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LETTER TO THE EDITOR

GINA step 1-2 therapy: Low-dose ICS-formoterol combination taken as needed or moderate-dose ICS-formoterol combination taken as needed?

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To the editor,

Combination therapy of low-dose inhaled corticosteroids (ICS) with formoterol taken as needed for symptom relief is now recommended for the first two steps of asthma treatment (1). As an alternative approach, for step one therapy, use of low-dose ICS is recommended whenever short-acting beta-agonist (SABA) is used (1). For step one therapy, previous studies have shown that use of low-dose ICS-formoterol as needed for symptom relief significantly reduces the risk of asthma exacerbations compared to as-needed SABA alone (2). For step two therapy, it has been shown that taking low-dose ICS-formoterol as needed is non-inferior to daily ICS+ as-needed SABA and even reduces asthma exacerbations with lower ICS use (3,4). In the alternative approach, it has also been shown that low-dose ICS taken whenever SABA is needed significantly reduces the risk of asthma exacerbation compared to as-needed SABA alone (5,6).

For step one and two therapies, the recommended dose of ICS used in combination with a single inhalation of 4.5 mcg formoterol (the recommended maximum delivered dose is 54 mcg for formoterol) is low-dose ICS. The question we are curious about is what would happen if moderate-dose ICS is used with the same formoterol dose, i.e., the combination of moderate-dose ICS-formoterol when needed? Could using the same dose of formoterol with moderate-dose ICS combination instead of formoterol and low-dose ICS combination be a more reasonable approach, especially for step two therapy? To the best of our knowledge, no study that can

answer these questions has been conducted so far. However, we believe that there is an urgent need for these studies to be carried out. Prospective studies are needed to evaluate the outcomes such as exacerbation rates, total ICS doses used, asthma control status, and functional parameters as endpoints in both step one and step two when formoterol and low-dose ICS combination is compared to formoterol and moderate-dose ICS combination. Similarly, prospective studies are needed to compare the effectiveness of low-dose ICS taken whenever SABA is needed with moderate-dose ICS taken whenever SABA is needed in the alternative approach. The most important benefit of these studies is to determine the most effective ICS dose that will be used as needed with rapid-onset beta2-agonists in mild asthma. In particular, it will enable the determination of whether the same recommended treatment (formoterol and low-dose ICS) in steps one and two differs in step two, i.e., whether the use of formoterol and moderate-dose ICS is more appropriate.

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