Value of Melanoma Biopsy Technique Is Revised

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WAIKOLOA, HAWAII — An incisional biopsy that fails to remove all of a pigmented skin lesion suspected of melanoma certainly isn't optimal, but it doesn't adversely affect overall or disease-free survival, Dr. Daniel G. Coit said at the annual Hawaii dermatology seminar sponsored by Skin Disease Education Foundation.

"A complete excisional biopsy is clearly the gold standard. But I would rather have an incomplete shave biopsy than no biopsy at all. Not getting all the tumor out is actually not all that terribly important in terms of outcome," said Dr. Coit, a surgeon and coleader of the melanoma disease management team at Memorial Sloan-Kettering Cancer Center in New York, and member of the American Joint Committee on Cancer melanoma staging committee.

The key determinant of outcome in melanoma is not biopsy technique but rather tumor biology as expressed in factors including Breslow thickness, sentinel lymph node status, mitotic index, ulceration, and body site, he added. He also addressed the significance of the time interval between biopsy and definitive wide excision and the optimal margin of wide excision.

Regarding the clinical impact of biopsy technique, Dr. Coit cited a study by Dr. Barbara G. Molenkamp and colleagues at Vrije University Medical Center, Amsterdam, who reported on 471 patients who underwent initial complete or partial removal of what proved to be stage I/II melanoma. After reexcision and sentinel lymph node biopsy, patients were followed for a mean of more than 5 years.

The Dutch researchers found adjusted overall and disease-free survival were unaffected by whether the initial diagnostic biopsy was a wide or narrow excision, an excision with positive margins, or incisional. The presence of residual tumor—in 41 patients—did not adversely affect these key outcomes, either (Ann. Surg. Oncol. 2007;14:1424-30).

Similarly, when dermatologists at Case Western Reserve University, Cleveland, retrospectively studied 108 patients with invasive melanoma who initially underwent nonexcisional shave or punch biopsy then definitive wide excision, they found 88% of the initial biopsies were accurate as to Breslow depth (J. Am. Acad. Dermatol. 2003;48:420-4).

"If you take less than the whole lesion out, you should expect to be correct about 88% of the time. And that's not bad. It beats missing a melanoma altogether," Dr. Coit said.

The Scottish Melanoma Group studied 986 patients with primary cutaneous melanoma whose surgical interval between diagnosis and definitive wide local excision ranged from less than 2 weeks to more than 92 days, with a median of 30 days. Surgical interval wasn't predictive of overall survival, disease-free survival, or local recurrence at a median follow-up of 5 years (Br. J. Dermatol. 2002;147:48-54).

"The interval from biopsy to definitive wide excision does not make a whit of difference other than dealing with patient anxiety, which is important. You can reassure your patients that, while we're doing everything to move them along, most of that is to deal with their anxiety. It will not [affect] the outcome of their melanoma," Dr. Coit said.

There are good data from well-conducted prospective studies addressing the optimal width for excision margins. A recent meta-analysis of five randomized trials totaling 3,313 invasive melanoma patients showed no significant differences with wide as compared with narrow margins insofar as local recurrence, disease-specific survival, or overall survival (Arch. Surg. 2007;142:885-91).

The exception is melanoma in situ, for which there are no prospective data. The current recommendation is to aim for histologically negative margins, starting with a 0.5-cm margin beyond the visible disease. "Explain to patients with melanoma in situ that their disease may extend beyond that, and they may need to return," said Dr. Coit.

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Dermoscopy May Enhance Melanoma Risk Assessment

WAIKOLOA, HAWAII — Nevi displaying a specific high-risk pattern on dermoscopy appear to indicate a several-fold greater melanoma risk than is conferred by the presence of clinical dysplastic nevi, Dr. Allan C. Halpern said at the annual Hawaii dermatology seminar sponsored by Skin Disease Education Foundation.

This finding from a recent pilot study that he characterized as "very small, preliminary, but thought provoking" suggests dermoscopy may enable physicians to do a significantly better job of identifying patients at high risk of developing melanoma, said Dr. Halpern, chief of the dermatology service at Memorial Sloan-Kettering Cancer Center, New York, and cochairman of the National Council on Skin Cancer Prevention.

For the past couple of decades, experts have considered the presence of dysplastic nevi to be one of the most potent available markers of increased risk of developing melanoma. Dysplastic nevi are a stronger risk factor than total skin nevus number, which in turn conveys more information about melanoma risk than does skin complexion.

And while family history of melanoma is another important risk factor, having a parent or sibling with melanoma confers only a 2.5- to threefold increased relative risk. It's only in the much smaller subgroup of individuals with both an affected parent and sibling that the risk really soars to about ninefold.

Numerous studies have shown that dysplastic nevi are an independent risk factor for melanoma and that the relative risk climbs as the number of dysplastic nevi increases. Although risk estimates vary, two dysplastic nevi are often associated with a roughly twofold increased relative risk of melanoma, five with a five- or sixfold increased risk, and so forth.

Dysplastic nevi are present in 2%-8% of whites. They are defined clinically as nevi at least 5 mm in size with a flat component and at least two of the three following criteria: indistinct borders, variable pigmentation, and an irregular asymmetric outline. Dysplastic nevi are markers of risk, not obligate precursors. Although melanoma sometimes arises within a dysplastic nevus, the melanoma risk extends to normal-appearing skin, so there is no point in trying to prophylactically remove dysplastic nevi, he stressed.

To test the hypothesis that dermoscopic pattern might do a better job of defining patients at high risk for melanoma than might identification of clinical dysplastic nevi, Dr. Halpern and his coinvestigators assessed in unblinded fashion dermoscopic images of 187 individual nevi from the backs of 20 patients with invasive melanoma and 150 nevi from 20 age- and gender-matched controls at very high risk for melanoma. All participants had numerous moles, including multiple dysplastic nevi.

In a multivariate logistic regression analysis, the finding of what the investigators called a complex global dermoscopic pattern was associated with a highly significant 2.9-fold increase in melanoma risk. They defined a complex global pattern as one in which both a reticular pigment network and globules were seen in the lesion.

In contrast, the dermoscopic finding of dots in a nevus was associated with a 50% reduction in the likelihood of melanoma (Br. J. Dermatol. 2008 Jan. 17 [Epub doi:10.1111/j.1365-2133.2007.08404.x]).

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COBRA Trial Opens Door to All-Topical Therapy in Psoriasis

WAIKOLOA, HAWAII — Clobetasol propionate spray 0.05% resulted in dramatic clinical improvement with a low rate of adverse events and excellent acceptance in patients with moderate to severe generalized psoriasis in the largest community-based trial ever conducted in psoriasis.

Results of the 2,488-patient Clobex Spray Community-Based Research Assessment (COBRA) trial advance psoriasis therapy to the threshold of a breakthrough era, said Dr. John Koo at the annual Hawaii Dermatology Seminar sponsored by Skin Disease Education Foundation. For patients with moderate to severe generalized disease, there is now the prospect of entirely topical short-term and maintenance therapy that's practical and offers absolute systemic safety.

COBRA was an open-label study conducted at 455 U.S. sites. Participants received clobetasol propionate spray 0.05% (Clobex) twice daily for 4 weeks. The efficacy evaluation involved 1,254 patients with moderate to severe plaque psoriasis treated with clobetasol spray as monotherapy and 731 others with more treatment-resistant disease who received it as add-on therapy. Participants had a 14-year mean duration of psoriasis. Dr. Koo drew particular attention to the mean 11% body surface area involvement at baseline.

COBRA included 183 out of the evaluable 1,254 patients who received clobetasol spray as add-on therapy because they weren't responding adequately to a biologic agent. The other common ongoing treatments alone or in various combinations were topical calcipotriene, non–class-1 topical steroids, and oral antipsoriatic agents.

Treatment success on a target plaque severity measure was defined as clearing, near clearing, or at least a 2-point improvement on a 6-point severity scale. This was achieved at week 2 in 60% of the clobetasol monotherapy group and 59% who received the superpotent topical steroid spray as add-on therapy. After 4 weeks, the success rate was 80% in both populations, explained Dr. Koo, professor and vice chairman of the department of dermatology and director of the psoriasis treatment center at the University of California, San Francisco.

On the target plaque severity scale, success rates at week 4 for clobetasol spray as add-on therapy were 76%-84%.

The other outcome measure was physician global assessment of improvement. Success required a rating of clear or almost clear on whole body assessment. This was achieved in 30% of the monotherapy group and 27% of the add-on treatment group at week 2, and in 69% of monotherapy and 62% of add-on therapy patients at week 4.

Seventy-five percent of participants were reported by their physicians as being very satisfied with their treatment at week 4, while another 19% were somewhat satisfied. Ninety-five percent of patients completed the study.

Among the 2,242 patients included in the safety analysis, one-quarter to one-third experienced treatment-related erythema, stinging/burning, dryness, or peeling/scaling, but these side effects were rated severe in less than 1% of cases. Telangiectasias, skin atrophy, and folliculitis occurred in 1% or less of patients at 4 weeks; pruritus was noted in 5.9%.

Dr. Koo is on the scientific advisory board of Galderma, which sponsored the COBRA trial. He is also a consultant to several other drug and device companies.

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