# Eruption of squamous cell carcinomas after beginning nilotinib therapy

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## Abstract

Chronic myelogenous leukemia (CML) is characterized by a reciprocal translocation between the long arms of chromosomes 9 and 22 leading to the formation of a constitutively active tyrosine kinase. Tyrosine kinase inhibitors (TKIs) are the treatment of choice for patients diagnosed with CML and have many associated side effects including the rarely reported eruption of squamous cell carcinomas (SCCs). Herein, we report a patient with CML who presented with sudden onset of multiple scaly lesions on his legs and trunk after beginning treatment with nilotinib, a novel TKI. Six biopsies were performed at his initial presentation and four of these lesions were confirmed to be keratoacanthoma-type SCCs. One month later, the patient reported the development of multiple new similar lesions on his legs, arms, and face. Four more biopsies were performed revealing keratoacanthoma-type and well-differentiated SCCs. Certain tyrosine kinase inhibitors such as sorafenib and quizartinib have been reported to cause eruptive keratoacanthoma (KA)-type SCCs as seen in our patient. However, there is only one other report in the literature of nilotinib promoting the development of SCCs or KAs. Physicians should be aware of this potential adverse effect and patients taking nilotinib should be closely monitored by a dermatologist.

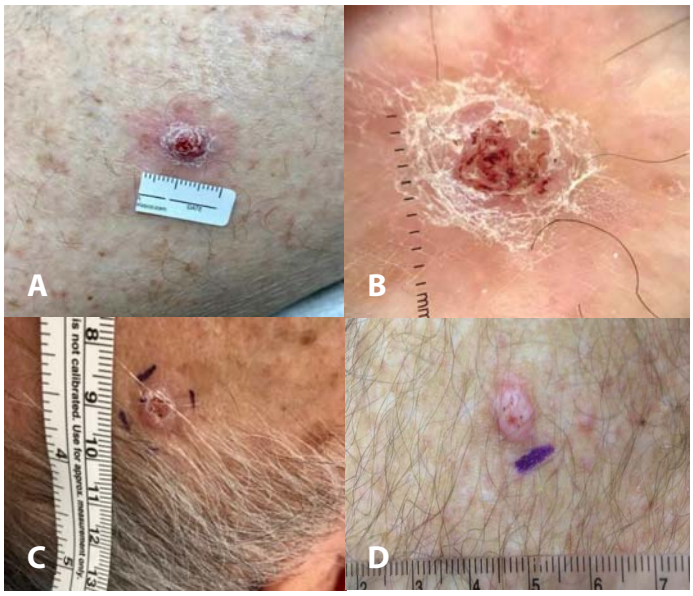
*Keywords: nilotinib, tyrosine kinase inhibitors, chronic myelogenous leukemia, eruptive keratoacanthomas, eruptive squamous cell carcinomas, BCR-ABL*

## Introduction

Chronic myelogenous leukemia (CML) is characterized by a reciprocal translocation between the long arms of chromosomes 9 and 22 resulting in the Philadelphia chromosome. This abnormality leads to the formation of a constitutively active tyrosine kinase, called BCR-ABL [1]. Tyrosine kinase inhibitors (TKIs) are the treatment of choice for patients diagnosed with CML and are used for long-term disease control. There are many associated side effects of TKIs including the rarely reported eruption of squamous cell carcinomas (SCCs), [2, 3]. Herein, we present a patient with CML who developed eruptive SCCs after beginning treatment with nilotinib, a novel TKI.

## Case Synopsis

A 72-year-old man presented with sudden onset of multiple scaly lesions on his legs and trunk, two months after beginning treatment with nilotinib for Philadelphia chromosome-positive (Ph+) CML. He reported that about one week after starting the medication he began to develop these lesions with associated mild pruritus. His history was significant for multiple nonmelanoma skin cancers. At his initial presentation, the patient had multiple hyperkeratotic, erythematous papules present on his thighs, shins, chest, and back (**Figure 1A**, **B)**. Six biopsies were performed at that time and four of these lesions were confirmed to be keratoacanthoma-type SCCs (**Figure 2**). These




**Figures *1*.** ***A)*** *Clinical, and* ***B)*** *dermoscopic images of a hyperkeratotic, erythematous papule on the patient's left lateral calf at initial presentation.* ***C)*** *Similar hyperkeratotic, erythematous papules on the patient's right temple, and* ***D)*** *right shin at follow-up visit.*

tumors were treated with electrodessication and curettage (ED&C). At a follow-up visit one month later, the patient reported the development of multiple new similar growths on his legs, arms, and face (**Figure 1C**, **D)**. Four more biopsies were performed and revealed both keratoacanthoma-type and well-differentiated SCCs. These lesions were treated with ED&C and the patient was counseled to discuss alternative treatment options for CML with his oncologist.

## Case Discussion

The prognosis of CML changed dramatically with the introduction of tyrosine kinase inhibitors. Nilotinib is a second-generation TKI used in patients with Ph+ CML in chronic phase or imatinib-resistant Ph+ CML in the chronic phase or accelerated phase [4]. Owing to the efficacy of tyrosine kinase inhibitors in CML and increased survival of these patients, the long-term side effects of TKIs have become an important focus of studies. Nilotinib has a favorable safety profile with its most common cutaneous side effects being rash (10-28% of patients), pruritus (17-24%), dry skin (13-17%), and alopecia (6%), [1].

Nilotinib affects the BCR-ABL-dependent MAP kinase pathway and may lead to its paradoxical activation in certain cell lines [5]. Activation of this pathway along with preexisting mutations related to UV radiation facilitate the development of keratoacanthomas and SCCs. As these hyperproliferative lesions have a low risk of metastasis and can spontaneously regress, discontinuation of TKI therapy is not generally required [6]. Typical management consists of surgical resection or local ablation, but in patients with multiple and/or unresectable lesions systemic retinoids should be considered [7].

Certain tyrosine kinase inhibitors such as sorafenib and quizartinib have been reported to cause eruptive keratoacanthoma-type SCCs as seen in our patient [2, 3]. However, there is only one other report in the literature of nilotinib promoting the development of SCCs or KAs [8]. In this case, a 72-year-old woman with Ph+ CML presented with multiple SCCs six months after the introduction of nilotinib. She was started on a systemic retinoid to decrease the proliferation of these tumors, but continued nilotinib therapy with close surveillance by her dermatologist.

## Conclusion

With only one other documented case of eruptive SCCs with the use of nilotinib, it is important for physicians to be aware of this potential adverse

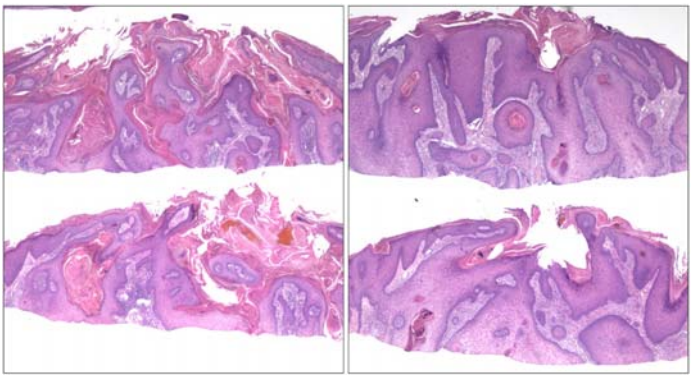


**Figure 2**. *Keratoacanthoma-type squamous cell carcinomas. Histopathological analysis reveals exo- and endophytic squamous proliferations with crateriform architecture, central keratin plugs, and well-differentiated squamous epithelium with pale-staining, eosinophilic, glassy cytoplasm. H&E, 20×.*

effect. Patients taking nilotinib should be closely monitored by a dermatologist. Also, switching to an alternative TKI or the addition of a systemic retinoid should be considered in patients with extensive sun damage or significant history of nonmelanoma skin cancers who develop eruptive SCCs on nilotinib therapy.

## Potential conflicts of interest

The authors declare no conflicts of interests.

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