Ipilimumab Extends Survival in Melanoma

Median survival was about 10 months in patients who received the agent vs. 6.4 months without it.

BY JANE SALODOF MACNEIL

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY

CHICAGO — After a 30-year drought during which 70 randomized trials failed to improve outcomes in advanced melanoma, the first agent in a new class of drugs has prolonged survival of advanced, pretreated patients in a large international phase III clinical trial.

"This is the first time we have shown a survival benefit in metastatic melanoma," Dr. Steven O'Day, the lead investigator, announced at the annual meeting of the American Society of Clinical Oncology.

The new agent, ipilimumab, is a monoclonal antibody targeting the cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), a gene that limits the ability of T cells to attack cancerous cells.

Median overall survival reached 10.1 months in 137 patients whose only active treatment was ipilimumab and 10 months in 403 patients given ipilimumab with an experimental vaccine. It was 6.4 months in 136 patients who received the vaccine without ipilimumab—a length of time that falls within the 6-9 month life expectancy for patients with metastatic melanoma, according to Dr. O'Day, chief of research and director of the melanoma program at the Angeles Clinic and Research Institute in Los Angeles.

The difference between the study arms treated with ipilimumab and patients who received only the vaccine was highly significant with a hazard ratio of 0.68 ($P = .0004$).

The one-year survival rate was nearly twice as high in the ipilimumab arms (46% vs. 25%), as was the two-year rate (24% vs. 14%). Some long-term survivors continue to be followed 4.5 years after treatment.

'This is the first time we have shown a survival benefit in metastatic melanoma.'

Disease-control rates were also significantly higher in the two ipilimumab arms (28.5% with ipilimumab alone and 20.1% with ipilimumab plus vaccine vs. 11% with the vaccine alone). Best overall response rates likewise were higher (10.9% and 5.7%, respectively, vs. 1.5%).

Addition of the GP 100 peptide vaccine did not appear to improve outcomes, Dr. O'Day noted. The investigators chose it for the control arm because it had drawn responses in a previous trial, and there is no standard of care for these patients. Dacarbazine (DTIC) has long and often been used, but no randomized trial has ever proven it superior to best supportive care.

Disclosures included that the research funding was provided by Medarex and Bristol-Myers Squibb, which is developing ipilimumab. ■

Indoor Tanning Appears to Quadruple Risk of Melanoma

BY HEIDI SPLETE

FROM CANCER EPIDEMIOLOGY, BIOMARKERS & PREVENTION

Indoor tanning is associated with a fourfold increased risk of melanoma, according to findings from the Skin Health Study, a population-based, case-control study of 1,167 cases and 1,101 controls.

Melanoma was 2.9 times more likely to occur in users of high-speed/high-intensity (UVB-enhanced) tanning devices and 4.4 times more likely in users of high-pressure (primarily UVA-emitting) devices, compared with individuals who had never used the devices.

VITALS

Major Finding: Overall, 63% of individuals with melanoma and 51% of controls reported any indoor tanning.

Data Source: A population-based, case-control study of 1,167 melanoma cases and 1,101 controls.

Disclosures: None of the study authors stated that they had any conflicts of interest. The study was supported in part by a grant from the American Cancer Society and the National Cancer Institute.

In addition, melanoma was 1.8 and 1.9 times more likely in users of conventional indoor tanning devices and sunlamps, respectively, compared with never users.

The study population included individuals aged 25-59 years who were diagnosed with invasive cutaneous melanoma between July 2004 and December 2007 in Minnesota and who were enrolled in a state cancer registry.

Controls were selected at random from the Minnesota state driver's license list. Study participants completed a self-administered questionnaire and a detailed 1-hour phone interview (Cancer Epidemiol. Biomarkers Prev. 2010 [doi: 10.1158/1055-9965.EPI-09-1249]).

DeAnn Lazovich, Ph.D., of the University of Minnesota, Minneapolis, and colleagues began the Skin Health Study in 2004 in Minnesota, a state with a documented high rate of indoor tanning.

The total amount of UV exposure in tanning beds over time is important. This study is going to be very helpful to further regulate the industry.

The data collected by the researchers included skin, hair, and eye color; presence of moles and freckles; lifetime routine sun exposure; age at which tanning beds were first used; duration and frequency of indoor tanning; and type of tanning device used. Overall, 63% of individuals with melanoma and 51% of controls reported any indoor tanning.

Melanoma risk increased significantly as the frequency of indoor tanning increased. In addition, individuals with melanoma were more than twice as likely as controls to report painful burns resulting from indoor tanning, and they reported significantly more of these painful burns than controls.

The researchers also noted that a dose-response relationship between the number of tanning sessions and the number of melanoma lesions on the trunk was identified in both men and women.

"We did not find lifetime routine sun exposure or sun exposure via recreational outdoor activities or occupations to be associated with melanoma risk," Dr. Lazovich and associates wrote.

"To the extent that sunburns are a marker of intermittent sun exposure, then our results adequately represent the independent effect of indoor tanning use on the risk of melanoma."

As physicians, "we see the horrible price paid for using these devices," Dr. Allan C. Halpern, chief of dermatology at Memorial Sloan-Kettering Cancer Center, New York, said during a teleconference last month to discuss the study findings.

Dr. Halpern was not involved in the study.

"We now know that the total amount of UV exposure in tanning beds over time is important," Dr. Halpern said. "I'm hopeful that this study is going to be very helpful in the hands of the FDA to further regulate the industry."

Dr. Halpern said that dermatologists have long understood the importance of educating patients about the dangers of indoor tanning devices, but that misinformation about the risks and benefits of indoor tanning persist.

"I think this study very much strengthens our hand," said Dr. Halpern, who added that he was encouraged to see the consumer video posted by the FDA earlier last month, which states than any UV indoor tanning device should be avoided.

In 2009, the International Agency for Research on Cancer classified tanning beds as carcinogenic to humans.

In 2010, a Food and Drug Administration advisory panel recommended tighter restrictions on the use of indoor tanning devices. However, the agency has yet to issue any guidelines based on these recommendations.

The findings address several limitations of previous investigations on this topic, including the ability to control for confounding variables such as sun exposure, the investigators noted. ■

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Melanoma was 2.9 times more likely to occur in users of UVB-enhanced tanning devices and 4.4 times more likely in users of primarily UVA-emitting devices, compared with nonusers.