Acitretin for the treatment of cutaneous T-cell lymphoma

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Background: Bexarotene is the only Food and Drug Administration–approved retinoid for the treatment of cutaneous T-cell lymphoma (CTCL) and is associated with a relatively high frequency of adverse effects. Acitretin has anecdotally been reported to be effective for CTCL.

Objective: We sought to determine the effectiveness and tolerability of acitretin as primary or adjuvant therapy for CTCL.

Methods: We conducted a retrospective chart review of patients with CTCL treated with acitretin at a single tertiary care center.

Results: A total of 32 patients with CTCL were included: 29 had mycosis fungoides, 2 had Sézary syndrome, and 1 had CTCL not otherwise specified. Median patient age was 55 years; 56% were male; 47% were white, 47% black, and 6% other. In all, 3% of patients were stage IA, 69% stage IB/IIA, 16% stage IIB, 6% stage III, and 6% stage IV. Six patients received acitretin alone; 26 received acitretin in addition to another CTCL therapy. The overall response rate was 59%. In all, 25% of patients had stable disease and 16% had progressive disease. Median duration of response was 28 months. Adverse effects were generally mild with 5 patients discontinuing therapy because of these.

Limitations: In this small retrospective chart review, many patients were on other CTCL therapies while on acitretin; therefore precise assessment of response to acitretin alone was difficult.

Conclusions: Acitretin is well tolerated and potentially effective for early-stage CTCL. Response to acitretin, either as adjuvant therapy monotherapy, is comparable with the response to oral agents currently approved for this disease. (J Am Acad Dermatol 2013;68:247-54.)

Key words: acitretin; adjuvant; cutaneous T-cell lymphoma; mycosis fungoides; response; retinoid; therapy.

Cutaneous T-cell lymphomas (CTCL) are a relatively heterogeneous group of disorders of which mycosis fungoides (MF) and Sézary syndrome are the most common subtypes. CTCL is rare (annual incidence 6.4/million persons)[1] and no cure is available, with the possible exception of very early-stage disease. Most patients with CTCL have an indolent course, but the disease can lead to

Abbreviations used:

BSA:	body surface area
CR:	complete response
CTCL:	cutaneous T-cell lymphoma
MF:	mycosis fungoides
PR:	partial response
PR1:	partial response, >50% improvement
PR2:	partial response but not meeting PR1

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Funding sources: None.
Disclosure: Dr Parker is currently an investigator on an industry (Eisai)-sponsored clinical trial using 2 different dosing schedules of bexarotene for cutaneous T-cell lymphoma. Drs Cheeley, Sahn, and DeLong have no conflicts of interest to declare.
Presented as a poster abstract at the Southeastern Consortium Meeting, Atlanta, GA, October 28, 2011.

Accepted for publication July 10, 2012.
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Published online August 22, 2012.
0190-9622/$36.00

http://dx.doi.org/10.1016/j.jaad.2012.07.013

significant disfigurement and adversely impact quality of life.[2] In the minority of cases, progression and even death can occur. Although many therapeutic options are available, no single therapy for CTCL has clearly shown a survival advantage,[3,4] and treatment with many of the currently available agents can lead to untoward adverse effects.

Retinoids are attractive agents for the treatment of CTCL because of their nonimmunosuppressive mechanism of action and ease of administration. The only Food and Drug Administration–approved systemic retinoid for the treatment of CTCL is oral bexarotene, which frequently induces adverse effects such as hyperlipidemia, hypothyroidism, and leukopenia. Acitretin is an orally administered synthetic retinoid familiar to dermatologic practice for the treatment of psoriasis and disorders of keratinization.[5] At our center, acitretin is often offered to patients with CTCL who have not had an adequate response to skin-directed therapy and/or have widespread cutaneous disease and/or contraindications to other accepted CTCL therapies. Although the use of retinoids in combination with other agents for CTCL has been evaluated, beyond case reports, very little is published regarding the efficacy of acitretin for MF/CTCL.[6] We sought to determine the effectiveness of acitretin, either alone or in combination, for patients with CTCL and to compare the response with that of currently approved oral agents. As a secondary objective we sought to determine whether response to acitretin was in any way predictive of response to oral bexarotene.

CAPSULE SUMMARY

- The only Food and Drug Administration–approved systemic retinoid for the treatment of cutaneous T-cell lymphoma is oral bexarotene, which frequently induces adverse effects.
- Acitretin may be a well tolerated and potentially effective therapy for early-stage mycosis fungoides/cutaneous T-cell lymphoma.
- Acitretin should be considered for treatment of patients with cutaneous T-cell lymphoma, either as an adjuvant to standard therapy or in scenarios where other therapies are not practical, not available, or not affordable.

METHODS

Institutional review board approval was obtained. We performed a retrospective chart review of patients with CTCL seen at Emory, a tertiary care/academic medical center in Atlanta, Ga, between 2000 and 2010.

Patient identification

We searched electronic records for patients with a diagnosis of CTCL (*International Classification of Diseases, Ninth Revision* codes 202.00-202.28) who had acitretin listed in their medication profile. Only patients with an unequivocal diagnosis of CTCL based on supportive clinical, histologic, immunophenotypical, and/or molecular parameters were included.[7] Patients who received acitretin for at least 1 month and for whom follow-up was available were included in the review. Information on the following was collected: patient demographics, stage of disease (based on World Health Organization/European Organization for Research and Treatment of Cancer revised staging),[8] duration of disease, number of prior and concomitant therapies, reason for discontinuation of therapies, response and duration of response to acitretin, adverse effects of acitretin, and status at study end (alive/deceased). Also noted was the patient's response to oral bexarotene, if applicable.

Definition of response

Complete response (CR) was defined as complete clinical resolution. Partial response (PR) was defined as unequivocal improvement in disease based on patient and physician assessment. Because this was a retrospective review and because in clinical practice precise cutaneous body surface area (BSA) measurements were not performed in all cases, PR was divided into 2 categories: PR1 = greater than 50% reduction in BSA involvement, and PR2 = unequivocal improvement (response) was noted based on resolution of previously documented index lesions and the absence of new lesions, but the precise percentage BSA improvement was not delineated. Stable disease was defined as disease in which no disease progression was noted. Patients who developed worsening of disease (new lesions or disease stage progression) while on therapy were designated as having progressive disease.

RESULTS

Forty-one patients with CTCL and electronic documentation of acitretin prescription were identified. Of these, 9 patients' responses to and/or actual use of acitretin could not be established or confirmed (eg, failed to fill prescription, lost to follow-up). Of the remaining patients, 32 who received acitretin for at least 1 month were identified and were included in the analysis. Acitretin dosage ranged from 10 to 50 mg daily. Most patients (53%) received 25 mg daily. In