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Brodalumab in the treatment of moderate to severe psoriasis in patients when previous anti-interleukin 17A therapies have failed

To the Editor: Brodalumab is an interleukin-17 (IL-17)-receptor A antagonist approved for the treatment of moderate to severe plaque psoriasis.[1] Other biologic drugs that target the IL-17 pathway include secukinumab and ixekizumab, although these inhibit IL-17A, not its receptor.

Data from the brodalumab pivotal trials showed that previous exposure to biologic drugs did not affect brodalumab's efficacy.[2] However, how patients respond to brodalumab after treatment specifically with anti—IL-17A agents has failed is unknown. This study evaluated the use of brodalumab in patients with moderate to severe plaque psoriasis in whom treatment with secukinumab or ixekizumab was unsuccessful.

The Icahn School of Medicine at Mount Sinai Institutional Review Board approved this study (10/5/2017). This open-label study was conducted on 39 patients with moderate to severe psoriasis enrolled at 3 sites. All investigators were Risk Evaluation and Mitigation certified. Patients received brodalumab, 210 mg, via subcutaneous injection at the standard dosing schedule up to week 16. All patients had previously experienced treatment failure with an IL-17A agent, defined as treatment with secukinumab or ixekizumab for at least 3 months, without achieving Psoriasis Area and Severity Index (PASI)-75 response or a 50% loss of original improvement.

The primary end point for this study was the proportion of patients achieving a score of "0, clear" or "1, almost clear" in the static Physician's Global Assessment (sPGA) score after 16 weeks of treatment. Secondary end points included improvement in PASI scores. Patients were assessed monthly. Statistical analysis was performed using Stata 15.1 software (StataCorp LLC, College Station, TX).

Table I. Baseline demographics and clinical characteristics of included patients

Baseline characteristic	No. (%) or mean ± SD (95% CI) (N = 39)
Age, y	50.74 ± 2.64 (45.57-55.91)
Sex	
Male	25 (64.10)
Female	14 (34.90)
Baseline PASI	20.36 ± 2.24 (15.97-24.75)
Baseline sPGA	3.41 ± 0.08 (3.25-3.57)
Previous treatment failed	
Secukinumab	16 (41.03)
Ixekizumab	19 (48.72)
Secukinumab and ixekizumab	4 (10.26)
Previously failed biologic drugs, No.	2.23 ± 0.29 (1.66-2.80)

CI, Confidence interval; *PASI*, Psoriasis Area and Severity Index; *SD*, standard deviation; *sPGA*, static Physician's Global Assessment.

Of 41 screened patients, 39 met eligibility requirements and were enrolled in the trial, with 34 patients completing all visits through week 16. The most common reason for early discontinuation was lack of efficacy. The demographics and baseline characteristics of the enrolled patients are detailed in Table I.

As-observed results at week 16 showed PASI-75, PASI-90, and PASI-100 scores in 76%, 50%, and 32% of patients who completed the trial, respectively, and 71% of these patients achieved an sPGA of 0 or 1. The data for the 39 patients, using the last observation carried forward, showed that PASI-75, PASI-90, and PASI-100 scores were achieved in 69%, 44%, and 28% of patients, respectively, with 62% achieving sPGA 0 or 1. Using a nonresponder imputation, PASI-75, PASI-90, and PASI-100 scores were seen in 67%, 44%, and 28% of patients, respectively, with 62% achieving sPGA of 0 or 1 (Fig 1) There were 6 adverse events, none of which were thought to be related to the study drug. There were no serious adverse events during the trial.

These results indicate that most patients whose previous treatment with an anti—IL-17A agent was unsuccessful had significant disease improvement with brodalumab. This may be due to the unique action of brodalumab, which inhibits the IL-17 receptor rather than the IL-17A ligand. Overall, these findings suggest that brodalumab may be a good treatment option for psoriasis patients when treatment with other biologic drugs has failed,

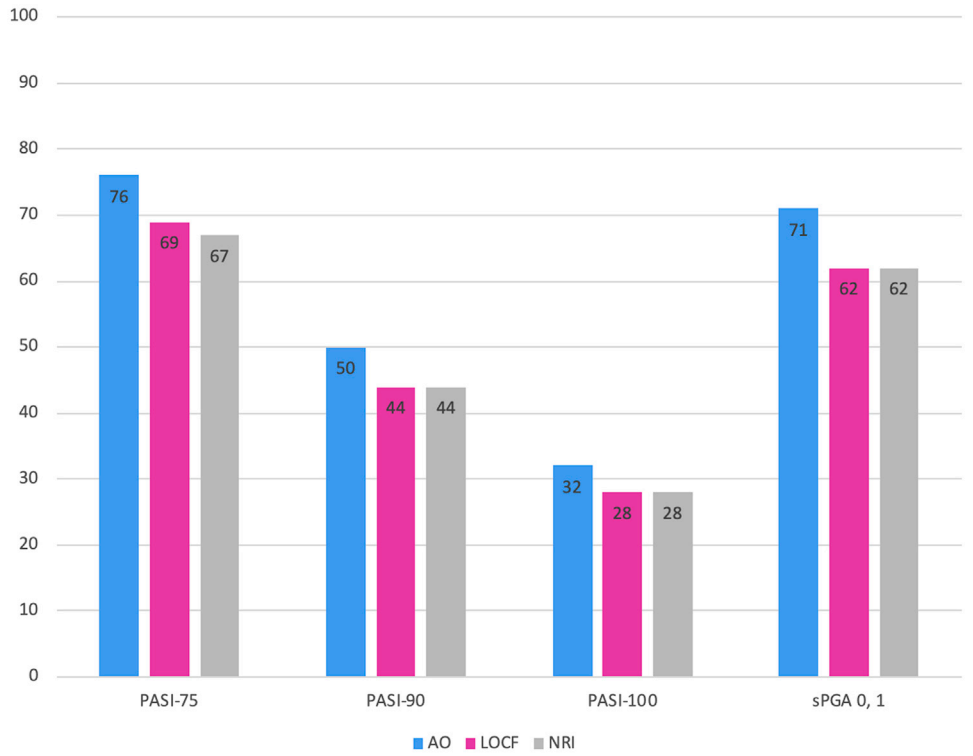

Fig 1. Week 16 results show the percentage of patients achieving Psoriasis Area and Severity Index (*PASI*)-100, PASI-90, PASI-75, and static Physician's Global Assessment (*sPGA*) scores of 0 or 1. *AO*, as observed; *LOCF*, last observation carried forward; *NRI*, nonresponder imputation.

including the anti—IL-17A agents. Although many factors must be considered in choosing the best treatment for psoriasis patients, efficacy is certainly among the most important.[3,4]

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Conflicts of interest: Dr Kimmel participated on an advisory board for Ortho Dermatologics, October 2018. Dr Chima is a consultant for Leo Pharma. Dr Bagel is an investigator, speaker, or advisory board for LEO, Abbvie, Amgen, Eli-Lilly, Novartis, Celgene, Janssen, Boehringer Ingelheim, BMS, and UCB. Dr Lebwohl receives research funds from Abbvie, Amgen, Arcutis, AstraZeneca, Boehringer Ingelheim, Celgene, Clinuvel, Corrona, Inc, Eli Lilly, Foundation for Research & Education in Dermatology, Incyte, Janssen Research & Development, LLC,Kadmon Corp, LLC, Leo Pharmaceuticals, MedImmune, Novartis, Ortho Dermatologics, Pfizer, Sciderm, UCB, Inc, and ViDac and is a consultant for Allergan, Almirall, Arcutis Inc, Boehringer Ingelheim, Bristol-Myers Squibb, Castle Biosciences, Leo Pharma, Menlo, Mitsubishi, Neuroderm, Pfizer, Promius/Dr. Reddy's Laboratories, Theravance, and Verrica. Drs H. Kim, Bares, and S. Kim, and Christopher J. Yao, and Giselle Singer have no conflicts of interest to declare.

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Adverse cutaneous drug reactions with antimalarials in cutaneous lupus and dermatomyositis: A retrospective cohort study

To the Editor: Aminoquinoline antimalarials are first-line systemic treatment for cutaneous lupus erythematosus (CLE) and dermatomyositis (DM). Their mechanism of action relates to their immunomodulatory, anti-inflammatory, and ultraviolet protective properties. Antimalarials can improve pruritus, photosensitivity, and erythema and eliminate the need for corticosteroid/immunosuppressant treatment in some patients with DM and CLE.[1]

Antimalarials may cause adverse cutaneous drug eruptions (ACDRs). Such reactions are uncommon in patients with CLE, whereas the opposite has been observed in patients with DM, in whom they have been reported with an incidence of 13% to 39%.[2-4]

We performed a retrospective review of adult patients with DM and CLE who were seen at the University of Utah Department of Dermatology from January 2013 to January 2018 to evaluate the frequency of antimalarial ACDRs. We included patients who were taking hydroxychloroquine (HCQ) or chloroquine and had at least 3 months of follow-up data noting reaction timing and severity. ACDRs were diagnosed by the treating physician on the basis of history, physical examination, and/or skin biopsy.

We identified 180 patients with DM or CLE (Table I). Demographic characteristics were similar, with the exception of age (mean age, 54 years with DM vs 48 years with CLE [$P = .03$]). The frequency of ACDRs was similar in both groups: 2 of 44 in the group with DM (5%) versus 4 of 136 in the group with CLE (4%) ($P = .68$). All eruptions were associated with HCQ use. More patients with DM were taking immunosuppressants (75% of those with DM vs 26% of those with CLE [$P < .001$]); however, diagnosis did not make a difference in number of ACDRs, even accounting for concomitant immunosuppressive therapy ($P = .83$).

ACDRs occurred 5 to 14 days after initiation of HCQ treatment and were non–life-threatening. Eruptions were characterized as lichenoid, urticarial, or exanthematous and resolved after discontinuation of HCQ treatment. One patient required a brief prednisone taper. No patients were hospitalized.

Two patients were later rechallenged with HCQ without ACDR recurrence. Successful rechallenge has been reported in patients with mild ACDRs to HCQ.[5] There are also reports of successful chloroquine treatment in patients with ACDRs to HCQ, suggesting the feasibility of alternate antimalarial therapy.[1]

The incidence of antimalarial ACDRs may be overestimated in the literature, and it varies between institutions. One possible explanation for the discrepancies may be differences in chemical compositions of generic HCQ formulations. Alternatively, rates of ACDRs may be related to dermatomyositis-specific autoantibody profiles. Ethnic/geographic differences in the frequencies of such autoantibodies are well documented. One recent report suggests that patients with small ubiquitin-like modifier-1 activating enzyme autoantibodies might be at increased risk of antimalarial ACDRs.[4] Interestingly, there is no evidence that patients with DM are at greater risk of ACDRs to other drugs or to other side effects of antimalarials than are patients with CLE. Further epidemiologic study is warranted.

Limitations to our study include its retrospective nature, a small sample size owing to the rarity of these diseases, and a single-institution population consisting of a primarily white demographic. DM-specific autoantibody testing was not available during much of the study period and was therefore not assessed.

We did not observe an increased frequency of antimalarial ACDRs in our patients with DM compared with in our patients with CLE. Antimalarial drugs should be offered to patients with DM and CLE. In patients who develop mild ACDRs, a re-challenge should be considered.

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