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# NEWS, VIEWS, & REVIEWS

## Anifrolumab for the Dermatologist

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### INTRODUCTION

The type 1 interferon (IFN) signaling pathway is considered a key player in the pathogenesis of systemic lupus erythematosus.[1,2] Elevated serum levels of type 1 IFNs and IFN-inducible gene expression in the peripheral blood of patients with SLE are associated with disease severity, activity, and clinical manifestations.[3-5] Type 1 IFNs are cytokines with myriad effects, including antiviral, antiproliferative, antitumor, and immunomodulatory activities[1]; autoimmune diseases such as SLE may be a result of chronic or dysfunctional activation of this pathway precipitated by self-nucleic acids in autoimmune complexes.[6] Targeting this pathway for the treatment of SLE is of interest; anifrolumab, a type 1 IFN-receptor antibody, is now approved for the treatment of SLE and emerging research suggests particular benefit for refractory cutaneous lupus erythematosus (CLE).[7-9] Dermatologists should be familiar with the mechanism of anifrolumab and its efficacy in treating SLE/CLE and other dermatologic diseases.

### Mechanism of Action

Anifrolumab is a humanized immunoglobulin (IgG)1k monoclonal antibody to the type 1 IFN-α receptor subunit 1 (IFNAR1), blocking the action of all type 1 IFNs and inducing internalization of IFNAR1. Through inhibition of receptor-mediated type 1 IFN signaling, anifrolumab disrupts IFN-responsive gene expression and the downstream, dysfunctional inflammatory and immunological cascades that lead to tissue damage associated with disease activity.[10]

### Indications, Efficacy, and Safety

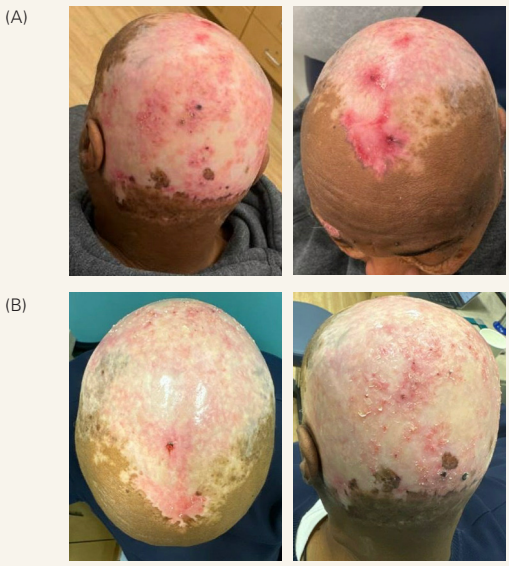
*Systemic Lupus Erythematosus*

Anifrolumab is FDA-approved for the treatment of patients with moderate to severe SLE on standard therapy.[10]Three randomized, double-blind, and placebo-controlled clinical trials – two phase III studies (TULIP-1 and TUILP-2) and one phase IIb study (MUSE)– established intravenous anifrolumab 300 mg administered every 4 weeks as efficacious across multiple clinical disease severity assessments. Notably, anifrolumab led to a sustained reduction in oral corticosteroid dosage, reduced number of flares, and improvement in the cutaneous lupus erythematous disease area and severity index (CLASI).[10-13] Anifrolumab was found to be safe and tolerable across all three trials; common adverse effects included upper respiratory tract infections, infusion-related reactions, and nasopharyngitis, and an increased incidence of herpes zoster was observed in the treatment arm.[10]

*Cutaneous Lupus Erythematosus Subtypes*

Although subtypes of CLE were not specifically characterized in the three major clinical trials, several case reports and series have found anifrolumab to effectively treat several subtypes, including discoid lupus erythematosus (DLE),[14-16] lupus erythematosus panniculitis,[17] and subacute CLE (SCLE),[18] among others. Additionally, a case report described the successful use of anifrolumab in treating Rowell syndrome (erythema multiforme-like lesions in the setting of SLE or CLE) with severe mucosal involvement after failing therapy escalation with multiple first-line treatments and belimumab.[19] Notably, anifrolumab is found to be rapidly effective even in refractory disease (Figure 1A and 1B).[20,21] For example, a case series describing 11 patients with SLE and one or more CLE subtypes (CLE, SCLE, chilblains lupus) treated with anifrolumab 300 mg intravenously every 4 weeks were all found to experience a decrease of CLASI activity of at least 50% at week 16, with a median time of 4 weeks to reach this point.[20] Furthermore, sustained improvement in CLASI activity was observed for all patients and 54% (6/11) experienced a complete response.[20]

**Figure 1.** Patient with DLE previously failed high-potency corticosteroids, topical calcineurin inhibitors, hydroxychloroquine, ustekinumab, and deucravacitinib. **(A)** Before treatment with anifrolumab, large well-defined hypopigmented and erythematous atrophic plaques extending from the mid-frontal to occipital scalp with scattered eroded papules and alopecia, and similar plaques with rims of hyperpigmentation were also present on bilateral cheeks. **(B)** Four weeks following the first infusion of 300 mg of anifrolumab, the patient endorsed less pain and pruritus, and plaques on the face and scalp decreased in size, had less erythema and scale, and had re-pigmentation.



### Future Directions

Anifrolumab may have therapeutic value for other dermatologic conditions involving dysregulation of the type 1 IFN pathway, including dermatomyositis and hidradenitis suppurativa.[22,23] Two individual case reports of adult[24] and juvenile dermatomyositis[25] with skin involvement recalcitrant to immunoglobulin and immunoglobulin and JAK inhibitor therapy, respectively, achieved rapid improvement and disease clearance with anifrolumab 300 mg monthly. Additionally, a clinical trial evaluating the safety and efficacy of intravenous anifrolumab in hidradenitis suppurativa is estimated to begin in June 2024, with a primary endpoint of achieving at least a 50% reduction in abscess and nodule count compared to baseline.[26]

## CONCLUSION

The use of anifrolumab for treating other autoimmune and autoinflammatory conditions appears promising; further exploratory research will determine the extent of its use in dermatology.

## DISCLOSURE

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