Cochrane Review: Surgery, Radiotherapy Best Treatments for Basal Cell Carcinoma

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AMSTERDAM — There has been "very little good quality research" overall on treatments for basal cell carcinoma, according to the latest Cochrane Systematic Review on the topic.

This is particularly hard to fathom since basal cell carcinoma (BCC) is the most common form of cancer in humans and an enormous volume of physician work is devoted to its treatment, Fiona J. Bath-Hextall, Ph.D., the review's lead author, noted at the 11th World Congress on Cancers of the Skin.

The review encompassed 27 published and unpublished randomized controlled trials involving surgical excision, radiotherapy, cryotherapy, photodynamic therapy (PDT), intralesional interferon, the plant-derived mixture of solasodine glycosides known as BEC-5 cream, topical 5-fluorouracil, and imiquimod.

The clear winners in terms of efficacy as reflected in the primary end point adopted for the review—BCC recurrence rates at 3-5 years—were surgery and radiotherapy. And in the sole head-to-head comparative trial of these two therapies, surgery had significantly fewer residual tumors and histologically proven recurrences as well as consistently better cosmetic outcomes than radiotherapy, said Dr. Bath-Hextall of the University of Nottingham (England).

Few of the other therapies have been compared directly with surgery, which is the most widely used form of treatment as well as the one supported by the strongest evidence of efficacy.

Most of the clinical trials involved only BCCs in low-risk locations. Only one focused on high-risk facial BCCs. Moreover, many of the studies didn't make it clear what type of BCC was included. Nor did most trials consider recurrent or morpheic BCCs separately, as is warranted given their lower treatment success rates.

Although the seven PDT trials included in the review collectively indicate that it is a promising modality with cosmetic outcomes significantly better than surgery, PDT also has a relatively high failure rate and is expensive. Longer-term efficacy data are needed before it is appropriate for PDT to enter routine clinical practice, according to the Cochrane reviewers (Cochrane Database Syst. Rev. 2007 Jan. 24;CD003412).

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DR. BATH-HEXTALL

Eight of nine studies on imiquimod for BCCs were industry sponsored. They suggest an 88% success rate for a once-daily 6-week regimen in superficial BCC and a more modest 76% treatment response in nodular BCC with 12 weeks of therapy. An ongoing trial of imiquimod versus surgery should help determine whether the topical therapy is a useful option, the reviewers said.

Dr. Bath-Hextall also presented a first look at a new Cochrane Systematic Review of interventions for prevention of nonmelanoma skin cancers in high-risk groups, namely organ transplant recipients and patients with xeroderma pigmentosa or a history of prior nonmelanoma skin cancers. Ten published randomized studies totalling more than 7,200 participants were identified. Only one focused on xeroderma pigmentosa: The 30-patient trial showed reductions in new actinic keratoses and BCCs during 1 year of topical T4N5, a repair enzyme specific for UV-induced DNA damage.

Several studies demonstrated preventive efficacy for retinoids. One study of a 24-month low-fat diet showed no difference in the rate of nonmelanoma skin cancer in year 1, versus controls, but a trend for fewer tumors in years 2-5, Dr. Bath-Hextall said at the congress, cosponsored by the Skin Cancer Foundation and Erasmus University, Rotterdam.

One particularly intriguing trial, she continued, involved more than 1,300 patients with a history of nonmelanoma skin cancer who were randomized in double-blind fashion to 10 years of supplemental selenium or placebo. The selenium group showed a nonsignificant increase in skin cancers, but a highly significant 37% reduction in nonskin cancers, including marked reductions in lung, colorectal, and prostate cancer and an adjusted 21% reduction in all-cause mortality (JAMA 1996;276:1957-63).

Audience members expressed puzzlement at selenium's divergent impacts on skin and internal malignancies. This prompted session chairman Dr. H.A. Martino Neumann, professor of dermatology and venereology at Erasmus, to propose an explanation: Perhaps participation in this study of an oral agent for skin cancer prevention caused some patients to feel a false sense of confidence and become more casual about sun protection. ■

Year 2 Results: Combo Tx Cuts BCC Recurrence

SANTA ANA PUEBLO, N.M. — Curettage followed by imiquimod therapy continues to show promise at 2 years as a way to treat nodular and superficial basal cell carcinoma, Dr. Darrell S. Rigel said at a meeting of the American Society for Mohs Surgery.

In a study that he and his associates first presented at the 2006 annual meeting of the American Academy of Dermatology, the researchers performed curettage on 57 patients who had nodular and superficial basal cell carcinomas. A week after curettage treatment, the patients were asked to apply imiquimod to the lesions five times a week for a total of 6 weeks.

After 1 year there were no disease recurrences. Mild hypopigmentation occurred at the site of about half of the lesions but overall the cosmetic results "were excellent," said Dr. Rigel, who is in private practice in New York. "The cosmetic results were superior to curettage and electrodesiccation," he said, adding that the study was limited to one lesion per patient.

At 2 years' follow-up, there remain no recurrences in the patients. "Combination therapy is going to change the way we're treating a lot of these lesions in the future," said Dr. Rigel, who is also president-elect of the American Society for Dermatologic Surgery. He noted that 60% of recurrent basal cell carcinomas clinically appear within 1 year of treatment. At 2 years, 90% of clinical recurrences will appear.

Dr. Rigel disclosed that he has served as a paid adviser and investigator for 3M Graceway Pharmaceuticals, Doak Dermatologics (a subsidiary of Bradley Pharmaceuticals Inc.), and DUSA Pharmaceuticals Inc.

—Doug Brunk

BCC Algorithm Praised

Mohs *from page 1*

caveat that a few patients remain yet to be counted in the extended follow-up, she said at the meeting, which was cosponsored by the Skin Cancer Foundation and Erasmus University.

Among the primary BCCs, 3% recurred after excision and 2% after Mohs during the first 30 months of follow-up. Although rates are higher at 5 years, they remain similar in the two arms. However, nearly one-quarter of all aggressive cancers 1 cm or greater in diameter were incompletely excised with a 3-mm margin.

Dr. Smeets presented an evidence-based BCC treatment algorithm informed by these updated trial results, as well as by the conclusions of the recent Cochrane Systematic Review of BCC therapies. (See related story, above.)

She stressed that the most important goal in treating BCCs is prevention of recurrence. Recurrences result in repeat procedures, larger defects, more cost, added pain and anxiety, and poorer cosmetic results. In Dr. Smeets' view, cosmetic outcomes—heavily promoted by companies marketing photodynamic therapy (PDT) as a major advantage for their treatment—only come into play as a tie breaker when therapies are of comparable efficacy.

Risk factors for recurrent BCC include a primary lesion 2 cm or more in diameter on the body or 1 cm on the face, location in the H zone of the face, and recurrent BCC. Histologically aggressive subtypes such as morpheaform or infiltrative BCC are also at increased risk for recurrence. For this reason, Dr. Smeets recommends always obtaining a biopsy before treating a BCC.

For a primary lesion on the face that is at least 1 cm and located in the H zone, or of an aggressive subtype, Mohs surgery is clearly the best option, she said. It is not as widely available in Europe as in the United States, though, and when it is unavailable surgical excision is next best. Other options are best reserved for patients who are poor surgical candidates.

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DR. SMEETS

For primary superficial BCCs less than 2 cm located in areas other than the face, the strongest supporting evidence is for surgical excision, but PDT with fractionated illumination has recently joined it as a legitimate first-line therapy in Dr. Smeets' view. She cited a Dutch randomized study involving 505 primary superficial BCCs in which the 1-year complete response rate following 5-aminolevulinic acid PDT with illumination using two light fractions 2 hours apart was a very acceptable 97%, compared with 89% with a single illumination (J. Invest. Dermatol. 2006;126:2679-86).

For nodular BCC outside the face, however, excision remains the sole first-line therapy. The recently completed 5-year follow-up of a previously published British trial (Arch. Dermatol. 2004;140:17-23) showed a 14% recurrence rate for PDT, compared with just 4% for excision in 93 randomized patients, she noted.

Dr. Perry Robins, honorary president of the congress, praised Dr. Smeets' algorithm, with its major role for Mohs surgery, as "a beautiful presentation."

"Mohs surgery is a misnomer," asserted Dr. Robins, chief of the Mohs micrographic surgery unit at New York University, New York. "What is Mohs surgery? Is it something complicated, something expensive, something difficult? Nonsense! Mohs surgery is surgical excision with instant pathology.

"I've done 47,000 Mohs cases, including 10% in the periorbital area. More than half were one layer. So what would you like to do: Excise something and have instant pathology, or excise something, send it to the laboratory, and tell the patient, 'I hope we got it all out'?

"Mohs surgeons are required to read their own slides, so the cost is not all that great," he added. "You don't have the cost for the pathologist, it's done in an office setting, and the patient goes home with a big smile. And because we have the luxury of going back a second time we don't have to do a guesstimate."

Dr. Smeets' trial was sponsored by the Dutch Foundation for Investigative Medicine, a governmental agency. ■