

# SLN Microscopic Melanoma May Lower Survival

*Any patient with sentinel lymph node evidence of metastatic melanoma may be at risk for recurrence.*

BY DAMIAN McNAMARA

PALM BEACH, FLA. — The presence of microscopic or even submicroscopic melanoma in a sentinel lymph node may be clinically relevant, a retrospective study has shown.

"We believe patients with microscopic deposits of metastatic melanoma have biologically relevant, potentially life-threatening disease," Dr. David W. Ollila said at the annual meeting of the Southern Surgical Association.

Although other investigators have proposed that submicroscopic disease (a sentinel node tumor that is less than 0.1 mm) is not associated with a significantly increased risk of recurrence or death (Br. J. Surg. 2007;94:1293-9), Dr. Ollila and his associates hypothesized that any sentinel node evidence of metastatic melanoma, regardless of size or stage, may be a cause for concern.

He and his associates retrospectively studied 586 patients (mean age, 55 years) with invasive melanoma and a sentinel node biopsy from 1998 to 2007 in a prospectively maintained database. They classified the 322 men and 264 women as node negative or as having a tumor burden of less than 0.1 mm, 0.1-1.0 mm, or greater than 1.0 mm.

The investigators found a statistically significant difference in recurrence of any type between node-negative patients and those with a tumor burden less than 0.1 mm. During a mean follow-up of 2.7 years, 57 (11%) of the 496 node-negative patients had a recurrence, compared with 8 (24%) of the 33 patients with a sentinel node tumor less than 0.1 mm.

"We [also] found a significant difference in disease-free survival between sentinel node-negative [patients] and the submicroscopic group. They cannot be

considered equivalent," said Dr. Ollila, director of the sentinel node program and codirector of the multidisciplinary melanoma program at the University of North Carolina at Chapel Hill.

In the node-negative group, 51 patients (10%) died, as did 5 (15%) of those with a tumor burden less than 0.1 mm, 6 of 27 patients (22%) in the 0.1- to 1.0-

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mm group, and 12 of 30 patients (40%) who had tumors larger than 1.0 mm.

Dr. Ollila pointed out that the stepwise decrease in survival with increasing diameter of the metastatic deposit was statistically different among the four groups. "This is an interesting [finding], contrary to Rotterdam criteria. I submit

to you that these patients are on a continuum, and this is clinically relevant disease," he said.

An increased sentinel node tumor burden was also associated with a greater risk of metastatic disease in other nodes. A total of 7% of node-negative patients had distant recurrence, as did 15% of those with tumors less than 0.1 mm, 22% of the 0.1- to 1.0-mm group, and 47% of those with tumors larger than 1.0 mm.

Dr. Marshall M. Urist, professor of surgery, University of Alabama at Birmingham, commented that this is an excellent study and asked, "Why did you measure these metastases in a two-dimensional way for a three-dimensional process?"

Dr. Ollila replied: "Point well taken. It's a volume disease. It would be more representative if we could do volumetric measures." The two-dimensional measurement was a limitation of the database used in the study, he said. ■

## Vitamin D and Other Melanoma Controversies Examined

BY KERRI WACHTER

Vitamin D, skin cancer screening, and chemoprevention top the list of current melanoma prevention controversies, according to Dr. Clara Curiel-Lewandowski.

Vitamin D has been a contentious subject for many years with its being suggested that increased sun protection may be associated with lower vitamin D levels, noted Dr. Lewandowski at the annual Hawaii dermatology seminar sponsored by Skin Disease Education Foundation in Maui.

"A decrease in the serum level of vitamin D has been observed in the general population, particularly here in the United States.

"The challenge is to understand to which degree each modulating factor—such as vitamin D dietary intake, photoprotection, body mass index, and geographical location—contributes to the observed decline in serum levels," she said in an interview.

"There is no randomized prospective study linking vitamin D deficiency to excessive photoprotection. Those studies are very difficult to carry out," said Dr. Curiel-Lewandowski, who is director of the pigmented lesion clinic and multidisciplinary oncology at the Arizona Cancer Center in Tucson.

Another component in de-

clining vitamin D levels is that humans produce less vitamin D as they age. Therefore, rising life expectancy may have a role in decreased vitamin D levels. "We're now living to 60, 70, 80 years and we are converting less vitamin D, irrespective of other sources," she said.

**'We're now living to 60, 70, 80 years,' and humans produce less vitamin D as they age; therefore, life expectancy may have a role in decreased vitamin D levels.**

In addition, normal levels of serum 25(OH)D are now in the 70-nmol/L range, where it used to be 35-40 nmol/L, she said. With all of these variables, it is very difficult to tease out which of the components are responsible for declining vitamin D levels.

Advice to skin cancer patients about vitamin D should be based on common sense, said Dr. Curiel-Lewandowski.

She recommends that patients pursue a balanced diet, take daily vitamin D supplements above 400 IU if needed, and limit sun exposure to early morning and late afternoon hours. The specific dose supplementation for individuals with suspected risk factors for vitamin D deficiency should be based on their serum 25(OH)D levels.

### Skin Cancer Screening

It's important to make the distinction between screening the general population and screening specific high-risk groups for skin cancer, said Dr. Curiel-Lewandowski.

"Cost effectiveness of massive skin cancer screening in the general population has been questioned," she said. An agreement needs to be reached on who is at risk for melanoma and how to target them for skin cancer screening.

The United States Preventive Services Task Force just released new recommendations on skin cancer screening for the general population (Ann. Intern. Med. 2009;150:188-93).

The task force said that there is insufficient evidence to recommend for or against skin cancer screening in the general population. (See story on pg. 4.)

"It is important to understand—no one is against skin cancer screening," said Dr. Curiel-Lewandowski. There simply are not enough data to recommend for or against it in the general population.

"In order to properly validate the effectiveness of massive or selective screening, randomized prospective studies will need to be completed. However, the incidence of melanoma is lower compared with other cancers

and in order to get significance, you need more than 400,000 subjects involved and followed for over 10 years to achieve reasonable outcome data. ... It's a very difficult study to accomplish," she said.

The task force did identify high-risk groups of individuals: fair-skinned men and women older than 65 years, patients with atypical nevi, patients with more than 50 nevi, and those with a family history of melanoma.

"What's not clear from this message is what to do with people that are known to be at high risk," she said, noting that the new recommendations identify these groups "but they don't tell you the type of screening and frequency that is recommended."

These are precisely the patients that many dermatologists see—patients with atypical nevi, those with a family history of melanoma, and transplant patients. Screenings should be done for these individuals, said Dr. Curiel-Lewandowski.

### Chemoprevention

"The reason why the concept of melanoma chemoprevention is emerging is because new alternatives are necessary to decrease the burden of disease, especially in high risk individuals. This rationale is particularly compelling since we haven't been successful in decreasing mortality rates. ... It

opens up another option, which is trying to identify systemic agents that can be used in individuals at higher risk for melanoma to slow down the development of disease or even prevent it," Dr. Curiel-Lewandowski commented.

In the 1980s, studies were performed using topical retinoids for atypical nevi. In the late 1990s, statins became the hot topic. Neither option panned out. "What is emerging now among several candidate agents are nonsteroidal anti-inflammatories and green tea derivatives" she said.

The idea of using NSAIDs for the chemoprevention of melanoma comes from experimental and limited epidemiologic and clinical data suggesting that the extended use of NSAIDs decreases the risk of melanoma development. Ongoing larger epidemiologic studies looking in more detail at the strength of this association are expected to be released within the next year.

"Since multiple melanoma pathways have been identified, the effectiveness of a specific chemopreventive agent in a given high-risk population needs to be carefully thought out," Dr. Curiel-Lewandowski said.

Some have advanced this as an argument against chemoprevention.

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