Ongoing Study Suggests Tacrolimus Is Safe for Kids

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WASHINGTON — Preliminary data from an ongoing observational study suggest no safety concerns associated with the use of tacrolimus ointment for the treatment of atopic dermatitis in children, Dr. M. Joyce Rico reported in a poster presentation at the annual meeting of the American Academy of Dermatology.

"The data to date confirm the established safety profile of tacrolimus ointment," said Dr. Rico, vice president of research and development at Astellas Pharma US, Inc.

In March 2005, concerns about possible malignancy prompted the Food and Drug Administration to add a boxed warning to the product labels of tacrolimus (Protopic) and to pimecrolimus (Elidel), advising physicians that the two topical nonsteroidal immune suppressants should be used only as directed and only as second-line therapy after other treatments have failed.

Forty-four percent of patients were using the 0.03% concentration, the one approved for children; 56% were using the 0.1% formulation, approved for adults only.

Two months later, Astellas began enrolling patients in a phase IV prospective study to evaluate the long-term safety of tacrolimus ointment in patients who first began using it for the treatment of atopic dermatitis prior to age 16 years, for a minimum of 6 weeks (either continuously or intermittently). Patients are being followed for 10 years with annual physical examinations and dermatologic examinations every 2 years, along with phone calls twice a year to collect additional safety information.

The planned study enrollment is 8,000 patients. Although tacrolimus ointment is indicated for the treatment of moderate to severe atopic dermatitis in nonimmunocompromised children aged 2 years and older, data are being collected on "actual use" conditions, including off-label use in children under 2 years of age.

To date, 1,779 patients from the United States, Germany, Ireland, and the United Kingdom have been enrolled. They are 52% female and 48% male, with a median age of 4 years at the time of first tacrolimus exposure and 6 years at study enrollment. Of note, 24% were first exposed to tacrolimus before 2 years of age, contrary to the package labeling, Dr. Rico remarked.

At the time of study enrollment, severity of atopic dermatitis was moderate in 41%, severe in 12%, not currently active in 6%, and mild in 41%. Not all of the latter two groups constituted off-label use, since some of those with mild or inactive disease may have had moderate to severe disease at the time they began using the ointment.

The median cumulative duration of tacrolimus ointment use was 1.9 patient-years, with a median 9.0 months of actual usage. Less than half of the patients (44%) were using the 0.03% concentration, the only one approved for use in children aged 2-15 years; the other 56% were using the 0.1% formulation, which is approved for adults only. At baseline, 70% of the study population was currently using the ointment.

Data were also collected on the patients' use of pimecrolimus cream, for which the median cumulative duration of use was 2.2 patient-years, with a median 4 actual months of usage. At baseline, 19% of the patients were currently applying pimecrolimus, Dr. Rico reported.

Before enrollment, three patients reported a history of malignancy, including one neuroblastoma and two leukemias. However, no malignancies have been reported since study enrollment. Among the serious adverse events reported so far were pneumonia and asthma-associated bronchitis in one patient, cellulitis in another, viral gastroenteritis in a third, and anaphylaxis in a fourth. All events were deemed by the investigators to be "not related" or "unlikely" to be related to the tacrolimus ointment.

Dr. Rico appealed to the dermatologic community to assist in enrolling patients into this study. "To be able to address this important issue, we need to enroll 8,000 patients. … We're trying to make this very user friendly for both patients and physicians." For more information, the number to call is 877-277-7530. ■