REVIEWER COMMENTS. FP is a common medication started for initial asthma maintenance therapy shown to improve patients' symptoms and PEF measurements. The study also suggests that a less commonly used medication, FF, has comparable efficacy with no new concerning adverse effects. This study shows there is a comparable alternative choice for providers to recommend on initiation of treatment as well as escalation of therapy for uncontrolled asthma.

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Serious Asthma Events With Budesonide Plus Formoterol Vs. Budesonide Alone

Peters SP, Bleecker ER, Canonica GW, et al. *N Engl J Med*. 2016;375(9):850–860

PURPOSE OF THE STUDY. To evaluate whether the addition of formoterol to budesonide maintenance therapy increased the risk of serious asthma-related events in asthma patients.

STUDY POPULATION. The study included patients, 12 years and older, with persistent asthma who were receiving daily asthma medication and had 1 to 4 asthma exacerbations in the previous year. Patients with a history of life-threatening asthma were excluded. A total of 11 693 patients were enrolled at 534 centers, spanning 25 countries; 11 551 patients completed the study.

METHODS. In this double-blind study, patients were randomly assigned in a 1:1 ratio to receive either budesonide-formoterol or budesonide alone. Patients were stratified to a dose of inhaled glucocorticoid on the basis of initial assessment of asthma control and previous asthma therapy. Both treatment groups had similar demographic profiles and baseline characteristics, providing a broad representation of the overall asthma population. Adherence was assessed by utilizing a dose-actuation counter on the inhalers. During the treatment period, patients had 3 scheduled clinic visits (days 28, 84, and treatment end) and received monthly telephone calls. The primary end point of the study was the first serious asthma-related event, which was assessed as a time-to-event analysis. Serious events included adjudicated death, intubation, and hospitalization. The primary efficacy end point was the first asthma exacerbation, again assessed as a time-to-event analysis.

RESULTS. Serious asthma-related events occurred in 43 patients from the budesonide-formoterol group compared with 40 patients in the budesonide group (hazard ratio of 1.07; 95% confidence interval [CI] 0.70–1.65). There were 2 asthma-related deaths, both in the budesonide-formoterol group. Asthma exacerbation risk was 16.5% lower in the budesonide-formoterol group compared with budesonide alone (hazard ratio of 0.84; 95% CI 0.74–0.94; $P = .002$). The budesonide-formoterol group was shown to be statistically noninferior to budesonide alone for the time to first serious asthma-related event. Finally, analyses in prespecified subgroups defined by age, sex, race, and region were also consistent with the profile of the overall population studied.

CONCLUSIONS. In patients aged 12 and older with moderate-to-severe asthma, budesonide-formoterol combination therapy was associated with a lower risk of asthma exacerbations and a similar risk of serious asthma-related events compared with budesonide treatment alone.

REVIEWER COMMENTS. This randomized clinical trial showed that the addition of formoterol to budesonide did not appear to increase the risk of serious asthma-related events in patients with moderate-to-severe asthma. Furthermore, the risk of asthma exacerbation was significantly lower in patients taking budesonide-formoterol despite the high percentage of patients who reported asthma control at baseline. The AUSTRI trial, a US Food and Drug Administration–mandated study looking at safety of long-acting β adrenoceptor agonists (LABAs), was also recently published showing similar results of no evidence of an increased risk of serious asthma-related events with the addition of a LABA to inhaled corticosteroid monotherapy. One important limitation in this study to note is the exclusion of patients who have a history of life-threatening asthma. Although this exclusion was needed for patient safety, it is important to consider that these results may not be applicable in this patient population. Overall, these results are an important addition to the growing amount of evidence reviewing the risks and benefits associated with the use of LABAs in a fixed-dose combination with an inhaled corticosteroid.

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Individualized Therapy for Persistent Asthma in Young Children

Fitzpatrick AM, Jackson DJ, Mauger DT, et al. *J Allergy Clin Immunol*. 2016;138(6):1608–1618.e12

PURPOSE OF THE STUDY. To determine if a differential response to asthma controller medications exists among young children with a history of wheezing requiring step 2 therapy and if this response can be predicted by phenotype and clinically available biomarkers.

STUDY POPULATION. Enrolled subjects were 300 children aged 12 to 59 months who required step 2 asthma therapy,

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