Inhaled Corticosteroid Does Not Suppress Growth

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MONTREAL — New data show that the novel inhaled corticosteroid, ciclesonide, has no detectable effect on growth, body height, or hypothalamic-pituitary-adrenal axis function when administered once daily for a year in prepubertal children with mild, persistent asthma.

The results are reassuring because all other inhaled corticosteroids have been associated with a small degree of growth suppression in pediatric patients, principle investigator Dr. David Skoner said in an interview. The study was performed using tougher clinical trial guidelines established in the late 1990s by the U.S. Food and Drug Administration, requiring larger numbers of children and longer run-in periods to gauge the effect of a steroid on growth.

"There is a lot of steroid phobia, including among doctors, that prevents people from using or adhering to steroids. This should defuse some of that phobia, improve adherence, and get better outcomes," said Dr. Skoner, director of the division of allergy, asthma, and immunology at Allegheny General Hospital in Pittsburgh. Dr. Skoner and associates reported their data in a poster at the Seventh International Congress on Pediatric Pulmonology. Ciclesonide (Alvesco) is under development in the United States, and has been approved for the treatment of persistent asthma in adults, aged 18 years or older, in some European and South American countries.

The phase III, double-blind, multicenter study randomized 661 children (aged 5-8.5 years) to receive one puff in the morning of ciclesonide 160 mcg/day, ciclesonide 40 mcg/day, or placebo for 1 year. Of those, 52 were excluded because they did not receive treatment for 4 months or more, or had missing height data, leaving a modified intent-to-treat population of 609 patients.

There were three phases; a 6-month run-in or baseline period, a 12-month treatment period, and a 2-month follow-up period. Rescue medications, including inhaled short-acting β-2 agonists, leukotriene receptor antagonists, cromones such as cromoglycate and nedocromil, and xanthine derivatives, were permitted on an as-needed basis during the baseline and double-blind treatment periods. No corticosteroids, other than the study medication, were permitted. The overall mean growth velocity, or growth rate, was slightly lower in the ciclesonide 160 group during the baseline period, compared with that in the other two groups. All other baseline characteristics were comparable among groups.

The study's primary end point of growth velocity during the 12-month treatment period was comparable among the groups, Dr. Skoner reported. Growth velocity averaged 5.6 cm/yr in the ciclesonide 160 group; 5.73 cm/yr in the ciclesonide 40 group; and 5.75 cm/yr in the placebo group. During the follow-up period, growth velocity was 5.64 cm/yr; 6.06 cm/yr; and 5.75 cm/yr, respectively.

Cortisol measures for 308 patients showed the mean change from baseline to study end in 24-hour urinary free cortisol, corrected for creatinine levels, remained relatively unchanged in the three groups. The differences were not significant.

In a separate study in adolescents with severe asthma, investigators reported a negative impact on the hypothalamic-pituitary-adrenal axis, as assessed by a decrease in urinary free-cortisol levels, associated with budesonide 800 mcg/day but not with ciclesonide 320 mcg/day.

The randomized, double-blind, multinational study included 403 adolescents in the intent-to-treat population, 371 in the per-protocol population, and 207 in a safety analysis. Their mean age was 14 years (range 12-17 years), and there were more male than female patients in both groups.

In the safety analysis, there was a slight increase after 12 weeks of treatment in creatinine-adjusted 24-hour urinary free cortisol in the ciclesonide group. Urinary free cortisol decreased significantly in the budesonide group, Dr. J. Vermeulen of Panorama Medical Practice, Cape Town, South Africa, and associates said in a separate poster at the meeting. The study's primary end point of change in forced expiratory volume in 1 second from baseline to end of treatment was similar among the groups, increasing by 518 mL with ciclesonide and by 533 mL with budesonide.

Both studies were supported by Altana Pharma and Sanofi-Aventis, which are jointly developing and marketing ciclesonide. Dr. Skoner has served on the speakers' bureau and received grant support from Sanofi-Aventis. ■