

CONCLUSIONS. The estimated incidence of symptomatic AS in the pediatric population is small, but it is potentially much higher in at-risk groups (children treated with GC). The close monitoring of growth and asking about nonspecific symptoms such as fatigue, nausea, and myalgia may help with earlier detection. To reduce the risk of AS, physicians must be aware that AS can occur, evaluate GC doses frequently, and use the lowest effective dose.

REVIEWER COMMENTS. This study is a good reminder that we must be aware of the risk of adrenal suppression in children treated with glucocorticoids. Although inhaled corticosteroids have dramatically improved asthma care, the close monitoring of growth and attention to nonspecific or vague symptoms suggesting AS is essential. Our goal for asthma treatment is to use the least amount possible to keep asthma in control.

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Tiotropium Add-on Therapy in Adolescents With Moderate Asthma: A 1-Year Randomized Controlled Trial

Hamelmann E, Bateman ED, Vogelberg C, et al. *J Allergy Clin Immunol*. 2016;138(2):441–450.e8

PURPOSE OF THE STUDY. Phase II studies in children and adolescents have demonstrated that tiotropium is an effective add-on to inhaled corticosteroid (ICS) maintenance therapy. This study sought to assess the safety and efficacy of once-daily tiotropium Respimat added to ICS in a phase III trial in adolescents with moderate symptomatic asthma.

STUDY POPULATION. Eligible patients were aged 12–17 years with histories of asthma of >3 months and who were symptomatic at screening, as defined by the 7-question Asthma Control Questionnaire (ACQ-7). Patients were required to have been receiving ICS +/− long-acting β agonist (LABA) or leukotriene receptor antagonist (LTRA), FEV1 60% to 90% of predicted normal, at least 12% reversibility after albuterol, FEV1 variability within 30% between screening and randomization, and no history of smoking or other lung disease.

METHODS. In this 48-week, double-blind, placebo-controlled, parallel-group study, 398 patients were randomized to receive 5 mcg or 2.5 mcg of tiotropium or placebo via a Respimat device once daily as an add-on to usual ICS, with or without LTRA. LABA use was not permitted. The primary efficacy end point was change from baseline in FEV1 within 3 hours after dosing at week 24. Blinded efficacy and safety monitoring continued to week 48. Secondary end points included trough FEV1, area under the curve (AUC) for FEV1 within 3 hours after dosing, various other pulmonary function measures after 24 weeks of treatment, time to first asthma exacerbation, asthma control (ACQ-6 and ACQ-7), and quality of life as evidenced with the Asthma Quality of Life Questionnaire with Standard Activities (ACLQ).

RESULTS. Both active treatment doses resulted in significantly greater improvement in the FEV1 primary end point versus the placebo ($P < .001$ for 5 mcg, $P < .01$ for 2.5 mcg). Trough FEV1 improved significantly only for the 5-mcg dose versus the placebo ($P < .03$). Also significant were changes in FEV1 AUC for both 5-mcg ($P < .001$) and 2.5-mcg ($P < .008$) doses. Trends for improvement in asthma control and health-related quality of life were observed over the 48-week course but were not statistically significant. No significant side effects occurred with use of either active dose.

CONCLUSIONS. Once-daily tiotropium significantly improved lung function and was safe and well tolerated as an add-on to maintenance ICS in adolescents with moderate symptomatic asthma, especially at the 5 mcg dose. This finding adds to the growing body of evidence supporting the inclusion of tiotropium as an option in step therapy for uncontrolled asthma in adolescents.

REVIEWER COMMENTS. The authors point out that there is considerable heterogeneity in individuals' responses to LABAs and long-acting anticholinergics, and there are no clinical markers we can employ to choose 1 agent versus the other. So, we are not in the "either or" circumstance, at least not yet, in the adolescent population. Given current evidence, tiotropium could be considered as a treatment option for adolescents with moderate persistent disease, in combination with ICS +/− LTRA.

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Real-life Effectiveness of Omalizumab in Severe Allergic Asthma Above the Recommended Dosing Range Criteria

Hew M, Gillman A, Sutherland M, et al. *Clin Exp Allergy*. 2016;46(11):1407–1415

PURPOSE OF THE STUDY. To determine if omalizumab (anti-IgE) above the standard dosing ranges can be beneficial in severe asthmatics and compare responses to patients who are within normal dosing ranges.

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James R. Banks and Timothy Andrews

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