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Advancing the Identification and Management of Cutaneous Lupus Erythematosus: Bridging Clinical Challenges and Emerging Therapeutic Strategies

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Learning Objectives

- Describe the pathogenesis, clinical variations, and diagnosis of acute, subacute, and chronic CLE to support comprehensive assessment and timely treatment

- Evaluate current clinical data associated with available and emerging treatment options for CLE

- Implement evidence-based and individualized CLE care that incorporates an interdisciplinary approach to management

CLE = cutaneous lupus erythematosus.

Presentation Overview

01

CLE Introduction and Subtypes

ACLE • SCLE • CCLE classification and clinical features

02

Chronic CLE: DLE and More

Discoid LE • LE profundus • LE tumidus • Chilblain LE

03

Association with SLE and Pathogenesis

Co-prevalence data • Type I IFN • UV injury • T/B cell dysregulation

04

Diagnosis

Labs • Biopsy • Differentiation from rosacea, contact dermatitis, DM

05

Burden and Impact of CLE

QOL • Morbidity • Chronic skin changes • Patients of color

ACLE = acute CLE; SCLE = subacute CLE; CCLE = chronic CLE; SLE = systemic LE; IFN = interferon; UV = ultraviolet; QOL = quality of life; DM = dermatomyositis.

CLE Introduction and Subtypes

Acute • Subacute • Chronic Cutaneous Lupus Erythematosus

Classification of Cutaneous Lupus Erythematosus

Cutaneous Lupus Erythematosus (CLE)

Acute CLE (ACLE)

- Localized (malar/butterfly rash)
- Generalized (photosensitive eruption)
- Bullous LE (tense blisters, anti-type VII collagen Ab)

Subacute CLE (SCLE)

- Annular (polycyclic/centrifugal rings)
- Papulosquamous (psoriasiform)
- Drug-induced SCLE

Chronic CLE (CCLE)

- Discoid LE (DLE)—localized/generalized
- LE profundus (panniculitis)
- LE tumidus
- Chilblain LE

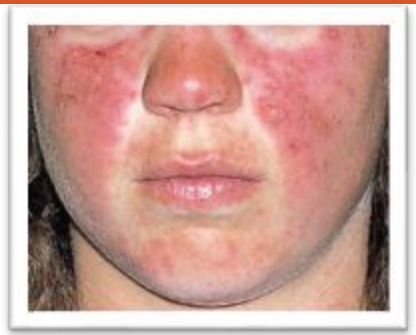
⚠ **SLE Association: ACLE >90% | SCLE ~58% | Localized DLE ~5% | Generalized DLE ~21%**

Gilliam JN, Sontheimer RD. *J Am Acad Dermatol*. 1981;4(4):471-475. Kuhn A, et al. *J Am Acad Dermatol*. 2011;65(6):e195-e213.

Acute Cutaneous Lupus Erythematosus (ACLE): Clinical Features

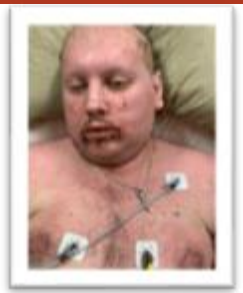
>90%	Malar rash	Transient	ANA+
co-prevalent SLE	ACR/EULAR SLE criterion	heals without scarring	nearly universal

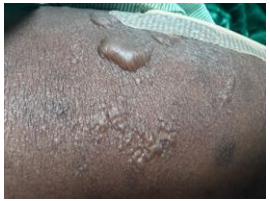
LOCALIZED ACLE—Malar (Butterfly) Rash



- Erythematous, edematous eruption over cheeks + nasal bridge
- SPARES nasolabial folds (key distinguishing feature vs rosacea)
- Photosensitive—worsens with UV exposure
- May have fine scale; generally non-pruritic or mildly pruritic
- Transient; resolves without atrophy or scarring
- Strongly associated with active SLE (>90% co-prevalence)

GENERALIZED ACLE + BULLOUS LE





- Widespread maculopapular photosensitive eruption on trunk, arms
- Hand/finger dorsa: involvement between MCP joints (vs DM: over MCP joints)
- May resemble viral exanthem or drug eruption—biopsy critical
- Bullous LE: tense blisters; anti-type VII collagen antibodies; DIF positive
- Bullous LE often responds to dapsone

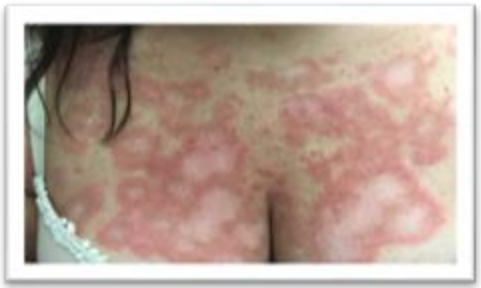
ACR = American College of Rheumatology; EULAR = European Alliance of Associations for Rheumatology; ANA = antinuclear antibody; MCP = metacarpophalangeal; DIF = direct immunofluorescence.

Sontheimer RD, et al. *Arch Dermatol Res*. 2009;301(1):65-70. Kuhn A, et al. *J Am Acad Dermatol*. 2011;65(6):e179-e193.

Subacute Cutaneous Lupus Erythematosus (SCLE): Clinical Features

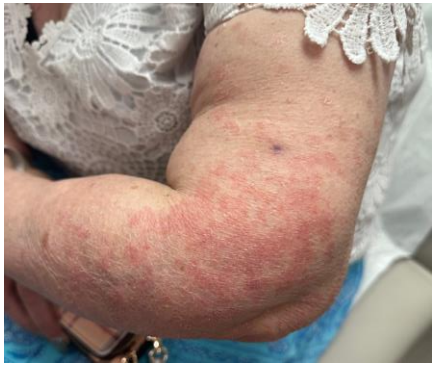
~58%	HLA-DR3	anti-Ro/SSA	Photodistributed
co-prevalent SLE	strong association	positive in ~70-90%	upper trunk, arms, neck

ANNULAR (POLYCYCLIC) SCLE—~50% of SCLE



- Erythematous polycyclic rings that expand centrifugally
- Central clearing; trailing scale at advancing edge
- Photodistributed: upper back, V-chest, shoulders, outer arms
- Heals without scarring (may leave post-inflammatory dyspigmentation)
- Most common SCLE morphology (~50% of cases)

PAPULOSQUAMOUS (PSORIASIFORM) SCLE—~50% of SCLE



- Scaly, erythematous, psoriasis-like plaques
- Same photodistribution as annular subtype
- Key culprit drugs: hydrochlorothiazide, PPIs, calcium channel blockers, TNF-α inhibitors, terbinafine
- Drug-induced SCLE often (but not always) resolves after offending drug withdrawal
- Overlap with annular morphology common

PPI = proton pump inhibitor; TNF = tumor necrosis factor.

Callen JP. *Lupus*. 1997;6(2):203-208. Patel P, Werth V. *Dermatol Clin*. 2002;20(3):373-385. Marzano AV, et al. *Br J Dermatol*. 2011;165(2):335-341.

Chronic CLE: DLE and More

Discoid LE • LE Profundus • LE Tumidus • Chilblain LE

Discoid Lupus Erythematosus (DLE): Clinical Features

Classic Presentation

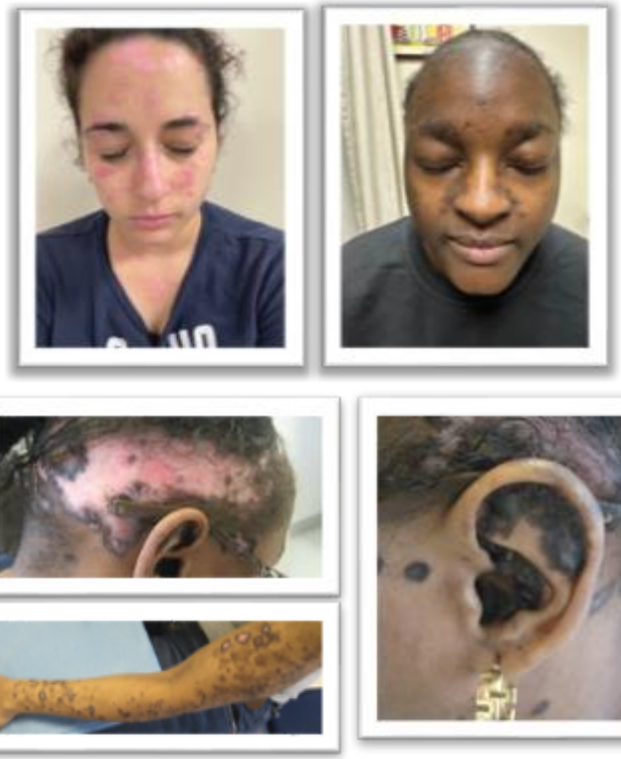
- Indurated, erythematous/violaceous papules or plaques
- Follicular plugging (“carpet-tack sign”) on scale underside
- Photodistributed: scalp, face, ears, V-neck area

Disease Evolution and Scarring

- Active lesions → central atrophy and scarring
- Hyperpigmented border, hypopigmented/atrophic center
- Permanent follicular destruction → scarring alopecia on scalp

Localized vs Generalized DLE

- Localized (above neck only): ~5% SLE co-prevalence
- Generalized (above AND below neck): ~21% SLE co-prevalence
- Generalized DLE requires closer SLE surveillance

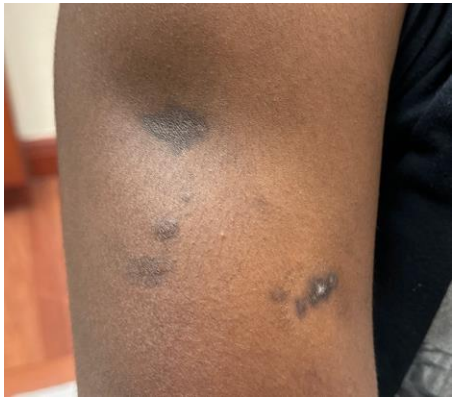


SLE Risk: Localized ~5% | Generalized ~21%

Okon LG, Werth VP. *Best Pract Res Clin Rheumatol.* 2013;27(3):391-404. Vera-Recabarren MA, et al. *Br J Dermatol.* 2010;162(1):91-101. Kuhn A, et al. *J Am Acad Dermatol*. 2011;65(6):e179-e193.

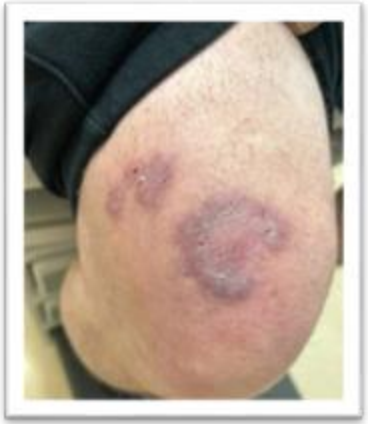
Other Chronic CLE Subtypes: LE Profundus, LE Tumidus, Chilblain LE

LE Profundus (Lupus Panniculitis)



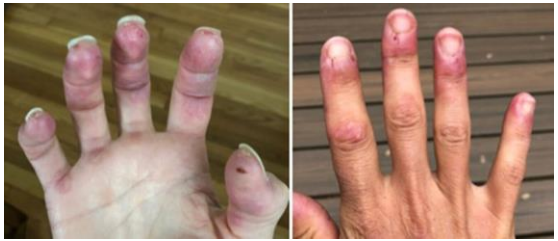
- Deep, firm, rubbery subcutaneous nodules/plaques
- Predilects cheeks, scalp, upper arms, buttocks, breasts
- Often overlies classical DLE lesion in the overlying epidermis
- Resolves with “hammered-out” depressed atrophic scars
- ~30-35% have co-prevalent SLE; may overlap with SCLE/DLE

LE Tumidus



- Urticarial, edematous, smooth papules and plaques
- No surface change: NO scale, NO follicular plugging—key distinction
- Exquisitely photosensitive; often clears in winter
- Generally heals without scarring (lowest scarring risk of CCLE)
- Lowest SLE association among CCLE subtypes

Chilblain LE (Lupus Pernio)



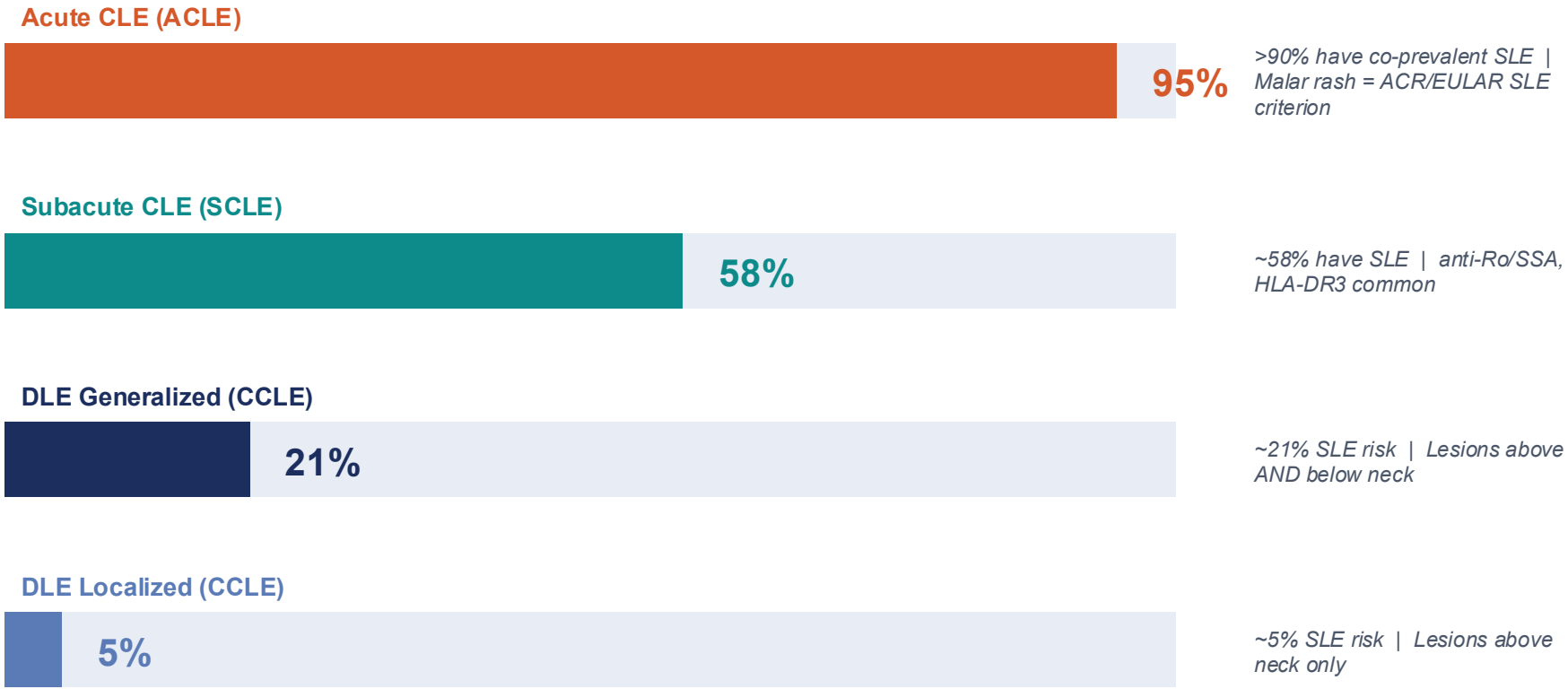
- Perniosis-like erythematous-violaceous plaques on acral sites (toes, fingers, heels, ears, nose)
- Precipitated by cold, wet, damp exposure
- Must distinguish from idiopathic pernio (both worsen in cold)
- Associated with TREX1 mutations in familial cases (Aicardi-Goutières)
- ANA positivity and SLE co-prevalence variable; serologic workup essential

Patel P, Werth V. *Dermatol Clin*. 2002;20(3):373-385.

Association with SLE and Pathogenesis

Co-prevalence data • Immune mechanisms • UV injury cascade

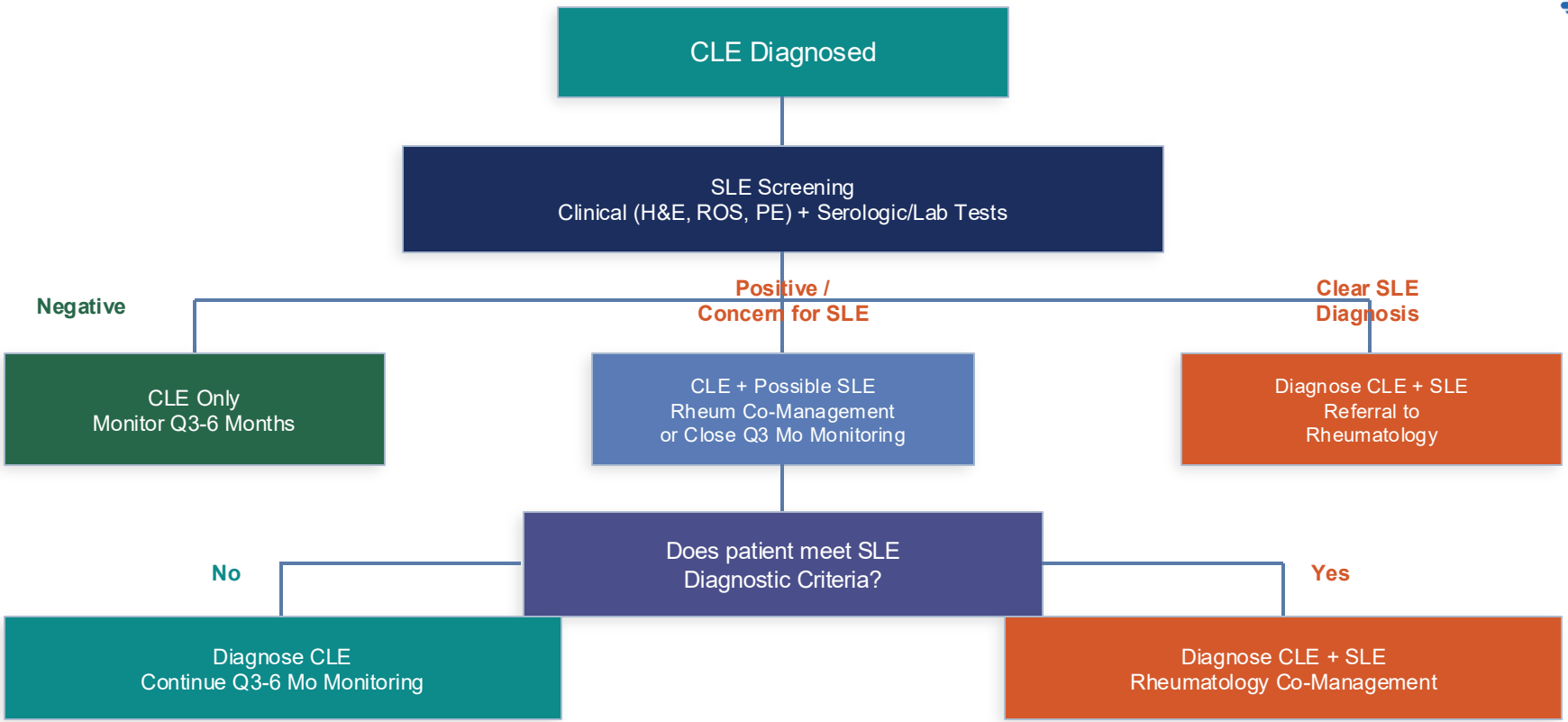
Co-Prevalent SLE Disease by CLE Subtype



Important: Up to 30% OVERLAP between CLE subtypes. CLE can occur without SLE—systematic serologic and clinical SLE screening at every visit is essential.

Merola JF [www.uptodate.com]. Last updated January 26, 2026. https://www.uptodate.com/contents/overview-of-cutaneous-lupus-erythematosus. Biazar C, et al. *Autoimmun Rev*. 2013;12(3):444-54. Watanabe T, et al. *Dermatology*. 1995;190(4):277-283. Klein RS, et al. *Rheum Dis Clin North Am*. 2010;36(1):33-51, vii.

Approach to CLE Patient Monitoring for SLE



H&E = hematoxylin and eosin; ROS = review of systems; PE = pulmonary embolism.
Adapted from Childs B, Merola JF. *J Clin Aesthet Dermatol*. 2025;18(10):40-47.

Pathogenesis of CLE: The Type I Interferon Axis

Key concept: UV radiation → keratinocyte apoptosis → nuclear antigen exposure → innate immune activation → type I IFN production → adaptive immune cascade → skin inflammation and damage

UV-Induced Keratinocyte Injury

- UVB → pyrimidine dimers → keratinocyte apoptosis and necrosis
- Defective clearance of apoptotic debris in lupus (impaired DNase I, C1q)
- Nuclear antigens (Ro/SSA, La/SSB, dsDNA) translocate to cell surface
- NETs (neutrophil extracellular traps) amplify antigen release
- Creates the “danger signal” driving innate immune activation

Type I Interferon Pathway — Central Driver

- pDCs (plasmacytoid dendritic cells) activated by nuclear debris via TLR7/9
- Robust IFN-α production — “IFN signature” detectable in skin and blood
- IFN-I upregulates ICAM-1 on keratinocytes → T cell recruitment
- Basis for anifrolumab (anti-IFNAR1) and litifilimab (anti-BDCA2 on pDCs)
- BAFF upregulated by IFN-I → B cell survival and autoantibody production

Adaptive Immune Dysregulation

- CD4+ Th1/Th17 cells: IFN-γ, IL-17 → sustained inflammation
- CD8+ T cells: key effectors of epidermal injury (lichenoid interface dermatitis)
- Treg cell deficiency → loss of peripheral tolerance
- B cell activation → autoantibodies (anti-Ro, anti-dsDNA, anti-Sm)
- TYK2 (JAK family): critical signaling → deucravacitinib target

Skin-Specific Inflammatory Pathways

- Interface (lichenoid) dermatitis: basal keratinocyte apoptosis, vacuolization
- DIF: granular IgG/IgM/C3 deposits at DEJ = “lupus band” (specific for CLE/SLE)
- Follicular involvement in DLE → follicular plugging → permanent follicle loss
- Melanocyte damage from inflammation → post-inflammatory dyspigmentation
- LE profundus: lobular panniculitis with lymphoplasmacytic infiltrate

Wenzel J. *Nat Rev Rheumatol*. 2019;15(9):519-532. Pellerin A, et al. *EMBO Mol Med*. 2015;7(4):464-476. Niebel D, et al. *Am J Clin Dermatol*. 2023;24(4):521-540.

Diagnosis

Laboratory and Serologic Testing • Skin Biopsy • Differential Diagnosis

Laboratory and Serologic Testing in CLE

Test	Clinical Significance	CLE Subtype Association
ANA (anti-nuclear antibody)	Positive in ~95% of SLE; present in many CLE patients; low titer ANA may be non-specific; high titer or specific patterns (homogeneous) more concerning	All CLE subtypes; required for SLE classification criteria
anti-Ro/SSA	Highly associated with photosensitivity; crosses placenta → neonatal LE and congenital heart block; critical to screen in pregnant patients	SCLE (~70-90%), ACLE, LE tumidus, neonatal LE
anti-La/SSB	Usually co-occurs with anti-Ro; associated with secondary Sjögren features; neonatal LE risk	SCLE, neonatal LE
anti-dsDNA	Highly specific for SLE; correlates with disease activity and lupus nephritis; useful for flare monitoring	SLE-associated CLE, especially ACLE
anti-Smith (anti-Sm)	Highly specific for SLE (~25% sensitivity); pathognomonic for SLE when positive; does not fluctuate with activity	SLE-associated CLE
Complement (C3, C4, CH50)	Low levels indicate complement consumption by immune complexes; correlates with active SLE, especially nephritis; may be normal in pure CLE	SLE co-prevalence monitoring
CBC, CMP, urinalysis + microscopy	Screen for hematologic cytopenias (hemolytic anemia, thrombocytopenia), renal involvement (proteinuria, casts), hepatic disease—SLE criteria domains	All CLE patients as SLE screening
Skin biopsy (H&E + DIF)	H&E: lichenoid interface dermatitis, follicular plugging, perivascular infiltrate. DIF: granular IgG/IgM/C3 at DEJ (“lupus band”)—specific for CLE/SLE; negative DIF does not exclude CLE	Essential for CCLE/DLE diagnosis and DDx

DEJ = dermal-epidermal junction; DDx = differential diagnosis.

Merola JF [www.uptodate.com]. Last updated January 26, 2026. https://www.uptodate.com/contents/overview-of-cutaneous-lupus-erythematosus Sontheimer RD, et al. *Arch Dermatol Res.* 2009;301(1):65-70. Kuhn A, et al. *J Am Acad Dermatol.* 2011;65(6):e179-e193.

Differential Diagnosis: CLE vs Rosacea vs Contact Dermatitis

Feature	ACLE/CLE	Rosacea	Contact Dermatitis
Distribution	Malar eminences + nasal bridge; photodistributed areas	Malar, nose, chin, forehead—centrofacial; telangiectasias	Corresponds to contactant exposure pattern
Nasolabial folds	SPARED (key feature)	INVOLVED	Variable; may be involved
Surface change	May have fine scale; edema; no papules/pustules	Papulopustules, telangiectasias, rhinophyma	Vesicles, oozing, crusting (acute); lichenification (chronic)
Symptoms	Often asymptomatic or mild burning/photosensitivity	Flushing (alcohol, heat, spicy food, sun); burning	Intense pruritus (hallmark of allergic contact dermatitis)
Triggers	UV light; stress; infections (SLE flare)	Alcohol, heat, sun, emotional stress, spicy food	Specific contactant (metal, latex, preservatives, plants)
Serology	ANA positive (often); anti-Ro may be positive	ANA negative	ANA negative
Biopsy	Interface dermatitis; DIF: granular IgG at DEJ	Lymphocytic perivascular infiltrate; dilated vessels; no interface change	Spongiosis; eosinophils; lymphocytic infiltrate; no DIF deposits
Key diagnostic step	ANA, complement, anti-Ro; biopsy if uncertain	Clinical diagnosis; biopsy if uncertain	Patch testing; exposure history

Clinical Pearl: Nasolabial fold sparing = think CLE. Involvement = think rosacea. Intense pruritus = think contact dermatitis.

Differential Diagnosis: CLE vs Dermatomyositis (DM)

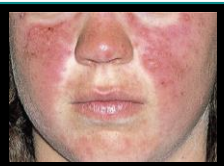
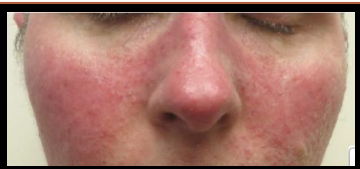
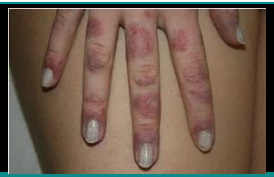
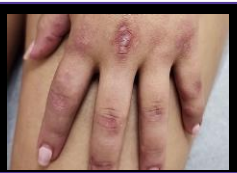
Critical Distinction: DM Gottron papules are OVER the MCP/IP knuckles (extensor skin); ACLE affects the skin BETWEEN the fingers and knuckles (spares the joints). This is one of the most important subtle distinctions in cutaneous lupus vs DM.

Feature	ACLE/CLE	Dermatomyositis (DM)
Facial rash	Malar butterfly rash; spares nasolabial folds	Heliotrope rash (violaceous periorbital erythema + edema); V-sign on chest
Hand/finger rash	Erythema BETWEEN knuckles (interdigital spaces, periungual)	Gottron papules OVER MCP/IP knuckles (extensor surface)—CLASSIC
Nailfold changes	Periungual erythema; nailfold telangiectasias	Dilated, tortuous nailfold capillaries; ragged cuticles; dropout areas (capillaroscopy)
Muscle involvement	Not a feature of CLE (may occur in SLE: myositis)	Proximal muscle weakness is a hallmark; dysphagia; elevated CK/aldolase
Antibodies	ANA, anti-dsDNA, anti-Ro, anti-Sm	ANA, anti-Mi-2 (classic DM), anti-MDA5 (CADM, ILD risk), anti-Jo-1 (antisynthetase), anti-TIF1γ (cancer risk)
Biopsy	Lichenoid interface dermatitis; DIF positive (lupus band)	Vacuolar interface dermatitis; mucin deposition; vascular dilation; DIF typically negative
Systemic associations	SLE; serositis; nephritis; cytopenias	Interstitial lung disease; malignancy (especially adult DM); Raynaud's; esophageal dysmotility
Key diagnostic step	ANA panel, complement, biopsy + DIF	CK, aldolase, myositis antibody panel, biopsy; screen for ILD and malignancy

dsDNA = double-stranded DNA; CK = creatine kinase; ILD = interstitial lung disease.

Callen JP. *Curr Rheumatol Rep*. 2010;12(3):192-197.

Visual Aid: Subtle Diagnostic Features—Side-by-Side Comparison

Nasolabial Folds	 ACLE—SPARED	VS	 Rosacea—INVOLVED
Knuckle Distribution	 ACLE—Between knuckles	VS	 Dermatomyositis—Over knuckles

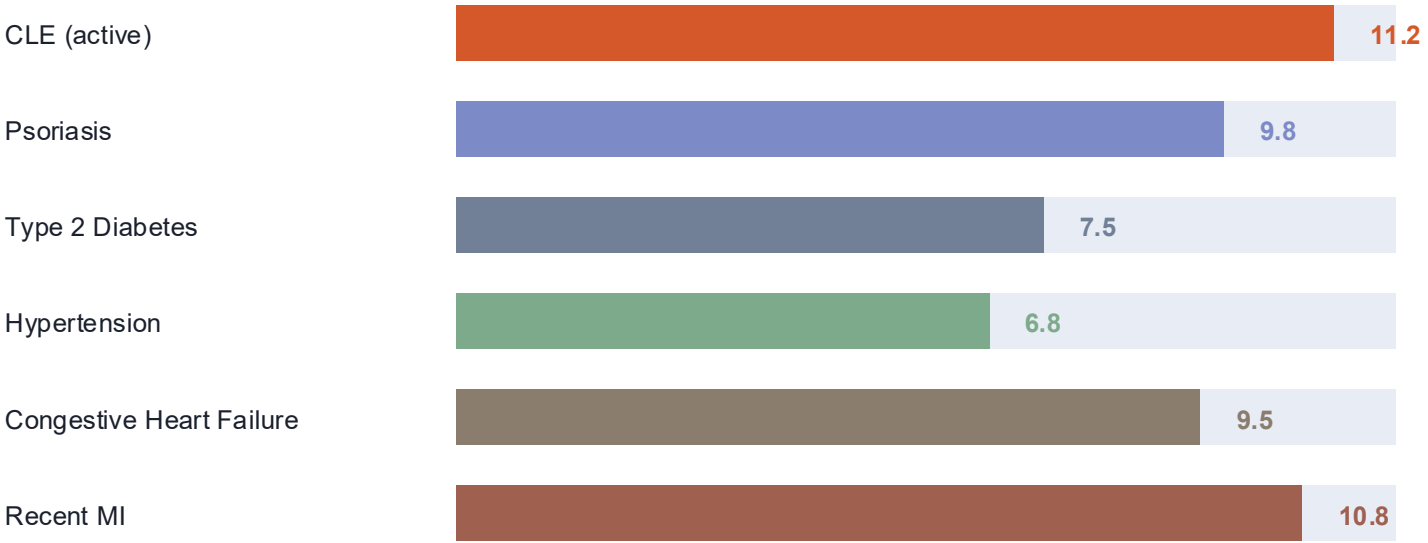
Burden and Impact of CLE

Quality of Life • Morbidity • Chronic Skin Changes

CLE Severely Impairs Quality of Life

CLE-associated QOL impairment is comparable to—or worse than—hypertension, type 2 diabetes, congestive heart failure, and recent myocardial infarction

Mean DLQI Score by Condition (illustrative—data from literature)



Key QOL Predictors

- Facial involvement
- Scarring
- Dyspigmentation
- Generalized disease
- Pain severity
- Fatigue
- Body dissatisfaction
- Activity limitation

DLQI = Dermatology Life Quality Index.

Klein R, et al. *J Am Acad Dermatol*. 2011;64(5):849-858. Ogunsanya ME, et al. *Br J Dermatol*. 2019;180(6):1430-1437. Verma SM, et al. *Br J Dermatol*. 2014;170(2):315-321. Merola JF, et al. Presented at: European Academy of Dermatology and Venereology (EADV) Congress; 2025.

Morbidity and Comorbidities in CLE

Psychological Comorbidities

- Depression: ~25-40% of CLE patients (2-3× general population)
- Anxiety disorders significantly elevated
- Body image disturbance—particularly with facial, scalp involvement
- Social isolation due to visible skin disease
- Suicidal ideation rates elevated in studies of CLE/SLE patients

Cardiovascular Disease

- Accelerated atherosclerosis: CLE/SLE patients have 5-7× increased risk of MI
- Chronic inflammation drives endothelial dysfunction
- Corticosteroid use contributes to metabolic syndrome risk
- Traditional CV risk factors (HTN, DM, dyslipidemia) more prevalent
- Annual lipid panel, BP monitoring essential in management

Photosensitivity Burden

- Activity restriction: outdoor work, recreation, social events
- Occupational impact: up to 30% report work productivity loss
- All CLE subtypes require rigorous sun protection (SPF50+, UPF clothing)
- UV avoidance may worsen vitamin D deficiency—supplementation needed
- Psychosocial impact of activity restriction is underrecognized

Disease Activity and Monitoring Burden

- CLASI (Cutaneous Lupus Erythematosus Disease Area & Severity Index): validated disease activity tool
- Regular labs: CBC, CMP, urinalysis, complement, anti-dsDNA every 3-6 months
- Medication monitoring: hydroxychloroquine eye exams annually (10 mg/kg/day max dose)
- Polypharmacy in SLE-associated CLE adds to monitoring complexity
- Patient education and self-monitoring empower better outcomes

SPF = sun protection factor; UPF = ultraviolet protection factor; CV = cardiovascular; HTN = hypertension; DM = diabetes mellitus; BP = blood pressure; CBC = complete blood count; CMP = complete metabolic panel.

Merola JF, et al. Presented at: European Academy of Dermatology and Venereology (EADV) Congress; 2025. Verma SM, et al.*Br J Dermatol*. 2014;170(2):315-321. Ogunsanya ME, et al. *Br J Dermatol.* 2019;180(6):1430-1437. Klein R, et al. *J Am Acad Dermatol.* 2011;64(5):849-858.

Special Focus: CLE in Patients of Color

Why this matters: CLE disproportionately affects patients with Fitzpatrick IV-VI skin tones. Diagnostic challenges, greater dyspigmentation burden, and underrepresentation in clinical trials compound health disparities.

Diagnostic Challenges

- Erythema is less visually obvious in darker skin—may be subtle or appear violaceous/brown
- Malar rash may present as hyperpigmentation or postinflammatory pigment change rather than erythema
- DLE: dyspigmentation (hyperpigmentation) may be presenting concern rather than active plaque
- Higher biopsy threshold reported in clinical practice—delays in diagnosis are documented
- CLASI scoring validated but may undercount erythema severity in skin of color

Dyspigmentation Burden

- Post-inflammatory hyperpigmentation (PIH) is pronounced in darker skin types
- Hyperpigmented rim of DLE lesions particularly visible and distressing
- PIH persists even after disease activity is controlled—requires separate management
- Significant contributor to QOL impairment, body image concerns, and social impact
- Camouflage cosmetics and PIH-directed treatment (hydroquinone, azelaic acid, retinoids) important adjuncts

Scarring Alopecia Disproportionate Impact

- Scalp DLE-driven scarring alopecia carries profound cultural and psychosocial significance
- Natural hair texture in patients of African descent may initially obscure scalp DLE lesions
- Later-stage diagnosis means more follicular damage by the time of presentation
- Dermatoscopy: white fibrosis, perifollicular erythema, follicular plugging—key early signs
- Hair care practices should be discussed sensitively and incorporated into patient education

Nozile W, et al. *J Drugs Dermatol*. 2015;14(4):343-349.

DLE: Dyspigmentation and Scarring Alopecia

Early Identification • Lesion Evolution • Key Learning Points

DLE: Dyspigmentation—Types, Mechanisms, and Impact

Types of Dyspigmentation in DLE

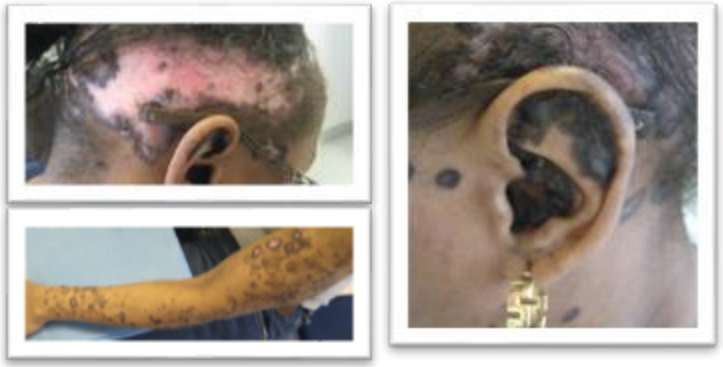
- Post-inflammatory hyperpigmentation (PIH): hyperpigmented rim/periphery—dominant in patients of color
- Central hypopigmentation/depigmentation: follicular dropout and melanocyte loss in healed center
- “Cigarette paper” atrophy: shiny, whitish, wrinkled center in fully healed lesions
- Combination pattern (hyper-rim, hypo-center) is characteristic of resolving DLE

Mechanisms of Pigment Disruption

- Basal keratinocyte and melanocyte damage from interface dermatitis
- Melanin incontinence: melanin drops into dermis → engulfed by macrophages (melanophages)
- Active inflammation → post-inflammatory hyperpigmentation
- Sustained or severe inflammation → permanent melanocyte destruction → hypopigmentation

Clinical Significance

- Dyspigmentation persists even after inflammatory activity is controlled
- Major source of QOL impairment—often more distressing to patients than the active disease
- Particularly prominent and persistent in Fitzpatrick IV-VI skin types
- Post-disease dyspigmentation requires active treatment (see management notes)



Dyspigmentation Management

- Strict photoprotection (SPF 50+, UPF clothing, sun avoidance)
- Treat active CLE to prevent further pigment disruption
- Topical hydroquinone 4% or compounded
- Azelaic acid 15-20% (safe in pregnancy)
- Topical retinoids (tretinoin): promote pigment normalization
- Tranexamic acid (oral/topical) for PIH
- Chemical peels (low-risk superficial): with caution
- Camouflage cosmetics for immediate coverage

Chambers S, et al. *Lupus Sci Med*. 2025;12(2):e001637.

DLE: Scalp Involvement and Scarring Alopecia

Scarring (cicatricial) alopecia from scalp DLE is IRREVERSIBLE once established. The follicle is permanently destroyed. Prevention through early diagnosis and treatment is the only effective strategy.

Early Recognition on the Scalp

- Peripilar casts (scale around hair shaft at follicular ostium)
- Peripilar erythema and edema—often subtle
- Pruritus or burning on the scalp
- Dermoscopy: peripilar erythema, follicular plugging, white fibrosis (late)
- Scalp biopsy (4 mm punch, horizontal section): definitive—shows lichenoid interface folliculitis

Established Scarring Alopecia

- Smooth, shiny atrophic patches—absent follicular ostia
- Central hypopigmentation; hyperpigmented periphery
- Permanent follicular destruction—hair does not regrow
- SCC (squamous cell carcinoma) in chronic DLE scars: rare but documented
- Psychological impact: profound in all patients; amplified by cultural and social factors

Treatment Imperative: Act Early

- Topical superpotent corticosteroids (clobetasol) or intralesional triamcinolone (5-10 mg/mL) first-line
- Hydroxychloroquine (200-400 mg/day; max 5 mg/kg/day)—foundational systemic therapy
- Strict photoprotection: SPF 50+, hats, UV-protective clothing
- Cosmetic camouflage options: scalp micropigmentation, hairpieces (once stabilized)
- Hair transplantation: only in QUIESCENT disease (DLE-free for ≥2 years)

Fabbri P, et al. *Lupus*. 2004;13(6):455-462.

The Importance of Identifying and Addressing DLE Early

DLE is a chronic, scarring condition. Damage is cumulative and IRREVERSIBLE. The window for preventing permanent disfigurement closes once follicular destruction is established.

Scarring is permanent

Once follicular units and dermal architecture are destroyed, restoration is not possible with current therapies. Prevention requires early recognition and adequate treatment. The “treatable window” is during active—not burnt-out—disease.

Dyspigmentation causes lasting distress

Post-inflammatory dyspigmentation, especially in patients of color, is persistent long after inflammation resolves. Early treatment minimizes melanocyte disruption and post-inflammatory hyperpigmentation burden.

Key Learning Points

1. CLE encompasses three major subtypes—ACLE, SCLE, and CCLE—each with distinct clinical features, SLE associations, and treatment implications. Accurate subtype identification is foundational to management.

2. SLE co-prevalence varies widely: >90% in ACLE, ~58% in SCLE, ~21% in generalized DLE, and ~5% in localized DLE. Systematic clinical and serologic SLE screening at every CLE visit is essential, with monitoring every 3-6 months.

3. Pathogenesis centers on UV-induced keratinocyte apoptosis, impaired nuclear debris clearance, and robust type I IFN production by pDCs. Targeted therapies (anifrolumab, litifilimab, deucravacitinib) address these specific pathways.

4. Distinguishing CLE from rosacea (nasolabial fold sparing), contact dermatitis (distribution, pruritus, patch test), and dermatomyositis (Gottron papules OVER vs ACLE BETWEEN knuckles) requires careful clinical and histopathologic assessment.

5. CLE significantly impairs QOL—comparable to or worse than major chronic diseases. Facial involvement, dyspigmentation, and scarring drive the greatest burden, particularly in patients of color where diagnosis may be delayed.

6. DLE is IRREVERSIBLE once scarring is established. Early recognition, aggressive photoprotection, and prompt stepwise treatment (topical → hydroxychloroquine → systemic agents) prevent permanent dyspigmentation and scarring alopecia—the most consequential outcomes of chronic CLE.

Part II: Presentation Overview

05

Innovation: A Path Forward for CLE

Innovations in clinical trials to bring the next generation of targeted therapies

06

Current (Historic) Treatment Algorithm

Discoid LE • LE profundus • LE tumidus • Chilblain LE

07

Future Treatment Algorithm and Emerging Therapies

Where we are in 2026 and where we are going

08

Co-management of CLE/SLE

Treatment considerations

Innovation: A Path Forward for CLE

Innovations in clinical trials to bring the next generation of targeted therapies

LUPUS SCIENCE & MEDICINE™

Development of a working core outcome set for cutaneous lupus erythematosus: a practical approach to an urgent unmet need

Lisa N Guo ,[1,2] Lourdes M Perez-Chada,[2,3] Robert Borucki,[4] Vinod E Nambudiri,[2,3] Victoria P Werth ,[4] Joseph F Merola[2,3,5]

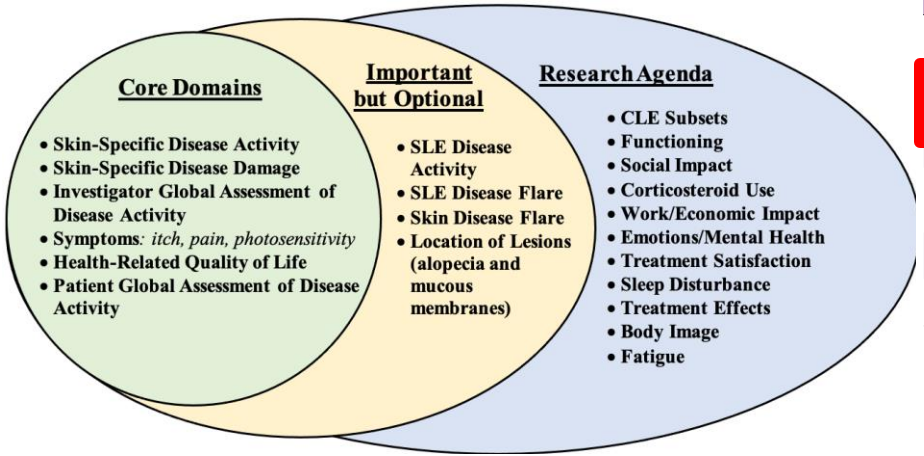


Table 1 Working core outcome measurement set

Core domain	Outcome measurements: CLE-specific	Dermatologic	Generic
Skin-Specific Disease Activity	CLASI-A	–	–
Investigator Global Assessment of Disease Activity	CLA-IGA*		
Skin-Specific Disease Damage	CLASI-D	–	–
Symptoms (pruritus, pain and photosensitivity)	CLEQoL (includes Skindex-29 +3)	DLQI Skindex-29+3 12-Item Pruritus Severity Scale	Itch VAS/NRS Pain VAS/NRS
Health-related Quality of Life	CLEQoL (includes Skindex-29 +3) LEQoL	Skindex-29+3 DLQI	SF-36 EQ-5D
Patient Global Assessment of Disease Activity	–	–	–

CLASI-A = CLASI-Activity; CLA-IGA = cutaneous lupus activity-investigator global assessment; CLASI-D = CLASI-Damage; CLEQoL = cutaneous lupus erythematosus quality of life; LEQoL = Quality of Life of Patients with Lupus Erythematosus Instrument; VAS = visual analog scale; NRS = numerical rating scale; SF-36 = 36-Item Short Form Survey; EQ-5D = EuroQol 5 Dimension survey.

Guo LN, et al. *Lupus Sci Med*. 2021;8(1):e000529.

Letter

LUPUS SCIENCE & MEDICINE

Expert consensus achieved on a working core outcome set for cutaneous lupus erythematosus research in survey following the 5th International Conference on Cutaneous Lupus Erythematosus (ICCLE)

Arianna J Zhang ,[1] Lourdes M Perez-Chada,[1,2] Victoria P Werth,[3] Joseph F Merola[4]

Zhang AJ, *et al. Lupus Science & Medicine* 2024;**11**:e001165. doi:10.1136/lupus-2024-001165

RESULTS

Survey results were collected from 46 out of 114 emailed meeting attendees (40.3% response rate). Respondents primarily identified themselves as dermatologists (95.6%), but also included one rheumatologist (2.2%) and one researcher (2.2%). The majority of respondents reported residency in Asia (65.2%), with smaller subsets from North America (26.1%) and Europe (8.7%). All 46 respondents endorsed the proposed working 'core domain set', and all but one (97.8%) endorsed the 'full core domain set'. All respondents voted to endorse the 'core outcome measures set', including the CLASI and CLA-IGA/CLA-IGA-R. Preference for CLASI percentage change from baseline endpoint was mixed; 43.5% voted in favour of CLASI50, while 39.1% preferred CLASI70 and 17.4% preferred CLASI90.

Zhang AJ, et al. *Lupus Sci Med*. 2024;11(1):e001165.

Journal of INVESTIGATIVE DERMATOLOGY

Articles Publish Topics About Contact

LETTERS TO THE EDITOR · Articles in Press, February 07, 2025

INTER-RATER AND INTRA-RATER RELIABILITY OF THE CUTANEOUS LUPUS ACTIVITY-INVESTIGATOR GLOBAL ASSESSMENT-REVISED (CLA-IGA-R) INSTRUMENT

Joseph F. Merola [1,*] · Arianna J. Zhang [2,*] · Beth A. Childs [3,*] · ... · Victoria P. Werth [8] · Scott A. Elman [9,**] · Lourdes M. Pérez-Chada [5,**]... Show more

Merola JF, et al. *J Invest Dermatol*. 2025;145(8):2085-2088.e2.

- Monash University

  Developing and validating a new treatment response measure for systemic lupus erythematosus clinical trials (TRM-SLE)

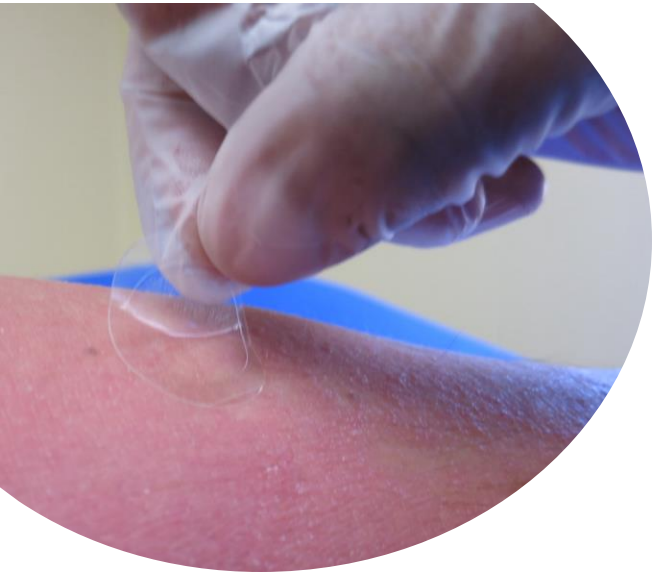
- Lupus Research Alliance

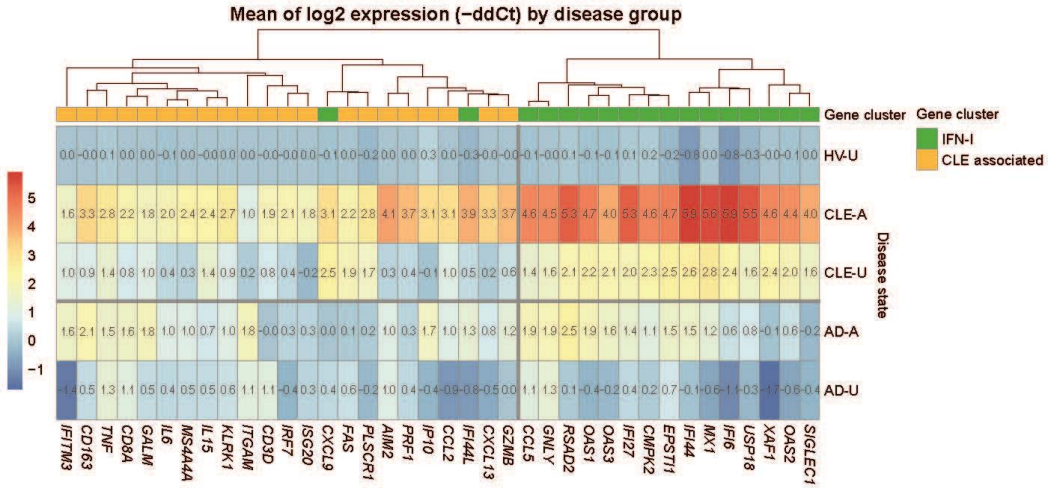
  Lupus Research Alliance Unites the U.S. Food & Drug Administration (FDA) & Lupus Community to Launch Novel Public-Private Partnership

  *Lupus **A**ccelerating **B**reakthroughs **C**onsortium to address challenges impacting lupus trial success and to accelerate treatment breakthroughs*

- International Dermatology Outcome Measures (IDEOM)
- Outcome Measures in Rheumatology (OMERACT)

RNA Tape Sampling in Cutaneous Lupus Erythematosus Discriminates Affected from Unaffected and Healthy Volunteer Skin

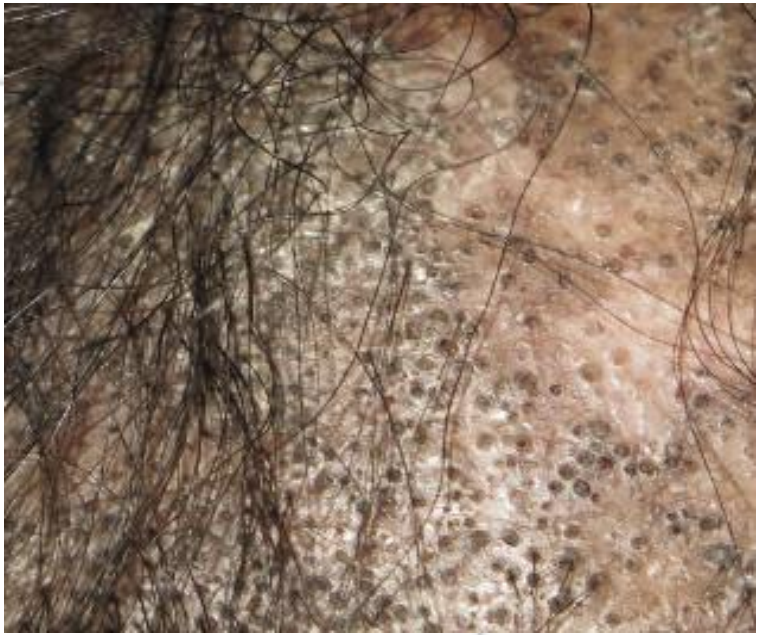




Heat map of interferon (IFN)- and cutaneous lupus erythematosus (CLE)-associated gene expression by disease group

Merola JF, et al. *Lupus Sci Med*. 2021;8(1):e000428.

DLE Classification Criteria



DLE Classification Criteria

Clinical feature	Points assigned
Atrophic scarring	3
Location in the conchal bowl	2
Preference for head and neck	2
Dyspigmentation	1
Follicular hyperkeratosis / plugging	1
Erythematous - violaceous in color	1

A score of **5** yields classification as DLE with 84.1% sensitivity and 75.9% specificity.

A score of 7 yields 73.9% sensitivity 92.9% specificity

Elman SA, et al. *JAMA Dermatol*. 2020;156(8):901-906.

Development and Validation of Algorithms to Identify Cutaneous Lupus Patients using Diagnostic Codes and Prescription Data

Lisa N. Guo, MD[1], Jordan T. Said, MD[2], Vinod E. Nambudiri, MD, MBA, EdM[1*], Joseph F. Merola, MD, MMSc[1,2*]
Brigham and Women's Hospital, Departments of [1]Dermatology and [2]Internal Medicine; **co-senior authors*

Background

- Well-validated methods to identify cases of cutaneous lupus erythematosus (CLE) are lacking
- Without accurate methods to identify CLE patients, large-scale studies are difficult to conduct

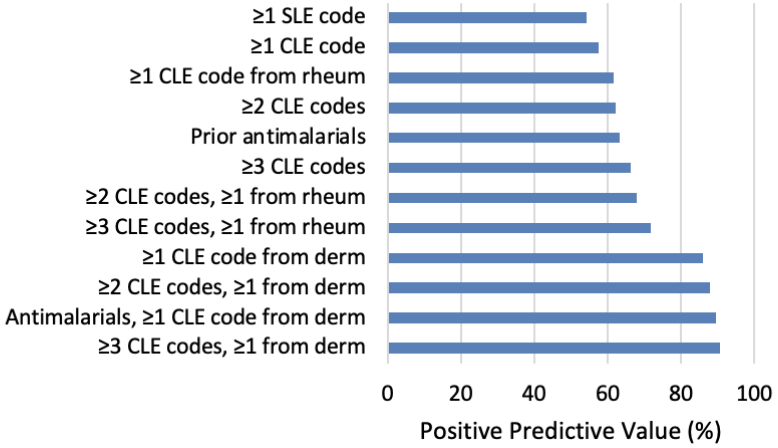
Objective

- Develop and validate the performance of novel algorithms to identify identify patients with CLE from electronic health records

Methods

- Study participants were identified from the Mass General Brigham's clinical data repository
- Inclusion criteria: adults with at least 1 ICD-10 code for cutaneous lupus (L93.0, L93.1, L93.2) from Jan 2016 - Apr 2021
- 300 patients were randomly selected to form the testing cohort
- 12 algorithms were developed to test
- Algorithms were validated using dermatologist or rheumatologist documentation of a CLE diagnosis in clinical notes as the CLE case definition, which was determined by chart review
- Positive prediction values (PPVs) were calculated for each algorithm

Results



- Most patients were white (69.3%) and female (85.7%)
- The most common CLE ICD-10 code was L93.0 (discoid lupus erythematosus)
- 173 patients were validated as truly having CLE (57.7%)
- Algorithms with an ICD-10 code for CLE from a dermatologist had highest PPVs
- The greater the number of CLE ICD-10 codes, the higher the PPV

Disclosures: VN: Imaging Endpoints, McGraw-Hill; JM: AbbVie, Biogen, BMS, Dermavant, Eli Lilly, Janssen, Novartis, Pfizer, Sun Pharma, UCB Pharma, Arena, Avotres, EMD, LEO Pharma, Merck, Regeneron, Sanofi.

Discussion

- Requiring a CLE code from dermatology yielded the highest PPVs, suggesting dermatologists may be particularly accurate in their coding for CLE
- Prior antimalarial prescription with at least one CLE code from a dermatologist had high PPV, but may under-capture less severe cases
- Of note, biopsy results were not used as the case definition to avoid skewing algorithms towards more challenging cases that necessitated biopsy
- Limitations: The study population was drawn from a single healthcare network and was primarily white and female
- Future studies can validate the performance of specific codes to identify subsets of CLE, e.g. L93.0 for discoid lupus

Conclusion

- The algorithm requiring at least 3 CLE codes with at least one code from a dermatologist had the highest PPV
- Validated algorithms that accurately identify CLE cases will allow for further study of CLE patients using EMR, claims data and large real-world databases

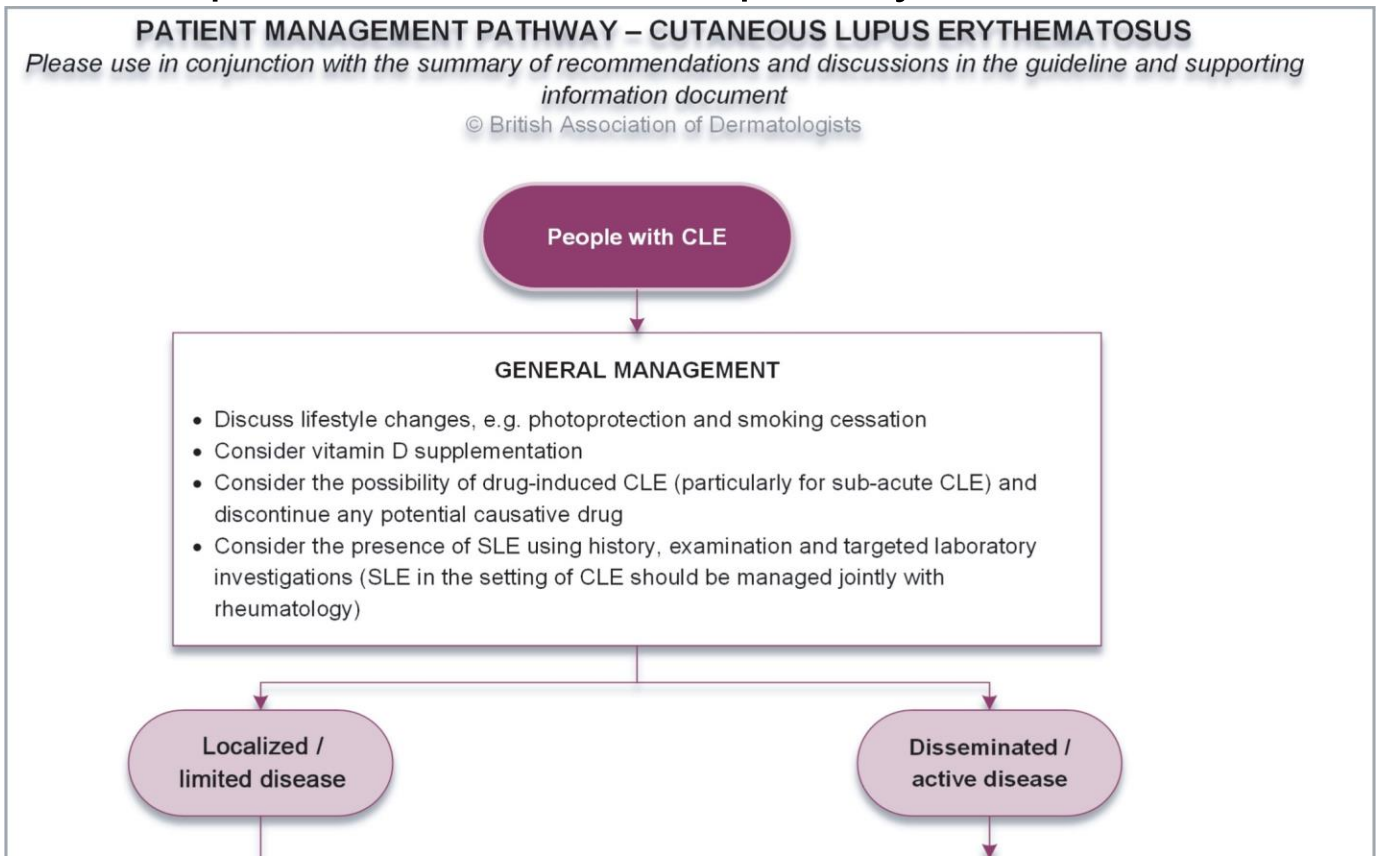
ICD-10 = International Statistical Classification of Diseases and Related Health Problems 10th Revision.

Guo L, Said J, Nambudiri V, Merola J. Development and Validation of Algorithms to Identify Cutaneous Lupus Patients Using Diagnostic Codes and Prescription Data [abstract]. Arthritis Rheumatol. 2022; 74 (suppl 9). https://acrabstracts.org/abstract/development-and-validation-of-algorithms-to-identify-cutaneous-lupus-patients-using-diagnostic-codes-and-prescription-data/. Accessed November 17, 2023.

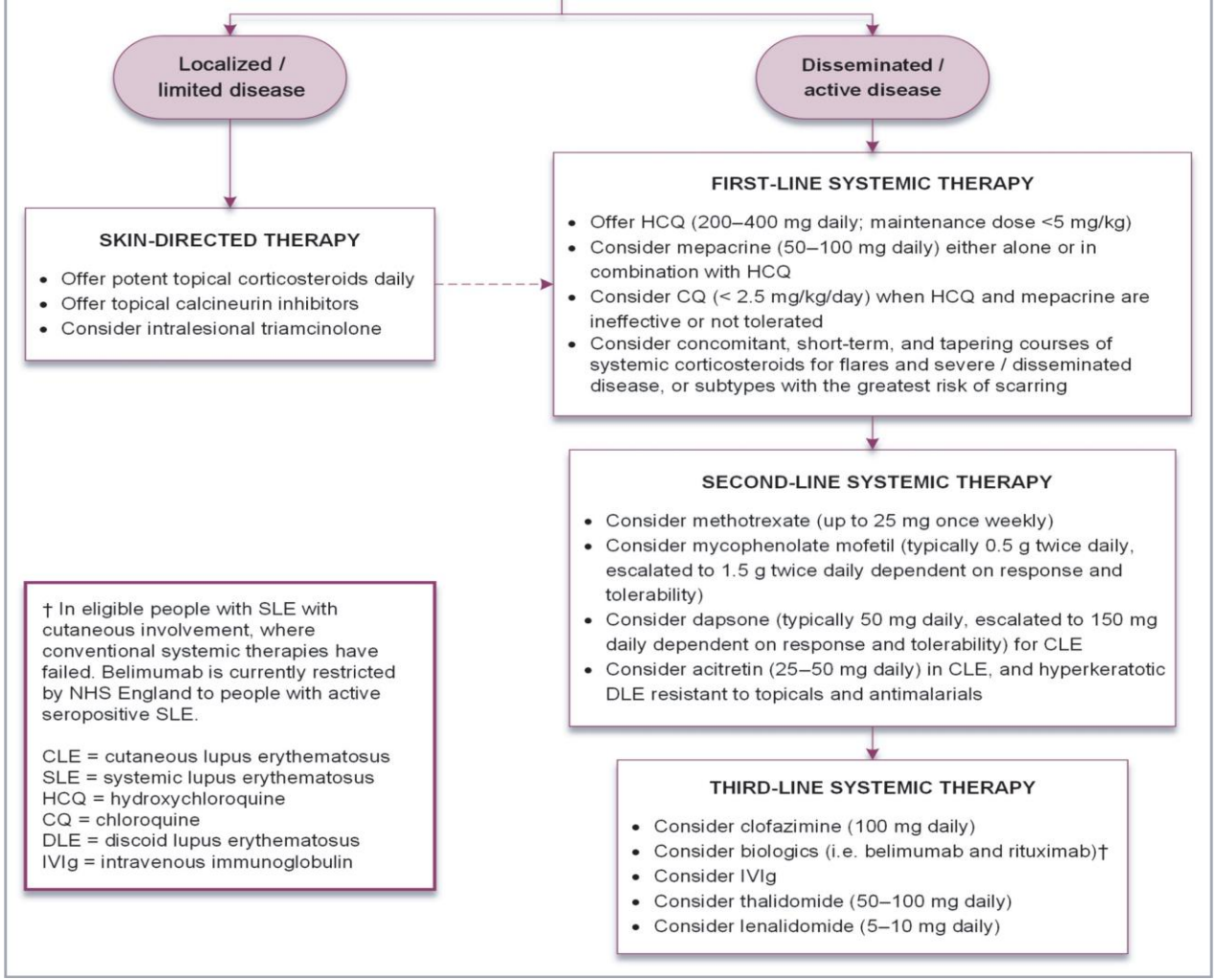
Current (Historic) Treatment Algorithm

Discoid LE • LE profundus • LE tumidus • Chilblain LE

British Association of Dermatologists Guidelines for the Management of People with Cutaneous Lupus Erythematosus 2021



O'Kane D, et al. *Br J Dermatol*. 2021;185(6):1112-1123.

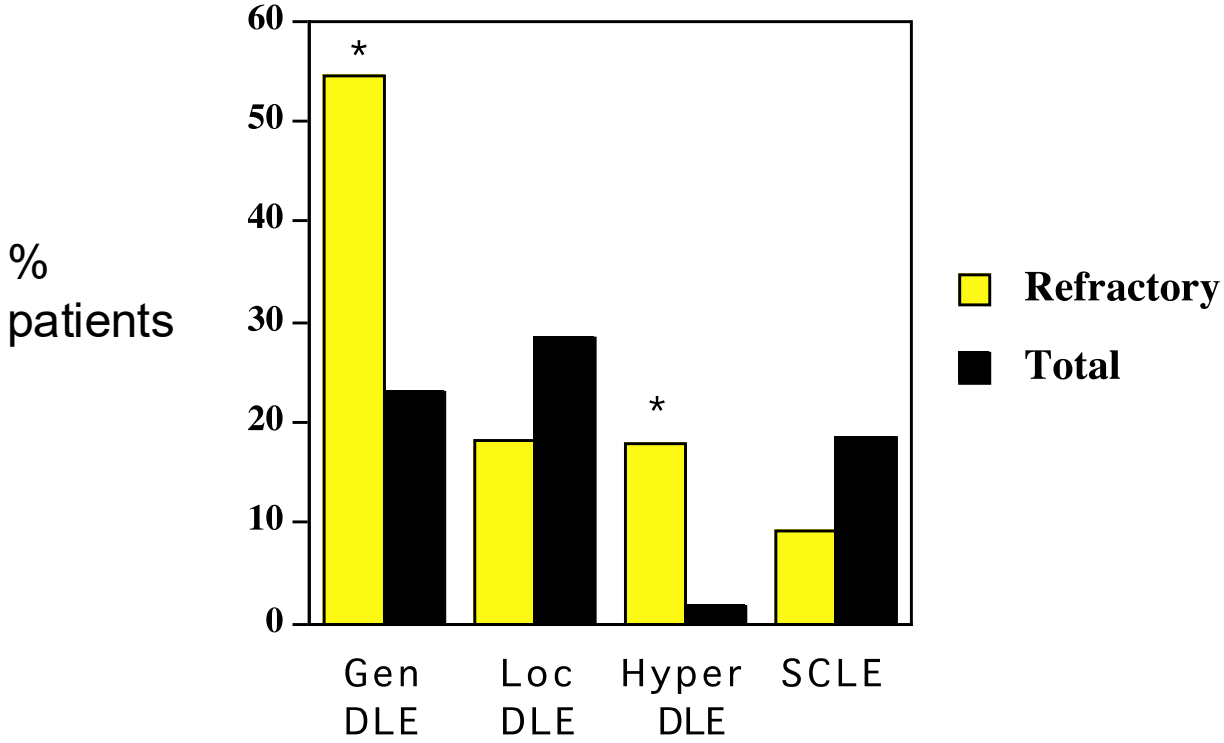


Take-Home Points

1) **First Line:** Anti-malarial first line; consider HCQ->CQ
2) **Second Line:** Consider MTX, MMF 2nd line (also dapsone, acitretin)
3) **Third Line:** Consider thalidomide/ lenalidomide, biologics (belimumab, others)

CQ = chloroquine; HCQ = hydroxychloriquine; MTX = methotrexate; MMF = mycophenolate mofetil.
O'Kane D, et al. *Br J Dermatol*. 2021;185(6):1112-1123.

Subsets of CLE with Refractory Disease



Adapted from Werth V. Moghadam-Kia S, et al. *Arch Dermatol*. 2009;145(3):255-260.

The effect of increasing the dose of hydroxychloroquine (HCQ) in patients with refractory cutaneous lupus erythematosus (CLE): An open-label prospective pilot study

François Chasset, MD,[a] Laurent Arnaud, MD, PhD,[b,c] Nathalie Costedoat-Chalumeau, MD, PhD,[d,e] Noel Zahr, PharmD, PhD,[f] Didier Bessis, MD,[g] and Camille Francès, MD[a]
Paris and Montpellier, France

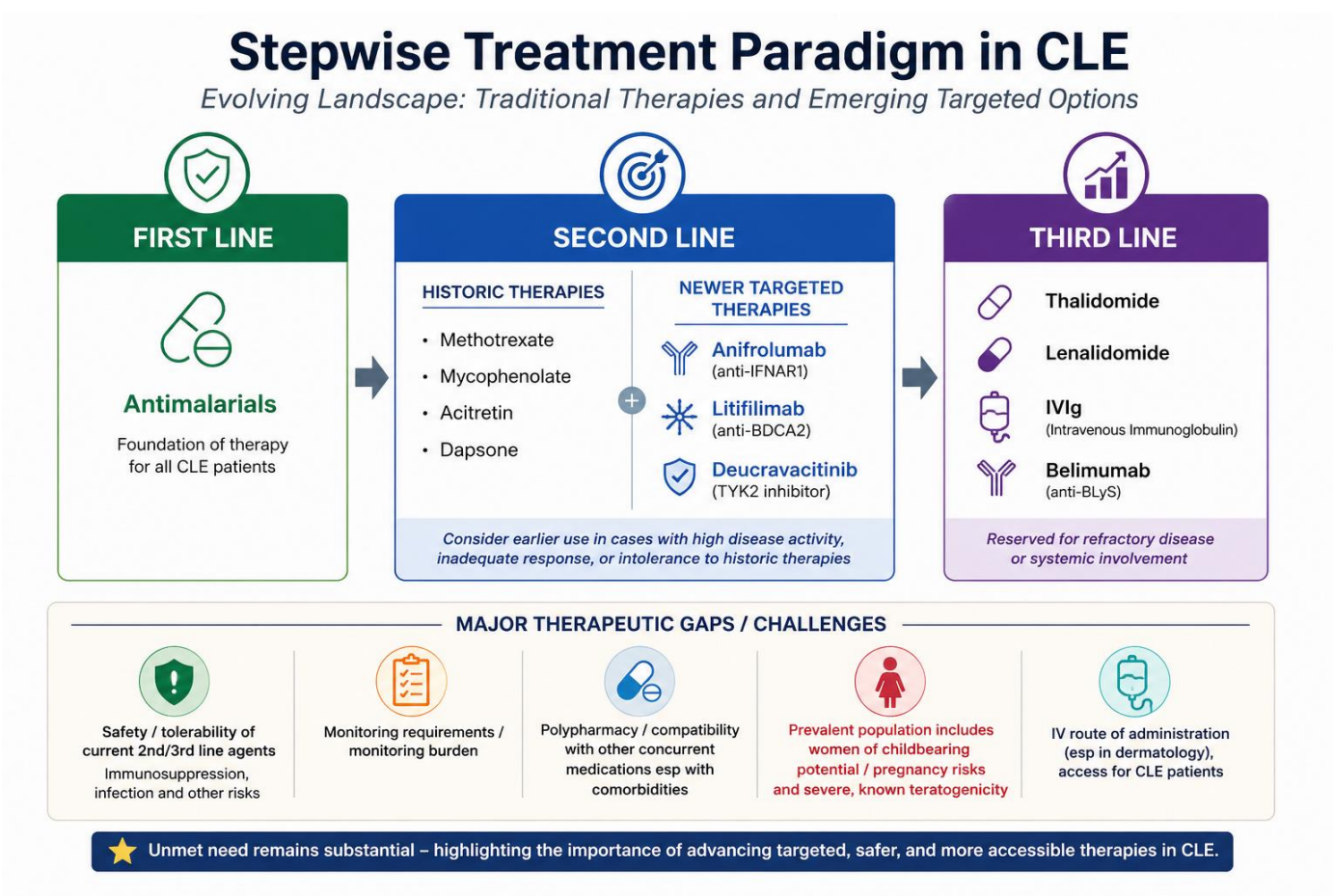
Low Blood Concentration of Hydroxychloroquine in Patients With Refractory Cutaneous Lupus Erythematosus

A French Multicenter Prospective Study

Camille Francès, MD; Anne Cosnes, MD; Pierre Duhaut, MD, PhD; Noël Zahr, PharmD, PhD; Boutros Soutou, MD; Saskia Ingen-Housz-Oro, MD; Didier Bessis, MD; Jacqueline Chevrant-Breton, MD; Nadège Cordel, MD; Dan Lipsker, MD, PhD; Nathalie Costedoat-Chalumeau, MD, PhD

Consider hydroxychloroquine therapeutic blood level testing

Chasset F, et al. *J Am Acad Dermatol*. 2016;74(4):693-699.e3. Francès C, et al. *Arch Dermatol*. 2012;148(4):479-484.

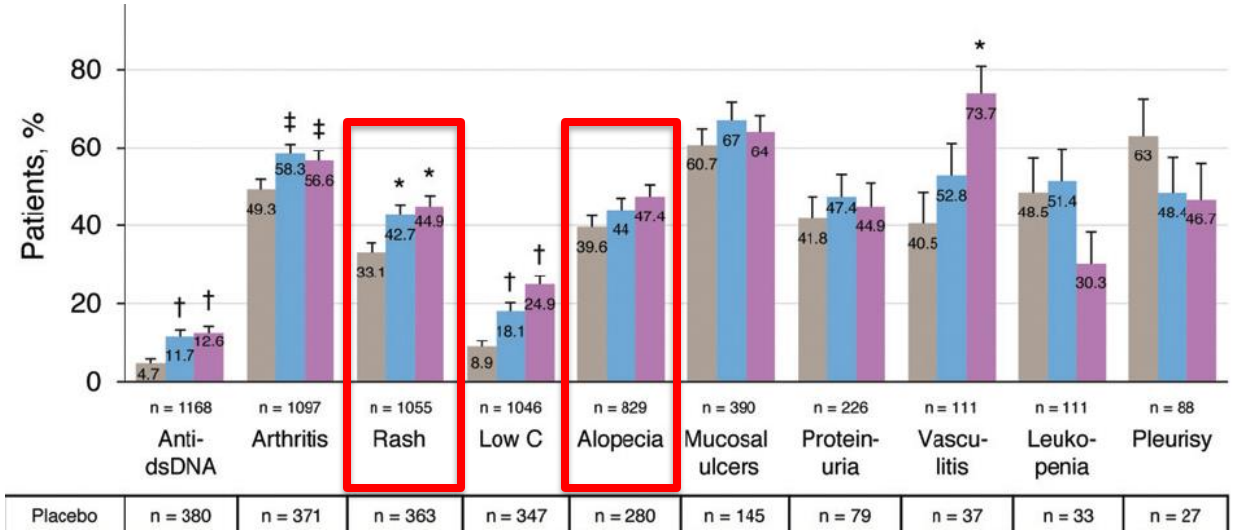


Courtesy of Merola JF.

Future Treatment Algorithm and Emerging Therapies

Where we are in 2026 and where we are going

Belimumab (Anti-BLyS Monoclonal Antibody)

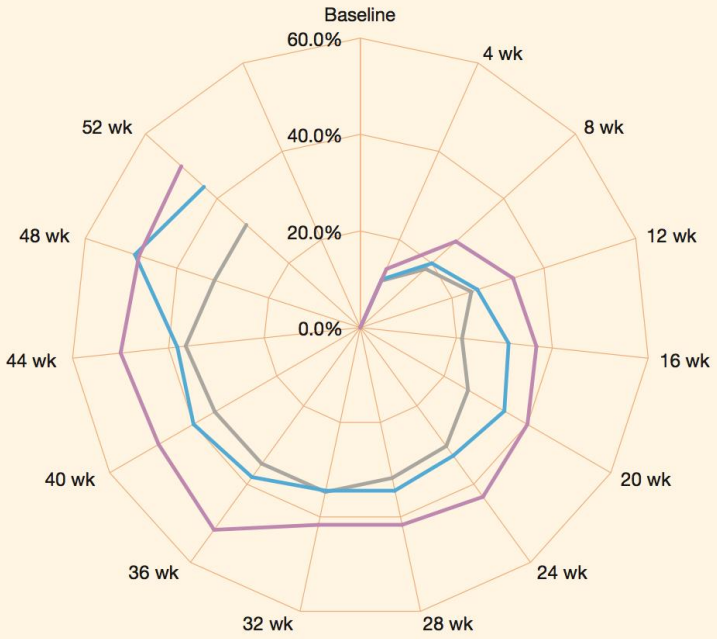


Manzi S, et al. *Ann Rheum Dis*. 2012;71(11):1833-1838.

Post-Hoc BILAG of Phase 3 Belimumab

Mucocutaneous items; pooled data

Active Discoid Lesions (Localized, Includes Lupus Profundus)



Item Not Present

		Belimumab	
Visit wk	Placebo	1 mg/kg	10 mg/kg
8	18%	20%	27%
36	35%	38%	52%
52	32%	44%	50%
	p =	0.18	0.037

Treatment Group[a]

- Placebo (n = 66)
- Belimumab 1 mg/kg (n = 55)
- Belimumab 10 mg/kg (n = 60)

[a]n = number of patients scored positive at baseline.

[ISE_pub_M6 T117]

BILAG = British Isles Lupus Assessment Group.

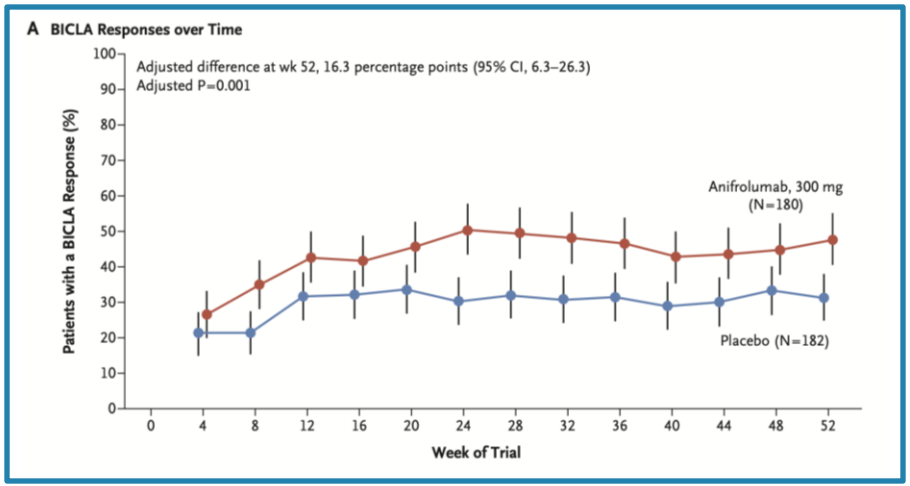
Manzi S, et al. Presented at: ACR/Association of Rheumatology Health Professionals (AHRP) Annual Meeting; 2011.

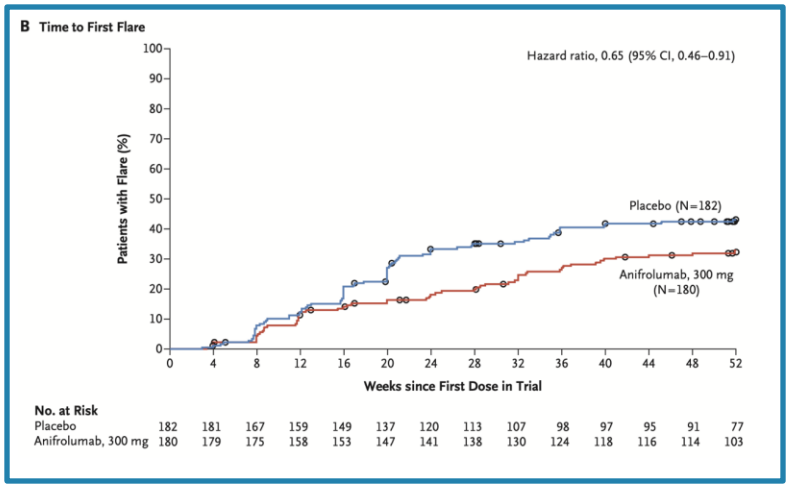
Anifrolumab

Trial of Anifrolumab in Active Systemic Lupus Erythematosus

E.F. Morand, R. Furie, Y. Tanaka, I.N. Bruce, A.D. Askanase, C. Richez, S.-C. Bae, P.Z. Brohawn, L. Pineda, A. Berglind, and R. Tummala, for the TULIP-2 Trial Investigators*

- Type I interferon receptor antagonist
- FDA-approved for SLE



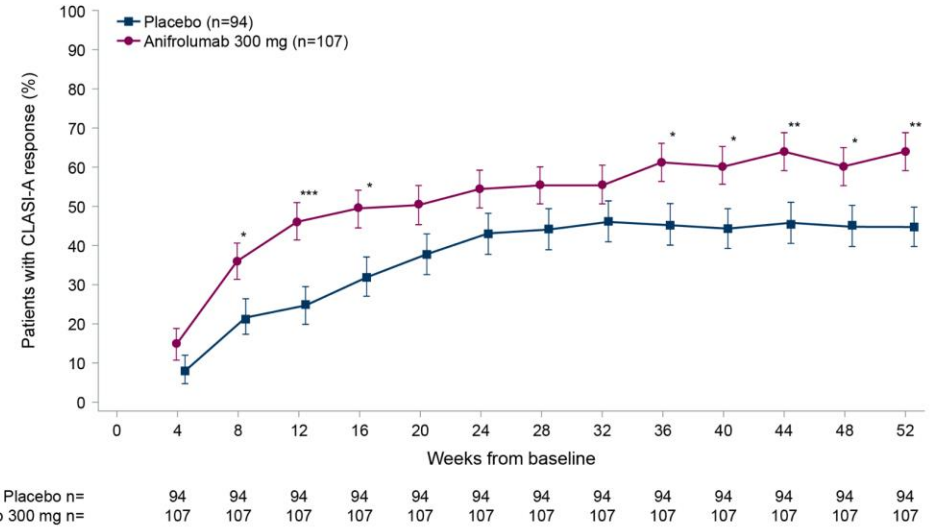


Morand EF, et al. *N Engl J Med*. 2020;382(3):211-221.

Improvement in Cutaneous Symptoms in Patients with SLE Treated with Anifrolumab

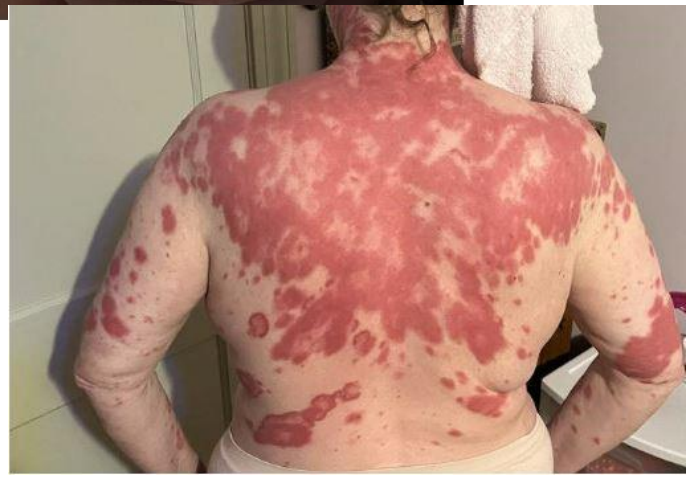
Early and Sustained Reduction in Severity of Skin Disease with Anifrolumab Treatment in Patients with Active SLE Measured by the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI): Pooled Data from 2 Phase 3 Studies

Percentage of Patients with CLASI-A ≥10 at Baseline Achieving ≥50% Reduction in CLASI-A from Baseline over Time in Pooled Data from the TULIP-1 and TULIP-2 Trials

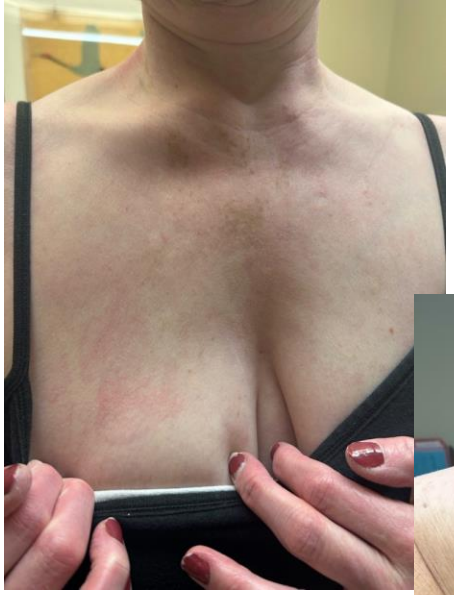


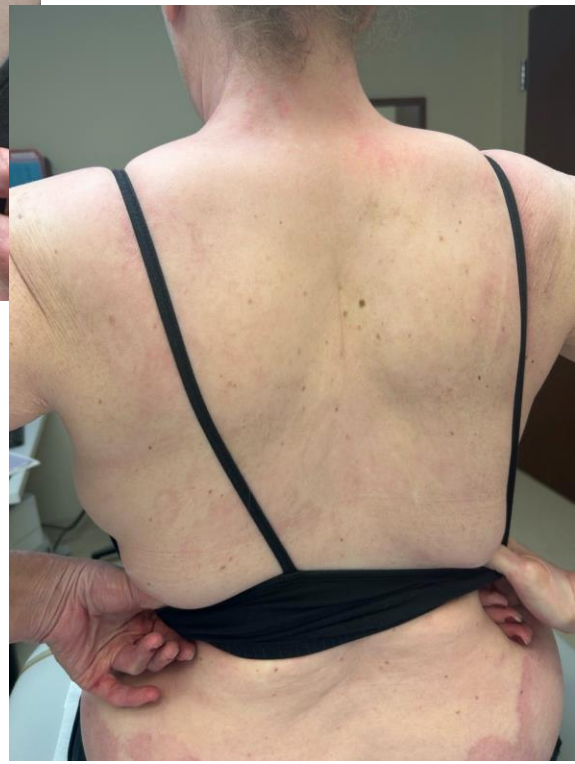
CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; CLASI-A, CLASI activity score; n, number of patients in analysis; OCS, oral corticosteroids.
Points are estimates and bars are standard errors. A response is defined as ≥50% reduction in CLASI-A from baseline for patients with baseline CLASI-A ≥10. Responder rates are calculated using a stratified Cochran–Mantel–Haenszel approach, with stratification factors SLEDAI-2K score at screening, Day 1 OCS dosage, type I IFN gene signature test result at screening, and study (TULIP-1 and TULIP-2).
Nominal *P*-values are presented,*$P<0.05$; **$P<0.01$; ***$P<0.001$.

Werth V, et al. Presented at: ACR Convergence; 2020.



After 1 dose anifrolumab IV





Gaffney RG, Merola JF. *JAAD Case Rep*. 2023;44:71-73.

Efficacy and Safety of Litifilimab in Cutaneous Lupus Erythematosus (CLE): 24-Week Results of the Phase 2 Study,

LATE BREAKER!!!
AAD 2026

AMETHYST Part A

Joseph F. Merola[1,2,3], Victoria P. Werth[4,5], Benjamin F. Chong[1], Filippa Nyberg[6,7], Eric F. Morand[8], David Fivenson[9], Francois Chasset[10], Qianyun Li[11], Michael Schindelar[11], Effie Pournara[12], Weihong Yang[11]

[1]Department of Dermatology, UT Southwestern Medical Center, Dallas, Texas, USA;[2]Division of Rheumatic Diseases, Department of Internal Medicine, UT Southwestern Medical Center, Dallas, Texas, USA; [3]Peter O'Donnell Jr. School of Public Health, UT Southwestern Medical Center, Dallas, Texas, USA; [4]Department of Dermatology, Penn Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA; [5]Corporal Michael J. Crescenz VA Medical Center, Philadelphia, Pennsylvania, USA; [6]Department of Medicine, Karolinska Institution for Medicine, Stockholm, Sweden; [7]Department of Dermatology, Karolinska University Hospital, Stockholm, Sweden; [8]Centre for Inflammatory Disease, Monash University, Melbourne, Victoria, Australia; [9]Fivenson Dermatology, Ann Arbor, MI, USA; [10]Service de Dermatologie, allergologie et médecine vasculaire AP-HP. Sorbonne Université - Hôpital Tenon, Paris, France; [11]Biogen, Cambridge, MA, USA; [12]Biogen, Baar, Zug, Switzerland

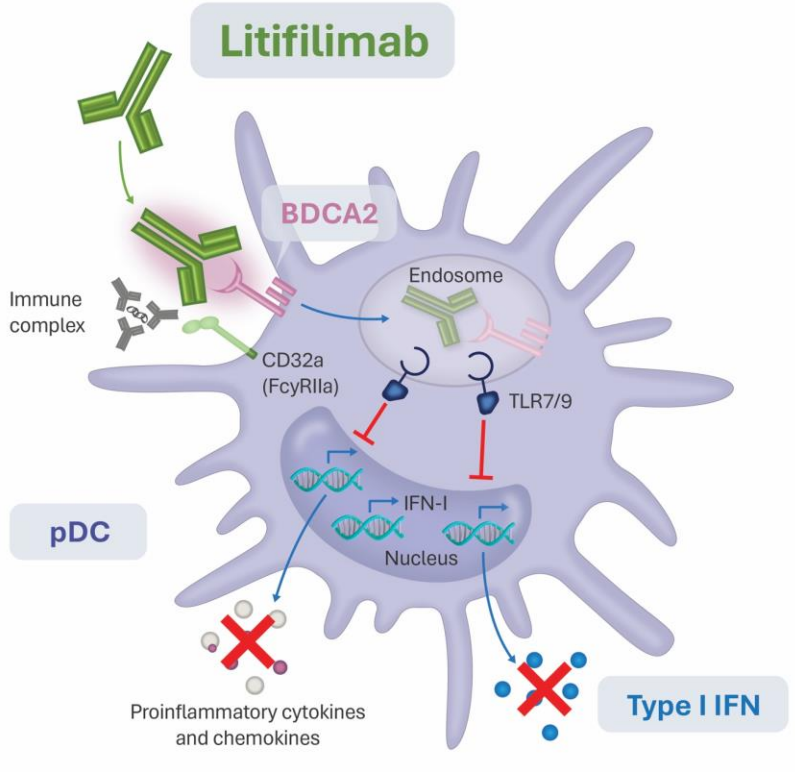
Merola JF, et al. Presented at: American Academy of Dermatology (AAD) Annual Meeting; 2026.

CLE/SLE and Litifilimab: BDCA2 Inhibition

Plasmacytoid dendritic cells (pDCs), specialized immune cells, are an important source of IFN-I and other proinflammatory cytokines and chemokines.[1-3]

Litifilimab is a humanized IgG1 monoclonal antibody that binds to BDCA2 on pDCs, inhibiting the production of IFN-I and other proinflammatory chemokines and cytokines, upstream of other immune pathways.[8-13]

FDA Breakthrough Therapy Designation for Litifilimab (January 2026)



BDCA2 = blood dendritic cell antigen 2; CD = cluster of differentiation; MoD = mechanism of disease; pDC = plasmacytoid dendritic cell; TLR = toll-like receptor.

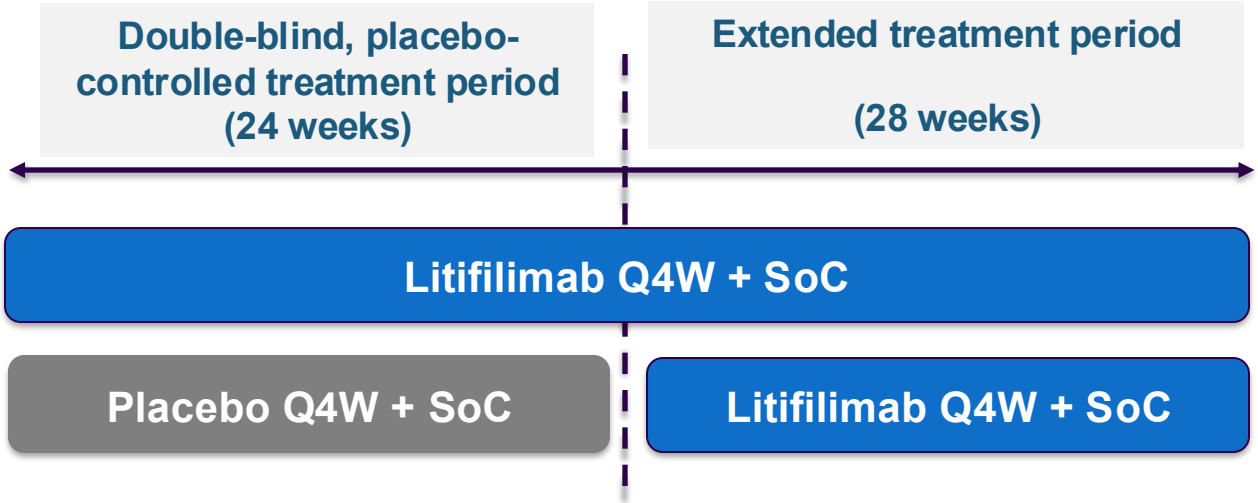
1. Niebel D, et al. *Am J Clin Dermatol.* 2023;24(4):521-540. 2. Maz MP, et al. *J Autoimmun.* 2022;132:102865. 3. Wenzel J. *Nat Rev Rheumatol.* 2019;15(9):519-532. 4. Fetter T, et al. *Front Med (Lausanne).* 2022;9:915828. 5. Fetter T, Wenzel J. *Exp Dermatol.* 2020;29(11):1123-1132. 6. Achtman J, Werth VP. *Arthritis Res Ther.* 2015;17(1):182. 7. Petty AJ, et al. *Curr Allergy Asthma Rep.* 2020;20(5):12. 8. Pellerin A, et al. *EMBO Mol Med.* 2015;7(4):464-476. 9. Furie RA, et al. *J Clin Invest.* 2019;129(3):1359-1371. 10. Furie R, et al. Arthritis Rheumatol. 2025;77(12):1726-1738. 11. Gardet A, et al. *Front Immunol.* 2019;10:275. 12. Rönnblom L, Leonard D. *Lupus Sci Med.* 2019;6(1):e000270. 13. Kaul A, et al. *Nat Rev Dis Primers.* 2016;2:16039.

AMETHYST Part A Study Design[1,2]

AMETHYST is a seamless, two-part, phase 2/3, double-blind, placebo-controlled study.

Key Inclusion Criteria

- Age ≥18 years
- Histologically confirmed CLE ± systemic manifestations
- CLASI-A score ≥10
- Refractory/intolerant to antimalarials
- Stable on lupus SoC



SoC = standard of care.

1. Werth V, et al. *J Invest Dermatol*. 2023;143(Suppl. 5):S100 (Abstract 583). 2. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated April 23, 2026. Accessed February 20, 2026. https://clinicaltrials.gov/study/NCT05531565.

Baseline Characteristics

Baseline characteristics were well balanced between treatment groups

74.2% female
Litifilimab: **76.3%** (45/59)
Placebo: **70.6%** (24/34)

66.7% White
Litifilimab: **61.0%** (36/59)
Placebo: **76.5%** (26/34)

24.7% Hispanic or Latino
Litifilimab: **22.0%** (13/59)
Placebo: **29.4%** (10/34)

Characteristics	Litifilimab (n = 59)	Placebo (n = 34)	Total (N = 93)
CLASI-A total score, mean (SD)	20.2 (9.4)	19.4 (7.2)	19.9 (8.6)
CLASI-A total score > 20 (Severe activity), % (n)	37.3% (22)	32.4% (11)	35.5% (33)
CLA-IGA-R erythema score, % (n)			
0 (Clear), 1 (Almost clear), 2 (Mild)	0	0	0
3 (Moderate)	66.1% (39)	70.6% (24)	67.7% (63)
4 (Severe)	33.9% (20)	29.4% (10)	32.3% (30)
Participants taking CLE/SLE concomitant medications, % (n)	76.3% (45)	76.5% (26)	76.3% (71)

Interpreting CLASI-A Scores[1]: 0–9: mild | 10–20: moderate | 21–70: severe

CLA-IGA-R = Cutaneous Lupus Activity of Investigator's Global Assessment–Revised; CLASI-A = Cutaneous Lupus Erythematosus Disease Area and Severity Index–Activity; CLE = cutaneous lupus erythematosus; SLE = systemic lupus erythematosus.

Klein R, et al. *Arch Dermatol*. 2011;147(2):203-208. Werth V, et al. *J Invest Dermatol*. 2023;143(Suppl. 5):S100 (Abstract 583). ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated April 23, 2026. Accessed February 20, 2026. https://clinicaltrials.gov/study/NCT05531565.

Baseline Characteristics

Concomitant medication use was balanced between treatment groups

Characteristics, % (n)	Litifilimab (n = 59)	Placebo (n = 34)	Total (N = 93)
Participants taking CLE/SLE concomitant medications, % (n)	**76.3% (45)**	**76.5% (26)**	**76.3% (71)**
Antimalarial	71.2% (42)	52.9% (18)	64.5% (60)
Immunosuppressant	22.0% (13)	20.6% (7)	21.5% (20)
NSAIDs	1.7% (1)	0	1.1% (1)
Oral corticosteroid	23.7% (14)	20.6% (7)	22.6% (21)
Topical steroid	13.6% (8)	8.8% (3)	11.8% (11)
Other	6.8% (4)	11.8% (4)	8.6% (8)

CLE = cutaneous lupus erythematosus; NSAIDs = non-steroidal anti-inflammatory drugs; SLE = systemic lupus erythematosus.

Werth V, et al. *J Invest Dermatol*. 2023;143(Suppl. 5):S100 (Abstract 583). ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated April 23, 2026. Accessed February 20, 2026. https://clinicaltrials.gov/study/NCT05531565.

Baseline Characteristics – CLE Subtypes

Majority of participants had DLE or DLE with SCLE

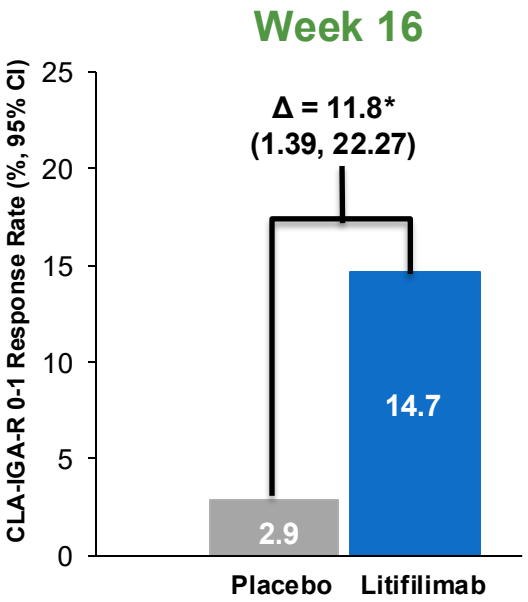
Active CLE Subtype, % (n)	Litifilimab (n = 59)	Placebo (n = 34)	Total (N = 93)
DLE[a]	54.2% (32)	50.0% (17)	52.7% (49)
SCLE[b]	27.1% (16)	35.3% (12)	30.1% (28)
Both DLE and SCLE	11.9% (7)	11.8% (4)	11.8% (11)
Other CLE combinations	6.8% (4)	2.9% (1)	5.4% (5)

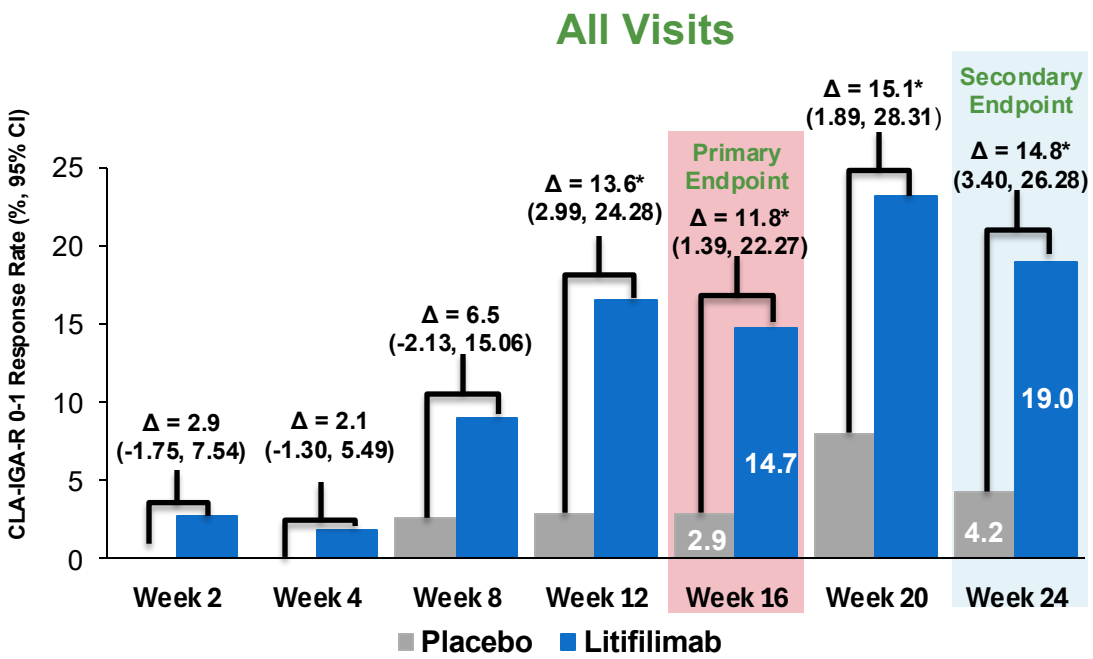
[a]Without SCLE. [b]Without DLE.
CLE = cutaneous lupus erythematosus; DLE = discoid lupus erythematosus; SCLE = subacute cutaneous lupus erythematosus.

Werth V, et al. *J Invest Dermatol*. 2023;143(Suppl. 5):S100 (Abstract 583). ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated April 23, 2026. Accessed February 20, 2026. https://clinicaltrials.gov/study/NCT05531565.

Primary Endpoint: CLA-IGA-R, 0-1 at Week 16

More participants treated with litifilimab had clear/almost clear skin



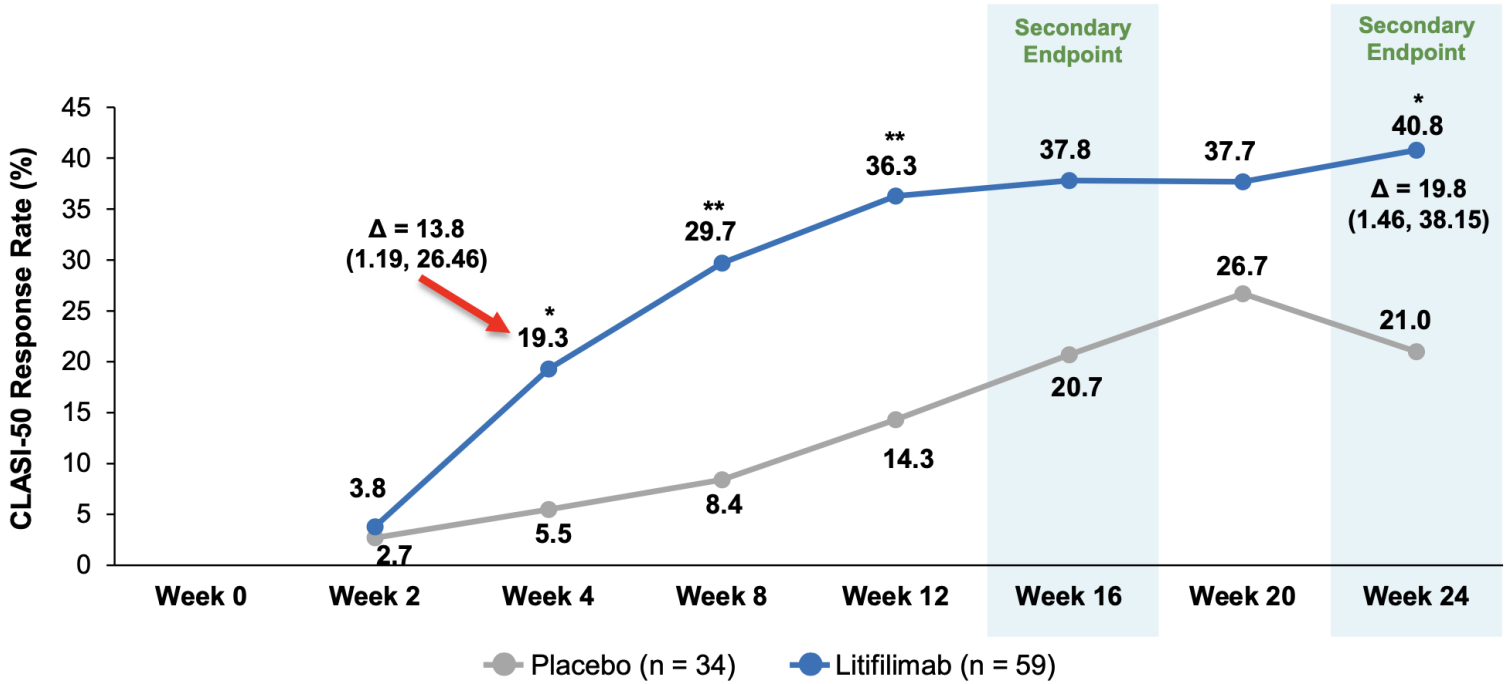


Nominal *P*-values <0.05 are marked with an asterisk (*) and *P*-values <0.01 are marked with double asterisk (**).

Werth V, et al. *J Invest Dermatol*. 2023;143(Suppl. 5):S100 (Abstract 583). ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated April 23, 2026. Accessed February 20, 2026. https://clinicaltrials.gov/study/NCT05531565.

CLASI-50

Litifilimab-treated participants showed early improvement in CLASI-A

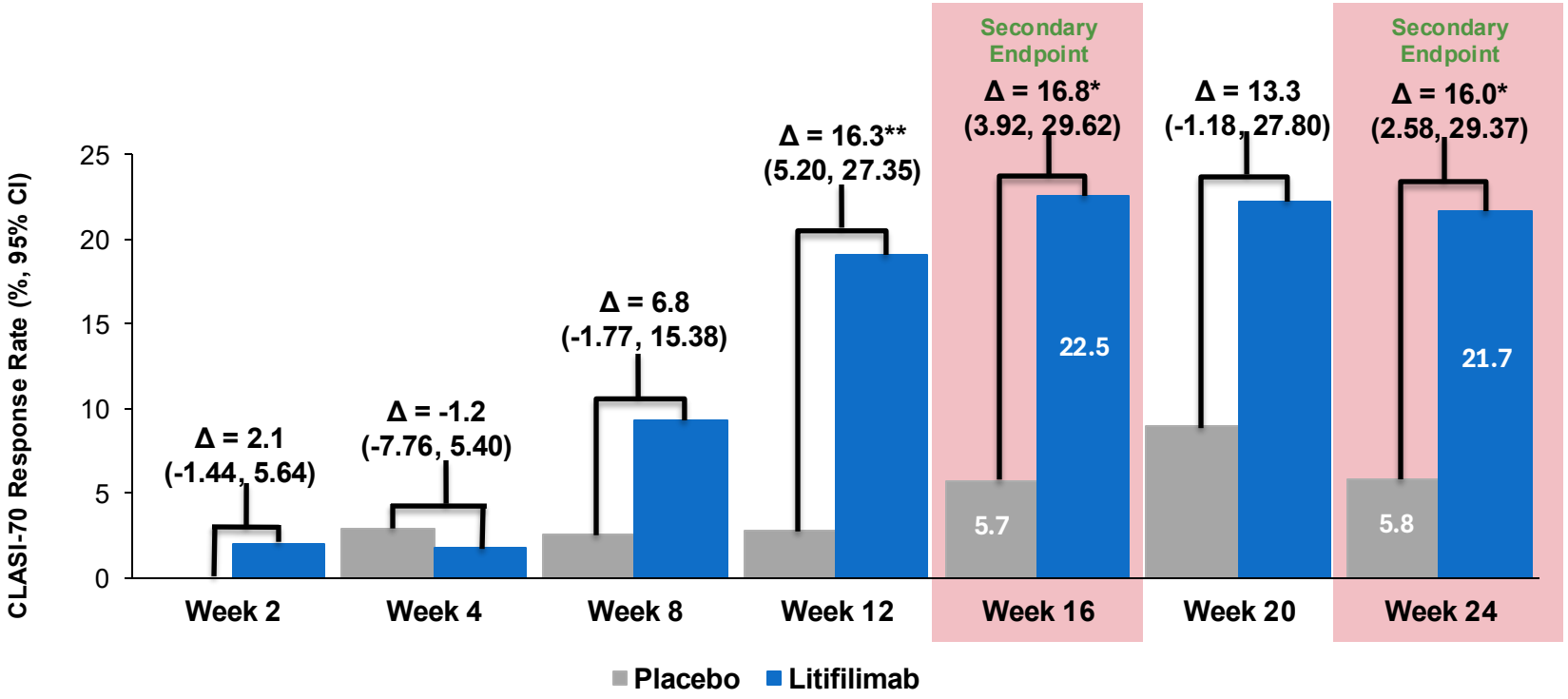


Nominal P values < 0.05 are marked with an asterisk (*) and nominal P values < 0.01 are marked with double asterisk (**). The unconditional treatment effect is estimated based on standardized estimator method using logistic regression model with covariates adjustment. Participants who used disallowed medication or discontinued study treatment due to safety or lack of efficacy were considered as non-responders after the event happened.
CLASI-50 = ≥50% improvement from baseline in Cutaneous Lupus Erythematosus Disease Area and Severity Index–Activity (CLASI-A).

Werth V, et al. *J Invest Dermatol*. 2023;143(Suppl. 5):S100 (Abstract 583). ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated April 23, 2026. Accessed February 20, 2026. https://clinicaltrials.gov/study/NCT05531565.

CLASI-70

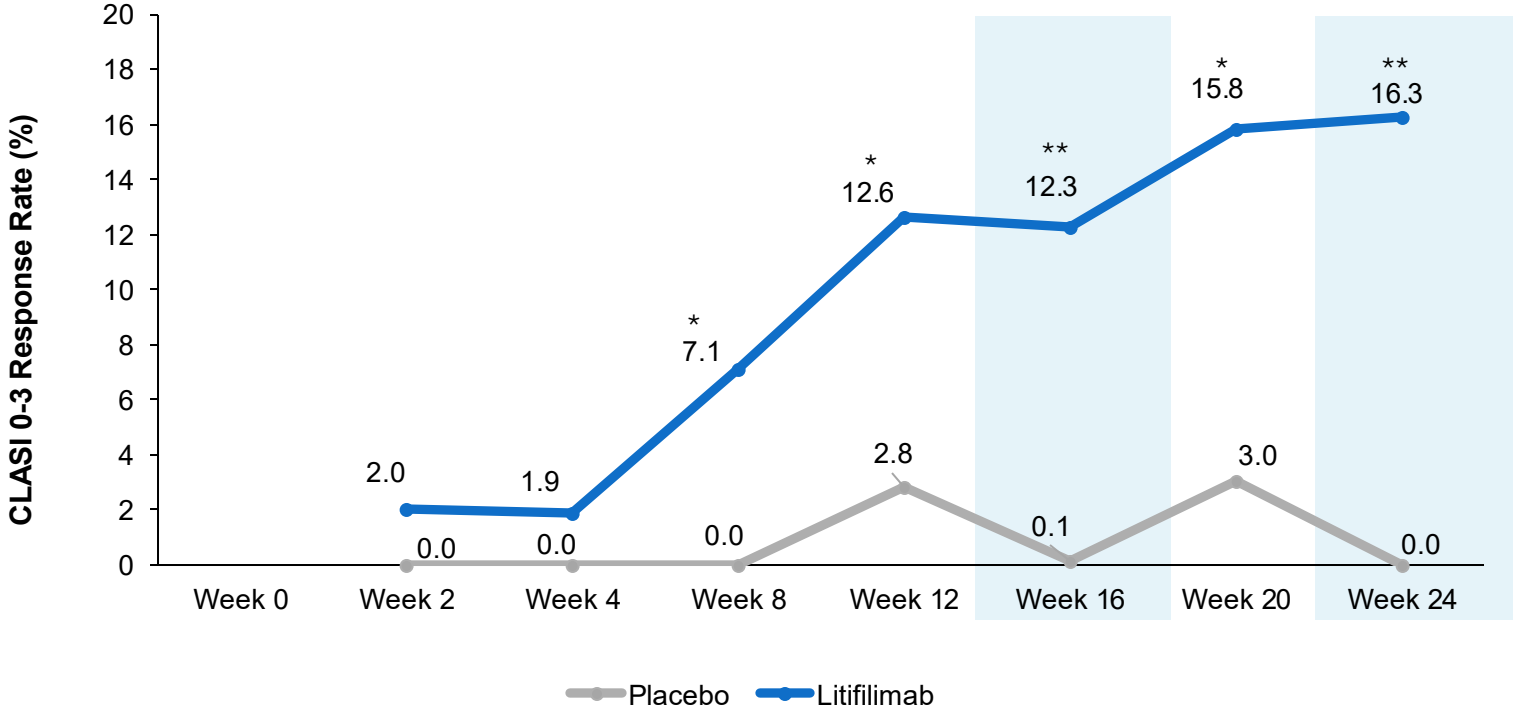
More participants treated with litifilimab had ≥70% reduction in CLASI from baseline



Nominal *P*-values <0.05 are marked with an asterisk (*) and *P*-values <0.01 are marked with double asterisk (**). CLASI-70 = ≥70% improvement from baseline in Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity. Werth V, et al. *J Invest Dermatol*. 2023;143(Suppl. 5):S100 (Abstract 583). ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated April 23, 2026. Accessed February 20, 2026. https://clinicaltrialsgov/study/NCT05531565.

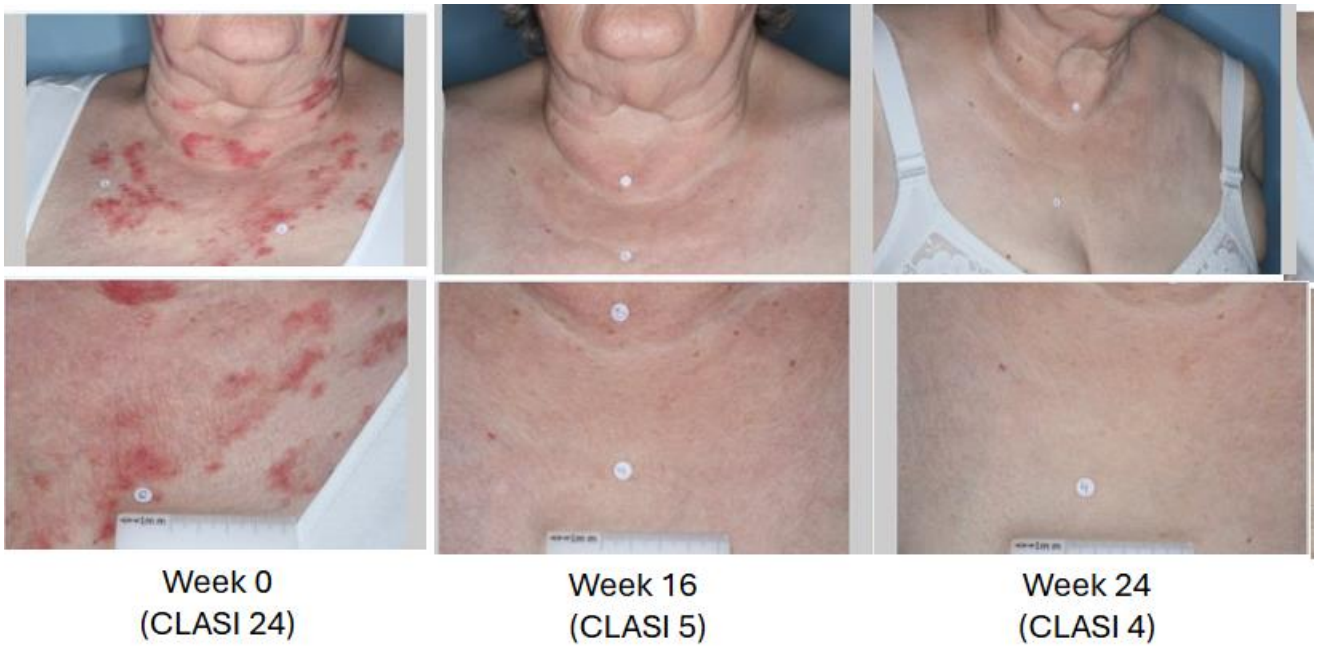
CLASI-A 0-3

More participants treated with litifilimab improved



Nominal *P*-values <0.05 are marked with an asterisk (*) and *P*-values <0.01 are marked with double asterisk (**). Werth V, et al. *J Invest Dermatol*. 2023;143(Suppl. 5):S100 (Abstract 583). ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated April 23, 2026. Accessed February 20, 2026. https://clinicaltrials.gov/study/NCT05531565.

Observed Skin Improvements in Participants



The outcomes shown are not intended to be representative of all participants treated with litifilimab. Results are individual and not indicative of typical outcomes for each participant.

The participants featured in these images provided written consent for the use of their photographs.

Werth V, et al. *J Invest Dermatol*. 2023;143(Suppl. 5):S100 (Abstract 583). ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated April 23, 2026. Accessed February 20, 2026. https://clinicaltrials.gov/study/NCT05531565.

Safety Outcomes

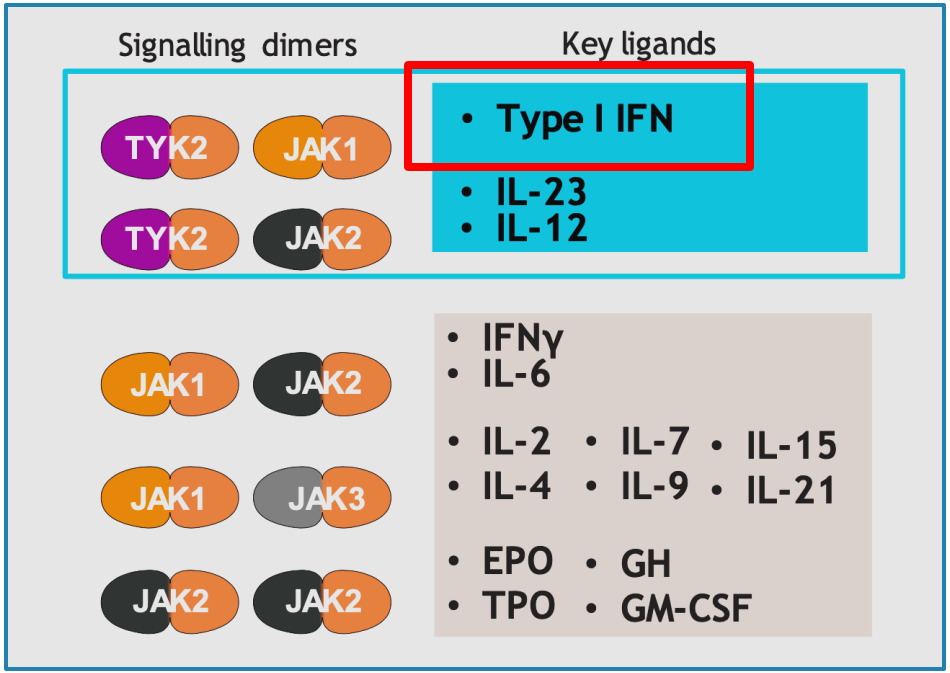
Litifilimab was generally well tolerated

Events, % (n)	Litifilimab (n = 59)	Placebo (n = 34)
Any event	74.6% (44)	64.7% (22)
Mild	54.2% (32)	41.2% (14)
Moderate	18.6% (11)	20.6% (7)
Severe	1.7% (1)	2.9% (1)
Related event[a]	20.3% (12)	26.5% (9)
Serious event[b]	6.8% (4)	2.9% (1)
Most common event (≥ 10% in either group)		
Nasopharyngitis	6.8% (4)	14.7% (5)
Headache	3.4% (2)	11.8% (4)
Viral infections occurring in > 1 participant in either group[c]		
COVID-19	3.4% (2)	0
Oral herpes	3.4% (2)	2.9% (1)
Viral upper respiratory tract infection	1.7% (1)	5.9% (2)

[a]AEs assessed by the investigator. [b]No fatal events. [c]Mild or moderate; no severe events.
AE = adverse event.

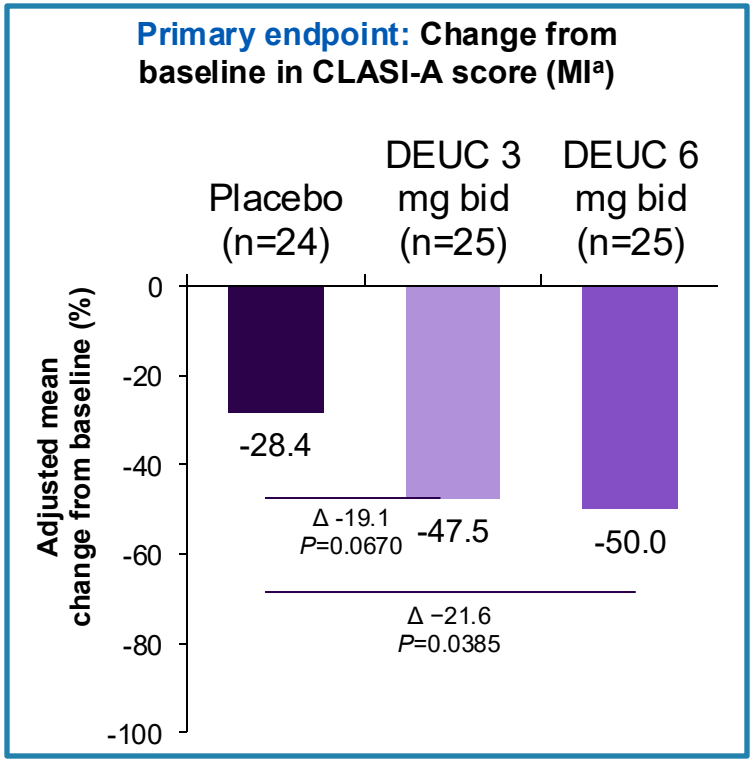
Werth V, et al. *J Invest Dermatol*. 2023;143(Suppl. 5):S100 (Abstract 583). ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated April 23, 2026. Accessed February 20, 2026. https://clinicaltrials.gov/study/NCT05531565.

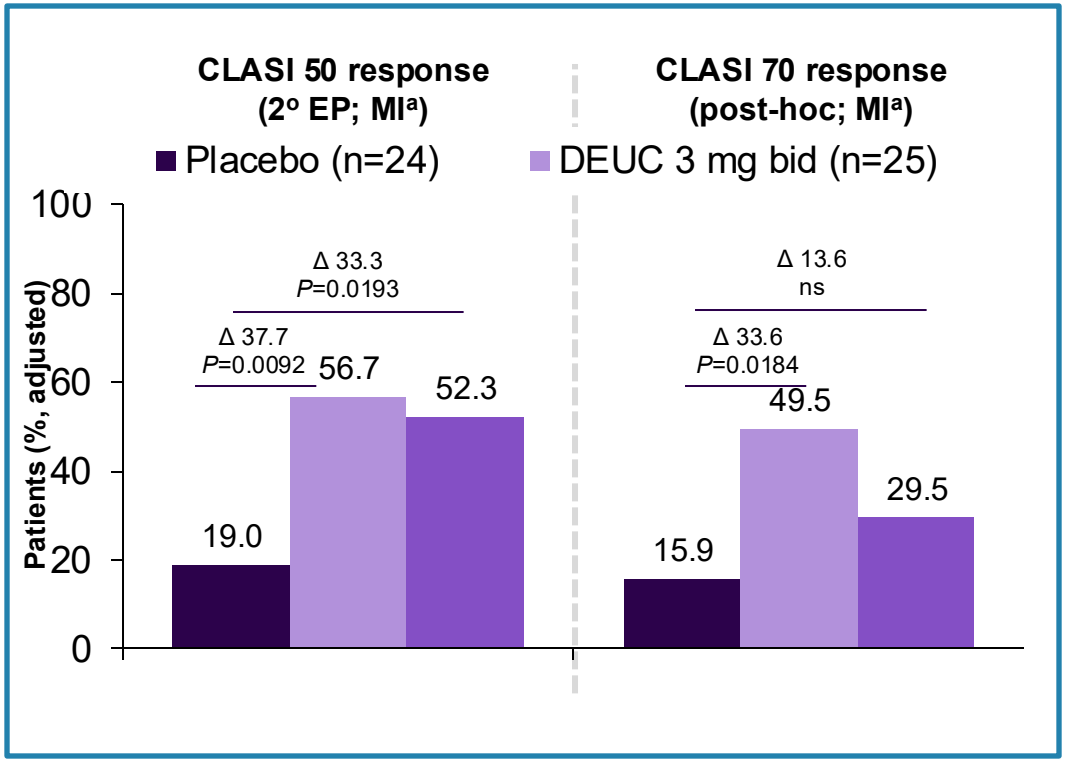
Efficacy and Safety of Deucravacitinib, an Oral, Selective, Allosteric TYK2 Inhibitor, in Patients With Active Systemic Lupus Erythematosus: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study



Morand E, et al. Presented at: EULAR Congress; 2022.

PAISLEY CLE: Efficacy at Week 16 of Oral Deucravacitinib in Patients with Cutaneous Lupus Erythematosus

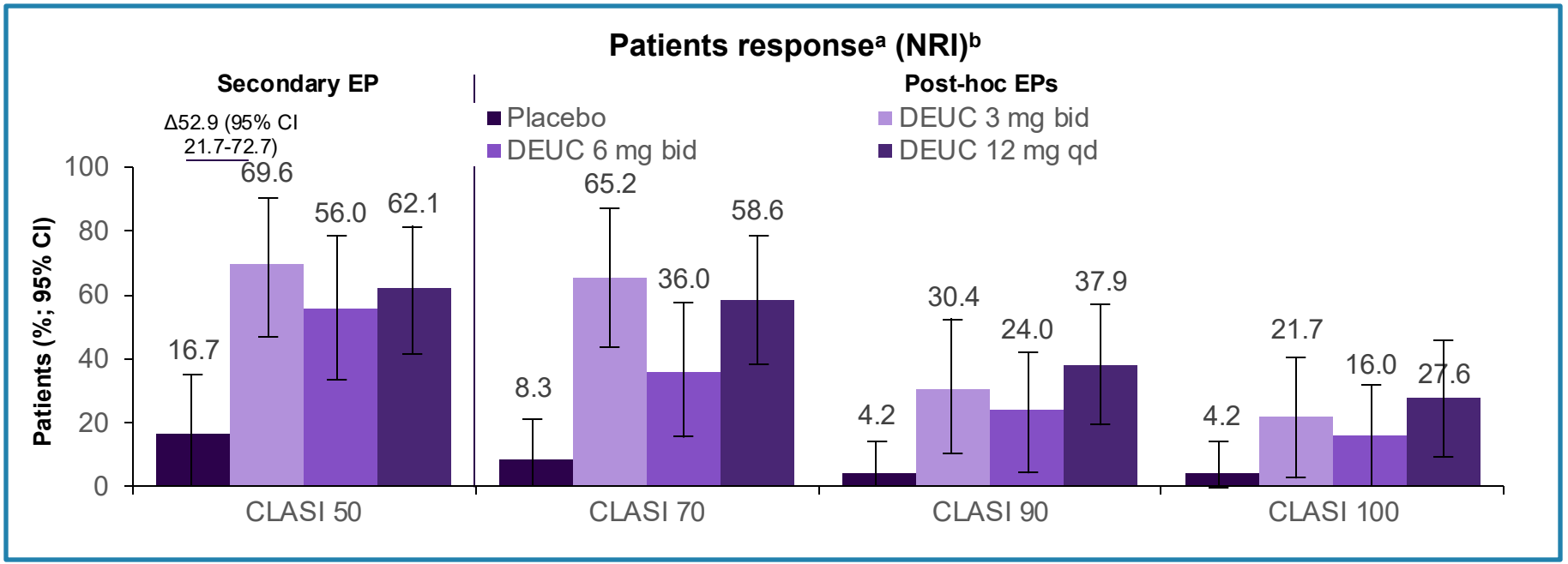




[a]A composite variable strategy was used that set CLASI-A scores to the baseline value after occurrence of key intercurrent events (ICEs). Subsequent missing data were addressed via multiple imputation under a missing not at random assumption. Regression analyses adjusting for stratification factors and baseline CLASI-A score were used for treatment effect inference. *P*-value <0.1 represents statistical significance.

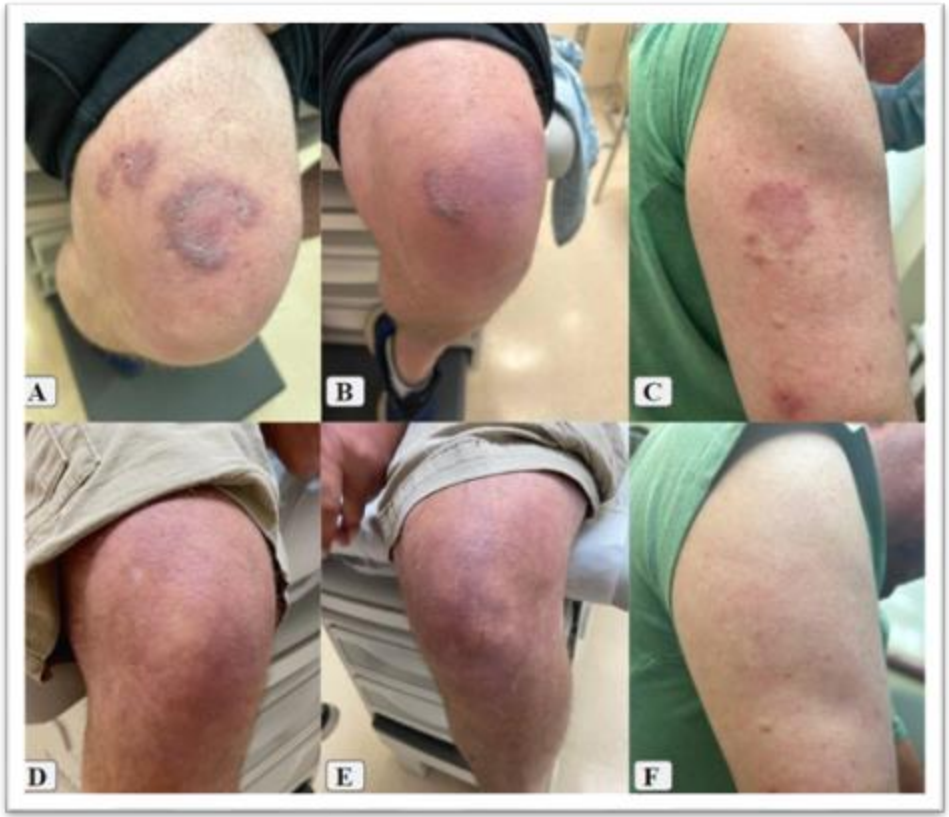
Werth VP, et al. Presented at: AAD Annual Meeting; 2025. Morand E, et al. Presented at: EULAR Congress; 2022.

PAISLEY SLE: CLASI Responses after Deucravacitinib Treatment for 48 Weeks in Systemic Lupus Erythematosus



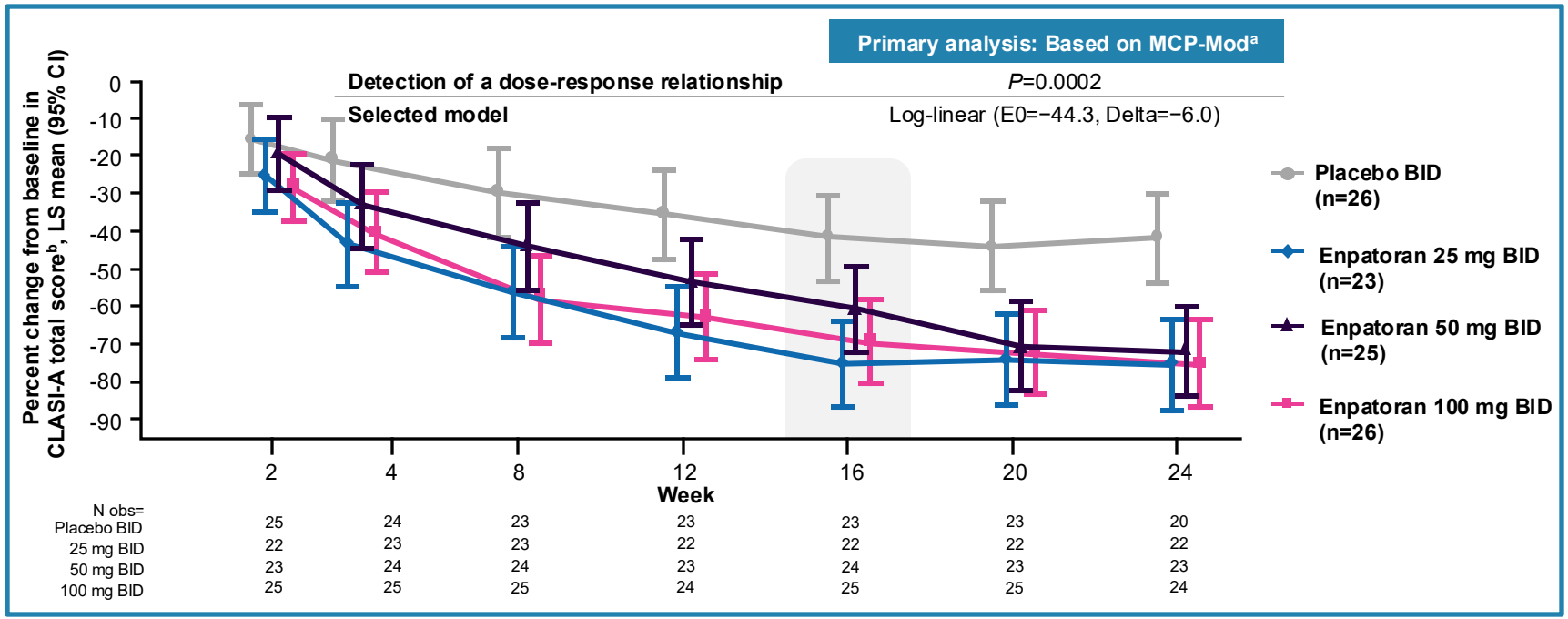
[a]Only patients with baseline CLASI-A score of ≥10 were included; [b]Missing data, prohibited medication use, or early discontinuation analyzed as nonresponse.
LP = lichen planus; LPP = lichen planus pigmentosus.
Morand E, et al. *Arthritis Rheumatol.* 2023;75(2):242-252. Morand E, et al. Presented at: EULAR Congress; 2022.

Deucravacitinib for CLE



Zhang A, et al. *JAAD Case Rep*. 2023;45:110-112..

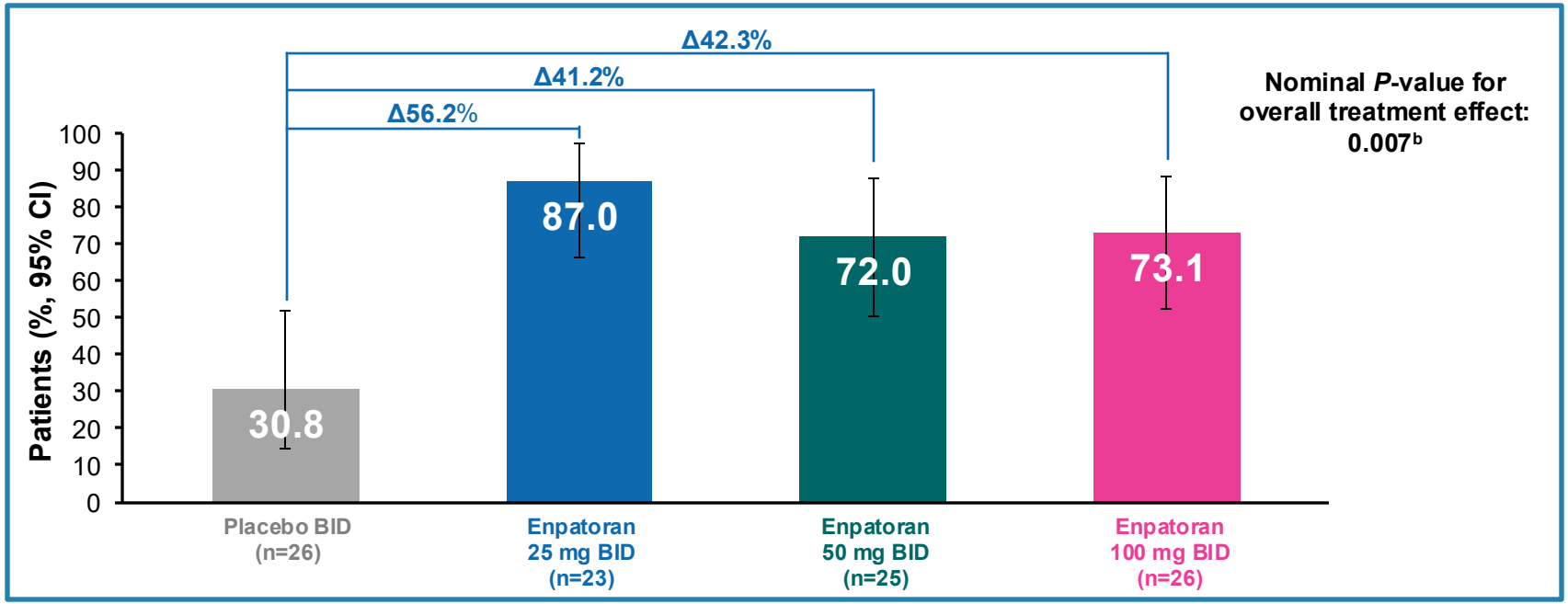
Oral Enpatoran Dual Inhibition of TLR7/8: Primary Endpoint



Significant dose response for enpatoran in reducing CLASI-A from baseline to week 16

[a]MCP-Mod adjusted for CLASI-A at baseline, region and disease diagnosis (CLE only vs CLE + SLE; FAS; N=100); [b]MMRM analyses (exploratory endpoint).
Enpatoran is an investigational product and has not been proven to be safe and effective in any country.
FAS = full analysis set; LS = least squares; MCP-Mod = multiple comparison procedures-modelling; MMRM = mixed model repeated measures.
Morand E, et al. Presented at: International Congress on SLE; 2025. LBA 827.

CLASI-50 Response at Week 24[a] with Enpatoran



Up to 87% of patients receiving enpatoran had ≥50% reduction in CLASI-A by week 24

[a]Exploratory endpoint. CLASI-50 response was defined as a decrease in CLASI-A total score of ≥50% from baseline values. [b]Logistic regression. Participants with any intercurrent events (early treatment discontinuation due to any reason, protocol-prohibited medications as determined by EAC or corticosteroid use not compliant with protocol rules) were considered as non-responders at all visits post-intercurrent event(s).
EAC = endpoint adjudication committee.
Morand E, et al. Presented at: International Congress on SLE; 2025. LBA 827.

Co-Management of CLE/SLE

Treatment Considerations

Treating the Patient with CLE and SLE

When choosing a second-line agent, consider

- (+ Arthritis?) ➔
  - Methotrexate, belimumab
- (+ Nephritis) ➔
  - Mycophenolate > azathioprine; combination therapy approaches such as MMF + belimumab, MMF + voclosporin, RTX, etc
- (+ ILD) ➔
  - Mycophenolate, ? rituximab, others
- (+ APLA/hypercoagulable?) ➔
  - Caution with thalidomide
- (+ Active systemic lupus despite other standard treatments?)
  - Belimumab, anifrolumab
- Mod-severe active systemic disease
  - Avoid thalidomide, or thalidomide monotherapy; consider combination therapy

Co-management and facilitated communication between the dermatologist and rheumatologist

APLA = antiphospholipid antibody.

Key Learning Points

1. There remains a substantial unmet need in CLE, driven by limitations of current therapies including incomplete efficacy, safety concerns with immunosuppressants, monitoring burden, and challenges in women of childbearing potential
2. The current treatment paradigm remains stepwise, with antimalarials as foundational therapy, followed by conventional immunomodulators such as methotrexate or mycophenolate, and escalation to thalidomide analogues or biologics in refractory disease
3. Advances in trial design and outcome measures, including CLASI and emerging tools such as CLA-IGA-R, are enabling more precise evaluation of therapeutic response and facilitating drug development in CLE
4. Targeted therapies are transforming the landscape, particularly agents addressing the type I interferon axis and upstream immune pathways, including anifrolumab, litifilimab, and deucravacitinib, with additional novel mechanisms such as TLR7/8 inhibition emerging
5. Clinical trial data increasingly demonstrate meaningful improvements in skin disease activity, supporting a shift toward higher treatment expectations and disease control
6. Future treatment algorithms will likely move earlier toward targeted therapies, incorporate mechanism-based selection, and emphasize combination approaches tailored to systemic involvement and comorbidities
7. Optimal management of CLE, particularly when associated with systemic lupus, requires coordinated co-management between dermatology and rheumatology, with therapy individualized based on extracutaneous manifestations such as arthritis, nephritis, or interstitial lung disease