# Investigational Gel Rapidly Clears Actinic Keratosis

BY PATRICE WENDLING
*Chicago Bureau*

CHICAGO — Topical therapy for 2 or 3 days with the investigational agent ingenol mebutate, also known as PEP005, provides substantial clearance of actinic keratosis lesions, according to findings from two phase II randomized studies.

"A comparison of efficacy outcomes with those of studies of diclofenac, 5-FU [fluorouracil], and imiquimod shows at least equivalent clearance of lesions over a much shorter period," Dr. Lawrence Anderson, one of the current study's lead investigators, reported at the American Academy of Dermatology's Academy 2008 meeting.

Ingenol mebutate gel has the potential to enhance compliance not only by its shorter course of therapy, but also by the truncated period of irritation in patients with actinic keratosis (AK), the investigators suggested.

PEP005 is a new class of compound derived from the sap of *Euphorbia peplus*, a readily available plant that has been used in Australia for centuries as a traditional treatment for skin conditions. The two current studies were sponsored by Peplin Ltd. of Brisbane, Australia, which is developing PEP005.

Dr. Anderson, who is in private dermatology practice in Tyler, Texas, and his associates randomized 222 patients with 4-8 visible AK lesions on the arm, shoulder, chest, back, or scalp, to one of four treatment groups. The primary end point was partial clearance, defined as the proportion of patients at day 57 with 75% reduction in the number of AK lesions identified at baseline.

Treatment with PEP005 gel once daily for 2 or 3 days produced significantly greater lesion clearance in a dose-dependent manner by all measures and at all dosing regimens, compared with a control vehicle applied once daily for 3 days.

The partial clearance rate was 22% for vehicle, 56% for ingenol mebutate gel 0.025% for 3 days, 62% for ingenol mebutate gel 0.05% for 2 days, and 75.4% for ingenol mebutate 0.05% for 3 days.

The proportion of patients at day 57 with complete clearance, defined as no clinically visible AK lesions, was 12%, 40%, 44%, and 54.4%, respectively.

All three active treatments were well tolerated, according to the investigators, one of whom was a Peplin employee. The most common lesion-site reactions on day 57 were erythema, experienced by 34% of 162 actively treated patients; flaking or scaling (29%); and crusting (9%).

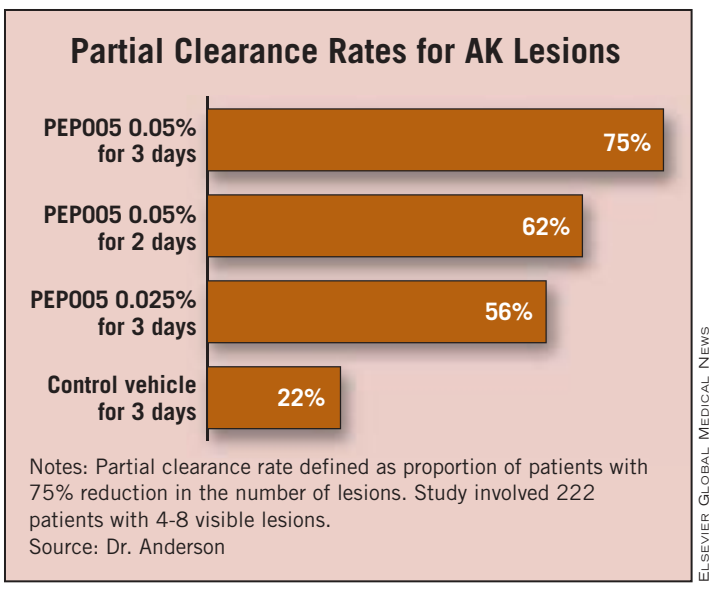
Because AK lesions on the trunk and extremities historically are more difficult to treat than scalp lesions, the investigators performed an ad hoc analysis to compare outcomes in patients with scalp and nonscalp lesions, Dr. Michael Freeman of the Skin Centre, Gold Coast, Australia, and his associates said in a separate poster.

Overall, scalp treatment areas had a higher complete clearance rate than nonscalp treatment areas (57% vs. 42.4%), although the gel was better tolerated when applied to nonscalp areas, regardless of concentration or dosing schedule, the investigators wrote.

The maximum tolerated dose (MTD) for face or face and scalp AK was determined to be once-daily ingenol mebutate gel 0.025% for 2 days, according to a second study that evaluated six formulation strengths ranging from 0.0025% to 0.025% in 86 patients with lesions limited to the face or face and scalp.

At the MTD, 26 of 36 patients (72%) achieved partial clearance and 14 of the 36 (39%) achieved complete clearance.

Ingenol mebutate gel was well tolerated across all strengths, with erythema the most common lesion site reaction. Three patients experienced four serious adverse events, none considered treatment related, according to the investigators, one of whom was also a Peplin employee. ■




Notes: Partial clearance rate defined as proportion of patients with 75% reduction in the number of lesions. Study involved 222 patients with 4-8 visible lesions.
Source: Dr. Anderson

ELSEVIER GLOBAL MEDICAL NEWS

# Ethnicity, Smoking, and BMI May Predict Tanning Dependence

BY SHARON WORCESTER
*Southeast Bureau*

Tanning dependence, sometimes called "tanorexia," is common in young adults and can be predicted by certain demographic and behavioral variables, according to a survey of 400 college students.

More than a quarter (27%) of survey respondents were classified as tanning dependent, and ethnicity, skin type, lack of skin protective behaviors, tanning behaviors, smoking, and body mass index each were found to be significant independent predictors of tanning dependence, reported Carolyn J. Heckman, Ph.D., of Fox Chase Cancer Center in Cheltenham, Pa., and her colleagues (Am. J. Health Behav. 2008;32:451-64).

The findings could assist clinicians in identifying individuals who are tanning dependent or who are at risk of becoming dependent, the investigators said.

In the article, which is now in press, the investigators stated that tanning dependence has a number of similarities to substance use, including higher prevalence among youth, an initial perception that the behavior is image enhancing, and high health risks and disregard for warnings about those risks. Although a primary motivation for tanning is appearance enhancement, tanners often report other benefits, such as mood enhancement, and socialization, commonly reported by individuals with other types of dependencies, Dr. Heckman and her associates noted.

Tanning dependence also has similarities to disorders such as obsessive compulsive disorder and eating disorders, thus the nickname "tanorexia," but it is unclear which comparisons are most applicable.

Prior studies have suggested that one possible mechanism for tanning dependence is endogenous opioid release during ultraviolet radiation (UVR) exposure: Blinded study participants demonstrated a preference for UVR vs. non-UVR tanning beds, and UVR exposure was associated with a more relaxed and less tense mood in those studies. Furthermore, in at least one other study, the preference for UVR tanning beds was reduced with increasing doses of the opioid antagonist naltrexone.

In the current study, which was sponsored by the National Cancer Institute, tanning dependence was assessed using measures developed to evaluate more traditional addictive behaviors such as substance use, which were adapted for the purpose of assessing tanning addiction. The scales used were the four-question CAGE alcohol evaluation and the American Psychiatric Association's Diagnostic and Statistics Manual IV–Text Revision substance dependence criteria.

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**Tanning dependence bears similarities both to substance use disorder and to eating disorders, thus the nickname "tanorexia."**

Participants, who had a mean age of 21 years and were mostly women (75%), were asked questions about tanning behaviors such as "Do you think you need to spend more and more time in the sun to maintain your perfect tan?" and "Does your belief that tanning can cause skin cancer keep you from spending time in the sun or going to tanning beds?"

Of the 400 individuals surveyed, 106 (27%) were classified as tanning dependent by one or both of the two scales used, the investigators found.

Race was found to be predictive of tanning dependence, with white participants having 7.6-fold greater odds than African Americans. Also predictive was moderate skin type, compared with fair and dark skin. Those with Fitzpatrick type III and IV skin had the highest risk: Sixteen percent of those with type I, 21% with type II, 39% with type III, 32% with type IV, and 4% with type V skin were tanning dependent.

Several exposure and skin protection factors were found to predict tanning dependence:

► Those with highest level of summer sunbathing were more likely to be tanning dependent (odds ratio 7.5) than were those with the lowest level.

► Respondents who had the highest number of sunburns were more likely to be tanning dependent (OR 2.85).

► Those who used moderate (OR 0.27) or high levels (OR 0.36) of sun protection were less likely than were those who used low levels to be tanning dependent.

► Those who tanned indoors during warm weather were more likely to be tanning dependent (OR 2.99) than were those who did not use indoor tanning.

The use of chemical sunless tanners and the overall rates of indoor tanning did not predict tanning dependence in this study.

Health-related behaviors that were linked with tanning dependence included current smoking, with smokers having 1.81 greater odds of tanning dependence, and obesity, with those considered obese having lower likelihood of being dependent (odds ratio 0.34).

The findings may offer new avenues for research as well as skin protection and skin cancer prevention interventions, the investigators concluded, but they also noted that "not all tanning behavior or even frequent behavior should be seen as indicative of tanning dependence."

Nonetheless, they expressed concern regarding the finding that about 40% of respondents had used tanning beds, with a mean age of 17 years at first tanning and a mean number of lifetime uses of 57. This is alarming, considering the mean age of 21 in the respondents, they stated. ■