13 by the end (54%) (Figure, B) (P < .008). Seven patients showed inflammatory lesions that waned after MEL treatment (P < .003), and 5 patients had hyperkeratotic lesions that subsequently disappeared (P < .02). Three of 13 patients’ areas of disease showed decreased infiltration during the study. Six patients reported scalp pain before or during the study, but none by the end (P < .008). While 10 of 13 patients reported itching at baseline or during the study, none indicated pruritus by the end of the study (P < .001). An increased growth of hair after 4 to 8 weeks was observed in 3 patients, with stable remission in 2. In 1 patient with canities, repigmentation of hair appeared.

Comment. After laser therapy, we found significantly reduced inflammatory activity in our patients, expressed by decreased erythema, pain, pruritus, and hyperkeratosis. The outcome seems to be in agreement with MEL features that cause significant depletion of T cells and alterations in cytokine expression.4,5 Furthermore, compared with topical therapies that require daily application, a twice-weekly laser regimen showed a greater rate of treatment compliance.

Another new approach, with possibly much lower costs, is treatment with pioglitazones. Controlled trials of PPAR antagonists are ongoing.

Weaknesses of our study include the limited number of patients, an unblinded half-side control, and no distinct control group. Stable hair regrowth was seen in 2 patients, for whom the process of scarring had not reached an irreversible stage. Considering these effects of MEL for active but not end-stage LPP, earlier intervention and improved patient selection and treatment protocol might yield better effects of MEL on hair regrowth. In the future, respawning strategies forming new hair follicles will hopefully complement the choice of therapeutic options for LPP.

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Cryimmunotherapy: Superficial Basal Cell Cancer and Squamous Cell Carcinoma In Situ Treated With Liquid Nitrogen Followed by Imiquimod

Superficial basal cell cancer (sBCC) and squamous cell carcinoma in situ (SCCIS) are common skin cancers limited to the epidermis and traditionally treated with liquid nitrogen with success rates of approximately 90%.1,2 Other treatments include electrodessication and curettage, 5-fluorouracil, topical tretinoin, photodynamic therapy, imiquimod cream, and excision.

In a multicenter study of 169 patients with sBCC treated daily with imiquimod for 6 weeks, high initial (94.1%) and 5-year sustained (85.4%) clearance rates were observed.3 Others report similar findings.4 Of 49 patients with SCCIS treated with imiquimod, 5%, cream, 86% had a complete clearance.5 Patel et al6 report similar results.

Herein, we report the results of a study examining the efficacy of combining liquid nitrogen and imiquimod therapy to treat superficial skin cancers.

Methods. Immunocompetent patients with histologically confirmed sBCC and/or SCCIS who were treated with liquid nitrogen followed by a 6-week course of imiquimod, 5%, cream were eligible for this retrospective study approved by our institutional review board. Only immunocompetent patients with untreated, biopsyproven sBCC or SCCIS who were observed for a period of 24 months or more were included. Patients were excluded if they (1) could not tolerate the treatment; (2) did not continue follow up for at least 24 months after treatment; or (3) were noncompliant with the regimen. Diagnosis of efficacy of treatment was based on the find-
ings of clinical examination and/or histologic evaluation, when available. Informed consent was obtained from all patients.

Lesions were treated by one of us (D.F.M.) using a CRY-AC container (Brymill Cryogenic Systems, Ellington, Connecticut) with an aperture C (0.022 inches) at a distance of 8 to 10 cm for a period of approximately 5 seconds for 2 cycles, obtaining a 2-mm margin around the lesion. One week following the spray with liquid nitrogen, patients were instructed to apply a thin coat of imiquimod for 5 consecutive nights, to take 2 days off, and repeat for a total of 6 weeks. Patients were seen halfway through this course and 2 weeks following the course. Records were reviewed from February 1, 2003, until June 1, 2011. If there was clinical suspicion of recurrence, a punch biopsy was performed.

Results. A total of 152 patients with SCCIS or sBCC treated with cryoimmunotherapy were identified; 73 had to be excluded owing to lack of a 24-month follow-up, and 5 owing to a severe reaction to the cream.

sBCC Findings. Fifty patients (27 men and 23 women) with 57 sBCC lesions were treated. No patients were lost to follow-up. Twelve cancers were located on the head or neck, 45 on the trunk and/or extremities. Seventeen patients underwent posttreatment biopsies; all results were negative. Biopsies were performed on patient request for confirmation purposes. Of the 17 patients biopsied, 14 showed scarring, and 3 showed solar elastosis. Sixteen patients were biopsied at 3 to 5 months, and 1 patient at 10 months following treatment. Disease recurred at the same site in 1 patient, giving a recurrence rate of 2% for sBCC. Three patients had a severe reaction and had to be withdrawn from the study. Another seven patients were not compliant with treatment and were excluded. Mean follow-up was 46.4 months (range, 24-88 months) (Table). Seven patients required application of tretinoin, 0.025%, cream to incite a reaction.

SCCIS Findings. Twenty-nine patients (14 men and 15 women) with 31 SCCIS lesions were treated. No patients were lost to follow-up. Nine cancers were located on the head or neck, 22 on the trunk and/or extremities. Five patients underwent posttreatment biopsies; all biopsies were negative. No recurrences were noted. Two patients experienced a severe reaction (ulcers, severe erythema, constitutional symptoms) and were withdrawn from the study. Four patients were non-compliant. Mean follow-up was 43.5 months (range, 24-83 months) (Table). Four patients required application of tretinoin, 0.025%, cream to incite a skin reaction.

Comment. The recurrence rate was 2% for sBCC and 0% for SCCIS. In the 1 sBCC recurrence, the patient failed to apply the cream to a sufficiently wide area. An excellent cosmetic outcome was noted in all cases. In those cases in which a severe reaction occurred, eventual cosmetic outcome was also acceptable.

The combination treatment of liquid nitrogen followed by the application of imiquimod, for which the term cryoimmunotherapy is proposed, was more effective than either treatment alone and would appear to be more effective than other nonsurgical treatments for superficial skin cancers. We believe that liquid nitrogen damages the integrity of the stratum corneum, thereby facilitating penetration of the cream. Larger randomized studies are needed to assess the efficacy of this combination treatment.

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Table. Summary of Results

<table>
<thead>
<tr>
<th>Lesions, No.</th>
<th>Tumor Type</th>
<th>Head and Neck</th>
<th>Trunk and/or Limbs</th>
<th>Recurrence, %</th>
<th>Severe Adverse Effects, No.</th>
<th>Follow-up, Mean, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>sBCC (n=57)</td>
<td>12</td>
<td>45</td>
<td></td>
<td>2</td>
<td>3</td>
<td>46.4</td>
</tr>
<tr>
<td>SCCIS (n=31)</td>
<td>9</td>
<td>22</td>
<td></td>
<td>0</td>
<td>2</td>
<td>43.5</td>
</tr>
</tbody>
</table>

Abbreviations: sBCC, superficial basal cell cancer; SCCIS, squamous cell carcinoma in situ.