

## BRIEF ARTICLE

## Successful Treatment of Refractory Discoid Lupus Erythematosus with Deucravacitinib

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### ABSTRACT

**Introduction:** Discoid lupus erythematosus (DLE) is the most common subtype of chronic cutaneous lupus erythematosus (CLE) that may present with or without systemic lupus erythematosus (SLE). Treatment for DLE remains limited, as there are no medications specifically approved to treat DLE. Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor, is currently being studied for adults with moderate-to-severe discoid and/or subacute CLE. We report a case of successful treatment of refractory DLE with deucravacitinib.

**Case Report:** A 65-year-old female with a longstanding history of systemic lupus erythematosus presented with prominent discoid lesions involving the nose, cheeks, and mid upper cutaneous lip. Having tried topical medications, multiple courses of systemic steroids were attempted, but the patient flared shortly after the tapers. Despite the patient experiencing some improvement on mycophenolate mofetil and prednisone, the decision to switch to deucravacitinib was made due to the patient developing multiple infections while on the former regimen. Three months after starting deucravacitinib, the patient returned with their skin completely clear.

**Conclusion:** A better understanding of the molecular pathogenesis of CLE is informing the development of more targeted therapeutic strategies. TYK2 and Janus Kinases (JAKs) both mediate the signaling of cytokines, some of which play a role in the pathogenesis of SLE. Deucravacitinib binds to TYK2 at the regulatory domain, which is unique to its respective kinase unlike conventional JAK inhibitors that bind to the active domain conserved across all JAKs. Deucravacitinib offers more targeted inhibition with a potentially improved safety profile compared to conventional JAK inhibitors.

### INTRODUCTION

Cutaneous lupus erythematosus (CLE) is an autoimmune disorder that includes a wide range of dermatologic manifestations that may present with or without systemic lupus

erythematosus (SLE).<sup>5</sup> Discoid lupus erythematosus (DLE) is the most common subtype of chronic cutaneous lupus erythematosus which classically presents with indurated coin-shaped scaly plaques that can subsequently progress to atrophy, dyspigmentation, and cicatricial alopecia in

hair bearing areas.<sup>11</sup> Treatment options for CLE remain limited, as there are only FDA approved medications for SLE, not CLE. Current treatment of DLE involves photoprotection, topicals (corticosteroids, calcineurin inhibitors, and retinoids), antimalarials, and systemic immunosuppressants (methotrexate, corticosteroids, and mycophenolate mofetil).<sup>6</sup> Despite recent efforts to develop more targeted therapies, there are no medications specifically approved to treat DLE.<sup>6</sup>

Deucravacitinib is an oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor approved for the treatment of adults with moderate-to-severe plaque psoriasis.<sup>7</sup> The efficacy of deucravacitinib is currently being evaluated in a phase II study in participants with active moderate-to-severe discoid and/or subacute cutaneous lupus erythematosus (SCLE), with or without SLE, that are not well controlled with the current standard of care therapy.<sup>4</sup> We recently reported a refractory case of SCLE that responded to deucravacitinib 6mg monotherapy.<sup>2</sup> Herein, we report a case of treatment refractory DLE that was also successfully treated with deucravacitinib.

## CASE REPORT

A 65-year-old female with a longstanding history of SLE presented for evaluation and management of her prominent discoid lesions. Patient was previously managed by rheumatology but was lost to follow up for over 10 years. Prior results from a punch biopsy of the nares were reviewed which demonstrated interface changes consistent with lupus erythematosus. On exam, the patient had erythematous scaly thin atrophic plaques with notable scarring involving the extensor arms, nose, cheeks, and mid upper cutaneous lip, as well as patchy scarring alopecia (**Figure 1**). Review of systems was

notable for joint pain, photosensitivity, and hair loss. The patient's medical history includes gastroesophageal reflux disease, hypothyroidism, osteoporosis, and Sjögren's syndrome. Laboratory tests revealed a positive ANA 1:320 and Anti-Ro (SSA).

The patient was initially treated with alternating tacrolimus 0.1% ointment, clobetasol 0.05% ointment, and ruxolitinib 1.5% cream which failed to lead to any notable improvement. Patient reported a serious hypersensitivity reaction to hydroxychloroquine in the past, so the decision was made along with her new rheumatologist to start methotrexate (maximum dose of 20mg weekly). Over the course of the next six months, the patient would require multiple courses of systemic steroids but flared shortly after tapering. Patient was subsequently changed to mycophenolate mofetil (MMP) (max dose 2g daily) and prednisone 20mg daily which finally led to some degree of control despite still having erosions in the mouth, nares, upper lip, and extensor arms. However, the patient developed multiple infections including numerous upper respiratory infections, sinusitis, pneumonia, and COVID-19 twice while on this regimen.

Due to the frequent number of infections the patient had experienced with MMP and prednisone, the decision was made to switch to deucravacitinib 6mg daily. At her 3-month follow-up, her skin had completely cleared, including her face and extensor arms (**Figure 2**). Patient tolerated the medication well with no notable adverse events and her 3-month follow-up comprehensive metabolic panel, complete blood count, and fasting lipid panel did not show any appreciable changes from baseline. The patient has been on deucravacitinib for 4 months and has not required any systemic steroids.



**Figure 1.** Presentation before treatment. Erythematous scaly thin atrophic plaques with scarring of the nose, cheeks, and mid upper cutaneous lip.



**Figure 2.** Three months after treatment with deucravacitinib (6mg daily)

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## DISCUSSION

Insights into the molecular landscape of CLE are informing the development of new therapeutic strategies, such as modulation of immune system activation or inhibition of the type I interferon (IFN) pathway.<sup>12</sup> There is an increase in the expression of type I IFN-regulated genes in individuals experiencing DLE and SLE, with IFN-regulated gene expression levels correlating with the severity of cutaneous disease.<sup>3</sup>

Anifrolumab is a fully humanized monoclonal antibody that selectively binds and inhibits the IFN- $\alpha$  receptor 1 and is approved for the treatment of adults with moderate-to-severe SLE.<sup>9</sup> Blum et al. recently reported a case series of three patients with refractory CLE that were successfully treated with anifrolumab, validating the importance of type 1 IFN signaling in CLE.<sup>1</sup> However, given the requirement for intravenous administration, an oral therapy may be preferable for some patients.

Deucravacitinib is an allosteric inhibitor of TYK2, and therefore moderates the signaling of cytokines (type I IFNs, interleukin-10, interleukin-12, and interleukin-23), some of which play a role in the pathogenesis of SLE.<sup>11</sup> Janus Kinases (JAKs) also play a role in mediating a variety of immune responses. Unlike TYK2, which signals select inflammatory pathways, JAK1/2/3 also influence cytokines that facilitate haematopoiesis, myelopoiesis, lipid metabolism, and bone metabolism.<sup>8</sup> Because deucravacitinib binds TYK2 at the regulatory domain which is unique to its respective kinase, unlike the active domain which is conserved across all JAKs, it offers more targeted inhibition with a potentially improved safety profile compared to conventional JAK inhibitors.

There is limited literature on the treatment of DLE with deucravacitinib; however, the use of deucravacitinib to treat CLE is currently being examined and shows promise. An individual with SCLE, whose CLE failed to be managed with topicals, oral steroids, and traditional immunosuppressants, experienced noticeable improvement of her cutaneous symptoms on deucravacitinib with no reported side effects.<sup>2</sup> In a phase II trial of individuals with active SLE, those who received deucravacitinib also reported significant improvement of their cutaneous lesions.<sup>10</sup>

Being a single case report, there are limitations with sample size, short duration of follow-up, and the inability to control for confounding variables. Nonetheless, we have shown a potential benefit of deucravacitinib in the treatment of DLE, adding to the growing body of literature that TYK2 is a valid therapeutic target for CLE. Further studies investigating the long-term safety, efficacy, and tolerability of deucravacitinib will be needed to corroborate our findings.

**Conflict of Interest Disclosures:**

AS: none

NB: none

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