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Why SMART About Second-Line Treatment When First-Line Treatment Is Being Ignored?

To the Editor:

In a recent issue of CHEST (January 2006), the Salmeterol Multicenter Asthma Research Trial (or SMART) demonstrated that the regular use of a twice-daily regimen of salmeterol in asthmatic patients was associated with an unerring increase in respiratory-related and asthma-related deaths, combined asthma-related deaths, or life-threatening experiences. However, surely one of the other most concerning observations was the fact that at study entry only 47% individuals in both the active treatment and placebo groups were receiving regular therapy with inhaled corticosteroids. Thus, > 26,000 subjects with asthma of approximately 16 years duration with a mean peak expiratory flow of 84% predicted were randomized to receive either a placebo inhaler or a long-acting beta-agonist over a 28-week period without therapy with inhaled corticosteroids.

Since guidelines advocate the early use of inhaled corticosteroids in the treatment of asthma, it is therefore incredulous to consider that the investigators felt it reasonable to enroll a majority of individuals who were being inappropriately managed in the community. Perhaps rigorous advertising campaigns are required to emphasize that therapy with inhaled corticosteroids is a long-established, effective, safe, and inexpensive treatment for the management of asthma. And perhaps clinicians and the pharmaceutical industry require reminding too.

Graeme P. Currie, MBChB, DCH, MD
Aberdeen Royal Infirmary
Aberdeen, Scotland, UK

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Correspondence to: Graeme P. Currie, MBChB, DCH, MD, Aberdeen Royal Infirmary, Chest Clinic, Foresterhill, Aberdeen AB25 2ZN, UK; e-mail: graeme.currie@sha.net
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To the Editor:

We thank Dr. Currie for his comments regarding the Salmeterol Multicenter Asthma Research Trial (SMART). It is important to note that SMART was conducted in the United States and was designed in collaboration with the US Food and Drug Administration to be a real-world, observational study evaluating the addition of salmeterol or placebo to usual pharmacotherapy for asthma.

The protocol required a physician diagnosis of asthma and current use of a prescription asthma medication. In addition, investigators were provided with current prescribing information for salmeterol and were asked to use their clinical judgment in determining which patients were appropriate for study inclusion. Therefore, patients could have been receiving inhaled corticosteroid (ICS) therapy to which either salmeterol or placebo would have been added. In addition, SMART was initiated in 1996, which was prior to the 1997 revision of the National Institutes of Health asthma guidelines. Furthermore, the reported use of ICSs at baseline in SMART (47%) was much higher than the average ICS use (10 to 20%) as reported by a large national survey in 1998.

In summary, although SMART was not designed to specifically evaluate the addition of salmeterol or placebo to current ICS therapy, we agree with Dr. Currie’s overall conclusions and current guideline recommendations that the most effective therapy for persistent asthma is ICSs; with the addition of a long-acting beta-agonist, as necessary, for treatment in patients with moderate and severe persistent asthma.

Harold S. Nelson, MD
National Jewish Research and Medical Center
Denver, CO
Paul M. Dorinsky, MD, FCCP
GlaxoSmithKline
Research Triangle Park, NC

Dr. Nelson is a consultant, speaker, and recipient of research grants from GlaxoSmithKline, and was also a member of the Morbidity and Mortality Review Committee. Dr. Dorinsky is an employee of GlaxoSmithKline. Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (www.chestjournal.org/misc/reprints.shtml).

Correspondence to: Paul M. Dorinsky, MD, FCCP, GlaxoSmithKline, 5 Moore Dr, Research Triangle Park, NC 27709; e-mail: paul.m.dorinsky@gsk.com
DOI: 10.1378/chest.130.3.929a

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Cause of Death in the SMART Trial

To the Editor:

The Salmeterol Multicenter Asthma Research Trial (SMART) found a higher incidence of death in African Americans with salmeterol therapy compared to placebo. The authors speculated on possible genetic causes, mentioning beta-receptor polymorphisms. But another genetic aspect is worth considering.