Author’s reply

Sir,

We thank Barthwal et al. - for showing interest in our work and sharing their views. We have answered their comments as follows:

Although previous studies have shown superiority of inhaled corticosteroid-long-acting beta agonist (ICS-LABA) combination over doubling the ICS dose in previous studies, GINA guidelines still provide both the options for stepping up the treatment. This suggests lack of sufficient evidence, to bring a change to the guidelines and hence, a research area of interest. We agree that ciclesonide, like other ICS, is likely to show the same results in terms of efficacy. However, ciclesonide is a relatively new drug, and there are very few studies comparing efficacy of ciclesonide with other ICS. Therefore, it may not be appropriate to assume equivalence of ciclesonide with other ICS. We value the author’s suggestion of comparing Formoterol-Ciclesonide (FC) with other ICS-LABA combination. However, such work has already been published. We compared our study with the study by Korn and Buhl to compare the extent of lung function improvement found in our study with that reported by Korn and Buhl. Since both the studies had independent groups of patients with asthma treated with a combination of ciclesonide and formoterol, we find the two studies comparable.

In our study, we had an independent subset of patients treated with ciclesonide single dose followed by doubling of the dose. This is consistent with a single sequence crossover study design allowing us to compare the effects of doubling of the dose of ciclesonide. So far, we are not aware of any published study evaluating the effect of doubling of the dose of ciclesonide in patients with asthma. Hence, comparison with previous studies on other ICS was important. The aim of our study was to compare the efficacy and safety of a combination of ciclesonide 80 µg and formoterol 4.5 µg with ciclesonide 80 µg, both given as one puff twice daily. Hence, our study was not designed to compare the effect of doubling the dose of ciclesonide with addition of LABA to the same dose of ciclesonide. The statement we made supports our finding that addition of LABA to ciclesonide provides additional benefit while doubling the dose does not provide benefit in terms of lung function. These two components should be interpreted separately.

In the Cochrane review cited by the authors, none of the studies included in the review evaluated ciclesonide. In our view, we are the first to report the effect of addition
of LABA to ciclesonide in patients with asthma. By conventional dose, we mean any dose of ciclesonide that the patient is taking and addition of ciclesonide to the same (or conventional) dose.

Our study was not aimed at comparing safety of ciclesonide with other ICS. Hence, we have not made any suggestion about FC as a better option than other ICS-LABA combinations. In fact, our conclusion suggests FC as a new combination and not a superior combination.

GINA guidelines provide the option of doubling the dose of ICS or adding LABA. Both the groups received guideline-recommended treatment. Hence, we do not find any ethical issue. Besides, the study was approved by the ethics committees of all the participating sites, and all the patients provided written informed consent before the study participation.

We did not use the word “significant” in the conclusion part of the abstract. Our conclusion was based on numerical improvements seen in the mean symptom scores between the two groups. Since symptom score was not our primary end point, our sample estimation was not based on obtaining significance levels in symptom scores. However, reading the abstract alone or along with the entire manuscript, one can clearly understand that the improvements in symptom scores between the two groups were not statistically significant, but the mean values were better with the FC group compared to the C group.

Although it is not relevant to the scientific discussion, we would like to mention that the ciclesonide-formoterol combination inhaler was introduced by Cipla Limited in 2006 and was available till 2009. The study was conducted using the approved product.

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Conflicts of interest
Authors Abhijit Vaidya and Jaideep Gogtay are employees of Cipla Limited. Authors Sundeep Salvi and Rahul Kodgule do not have any conflict of interest to declare.

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