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## Acute Pulmonary Injury in Association With Amiodarone

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genetic variation as well. Although this has not been proven in asthmatic patients treated with salmeterol or formoterol, it is worthy of further investigation.

Current data support the combination of ICS and long-acting  $\beta$ -agonists for the treatment of many patients with persistent asthma. While we agree that long-acting  $\beta$ -agonists should not be used for asthma treatment in the absence of ICS, the data presented by Mann and colleagues<sup>1</sup> are not sufficient to determine whether higher doses of the long-acting  $\beta$ -agonist, formoterol, in fact produce increased rates of serious asthma exacerbations. In order to appropriately address this concern, a prospective study designed and powered to answer this would need to be performed.

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## Formoterol and Asthma Exacerbations

To the Editor:

The paper by Mann et al (July 2003)<sup>1</sup> concludes that treatment with formoterol, 24  $\mu$ g bid, in patients with asthma may lead to more serious asthma exacerbations as compared to placebo. The authors based their conclusion on three studies in which 24  $\mu$ g of formoterol bid was compared with placebo, from which one study was performed in children. The number of serious exacerbations in these studies was slightly higher for formoterol but not statistically different between groups. We performed a 6-month study<sup>2</sup> with inhaled formoterol, 24  $\mu$ g bid, in 239 adult patients with moderate asthma, showing contrasting results. We found a

similar incidence of exacerbations as measured by the number of prednisolone courses: 26.4% of patients receiving formoterol needed at least one prednisolone course and 28.1% receiving placebo. Moreover, the number of patients who discontinued the study because of deterioration of asthma was higher in the placebo group ( $n = 6$ ) than in the formoterol group ( $n = 1$ ). Our patients continued their previously prescribed inhaled corticosteroids throughout this double-blind study. The finding that formoterol reduces and not increases the number of asthma exacerbations is consistent with studies<sup>3,4</sup> that were designed to measure the effect of lower dosages of formoterol on exacerbations in moderate asthma. Our study showed that a higher dose of formoterol in conjunction with inhaled corticosteroids is also safe and will not lead to extra concern. Though Mann et al<sup>1</sup> stated that patients of the three studies presented were allowed to continue their steroids, the article did not reveal whether the patients with the reported serious exacerbations received inhaled corticosteroids. This might be a more important explanation for the number of serious exacerbations than the difference in formoterol dosage between the studies cited by Mann et al<sup>1</sup> and other studies.

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To the Editor:

We are writing to highlight recent changes to the amiodarone (Cordarone; Wyeth-Ayerst; Philadelphia, PA) package insert (*ie*, product label). The label, as approved in 1986, states that amiodarone is indicated for the treatment of life-threatening, recurrent ventricular dysrhythmias in situations in which there has been no response to alternative agents or when those alternative agents could not be tolerated. The label further states that the frequency of pulmonary toxicity (*ie*, hypersensitivity pneumonitis and interstitial/alveolar pneumonitis) in retrospective cohorts at doses of 400 mg per day has been estimated at 10 to 17%, with fatality occurring in about 10% of cases. Although the acuity of the amiodarone-associated pulmonary toxicity was

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