



Published in final edited form as:

J Am Acad Dermatol. 2009 August ; 61(2): 360–361. doi:10.1016/j.jaad.2009.02.004.

The array of cutaneous adverse effects associated with sorafenib

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To the Editor: We read with interest “Dermatologic symptoms associated with the multikinase inhibitor sorafenib” by Robert et al¹ in the February 2009 issue of the *Journal*. The frequency of sorafenib-associated dermatologic side effects and their impact on quality of life highlight the important role of dermatologists in caring for these patients. We wish to share our experience with oncology patients receiving sorafenib at the National Cancer Institute. We found skin changes similar to those described by the authors in addition to some not included in their report.

Sixty-five patients on sorafenib therapy for solid tumors were evaluated in the Dermatology Clinic from August 2005 - December 2007: 24 individuals were examined at baseline and followed for the development of dermatologic side effects (prospective cohort) and 41 individuals were examined after developing cutaneous lesions (consultation cohort). The cutaneous adverse effects discussed by the authors were similarly encountered in both of our cohorts: hand-foot skin reaction/HFSR (63% prospective cohort; 78% consultation cohort), facial/scalp erythema/dysesthesias (63%; 68%), nail changes (33%; 32%), alopecia (21%; 39%), rash/exanthems (21%; 10%), cysts (8%; 27%), eruptive keratoacanthomas (4%; 7%), and eruptive nevi² (0%; 2%).

In comparison with the review by Robert et al, our cohorts had a much higher incidence of HFSR.³ Dermatologic adverse effects identified in our patients but not reported in Robert’s review include the development of a generalized keratosis pilaris-like eruption (21% prospective cohort; 41% consultation cohort); stomatitis (17%; 22%), inflamed seborrheic keratoses (13%; 10%), and leukocytoclastic vasculitis⁴ (0%; 2%).

The histology of the generalized keratosis pilaris-like eruption was typical for keratosis pilaris (Fig 1). The findings of a keratosis pilaris-like eruption, eruptive keratoacanthomas and multiple cysts support the hypothesis that sorafenib causes alterations in the keratinocyte differentiation/proliferation pathways.

While some of the exanthematous eruptions experienced by our patients resembled erythema multiforme (EM) clinically, multiple biopsies demonstrated only mild superficial perivascular lymphocytic infiltrates with no evidence of basal vacuolization nor necrotic keratinocytes as would be expected in EM. A previously reported patient, who presented with erythema multiforme-like lesions, was demonstrated to have leukocytoclastic vasculitis on histologic

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Conflicts of Interest Disclosure: The authors have no conflict of interest to disclose.

examination. We recommend biopsies from these skin lesions for more precise diagnoses. Sorafenib was successfully re-initiated at reduced doses after temporary rest periods despite these eruptions.

We concur with the assessment of Robert et al¹⁵ that the dermatologic side effects of sorafenib are often manageable with topical therapies and/or dose modifications. Increased awareness within the dermatologic community of the diversity, frequency, and treatment of sorafenib-induced cutaneous adverse reactions will be helpful to patients who require chronic therapy with this medication for their cancers.

Acknowledgments

Funding Sources: This research was supported by the Intramural Research Program of the NIH, Center for Cancer Research, National Cancer Institute.

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A



B

Fig 1. Keratosis pilaris-like lesions. **A**, Fine keratotic papules on thigh of a patient on sorafenib. **B**, Hyperkeratotic plug within hair follicle (Original magnification: x20.)