

As-needed budesonide-formoterol for adolescents with mild asthma: Importance of lung function



To the Editor:

We read with great interest the article by Reddel and colleagues that reported pooled adolescent-specific data from the Symbicort Given as Needed in Mild Asthma (SYGMA) trials regarding efficacy and safety of as-needed (prn) budesonide-formoterol (as-needed [prn] BUD-FORM) versus prn terbutaline alone and maintenance budesonide (BUD) and prn terbutaline.¹ These data are greatly valued because adolescent-specific data are lacking despite adolescents with asthma facing distinct challenges compared with children and adults.²

Over 52 weeks, benefits of prn BUD-FORM therapy included reduced severe exacerbations and improved symptoms scores, equivalent to maintenance BUD. However, prn BUD-FORM was associated with reduced median daily steroid exposure and in 12- to 14-year-olds greater linear growth. The authors concluded these data supported prn BUD-FORM as the preferred management strategy in adolescents with mild asthma.

Adolescence, however, is also an important period of lung function attainment, given peak lung function is achieved during early adulthood.³ In pooled analysis, maintenance BUD-FORM was associated with better improvement in baseline pre-bronchodilator forced expiratory volume in 1 second (FEV₁): Maintenance BUD mean improvement of 4.5% versus 2.1% with prn BUD-FORM (2.3% difference between groups; $P < .001$). The results of the Treating Children to Prevent Exacerbations of Asthma (TREXA) study, performed in children and adolescents with mild asthma, are also worth mentioning in this context.⁴ In TREXA, all 4 treatment arms were associated with declines in pre-bronchodilator FEV₁ over the 44-week study, but decline from baseline reached statistical significance only in arms not including maintenance inhaled corticosteroid: the decline was approximately 2% greater comparing 40 µg twice-daily beclomethasone treatment arm versus the beclomethasone rescue arm (80 µg prn plus albuterol), although not statistically significant when directly compared. In agreement with the findings of Reddel et al, in TREXA, rescue beclomethasone had no effect on linear growth whereas daily beclomethasone impaired growth (−1.1 cm lower height attained; $P < .0001$).

It is clear adolescent asthma management should target the optimal balance between improving asthma symptom control, preventing exacerbations, and minimizing growth impairment. However, detrimental effects on peak lung function attained should remain part of this and future evaluations, and the argument that these differences are not clinically relevant, citing thresholds of 5% to 10% from studies of people with cystic fibrosis, may not be appropriate to this setting.¹ Importantly, Vasquez et al⁵ have shown that differences in peak lung function attained by 21 to 35 years predict risk of early cardiopulmonary mortality, and further supported by similar findings within the

Coronary Artery Risk in Young Adults study.^{6,7} How this approximately 2% difference over 44 to 52 weeks translates to peak FEV₁ attained by early adulthood remains unclear, but Vasquez et al⁵ reported that every 10% decline in FEV₁ within their cohort was associated with a 15% increase in mortality risk.

The reduced lung function observed in the prn BUD-FORM group does not mean that this treatment should not be recommended for adolescents, especially given the challenges of maintaining adherence.⁸ However, future studies should clarify effects on peak lung function so that an informed decision can be made by adolescents, physicians, and families, weighing up the potential benefits (reduced burden, reduced steroid exposure, increased height) and risk (lower lung function) of prn BUD-FORM.

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