Rebuttal From Dr Pavord

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I find myself agreeing with almost all of Professor Chalmer’s comments. I accept that this is not in the spirit of a pro-con debate, but suggest it represents a much more important and exciting development: an emerging consensus on the use of inhaled corticosteroids (ICS) in patients with COPD. We both recommend that treatment be initiated in patients who have evidence of involvement of the relevant biologic pathway rather than in those who possess an arbitrary label. We agree that in the blood eosinophil count we have a convenient and consistently robust biomarker of corticosteroid-responsive eosinophilic airway inflammation. As the main impact of treatment is to reduce the frequency of exacerbations (particularly those requiring treatment with oral corticosteroids), and as prior exacerbations are the most important predictor of future events, we also agree that ICS should be applied in a secondary prevention–type fashion.

What should be done about the large number of patients who have been started on ICS, using old “one size fits all” criteria, but who have persistently low blood eosinophil counts? Because the blood eosinophil count is not responsive to ICS treatment, it retains its predictive value in a treated population. Professor Chalmers produces a helpful management algorithm to guide physicians who are contemplating withdrawal of ICS in patients with COPD. There are a few points that need to be emphasized and some aspects that might need to be modified. First, it is clearly critically important that physicians distinguish patients who have low exacerbation frequency because ICS treatment has been successful from those whose risk has always been low. The blood eosinophil count may be helpful, but good history taking is also essential. Second, is triple therapy always necessary in patients with an exacerbation history and an eosinophilic profile? In patients with the right biologic profile ICS/long-acting β2-agonist (LABA) combination treatment is as effective as combination treatment with long-acting muscarinic antagonist (LAMA)/LABA for prevention of exacerbations, and not all patients are in need of the additional bronchodilation and symptom improvement seen when a LAMA is added to a LABA. Finally, I would change the blood eosinophil count criteria for continuing ICS from > 300 to > 150 cells/mm³. Blood eosinophil counts below 150 cells/mm³ have a high negative predictive value for the presence of eosinophilic airway inflammation and were shown to be predictive of successful ICS withdrawal in the WISDOM (Withdrawal of Inhaled Steroids During Optimized Bronchodilator Management) trial. High confidence that the relevant pathology is not present seems to me to be appropriate when adding or removing a therapy with relatively low risks and cost.

These are minor quibbles that shouldn’t take too long to sort out. What might be more of a challenge is to move primary care treatment away from the current blanket, one-size-fits-all approach to the more targeted...
and precise biomarker-directed approach we advocate. Primary care physicians are perhaps more familiar with the nuances of biomarker-directed management than we think. The general principles (ie, consistently and/or highly abnormal results are more influential than a single borderline result; borderline evidence is more influential if the risk of the event we are seeking to prevent is high) are widely understood in primary care, where biomarker-directed cardiovascular risk reduction is carried out to a high standard. I can see no reason why this should not be the case in airways disease.

References
1. Chalmers JD. Point: Should an attempt be made to withdraw inhaled corticosteroids in all patients with stable GOLD 3 (30% ≤ FEV₁ < 50% predicted) COPD? Yes. Chest. 2018;153(4):778-782.