Published in final edited form as:

J Am Acad Dermatol. 2014 March ; 70(3): 583–584. doi:10.1016/j.jaad.2013.11.007.

Lenalidomide in treatment-refractory cutaneous lupus erythematosus: Efficacy and safety in a 52 week trial

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Patients with cutaneous lupus erythematosus (CLE) are frequently intolerant or refractory to traditional first-line treatment with antimalarials, and 10% remain recalcitrant to immunosuppressives or thalidomide.^{1,2} Thalidomide use is limited by side effects, including peripheral neuropathy and teratogenicity, and we thus studied lenalidomide (Revlimid®), a thalidomide analog.^{3,4}

A case series in which severe CLE patients were treated with lenalidomide showed at least a partial response in four out of five patients.⁵ The present study represents the longitudinal data from this initial case series.

We investigated the use of lenalidomide in five refractory biopsy-proven CLE patients, with or without systemic involvement, in a prospective, open-label trial. Subjects took 5 mg daily of oral lenalidomide for the initial 6 weeks. Patients who had responded at 6 weeks lowered their dose to 5 mg every other day, while non-responders were increased to a dose of 10 mg daily. The primary endpoints were the change in the CLASI, quality of life (QoL) measures (SKINDEX-29), and side effects. The physicians' and patients' global assessment, as well as pain, itch and fatigue scores were measured on a 10-point visual analogue scale.

All five patients experienced at least 4-point decreases in CLASI activity at 12-weeks, which met the MCID. Activity scores improved from a mean of 21.4 at week 0 pretreatment to means of 10.8 and 8.6 at weeks 6 and 12 of treatment, respectively. Subject 2 experienced

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Financial Disclosure:

Dr. Werth serves as a consultant to: Xoma, RPS, Janssen/Centocor, Biogen-Idec, Sanofi-Aventis, UVC, Novartis, Idera, Pfizer, Lupus Foundation of America, Medimmune, Rigel, Merck, Genentech, GSK Stiefel, Celgene.

Dr. Werth holds stock ownership/options in UV Therapeutics, grants from the NIH, Amgen, Celgene, Rigel, Novartis, and the VA, and the copyright for the CLASI is owned by the University of Pennsylvania.

a 10-point decrease in activity score at week 12 on the higher dose of 10mg daily. The patient felt this to be clinically inadequate, and she was withdrawn from the study. Subject 5 had an 18-point decrease in CLASI activity, however she was withdrawn at week 20 due to the development of arthralgias and new-onset proteinuria. In the three remaining patients, activity scores continued to improve throughout the 52 weeks (Figure 1). Personal skin scores improved from a mean of 6.0 at week 0 pretreatment to means of 3.0 and 3.8 at weeks 6 and 12, respectively. Skin scores continued to improve for the three patients who remained in the trial at 52 weeks. These findings correspond to improved physician impression scores throughout the duration of treatment. Itch scores, as well as all three QoL parameters improved for these three patients.

Lenalidomide was well tolerated in all but patient 5, described above. This patient may have been predisposed to the development of systemic lupus erythematosus (SLE), as she was the only subject to report arthralgias at baseline. EMGs performed before and after treatment showed no new or exacerbations of peripheral neuropathies, and subject 3's EMG showed moderate improvement after treatment.

Lenalidomide is a potential therapy that has more potent anti-TNF activity as compared to thalidomide, possibly without the risk of peripheral neuropathy. Patients with signs of systemic disease may not be candidates for therapy. This study is limited by the small sample size and lack of a randomized control. Despite this, our results suggest that lenalidomide should be given consideration as a potentially valuable entity in the treatment of antimalarial-resistant CLE.

Acknowledgments

This material is based upon work supported by the Department of Veterans Affairs (Veterans Health Administration, Office of Research and Development, Biomedical Laboratory Research and Development) and by the National Institutes of Health (NIH K24-AR 02207) to VPW. The Copyright for the CLASI is owned by the University of Pennsylvania.

Funding Sources: This funding was supported in part by the NIH.

Role of the Sponsors: The sponsors had no role in the design and conduct of the study; in the collection, analysis, and interpretation of data; or in the preparation, review, or approval of the manuscript. Celgene provided study drug but had no input into the trial design or manuscript.

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Figure 1. Discoid Lupus
Patient 1's discoid lupus lesions at (a) week 0 and (b) week 24.