Safety of Solaraze for Actinic Keratosis Confirmed

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AMSTERDAM — Diclofenac 3% gel was well tolerated and showed an excellent safety profile for treatment of multiple actinic keratoses in a postmarketing safety surveillance study.

The study, conducted in 140 primary care practices in the U.K., showed no severe treatment-related adverse events in 450 treated patients. The most common adverse events were mild to moderate dry skin, itching, and redness, each occurring in 16%-20% of patients, Dr. Ron Higson said at the 11th World Congress on Cancers of the Skin. Severe versions of these side effects occurred in fewer than 4% of patients.

Participants in this observational study applied diclofenac 3% gel (Solaraze) twice daily for 12 weeks to areas of actinic keratoses (AKs) in accord with the product labeling. The topical nonsteroidal anti-inflammatory drug is licensed for treatment of AKs in the United States, United Kingdom, and some other European countries. Patients were assessed during office visits at baseline and at weeks 6, 12, and 16.

There was also a secondary efficacy end point consisting of change over time in the longest AK axis from each patient's three largest AKs. The mean reduction in the size of AKs on the head, face, or neck was 2.8 mm at week 6 and 6.4 mm at the week 16 follow-up visit, Dr. Higson of Clitheroe (U.K.) Health Centre said at the congress.

Dr. Eggert Stockfleth, director of the skin cancer center at Charité University Hospital, Berlin, said diclofenac gel's two major advantages are its safety and the fact that it treats visible AK lesions as well as "field cancerization," the underlying dysplasia that gives rise to new AKs and eventually to skin cancers.

The congress was cosponsored by the Skin Cancer Foundation and Erasmus University, Rotterdam, the Netherlands. Shire Pharmaceuticals funded the study. ■

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vival (J. Clin. Oncol. 2006;24:4738-45).

Oblimersen failed to win regulatory approval in Europe or the United States based on this study because the trend for improved overall survival—the primary end point—didn't achieve significance, but overall survival was significantly better with combination therapy in the 508 patients with a normal baseline serum lactate dehydrogenase level, which was a prespecified stratification factor. Oblimersen's developer, Genta Inc., plans to conduct a repeat phase III trial, this time restricted to melanoma patients with normal lactate dehydrogenase levels, said Dr. Lebbé.

The Bayer drug Sorafenib is an antiangiogenesis agent by virtue of its inhibition of vascular endothelial growth factor 2, as well as an inhibitor of the mitogen-activated protein kinase signalling pathway with selectivity for the BRAF mutation present in 70% of melanoma patients. It quickly won regulatory approval in the United States and Europe for the treatment of renal cell carcinoma, and then for hepatocellular carcinoma, the most common malignancy worldwide. Results for melanoma have been mixed.

Clinical activity must be based on survival, and not response rates, which have not translated into improved survival.

DR. MIDDLETON

But Dr. Mark R. Middleton of Cancer UK and the University of Oxford (England) sounded a note of caution. "In melanoma we already have a wealth of therapeutic options. Untold numbers of drugs have been tested in our patients. Unfortunately, none of them work particularly well. The response rates are pretty dismal compared to those for most other solid tumors."

"The definition of promising clinical activity has to be based on survival rather than response rates … the higher response rates haven't translated into survival improvements," he said.

Dr. Middleton and Dr. Eggermont have received research funding from and are consultants to Schering-Plough. Dr. Eggermont is a consultant to Bayer, Boehringer Ingelheim, GlaxoSmithKline, Sanofi Pasteur, Onyx Pharmaceuticals, Genta Inc., and Synta Pharmaceuticals. Dr. Lebbé has received Novartis research funding. ■