Title: Safety of formoterol in asthma clinical trials

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Body: Background: We have previously reported safety data through 2006 from all AstraZeneca-sponsored, randomised, controlled, parallel-group trials with 3-12 months duration with formoterol. Data from 2007-2011 trials have now been added. Methods: Risks associated with formoterol relative to non-LABA-treatments (ICS, SABA, placebo), salmeterol treatments, and conventional best practice, were assessed using rate and rate ratios for multiple safety endpoints. Results: The 2007-2011 data added 15 trials and 22,509 patients including 17,447 treated with formoterol (all with concomitant ICS), increasing the combined dataset to 79 trials and 94,683 patients, of whom 67,380 received formoterol (94% using ICS). There were no asthma-related deaths in the new trials. In total, there were 8 asthma-related deaths among the formoterol-treated patients (exposure 33,700 years), vs. 2 among the non-LABA treated patients (N=18,740; exposure 9500 years) (RR 1.13; 95% CI: 0.23–10.9). No increased risk was observed for formoterol vs. non-LABA treatments for all-cause mortality (RR 0.94; 95% CI: 0.52–1.80), cardiac mortality (RR 0.47; 95% CI: 0.19–1.22), or cardiac-related SAEs (RR 0.94; 95% CI: 0.52–1.80). Asthma-related SAEs were significantly reduced for formoterol vs. non-LABA treatment (RR 0.63; 95% CI: 0.53–0.75). The new trials added a substantial number of black patients to the dataset, but no increased risk for asthma-related SAEs was observed for this subgroup in the combined dataset. Conclusion: Use of formoterol in asthma patients, most using ICS, is not associated with any increased risk of asthma- or cardiac-related deaths or SAEs.