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## ORIGINAL ARTICLE

# Effect of Imiquimod as Compared With Surgery on the Cancerization Field in Basal Cell carcinoma<sup>☆</sup>

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### KEYWORDS

Basal cell carcinoma;  
Imiquimod;  
Cancerization field;  
Risk;  
Cutaneous neoplasm;  
Second primary.

### Abstract

**Background:** Patients with basal cell carcinoma (BCC) have an increased risk of subsequent BCCs. It is possible that imiquimod might reduce this risk by acting on the cancerization field.

**Objective:** To examine the ability of imiquimod to reduce subsequent BCCs.

**Methods:** Retrospective cohort study of patients with BCC treated at our hospital between 2003 and 2011. The patients were divided into 2 groups depending on whether they had been treated with surgery or with imiquimod. Comparing the 2 groups, we analyzed the development of new BCCs, the time that elapsed between first and subsequent tumors, and the site of occurrence of the second BCC with respect to the first one (local, same lymphatic drainage basin or anatomic region, or other). Survival methods were used to analyze the data.

**Results:** We reviewed the charts of 623 patients. Of these, 550 had been treated with surgery (88.3%) and 71 with imiquimod (11.4%). Overall, a second BCC occurred in 36.4% of patients (n = 227). The rate of occurrence was 38.2% in the surgery group and 23.9% in the imiquimod group (P = .02). The hazard ratio for the occurrence of a subsequent BCC was 2.13 (95% CI, 1.28–3.53) for patients treated with surgery compared with those treated with imiquimod. Imiquimod reduced the risk of a second BCC locally, regionally, and in the lymphatic drainage area. Our findings are limited by the retrospective nature of our study and the small number of patients treated with imiquimod.

**Conclusions:** Imiquimod may reduce the risk of subsequent BCC in patients treated for BCC and its effect could last for up to 2 years in local, regional and lymphatic cancerization fields. We believe that the cancerization field concept should be expanded to include not only the local area, but also the pertinent anatomic region and the regional lymphatic drainage area.

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**PALABRAS CLAVE**

Carcinoma basocelular;  
Imiquimod;  
Campo de cancerización;  
Riesgo;  
Neoplasia cutánea;  
Segundo primario.

## Efecto del imiquimod comparado con la cirugía sobre el campo de cancerización en el carcinoma basocelular

**Resumen**

**Antecedentes:** Los pacientes con carcinoma basocelular (CB) tienen riesgo de CB subsiguientes. El imiquimod podría reducir dicho riesgo mediante su efecto sobre el campo de cancerización.

**Objetivo:** Examinar la capacidad de imiquimod para reducir CB subsiguientes.

**Métodos:** Estudio de cohorte retrospectivo de los pacientes con CB tratados en nuestro centro entre 2003 y 2011. Se establecieron 2 grupos según hubieran sido tratados con cirugía o imiquimod. Se comparó entre ambos la aparición de nuevos CB, analizando la proximidad del segundo CB respecto al primero (local, mismo territorio linfático, misma región anatómica, otro territorio) y el tiempo transcurrido entre el primer y segundo tumor. Para el análisis de los datos se emplearon estudios de supervivencia.

**Resultados:** Se revisaron 623 pacientes: 550 tratados con cirugía (88,3%), 2 con crioterapia y 71 con imiquimod (11,4%). Doscientos veintisiete pacientes (36,4%) presentaron un segundo CB (38,2% en el grupo cirugía, 23,9% en el grupo imiquimod,  $p=0,02$ ). La función de riesgo (hazard ratio) de sufrir un segundo CB cuando fueron tratados con cirugía comparado con imiquimod fue 2,13 (1,28-3,53). El imiquimod mostró menor riesgo de segundo CB a nivel local, regional y en el territorio linfático. Limitaciones: la naturaleza retrospectiva del estudio y el número de pacientes tratados con imiquimod fue limitado.

**Conclusiones:** El tratamiento del CB con imiquimod podría reducir el riesgo de segundos CB. Este efecto podría permanecer hasta 2 años y se presentaría en los campos de cancerización local, regional y linfático. Creemos que el concepto de campo de cancerización debería extenderse no solo a nivel local, sino también regional y linfático.

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**Introduction**

Basal cell carcinoma is the most common tumor in humans and its incidence has risen dramatically worldwide in recent decades.<sup>1</sup> Patients who have had BCC have a greater chance of developing subsequent BCCs, with the risk of a second BCC estimated at between 22% and 50%.<sup>2-5</sup>

Sun exposure is the main risk factor for skin cancer. The likelihood of a subsequent BCC developing at the site of a previous BCC and in the surrounding area is theoretically very similar as both areas have been subjected to a similar degree of sun damage. This concept is known as *field cancerization* and has been described in many epithelial tumors.<sup>6-8</sup> Whether or not it also applies to BCC, however, is still a matter of debate.<sup>8</sup>

Surgery is the treatment of choice for BCC. Other alternatives include local immunotherapy, which can cure BCC by stimulating a local immune response. One local immune response modifier is topical imiquimod 5%, which has been licensed for the treatment of small superficial BCCs in adults and has a cure rate of between 43% and 100%.<sup>9</sup>

Imiquimod exerts its effect as a topical immunomodulator by activating both the innate and acquired immune systems.<sup>10,11</sup> It has been shown to have an effect on the cancerization field in actinic keratosis.<sup>7</sup>

In this retrospective study we investigated the ability of imiquimod, when it is used to treat BCC, to prevent the development of second BCCs in the area treated, in the cancerization field, and beyond this field.

**Material and Methods**

The study was conducted in a secondary care level hospital serving a predominantly urban population of approximately 130 000 inhabitants.

We retrospectively compared 2 groups of patients with histologically confirmed BCC treated with either surgery or imiquimod. We reviewed the charts of patients treated for their first BCC at our hospital between January 2003 and December 2011 and recorded the date and type of treatment (surgery vs imiquimod). Due to the retrospective design of the study, we were unable to systematically record why the treating physician decided to choose one treatment over the other. The treatment regimen for imiquimod was 5 days a week for 6 weeks in all cases.

We also made note of the main variables that can influence the occurrence of subsequent BCCs based on the findings of previous studies, namely, age, sex, number of previous BCCs, and number of simultaneous BCCs. The follow-up data recorded included, where applicable, the date at which a second BCC was histologically confirmed; the proximity of the second BCC to the first one (local, same lymphatic drainage basin, same anatomic region, other); and the duration of follow-up (to diagnosis of the second BCC, discharge from care, last routine checkup, or loss to follow-up). The follow-up period analyzed was 60 months and patients followed for less than 3 months were excluded. BCCs diagnosed within 3 months of the first tumor were considered to be synchronous. Recurrent tumors were not classified as second BCCs.

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