

Beta-blocker for COPD

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To the Editor

We appreciate the interest in the Bisoprolol in COPD study (BICS) from Dr Hsu and Lai. This was a pragmatic study to investigate the effect of bisoprolol on exacerbations in COPD patients in the United Kingdom National Health Service, with any subgroup analysis considered exploratory and hypothesis generating¹. Moreover, the interpretation of any subgroup analyses in BICS is particularly limited because study recruitment was curtailed by the COVID-19 pandemic.

We did not expect any effect of bisoprolol in those patients with asthma-COPD overlap for the following reasons. Bisoprolol has a high selectivity ratio for β_1/β_2 receptor antagonism of 13.3:1². It has been shown in patients with persistent asthma that intravenous esmolol, which exhibits a similar degree β_1 selective antagonism, has no significant adverse effect on FEV₁ or peripheral airway resistance³. Notably, concomitant use of tiotropium in such patients protects against bronchoconstriction when used with the non-selective β -blocker propranolol³. In this regard, 90% of our cohort of COPD patients were taking long-acting muscarinic antagonists¹. Furthermore, chronic dosing with the propranolol versus placebo in patients with persistent asthma produced a 2.4% worsening of FEV₁ percent predicted along with unchanged airway hyper-responsiveness and asthma control⁴. Moreover, in patients with COPD in the presence of inhaled triple therapy, neither bisoprolol nor carvedilol was associated with a significant reduction in FEV₁ or peripheral resistance⁵.

In BICS, during the COVID pandemic, symptomatic deteriorations reported to be associated with SARS CoV2 infection were classified as COVID-19 infections and not infective exacerbations of COPD. These patients were equally distributed between the treatment and placebo groups. We note that in the UK, before and during the BICS trial, there was no routine vaccination for either respiratory syncytial virus or herpes zoster, although most

patients with COPD were routinely vaccinated against pneumococcus and influenza. Given the pragmatic nature of our study, we did not collect vaccination data and this is a study limitation. Notably, only 90 of the 514 participants were enrolled after the implementation of mass SARS CoV2 vaccination. Due to the sample size constraints, any further sub-group analysis of vaccination status is unlikely to be statistically or clinically meaningful, alter the interpretation of the main study findings or have implications for clinical practice.

References

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