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# Advances in Dermatomyositis: The Evolving Landscape and Potential Role of Novel Therapies to Improve Disease Outcomes

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# Disclosures

- **Victoria Werth, MD:** Consultant – Abbvie, Almirall, Amgen, Anaptysbio, Architect Therapeutics, Argenx, AstraZeneca, Atticus, Biogen, BMS, Boehringer Ingelheim, Cabaletta Bio, Celexor, CSL Behring, Duality Biologics, Evommune, Exo, Gilead, Glycoera, GSK, Immunovant, Inmagene, Innovaderm, Kwoya Kirin, Lilly, Merck, Novartis, Nuvig, Pfizer, Quotient, Regeneron, Sanofi, Takeda, UCB, Xencor; royalties – Abbvie Amgen, Argenx, Biogen, BMS, Cabaletta Bio, Chugai, EMD Serona, Gilead, Lilly, Merck, Pfizer; grant/research support – Amgen, Argenx, AstraZeneca, Biogen, Chugai, CSL Behring, Gilead, Glycoera, Horizon, Pfizer, Priovant, Regeneron; advisory board – Argenx, EMD Serona, GSK, Merck, Regeneron, Sanofi; speaker's bureau – EMD Serona
- **Scott Elman, MD, FAAD:** Consultant – Biogen, Blueprint, EMD-Serono; research/grant support – Clinuvel, Immunovant, Insmed, Pfizer

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# Learning Objectives

- Apply evidence-based strategies for timely DM detection, accurate diagnostic evaluation, and consistent use of validated assessment tools
- Evaluate the evolving DM treatment landscape, including emerging targeted therapies with promising mechanisms of action and the potential to improve patient outcomes
- Implement interdisciplinary strategies to manage DM and address patient needs

**DM = dermatomyositis.**

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# Dermatomyositis Overview

**Victoria Werth, MD**

*Professor of Dermatology*
*University of Pennsylvania*

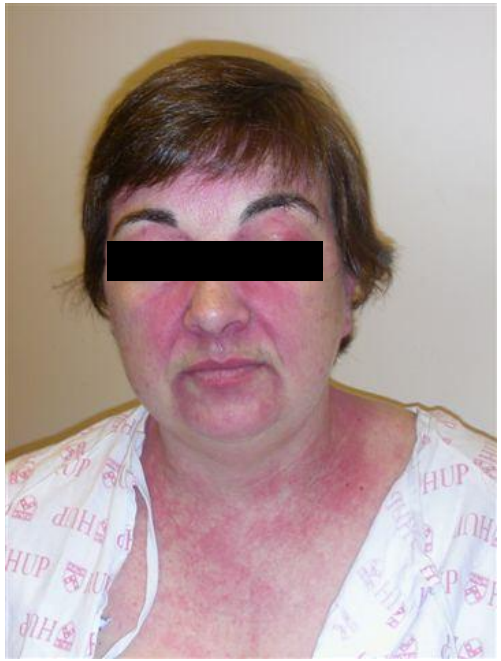
# Outline

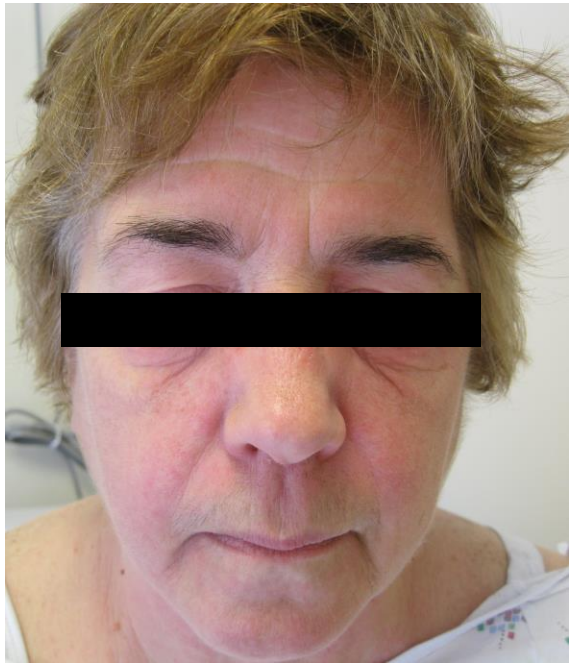
- **Cutaneous findings in dermatomyositis**
- Diagnosis of dermatomyositis
- Pathophysiology
- Evaluation of dermatomyositis
- Environmental triggers of DM
- Outcomes in dermatomyositis

# Clinical Findings in Skin in Dermatomyositis

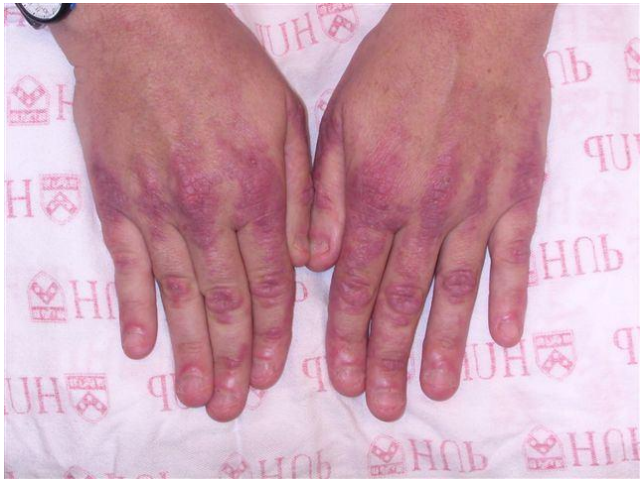
- Classic skin eruptions
  - Heliotrope
  - Gottron's sign/papules
  - V-neck sign
  - Shawl sign
  - Cuticular overgrowth
  - Photosensitivity

# Dermatomyositis

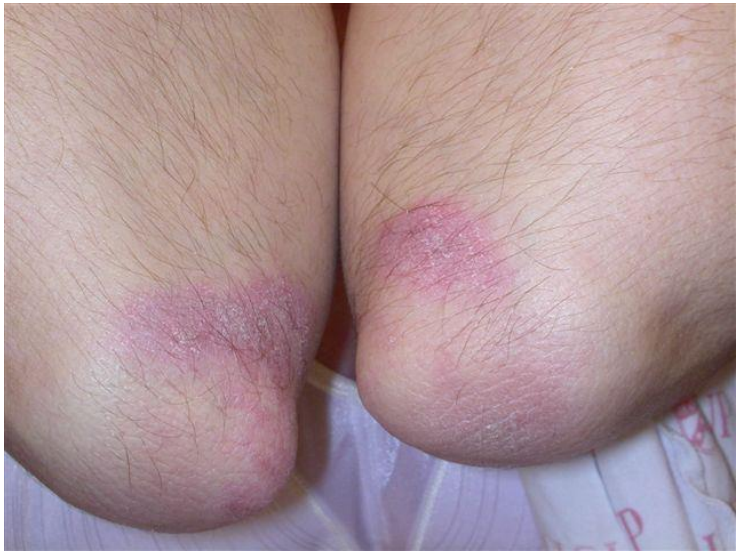




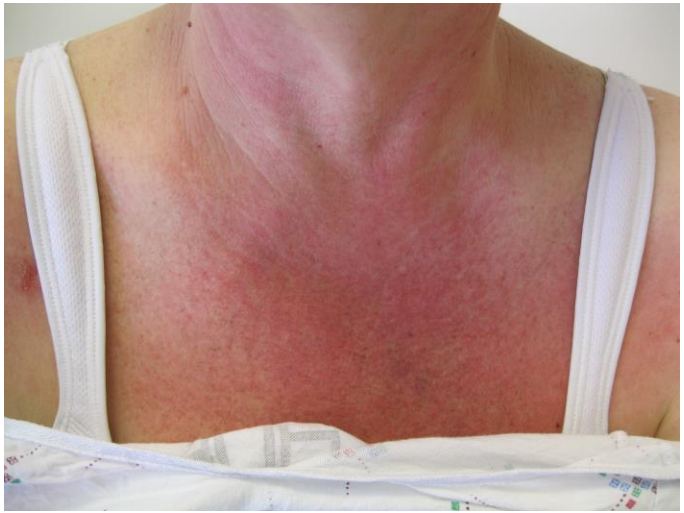
**Erythematous macules or papules over joints**



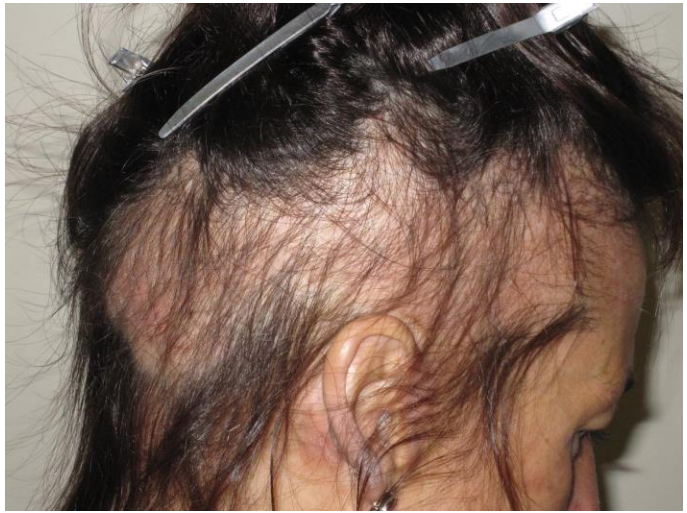
# Gottron's of the hands



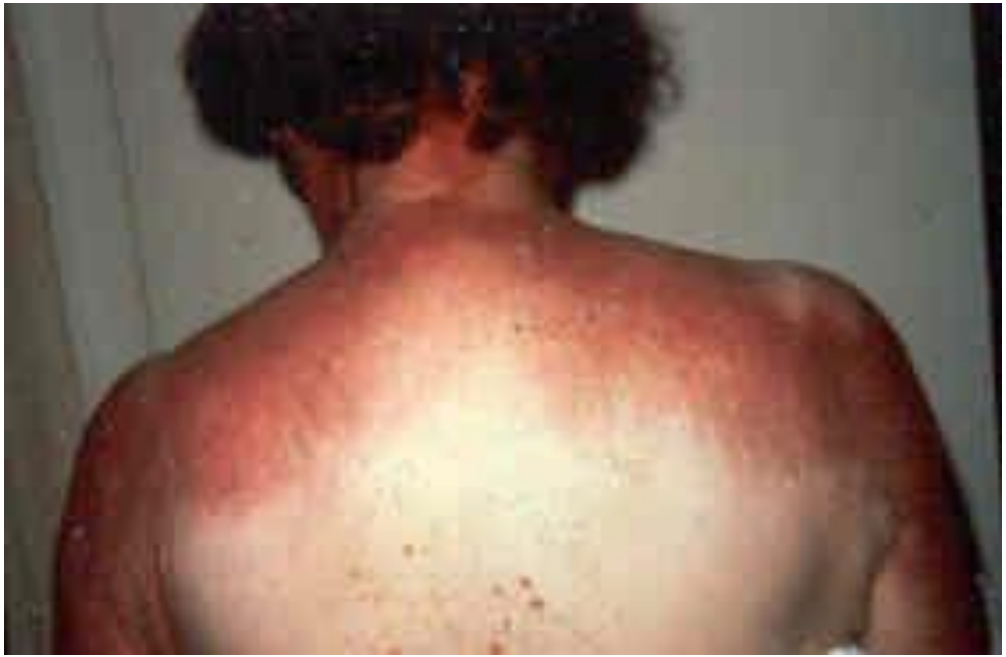
## V-neck erythema



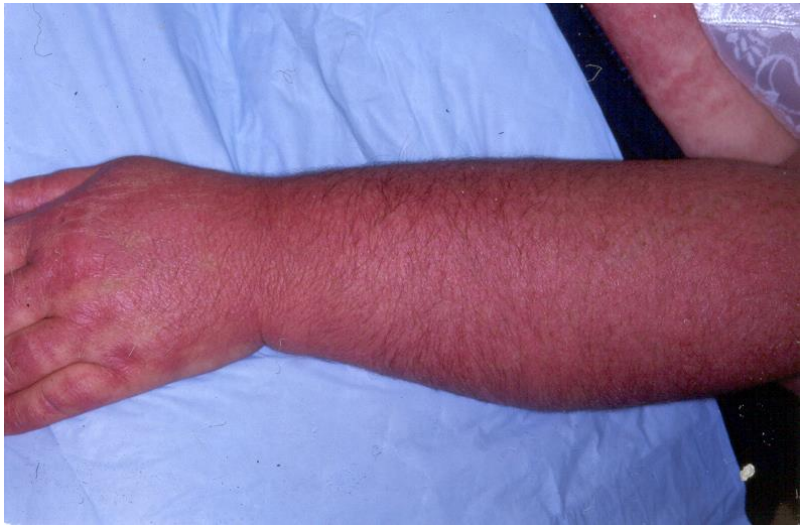
## Inflammatory alopecia



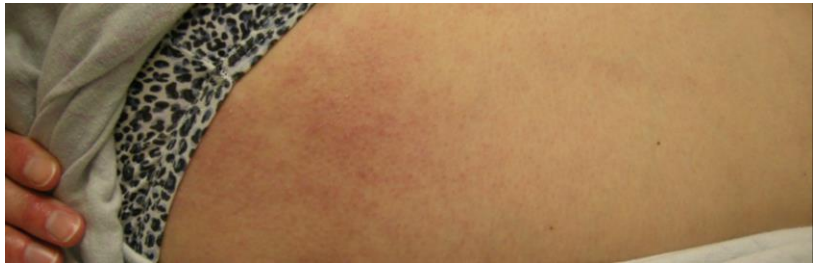
# Shawl sign



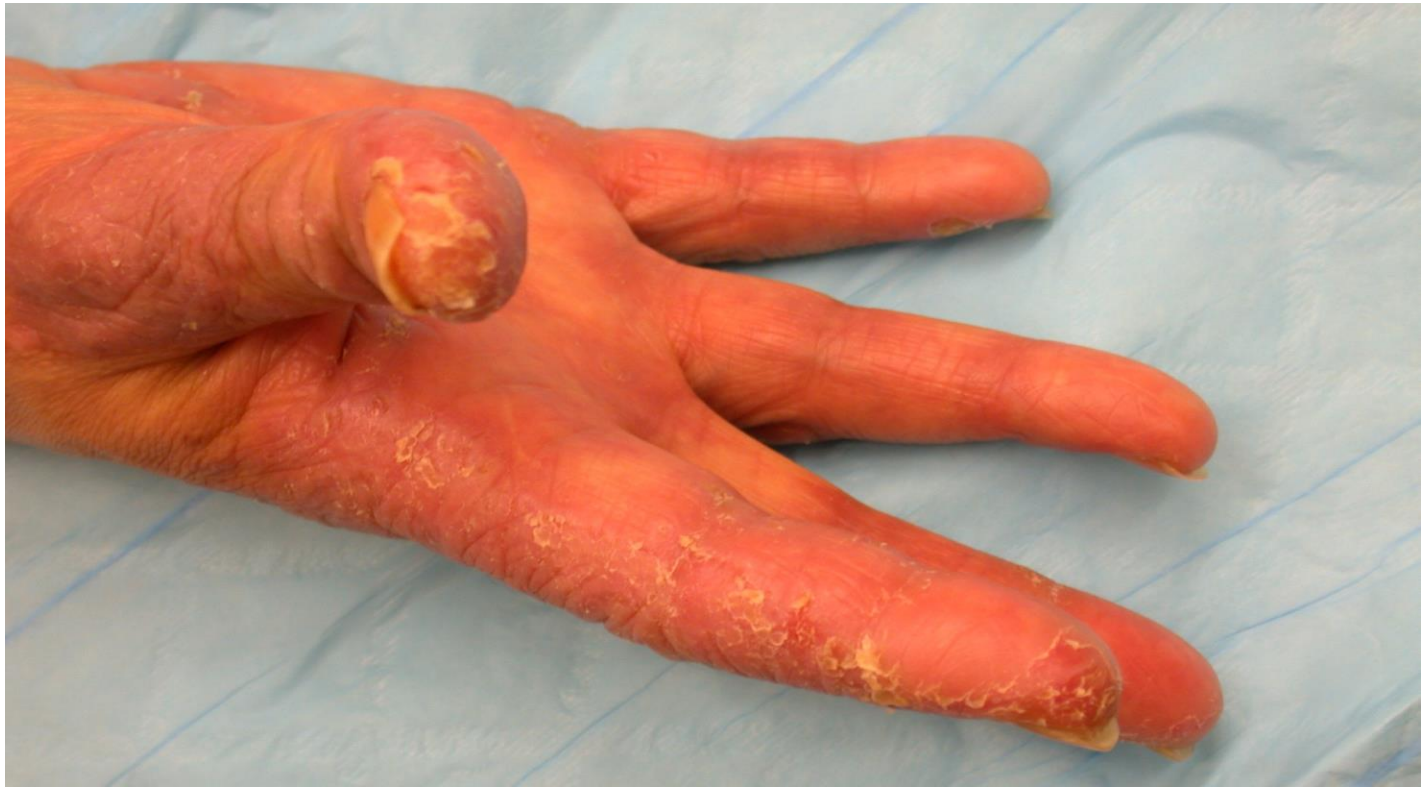
**Extensor arm erythema**

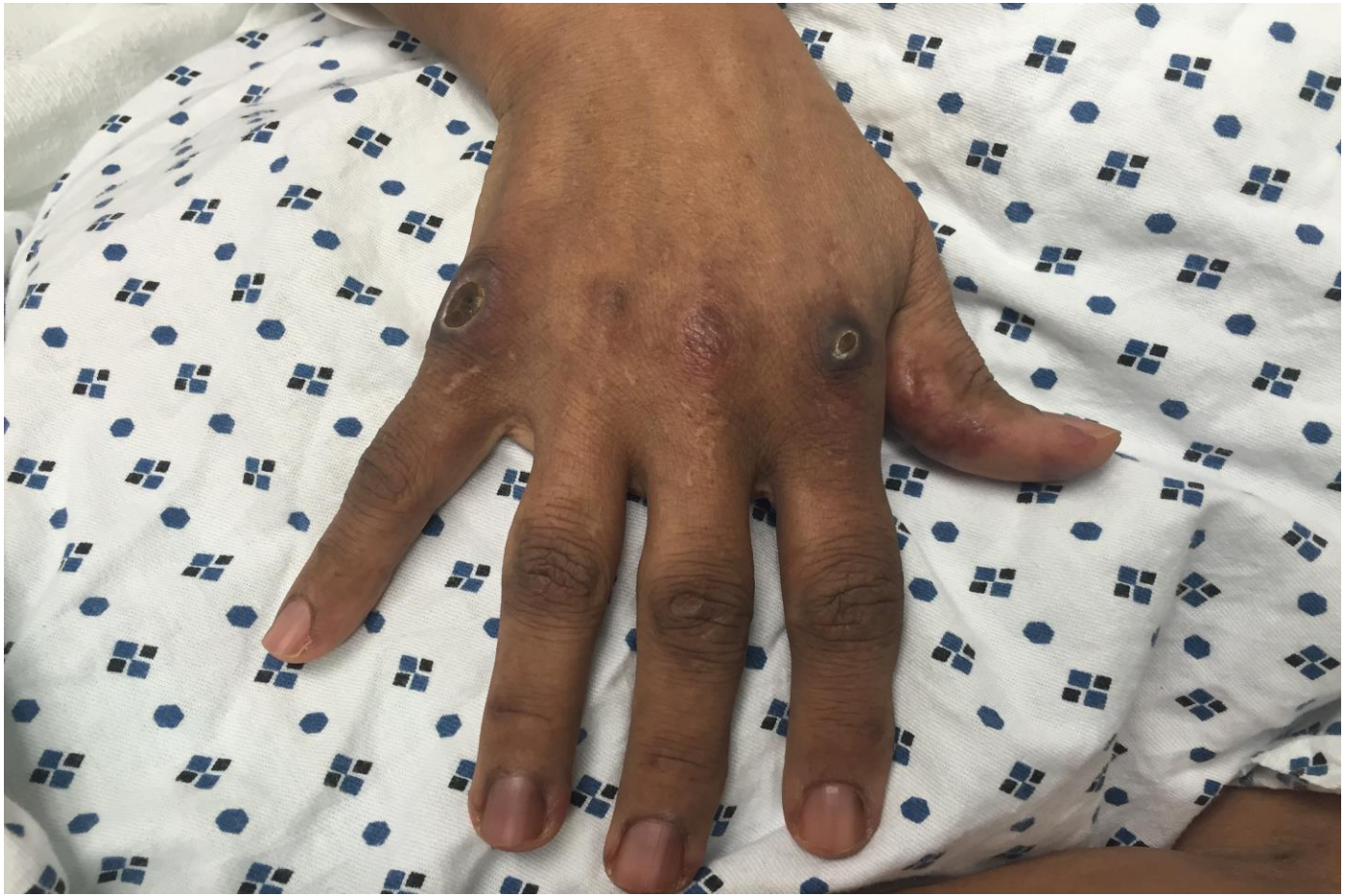


**Holster sign**



# Mechanic's hands





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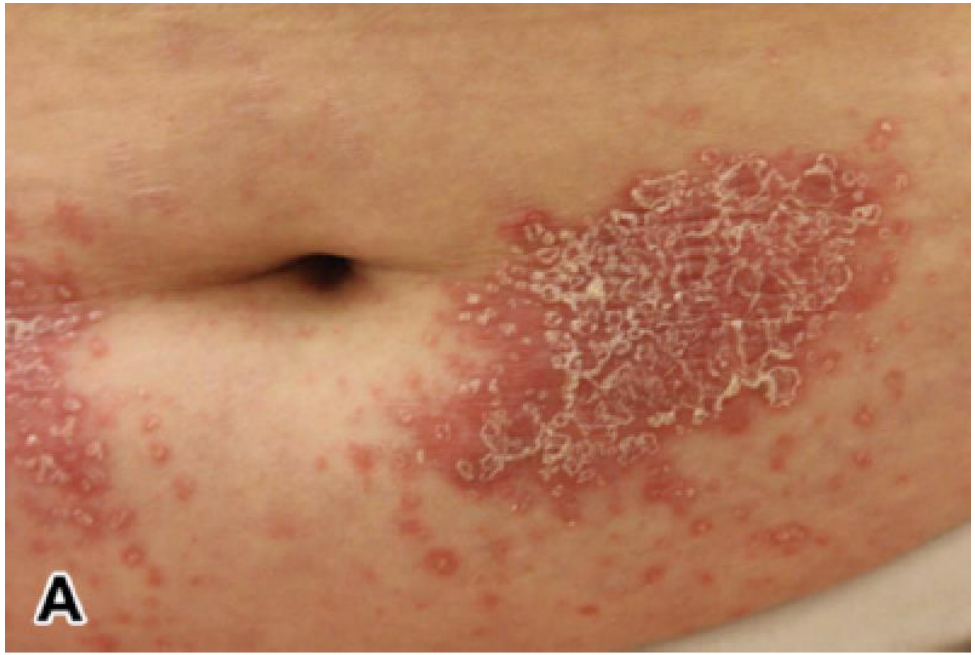
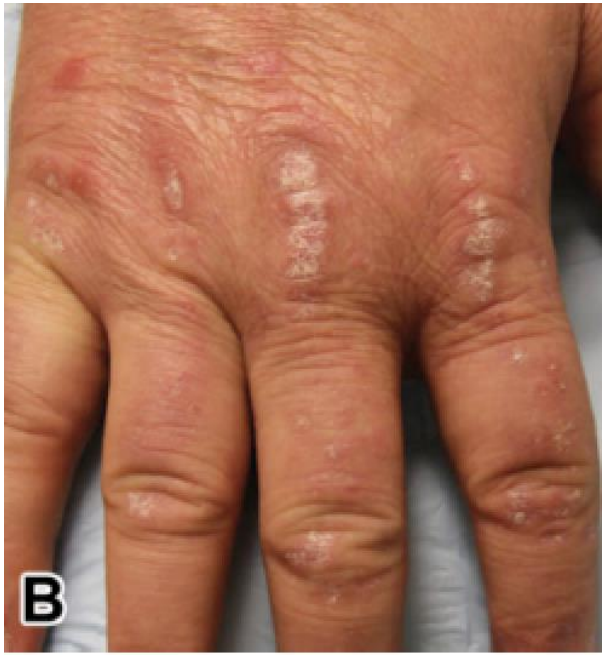
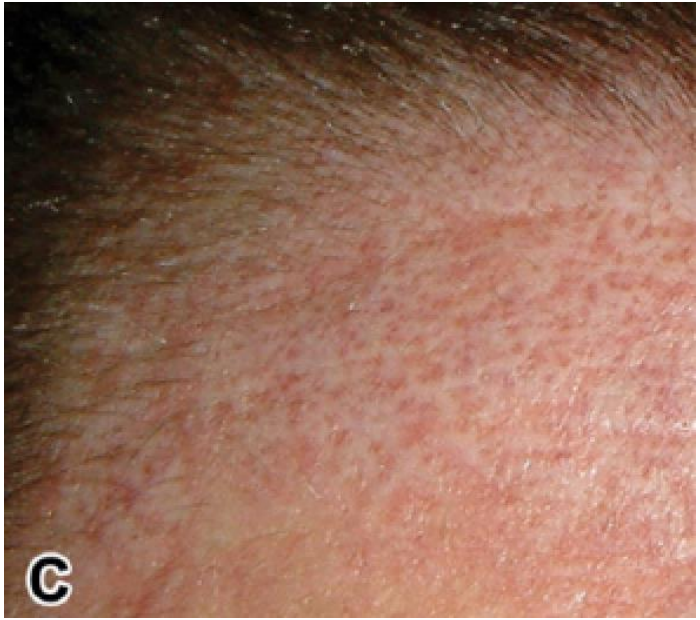
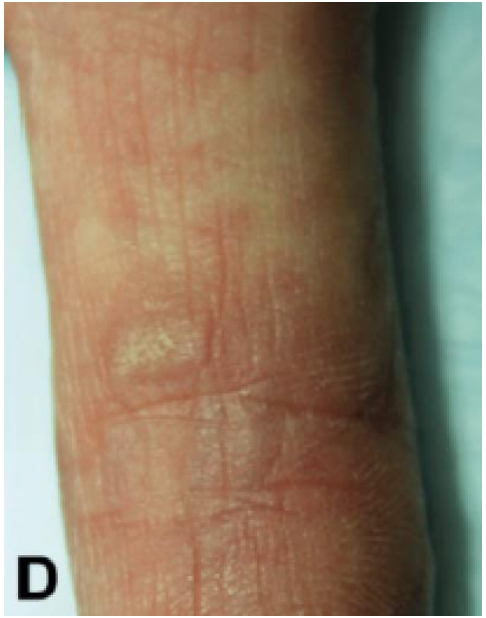



**TIF = transcription intermediary factor.**
**Fiorentino DF, et al. *J Am Acad Dermatol*. 2015;72(3):449-455.**

# Anti-TIF1




Fiorentino DF, et al. *J Am Acad Dermatol*. 2015;72(3):449-455.

# Dermoscopy Images of Nailfold Capillary Changes

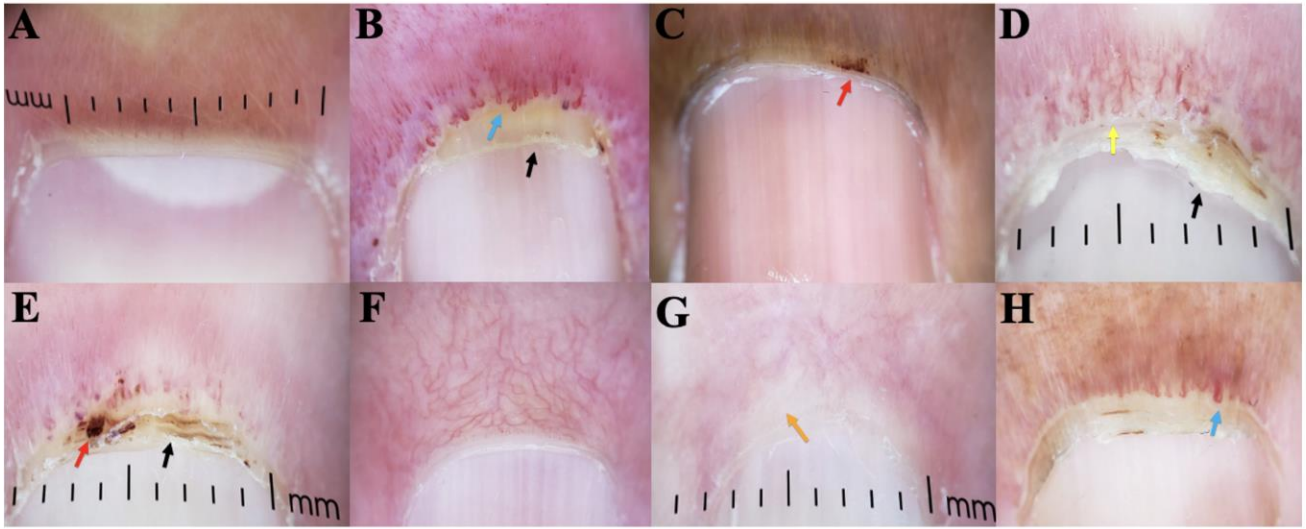



Figure 1: A. Normal nailfold capillary B. Dilated capillary loop (blue), cuticular dystrophy and overgrowth (black) C. Capillary hemorrhage (red) D. Abnormal morphology (yellow), cuticular dystrophy and overgrowth (black), and overall disorganization of the capillary bed E. Capillary hemorrhage (red), cuticular overgrowth and dystrophy (black) F. Visible subpapillary plexus G. Capillary dropout (orange) H. Dilated capillary loop (blue)

Dan J ... Werth V, et al. *Arthritis Rheumatol*. 2022;74(suppl 9).

# Outline

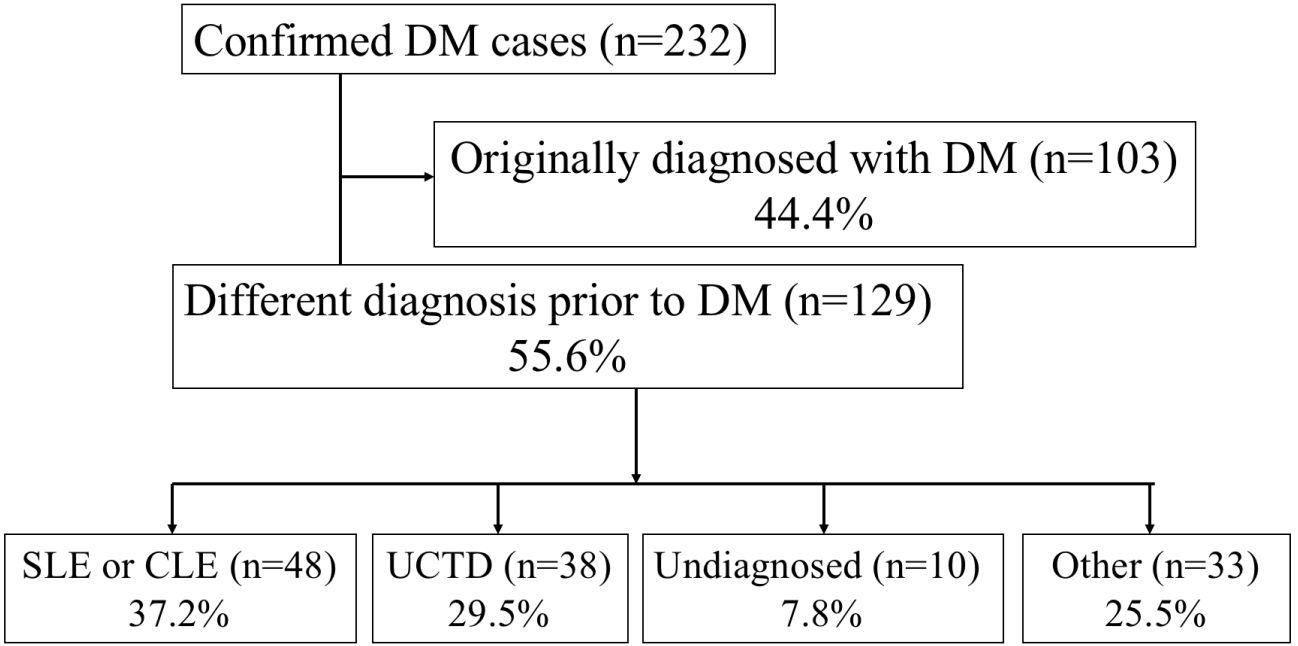
- Cutaneous findings in dermatomyositis
- **Diagnosis of dermatomyositis**
- Pathophysiology
- Evaluation of dermatomyositis
- Environmental triggers of DM
- Outcomes in dermatomyositis

# Diagnosis of Amyopathic DM

- Problems in getting a diagnosis
- Often misdiagnosed with SLE
- SLE criteria often positive (malar rash, photosensitivity, +ANA, oral ulcers)
- Skin biopsy indistinguishable between DLE and DM
- Bohan and Peter's criteria don’t identify these patients

**SLE = systemic lupus erythematosus; ANA = anti-nuclear antibody; DLE = discoid lupus erythematosus.**

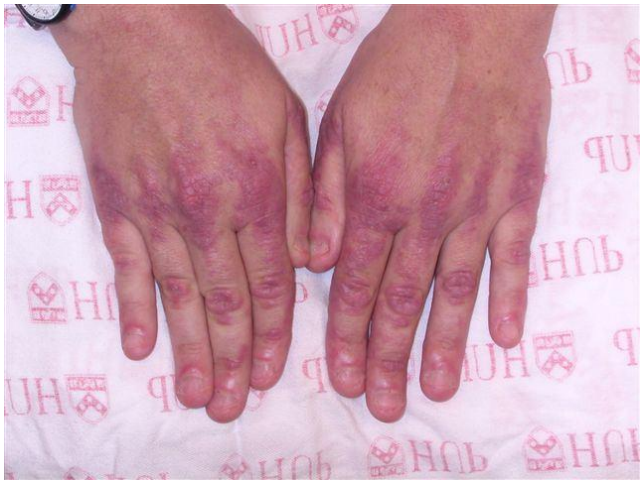
# Diagnoses of Dermatomyositis

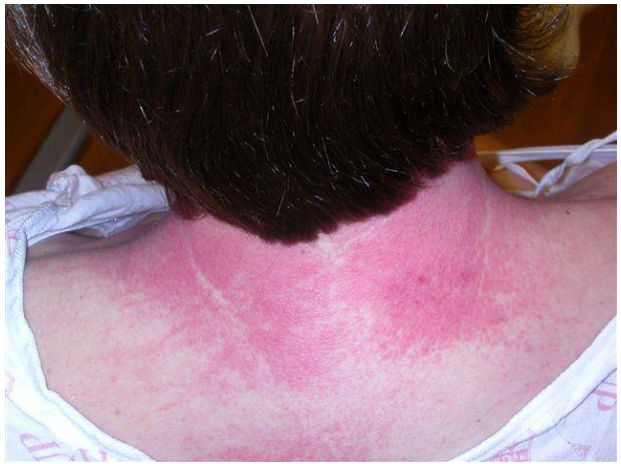


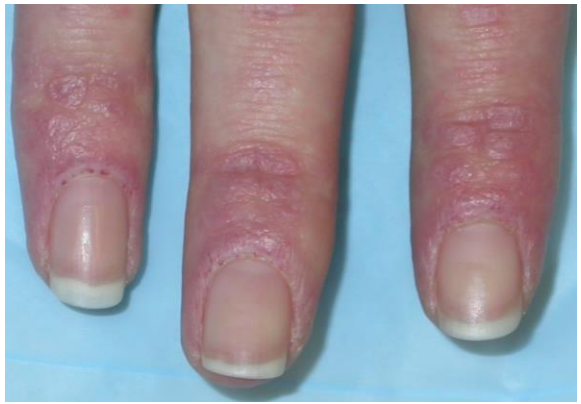

**CLE = cutaneous lupus erythematosus; UCTD = undifferentiated connective tissue disease.**

**Da Silva DM, et al. *J Am Acad Dermatol*. 2018;79(2):371-373.**

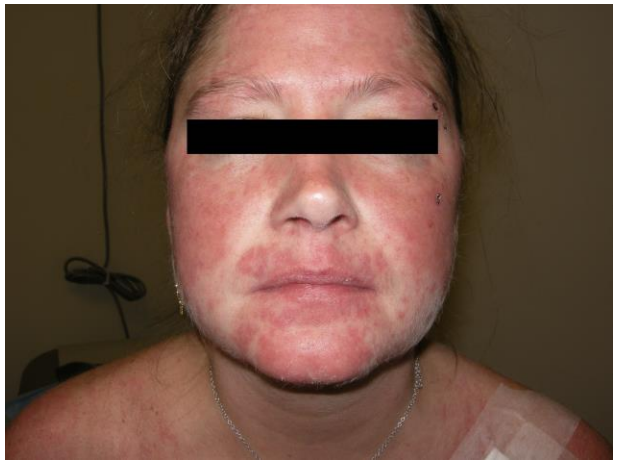
# Dermatomyositis Frequently Misdiagnosed as Lupus



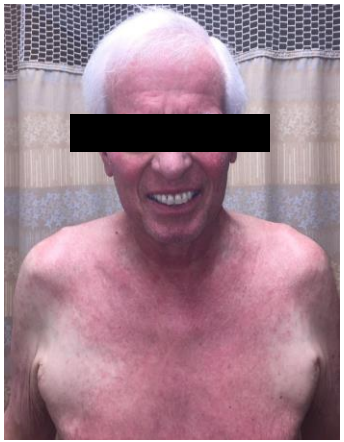


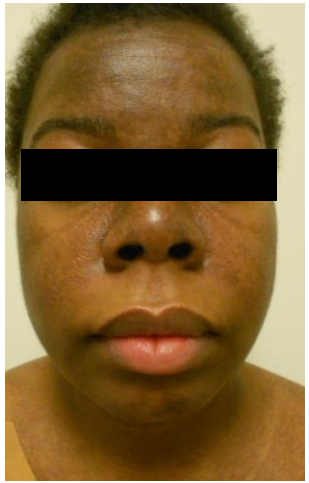


# Dermatomyositis Frequently Misdiagnosed as Lupus



SLE spares nasolabial fold





Dermatomyositis involves nasolabial fold

# Diagnostic Criteria for DM (Bohan and Peter's)

- Symmetric proximal weakness with or without dysphagia or respiratory muscle involvement
- Abnormal muscle biopsy specimen
- Elevation of skeletal muscle-derived enzymes
- Abnormal electromyogram
- Typical skin rash
  - Definite DM: Rash and 3 or 4 criteria
  - Probable DM: Rash and 2 criteria
  - Possible DM: Rash and 1 criterion

**Bohan A, Peter JB. *N Engl J Med.* 1975;292(8):403-407.**

# How Frequent Are Skin Manifestations of Rheumatic Diseases?

Skin findings in classic and CADM are similar in frequency and type

Cutaneous findings of patients with dermatomyositis as measured by CDASI activity at enrollment

| Cutaneous finding | All patients (N = 211) Total (%) | Classic DM (n = 101) Total (%) | CADM (n = 110) Total (%)* | *P* value |
|---|---|---|---|---|
| Gottron's sign | 190 (90.0) | 90 (89.1) | 100 (90.1) | .82 |
| Malar area† | 173 (82.0) | 83 (82.1) | 90 (81.8) | 1.00 |
| Periungual changes | 163 (77.3) | 81 (80.2) | 82 (74.5) | .41 |
| V area of the neck† | 161 (76.3) | 78 (77.2) | 83 (75.5) | .87 |
| Rest of face† | 160 (75.8) | 75 (74.2) | 85 (77.3) | .63 |
| Gottron's sign on areas other than the hands† | 153 (72.5) | 72 (71.3) | 81 (73.6) | .76 |
| Scalp† | 148 (70.14) | 65 (64.3) | 83 (75.5) | .10 |
| Arm† | 143 (67.8) | 66 (65.3) | 77 (70.0) | .56 |
| Periorbital† | 136 (64.5) | 68 (67.3) | 68 (61.8) | .47 |
| Posterior neck† | 126 (59.8) | 61 (60.4) | 65 (59.1) | .89 |
| Upper back and shoulders† | 124 (58.7) | 57 (56.4) | 67 (60.9) | .58 |
| Mechanic's hands† | 117 (55.4) | 51 (50.5) | 66 (60.0) | .17 |
| Dorsum of the hands (not over joints)† | 114 (54.0) | 52 (51.5) | 62 (56.4) | .33 |
| Lateral upper part of the thigh† | 74 (35.1) | 38 (37.6) | 36 (32.7) | .47 |
| Rest of back and buttocks† | 70 (33.2) | 33 (32.7) | 37 (33.6) | 1.00 |
| Rest of legs and feet† | 69 (32.7) | 35 (34.7) | 34 (30.9) | .66 |
| Alopecia | 64 (30.3) | 34 (33.7) | 30 (27.2) | .37 |
| Gottron's papules | 61 (28.9) | 26 (25.7) | 35 (31.8) | .36 |
| Abdomen† | 25 (11.9) | 11 (10.9) | 14 (12.7) | .83 |
| Average CDASI activity score (±SD)‡ | 19.7 (12.1) | 19.6 (12.3) | 19.7 (11.9) | .95 |

*CDASI*, Cutaneous Dermatomyositis Disease Area and Severity Index; *DM*, dermatomyositis; *SD*, standard deviation.
*Clinically amyopathic dermatomyositis includes hypomyopathic and amyopathic dermatomyositis.
†CDASI activity includes erythema, scale, erosion, or ulceration.
‡CDASI activity scores range from 0 to 100.

**CADM = clinically amyopathic dermatomyositis; CDASI = Cutaneous Dermatomyositis Disease Area and Severity Index; SD = standard deviation.**
**Da Silva DM, et al. *J Am Acad Dermatol*. 2018;79:7783;371-373.**

# New Dermatomyositis ACR/EULAR Classification Criteria: 3 Skin Criteria Determined

- S1 Heliotrope
- S2 Gottron's papules
- S3 Gottron's sign

**ACR = American College of Rheumatology; EULAR = European Alliance of Associations for Rheumatology.**
**Lundberg IE, et al. *Ann Rheum Dis*. 2017;76(12):1955-1964.**

# Probability of Classification for Patients with ADM by EULAR/ACR Criteria Skin Variables Using IMCCP Web Calculator

| Probability of IIM | ADM n=99 (%) |
|---|---|
| >55% | 73 (73.7) |
| 10-55% | 20 (20.2) |
| <10% | 6 (6.1) |
| *http://www.imm.ki.se/biostatistics/calculators/iim/ | |

**IIM = idiopathic inflammatory myopathies; ADM = amyopathic dermatomyositis.**
**Patel B, et al. *J Am Acad Dermatol*. 2018;79(1):77-83.e1.**

# Delphi Project to Expand DM Skin Criteria

| | |
|---|---|
| ***MORPHOLOGY*** | |
| Erythema to violaceous erythema | ☐ Present ☐ Absent |
| Erythematous papules/plaques (often flat-topped) +/- scale over the dorsal MCP/IP joints | ☐ Present ☐ Absent |
| Macular erythema over the dorsal MCP/IP joints | ☐ Present ☐ Absent |
| Dilated nailfold capillaries by eye or microscopy | ☐ Present ☐ Absent |
| Nailfold erythema | ☐ Present ☐ Absent |
| Cuticular dystrophy | ☐ Present ☐ Absent |
| Poikiloderma | ☐ Present ☐ Absent |
| Lateral digit fissuring/hyperkeratosis/papules | ☐ Present ☐ Absent |
| Linear extensor erythema of digits | ☐ Present ☐ Absent |
| Erythematous palmar macules and papules | ☐ Present ☐ Absent |
| ***DISTRIBUTION*** | |
| Scalp | ☐ Present ☐ Absent |
| Eyelid | ☐ Present ☐ Absent |
| Nasolabial fold | ☐ Present ☐ Absent |
| Upper chest in 'V' | ☐ Present ☐ Absent |
| Upper back in 'shawl' | ☐ Present ☐ Absent |
| Elbow and/or knee | ☐ Present ☐ Absent |
| Lateral upper thigh/hip | ☐ Present ☐ Absent |
| ***SYMPTOMS*** | |
| Scalp pruritus | ☐ Present ☐ Absent |
| Photosensitivity | ☐ Present ☐ Absent |
| ***LAB*** | |
| Presence of DM-specific myositis antibody (Jo-1, PL-7, PL-12, EJ, OJ, Mi-2, SRP, KS, TIF1γ/α, TIF1β, MJ/NXP-2, MDA5/CADM-140, SAE)<br><br>Note: Although not required, may indicate type of assay used (e.g. ELISA, immunoprecipitation etc.) and/or lab utilized (e.g. OMRF, ARUP etc.) in the space provided. | ☐ Present ☐ Absent<br>☐ Not assessed<br><br>_____<br>_____ |

Concha JSS, et al. *Br J Dermatol*. 2020;182(2):410-417.

# New EULAR/ACR Myositis Criteria Project Ongoing

- Evaluating skin variables found in this skin study
- Not clear how retrospective capture of skin data will be analyzed
  - Detection of skin variables should be done prospectively to be accurately assessed
  - Many skin variables not included in routine EMR records

# Outline

- Cutaneous findings in dermatomyositis
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- Outcomes in dermatomyositis

# Interface Dermatitis

- Inappropriate activation of type I IFN system
- IFN-regulated chemokines aid in recruitment of CXCR3-positive cytotoxic lymphocytes to dermal-epidermal junction
- Also see dendritic cells, macrophages
- Induce keratinocyte cell death
- Release of nuclear antigens
- Stimulate innate immune response in TLR-dependent and independent fashion

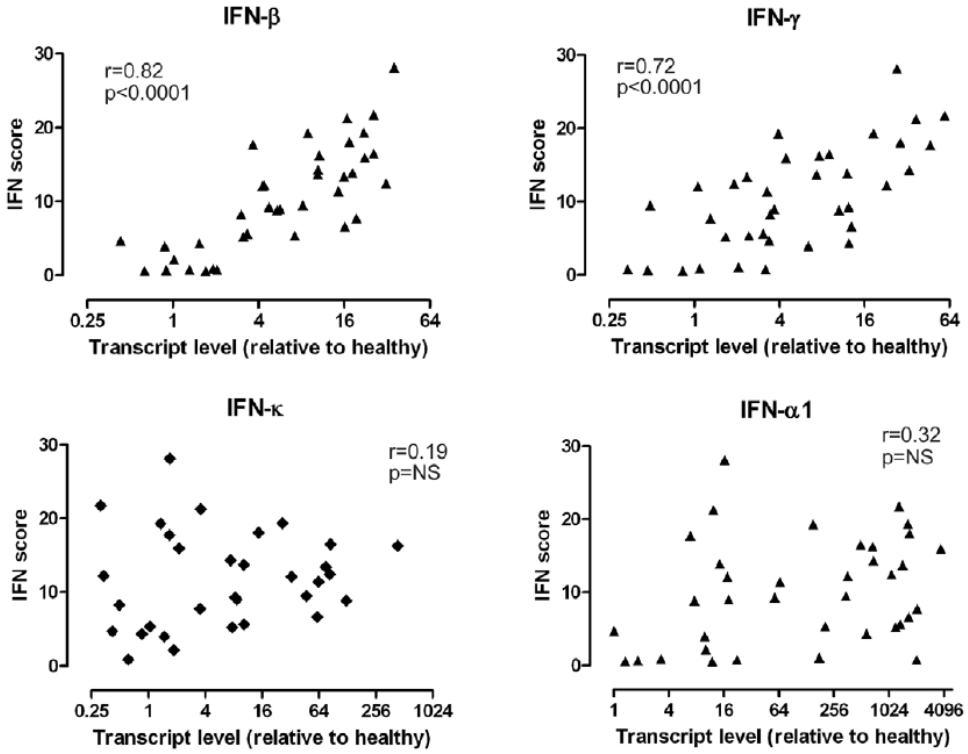
**IFN = interferon; TLF = toll-like receptor.**
**Patel J, et al. *J Invest Dermatol*. 2021;141(9):2151-2160.**

# Interferon Signature

- Present in skin, blood, muscle
- IFN-$\beta$ and IFN-$\gamma$ levels most closely correlate with activation of IFN-induced genes
- Very specific genes differentially regulated by Type I vs Type II IFN, but most IFN-response genes upregulated by both

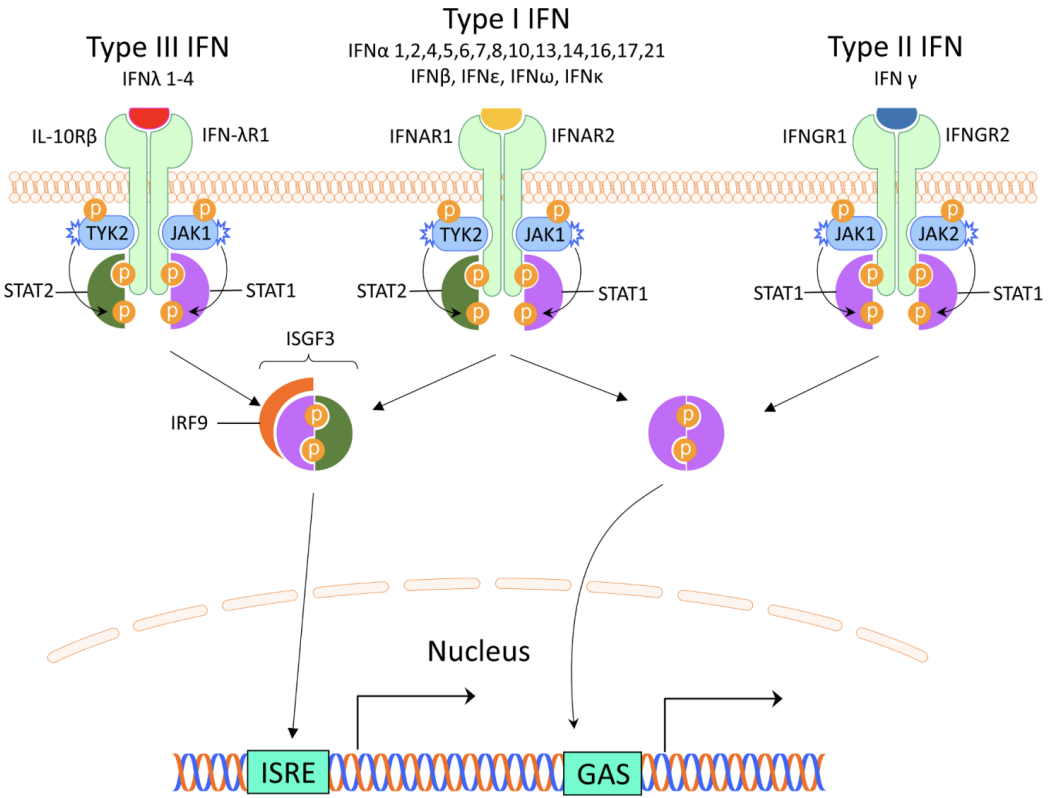
**Wong D, et al. *PLoS One*. 2012;7(1):e29161. Hall JC, et al. *Proc Natl Acad Sci U S A*. 2012;109(43):17609-170614.**

# Interferon Signature in Skin




Wong D, et al. *PLoS One*. 2012;7(1):e29161.

# Interferon Receptors and Signaling




Rönnblom L, Leonard D. *Lupus Sci Med*. 2019;6(1):e000270.

# Outline

- Cutaneous findings in dermatomyositis
- Diagnosis of dermatomyositis
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- **Evaluation of dermatomyositis**
- Environmental triggers of DM
- Outcomes in dermatomyositis

# Evaluation of Dermatomyositis

- History: Joint pain, proximal muscle weakness, dysphagia, shortness of breath
- Physical exam: Skin, muscle, joint, lung exams
- Skin biopsy: Interface dermatitis (80% +)
- CPK, aldolase
- If no muscle symptoms and muscle enzymes normal, no further muscle work-up
- Myositis antibodies

**CPK = creatine phosphokinase.**

# Autoantibodies and Phenotypes

- Help in diagnosis and patient assessment
  - Prediction of complications and prognosis
  - Therapeutic strategy

**Betteridge Z, McHugh N. *J Intern Med*. 2016;280(1):8-23. Satoh M, et al. *Clin Rev Allergy Immunol*. 2017;52(1):1-19. Gunawardena H. *Clin Rev Allergy Immunol*. 2017;52(1):45-57.**

# Dermatomyositis-Specific Antibodies

| Autoantibody | Autoantigen | Clinical Features |
|---|---|---|
| Anti-Mi-2 | DNA helicase | Skin, muscle, responsive to Rx |
| Anti-MDA5 | Melanoma differentiation-associated gene 5 | Skin, rapidly progressive ILD, distinct skin (ulcers, palmar papules) |
| Anti-155/140 | TIF-gamma | Cancer-associated |
| Anti-p140 (MJ) | Nuclear matrix protein (NXP-2) | Juvenile DM, calcinosis, cancer |
| Anti-SAE | Small ubiquitin-like modifier-activating enzyme | CADM, can get myositis, ILD rare |

# Positivity Rates of MSA, MAA, and ANA by DM Subtype

| | No. (%) | | |
|---|---|---|---|
| | Classic DM (n = 198) | Clinically amyopathic DM (n=122) | P-value |
| Any MSA positive | 94/198 (47) | 49/122 (40) | .20 |
| Any MAA positive | 48/168 (29) | 26/100 (26) | .65 |
| Any ANA positive | 90/143 (63) | 42/85 (49) | **.045 (< .05)** |
| Either MSA or MAA positive | 118/198 (60) | 63/122 (52) | .16 |
| Both MSA and MAA negative | 80/198 (40) | 59/122 (48) | .16 |
| Both MSA and MAA negative but ANA positive | 26/53 (49) | 13/36 (36) | .23 |

**MSA = myositis-specific; MAA = myositis-associated.**

**Yang X, et al. *JAMA Dermatol*. 2025;161(11):1184-1186.**

# Evaluation of Dermatomyositis

- History
  - Use of meds that can exacerbate DM (hydroxyurea, TNF blockers, statins)
  - Immunostimulatory herbs
  - Timing of onset or flares with COVID vaccination

# Evaluation of Dermatomyositis

- If muscle symptoms or elevated muscle enzymes (including ALT)
  - MRI or EMGs
- If skin findings typical for dermatomyositis, don't need muscle biopsy to confirm muscle involvement
- PFTs including DLCO for all with DM
  - High resolution CT of lungs if PFTs abnormal

**PFT = pulmonary function test; DLCO = diffusing capacity of the lungs for carbon monoxide.**

**Ahmed S. *J Am Acad Dermatol*. 2022;86(3):544-550.**

# Skin Biopsy: Differential Diagnosis

- Cutaneous lupus erythematosus
- Dermatomyositis

# Evaluation of Dermatomyositis for Malignancy

- Recent evidence-based guidelines
- Stratify based on risk
- Endoscopy/colonoscopy, mammogram, pelvic ultrasound
- In older ages or higher risk: CT with contrast of abdomen/pelvis and chest
- Possible role for PET scan

**Oldroyd AGS, et al. *Nat Rev Rheumatol*. 2023;19(12):805-817.**

# Evaluation of Dermatomyositis for Malignancy

- **High risk**
  - Dermatomyositis
  - Anti-TIF1y antibody positivity
  - Anti-NXP2 antibody positivity
  - Age >40 years at the time of IIM onset
  - Features of persistent high disease activity despite immunosuppressive therapy (including relapse of
  - previously controlled disease)
  - Dysphagia (moderate to severe)
  - Cutaneous necrosis or ulceration

**Oldroyd AGS, et al. *Nat Rev Rheumatol*. 2023;19(12):805-817.**

# Outline

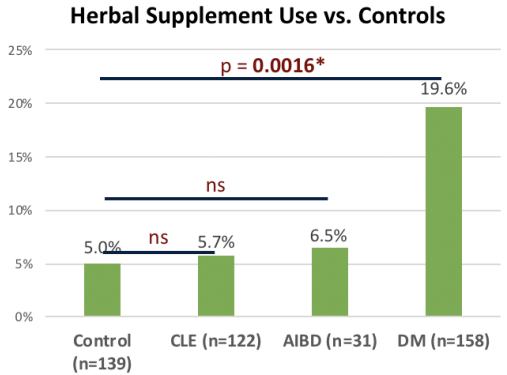
- Cutaneous findings in dermatomyositis
- Diagnosis of dermatomyositis
- Pathophysiology
- Evaluation of dermatomyositis
- **Environmental triggers of DM**
- Outcomes in dermatomyositis

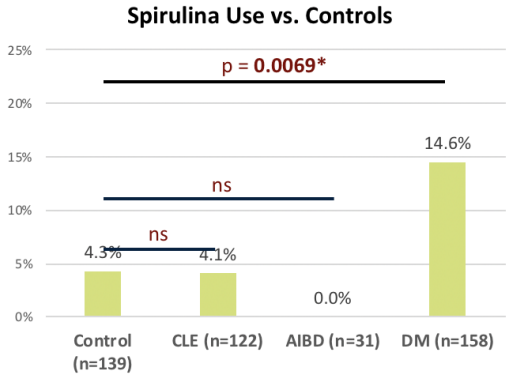



- Herbal supplement use is increasing in US
- Popular weight-loss powders associated with DM onset or flare
- Herbs stimulate the immune system, as determined by both in vitro and in vivo studies
  - *Spirulina platensis*
  - *Aphanizomenon flos-aqua* (blue-green algae)
  - Chlorella
  - Echinacea
  - Alfalfa
  - Elderberry
  - Ashwagandha

**Zeidi M, et al. *J Am Acad Dermatol*. 2019;80(3):801-804. Bax CE, et al. *J Am Acad Dermatol*. 2021;84(4):1051-1058.**

# Immunostimulatory Herbal Supplement Use among Dermatology Patients at Penn



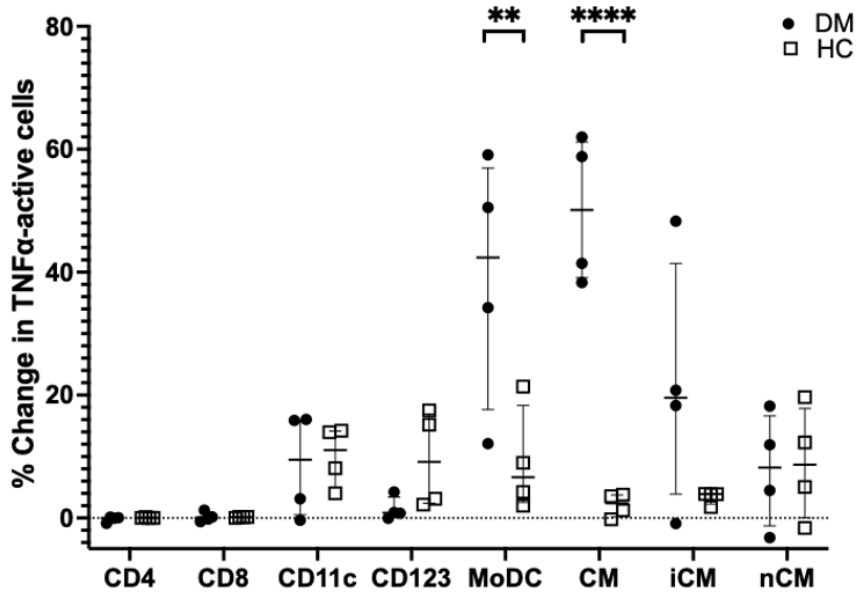



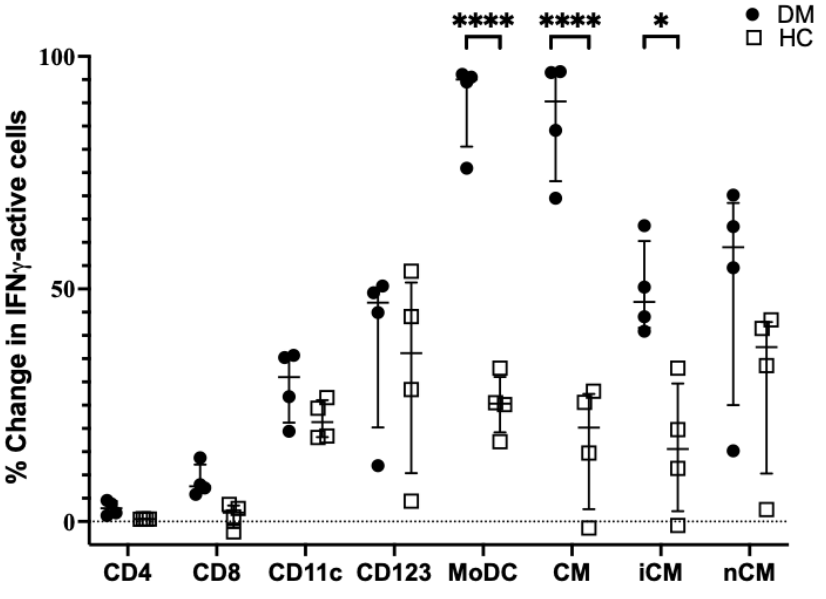

Herbal supplement use is **3.47x** more common in DM than in CLE & AIBD (p = 0.0032) and **4.0x** more common in DM than in healthy controls (p = 0.0016).

Spirulina use **3.63x** more common in DM than in healthy controls ( p = 0.0069) and **4.92x** more common in DM than in CLE and AIBD (p = 0.0027).

**Ravishankar A ... Werth VP, et al. *J Am Acad Dermatol*. 2022;87(5):1093-1095.**

# IFNg and TNFα Production in PBMCs in DM and HC after Spirulina




**PBMC = peripheral blood mononuclear cells; HC = healthy control; TNF = tumor necrosis factor.**
**Bax CE, et al. *iScience*. 2023;26(11):108355.**

# Immunostimulatory Herbs

## Think before you drink!

We are concerned that certain supplements may be harmful if you have an autoimmune disease

Avoid these ingredients:

- Spirulina
- Echinacea
- Green Algae
- Chlorella
- Alfalfa
- Elderberry (Sambucol)
- Ashwagandha

Before you try *supplements, powders, protein drinks, or juices,* **check the ingredients**! Look closely at anything marketed for "immune support" or "healthy immunity"

**Nutrition Facts**
Serving size 1 bottle

Amount Per Serving
**Calories 150**

| | % Daily Value* |
|---|---|
| **Total Fat** 0.5g | **1%** |
| **Cholesterol** 0mg | **0%** |
| **Sodium** 125mg | **5%** |
| **Total Carbohydrate** 32g | **12%** |
| Dietary Fiber 2g | **6%** |
| Total Sugars 26g | |
| Incl. 0g Added Sugars | **0%** |
| **Protein** 3g | |

Calcium 40mg 2% • Iron 1mg 4%
Potas. 670mg 10% • Vit. C 36mg 40%

Not a significant source of saturated fat, *trans* fat and vitamin D.

**INGREDIENTS:** COCONUT WATER FROM CONCENTRATE (WATER, COCONUT WATER CONCENTRATE) CUCUMBER JUICE, APPLE PUREE, PEACH PUREE, ORANGE JUICE, LEMON JUICE, KIWI PUREE, NATURAL FLAVORS, SPIRULINA, ALFALFA, BROCCOLI, SPINACH, BARLEY GRASS, WHEATGRASS, GINGER ROOT, PARSLEY, KALE, GARLIC.

# Immunostimulatory Herbs

- They may be found in
  - Bolthouse Farm™
  - Health-Ade Kombucha®
  - Synergy Kombucha™
  - Naked® Juice
  - Suja
  - Raw Juice Guru™
  - SmartFruit™
  - Juice Plus+®
  - Robitussin®
  - Melatonin
  - And many other products!


**Zeidi M, Chansky PB, Werth VP. *J Am Acad Dermatol*. 2019;80(3):801-804. Barak V, et al. *Eur Cytokine Netw*. 2001;12(2):290-296.**

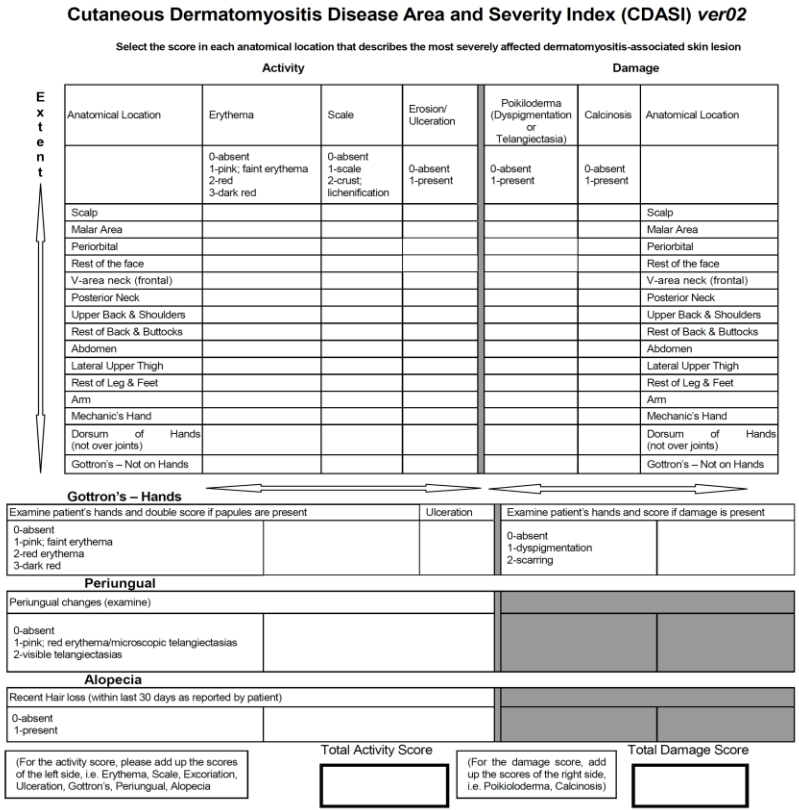
# Outline

- Cutaneous findings in dermatomyositis
- Diagnosis of dermatomyositis
- Pathophysiology
- Evaluation of dermatomyositis
- Environmental triggers of DM
- **Outcomes in dermatomyositis**

# Outcomes in DM

- 269 patients with DM
- 51% classic DM and 49% CADM at baseline
- Median (IQR) database follow-up time of 2.0 (4.0) years for patients with CADM and 2.0 (3.8) years
- 40% of classic DM became post-myopathic after median of 3.8 (7.1) years
  - Skin disease frequently persists after muscle disease better
- 5% of CADM went on to develop muscle disease after 6.3 (8.8) years

**Pandya R, et al. *J Am Acad Dermatol*. 2024;91(1):31-36.**



**Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) *ver02***

Select the score in each anatomical location that describes the most severely affected dermatomyositis-associated skin lesion

| | Activity | | | Damage | | |
|---|---|---|---|---|---|---|
| Extent | Anatomical Location | Erythema | Scale | Erosion/ Ulceration | Poikiloderma (Dyspigmentation or Telangiectasia) | Calcinosis | Anatomical Location |
| | | 0-absent<br>1-pink; faint erythema<br>2-red<br>3-dark red | 0-absent<br>1-scale<br>2-crust;<br>lichenification | 0-absent<br>1-present | 0-absent<br>1-present | 0-absent<br>1-present | |
| | Scalp | | | | | | Scalp |
| | Malar Area | | | | | | Malar Area |
| | Periorbital | | | | | | Periorbital |
| | Rest of the face | | | | | | Rest of the face |
| | V-area neck (frontal) | | | | | | V-area neck (frontal) |
| | Posterior Neck | | | | | | Posterior Neck |
| | Upper Back & Shoulders | | | | | | Upper Back & Shoulders |
| | Rest of Back & Buttocks | | | | | | Rest of Back & Buttocks |
| | Abdomen | | | | | | Abdomen |
| | Lateral Upper Thigh | | | | | | Lateral Upper Thigh |
| | Rest of Leg & Feet | | | | | | Rest of Leg & Feet |
| | Arm | | | | | | Arm |
| | Mechanic's Hand | | | | | | Mechanic's Hand |
| | Dorsum of Hands (not over joints) | | | | | | Dorsum of Hands (not over joints) |
| | Gottron's – Not on Hands | | | | | | Gottron's – Not on Hands |

**Gottron's – Hands**

| Examine patient's hands and double score if papules are present | | Ulceration | Examine patient's hands and score if damage is present | |
|---|---|---|---|---|
| 0-absent<br>1-pink; faint erythema<br>2-red erythema<br>3-dark red | | | 0-absent<br>1-dyspigmentation<br>2-scarring | |

**Periungual**

| Periungual changes (examine) | | | |
|---|---|---|---|
| 0-absent<br>1-pink; red erythema/microscopic telangiectasias<br>2-visible telangiectasias | | | |

**Alopecia**

| Recent Hair loss (within last 30 days as reported by patient) | | | |
|---|---|---|---|
| 0-absent<br>1-present | | | |

(For the activity score, please add up the scores of the left side, i.e. Erythema, Scale, Excoriation, Ulceration, Gottron's, Periungual, Alopecia)

Total Activity Score

(For the damage score, add up the scores of the right side, i.e. Poikioloderma, Calcinosis)

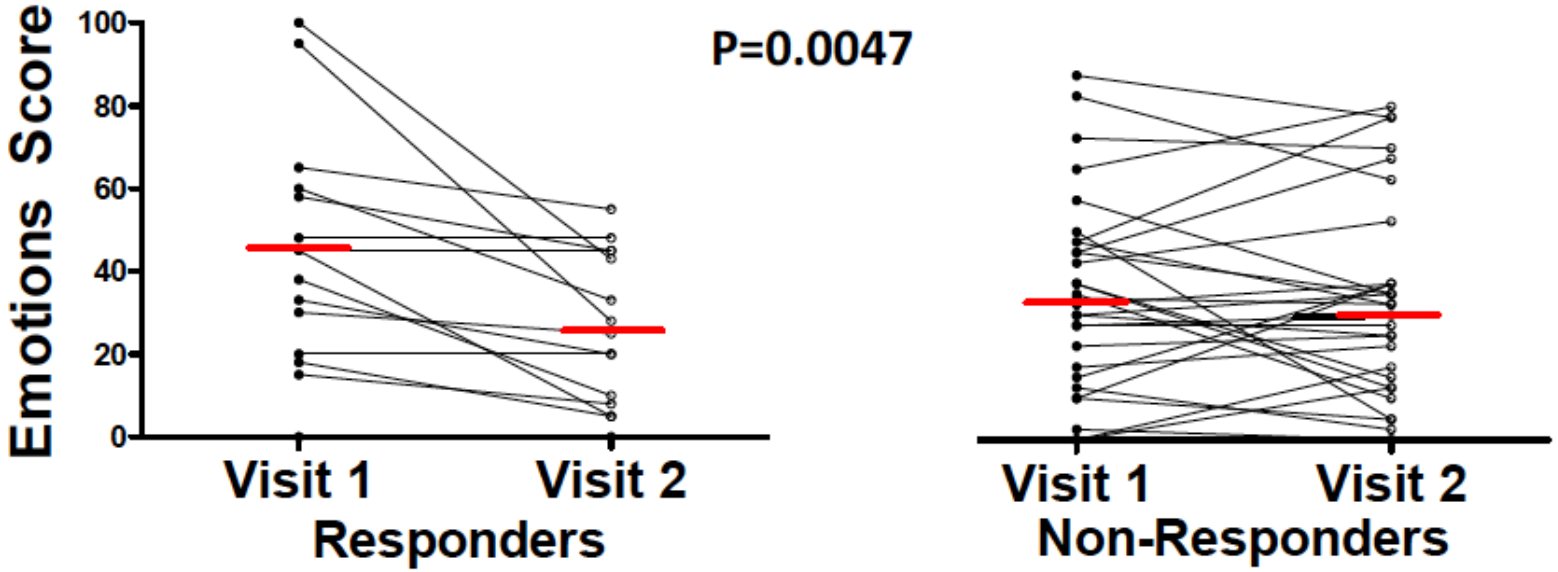
Total Damage Score

# CDASI

- Validated outcome measure
- Useful for early and accurate diagnosis
- Rate disease activity and damage at 15 anatomical sites
- Separate activity and damage scores
- Mild DM: CDASI activity score < 14
- Moderate–severe DM: CDASI activity score >14
- Clinically relevant improvement: 40% improvement in CDASI

**Klein RQ, et al. *Br J Dermatol.* 2008;159(4):887-894. Goreshi R, et al. *J Invest Dermatol.* 2012;132(4):1117-1124. Anyanwu CO, et al. *Arthritis Rheum.* 2013;65(10):2622.**

# CDASI Response Correlates with QoL




QOL = quality of life.

Robinson ES, et al. *Br J Dermatol*. 2015;172(1):169-174.

# Skindex

- Used in patients with skin disease of any sort
- Can be used to assess QoL over time

Mean Skindex scores in patients with different dermatological diagnoses

| | SKINDEX-29 SCORES* | | | | SKINDEX-16 SCORES* | | | |
|---|---|---|---|---|---|---|---|---|
| DIAGNOSIS | # | SYMPTOMS | EMOTIONS | FUNCTIONING | # | SYMPTOMS | EMOTIONS | FUNCTIONING |
| Eczematous dermatitis | 102 | 48 ± 23 | 41 ± 27 | 26 ± 26 | 84 | 42 ± 31 | 52 ± 30 | 24 ± 29 |
| Psoriasis | 44 | 42 ± 21 | 39 ± 27 | 23 ± 27 | 27 | 49 ± 29 | 68 ± 25 | 39 ± 33 |
| Acne vulgaris | 63 | 30 ± 19 | 41 ± 25 | 16 ± 16 | 38 | 31 ± 24 | 75 ± 23 | 38 ± 30 |
| Warts | 24 | 23 ± 18 | 22 ± 16 | 6 ± 13 | 33 | 23 ± 23 | 48 ± 31 | 24 ± 31 |
| Other benign growths | 76 | 22 ± 20 | 21 ± 21 | 9 ± 17 | 56 | 15 ± 20 | 34 ± 29 | 12 ± 21 |

*Mean ± SD

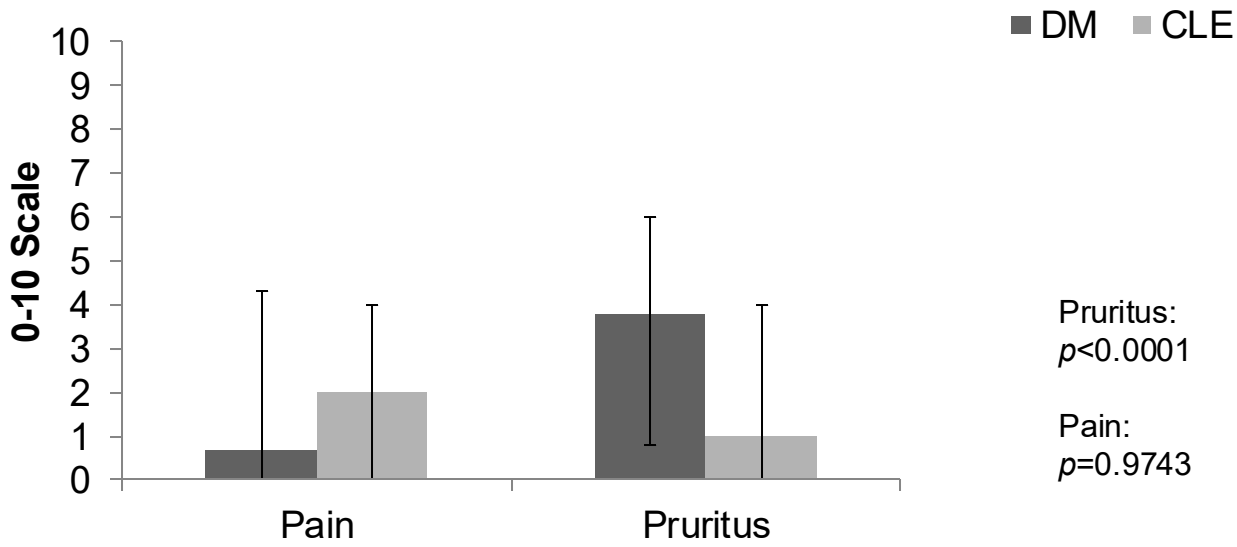
**Chren MM. *Dermatol Clin*. 2012;30(2):231-236, xiii.**

# QoL DM (SF-36)

- QoL in DM worse than other diseases (recent MI, HTN, type II diabetes)
- Particularly true in the emotional realm (vitality, social functioning, role-emotional, mental health)

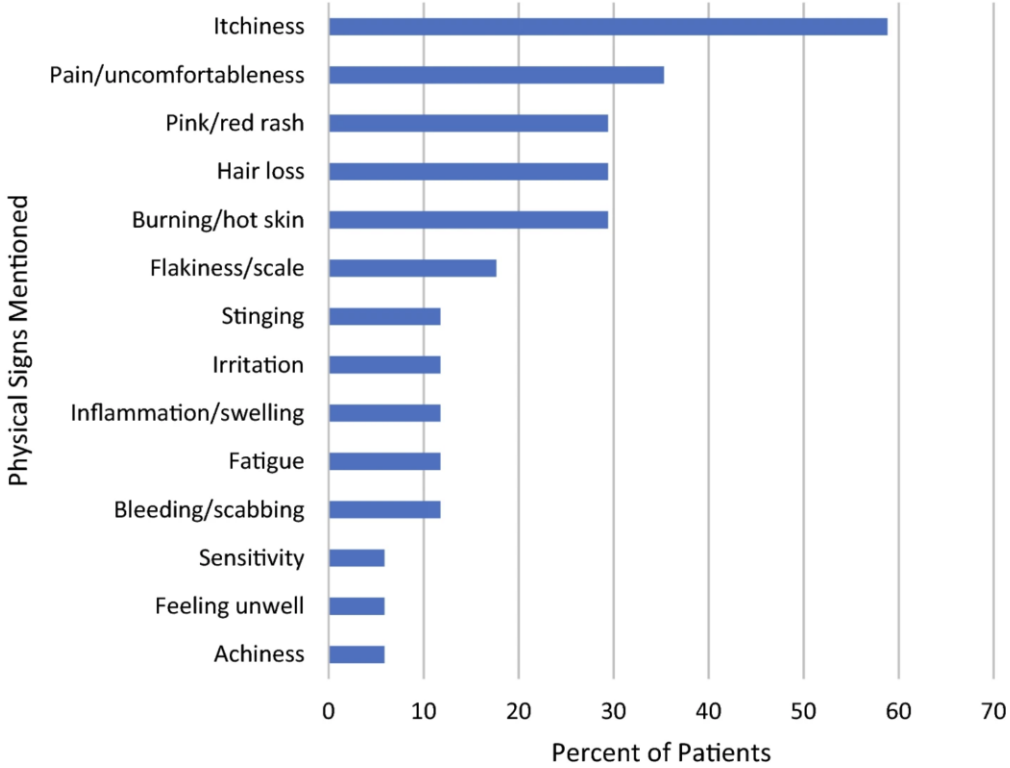
**Goreshi R, et al. *J Am Acad Dermatol*. 2011;65(6):1107-1116.**

# Median Pain and Pruritus Scores in DM and CLE




Goreshi R, et al. *J Am Acad Dermatol*. 2011;65(6):1107-1116.

# The Physical and Emotional Impact of Cutaneous Dermatomyositis




**Kleitsch J, et al. *Arch Dermatol Res*. 2023;315(8):2431-2435.**

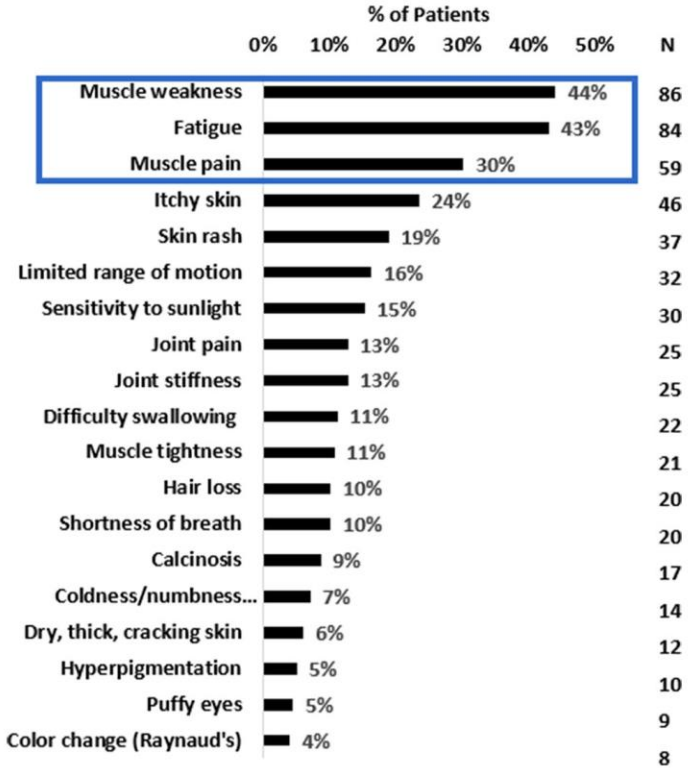
# In Classic DM (Skin and Muscle)

- More than 50% of participants said their social life and relationships are at least somewhat negatively impacted by DM
- DM limits their ability to perform daily activities (65%) and the ability to climb stairs (63%)
- Immunosuppressants were most commonly used (72%), then over-the-counter NSAIDs (56%) and oral corticosteroids (48%)

**NSAID = non-steroidal anti-inflammatory drug.**

**Christopher-Stine L, et al. *J Rheumatol*. 2024;51(12):1198-1207.**

# In Classic DM (Skin and Muscle)




Christopher-Stine L, et al. *J Rheumatol*. 2024;51(12):1198-1207.

# Key Learning Points

- Better classification criteria that includes amyopathic DM
- Further improvements to criteria ongoing
- Dermatomyositis frequently misdiagnosed as SLE or CLE
- Use CDASI for early and accurate diagnosis of DM
- Huge impact on quality of life for patients
- Check for lung disease and underlying malignancy
- Growing insights into the role of type I interferons, particularly IFNβ
- Validated outcome measures that measure skin activity

masterclasses in dermatology annual meeting
PRESENTED BY THE dermatologist

# Evolving Treatment Strategies in the Management of Dermatomyositis

**Scott Elman, MD, FAAD**

*Dr. Phillip Frost Department of Dermatology & Cutaneous Surgery*
*University of Miami Miller School of Medicine*

# Historical Approach to Treating Dermatomyositis

- Approach depends on
  - Presence/severity of underlying muscle disease
  - Presence of malignancy
  - Presence of ILD (ie. may favor MMF, RTX, etc.)
  - Presence of arthralgia (may prefer HCQ/MTX)

**ILD = interstitial lung disease; MMF = mycophenolate mofetil; RTX = rituximab; HCQ = hydroxychloroquine; MTX = methotrexate.**

# Historical Approach to Treating Dermatomyositis

- General
  - Strict sun protection
  - Emollient use

- Topical corticosteroids
- Topical calcineurin inhibitors

- Systemic corticosteroids

# Historical Treatment

- Antimalarials (?) +/-
- Methotrexate
- Mycophenolate mofetil
- Azathioprine
- IVIG *

- Others
  - Rituximab (muscle disease >> skin disease)
  - Apremilast
  - Abatacept
  - Cyclophosphamide
  - Dapsone
  - Leflunomide
  - Thalidomide
  - Tacrolimus
  - JAK inhibitors

**IVIG = intravenous immunoglobulin; JAK = Janus kinase.**

# Historical Approach to Treating Dermatomyositis

- **Adverse effects**
  - **Hydroxychloroquine**
    - **Cutaneous hypersensitivity reactions**
      - Drug eruptions more common in dermatomyositis vs lupus
      - May require discontinuation or switch to quinacrine
    - **Retinal toxicity**
      - Risk increases with cumulative dose, duration >5 years, renal disease
      - Requires baseline and routine ophthalmologic screening
    - **Myopathy and neuromyopathy**
      - Can mimic or worsen muscle weakness
  - Even “mild” therapy has DM-specific tolerability challenges

**Wolverton SE, Wu JJ. *Comprehensive Dermatologic Drug Therapy*. 4th ed. Elsevier; 2020.**

# Historical Approach to Treating Dermatomyositis

- **Adverse effects**
  - **Methotrexate**
    - **Hepatotoxicity**
      - Transaminase elevation, fibrosis risk with cumulative exposure
      - Increased risk with obesity, diabetes, alcohol use
    - **Bone marrow suppression**
      - Leukopenia, anemia, thrombocytopenia
      - Requires regular CBC monitoring
    - **Pulmonary toxicity**
      - Hypersensitivity pneumonitis, chronic interstitial injury
      - Particularly concerning in DM-associated ILD
    - **Mucositis, nausea, fatigue**
      - Common drivers of dose limitation or discontinuation

- Monitoring burden and organ toxicity limit **long-term tolerability**

**Wolverton SE, Wu JJ. *Comprehensive Dermatologic Drug Therapy*. 4th ed. Elsevier; 2020.**

# Historical Approach to Treating Dermatomyositis

- **Adverse effects**
  - **Mycophenolate mofetil**
    - **Gastrointestinal intolerance**
      - Diarrhea, nausea, abdominal pain → frequent dose-limiting toxicity
    - **Infection risk**
      - Viral reactivation (HSV, VZV, CMV), bacterial infections
      - Heightened concern with combination immunosuppression
    - **Leukopenia and anemia**
      - Requires CBC surveillance
    - **Long-term malignancy risk**
      - Non-melanoma skin cancer, lymphoproliferative disorders (rare but relevant in a malignancy association condition)

**HSV = herpes simplex virus; VZV = varicella-zoster virus; CMV = cytomegalovirus; CBC = complete blood count.**
**Wolverton SE, Wu JJ. *Comprehensive Dermatologic Drug Therapy*. 4th ed. Elsevier; 2020.**

# Historical Approach to Treating Dermatomyositis

- **Adverse effects**
  - **IVIG**
    - **Infusion-related reactions**
      - Headache, fever, chills, nausea
      - **Aseptic meningitis** in susceptible patients
    - **Thromboembolic events**
      - Increased viscosity increases risk of thromboembolic events (DVT, PE, stroke)
    - **Logistical and financial burden**
      - Repeated infusions, high cost, insurance barriers

**DVT = deep vein thrombosis; PE = pulmonary embolism.**

**Wolverton SE, Wu JJ. *Comprehensive Dermatologic Drug Therapy*. 4th ed. Elsevier; 2020.**

# Historical Approach to Treating Dermatomyositis

- **Patient challenges**
  - Delayed response
    - Most conventional systemic agents for dermatomyositis have slow time to meaningful clinical improvement
    - **HCQ 8-12 weeks, MTX 8-16 weeks, MMF 8-12 weeks**
  - Delayed efficacy contributes to
    - Prolonged disease activity
    - Extended corticosteroid exposure
    - Patient frustration and treatment switching
    - Time to response varies substantially by agent and cutaneous vs muscle domain

**Wolverton SE, Wu JJ. *Comprehensive Dermatologic Drug Therapy*. 4th ed. Elsevier; 2020.**

# Historical Approach to Treating Dermatomyositis

- **Patient challenges**
  - Delayed response
  - Repeated flares/hospitalizations
  - Frequent discontinuation (side effects)
  - Persistent corticosteroid dependence
  - Need for painkillers
  - Overall dissatisfaction of current landscape

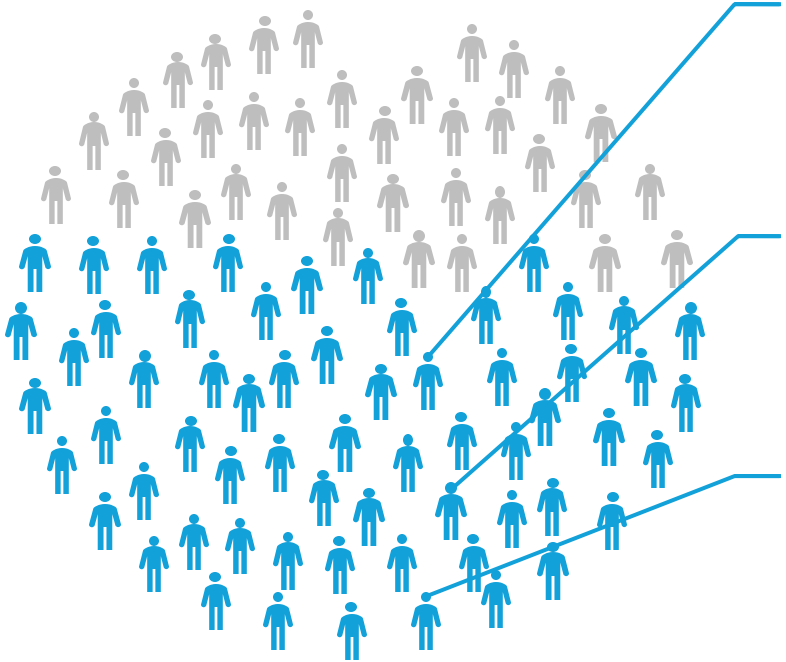
**Wolverton SE, Wu JJ. *Comprehensive Dermatologic Drug Therapy*. 4th ed. Elsevier; 2020.**

# Patients with DM Report Persistent Dissatisfaction with Current SOC

**62%**

**Dissatisfied with Current Treatment Options**

Patients with moderate to very severe DM are significantly more likely to be dissatisfied with their treatment regimen



### Persistent Symptoms Despite Treatment

**Many patients continue to experience debilitating symptoms** including muscle weakness and pain, skin rashes, joint pain, and fatigue even while on standard therapies. **More than half of patients report their current regimens only partially control symptoms**

### Patients Discontinue Treatment Due to Side Effects and Lack of Efficacy

Of patients who decide to discontinue treatment, **two-thirds describe side effects and poor efficacy as the primary drivers**. Prolonged non-specific, systemic immunosuppression can lead to challenging side effects

### Constant Fear of Disease Worsening

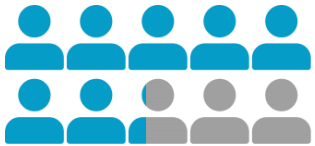
Nearly half of patients report being worried about disease flares and worsening of their DM. **Persistent anxiety reflects inadequate and unpredictable disease control**

**SOC = standard of care.**

**Christopher-Stine L, et al. *BMC Rheumatol*. 2025;9(1):23.**

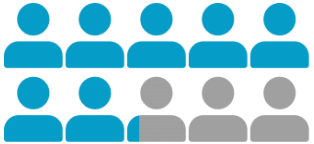
# High Rates of Disease Flares, Hospitalizations, Pain

**73%**
(N=524)



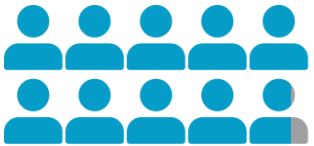
**Despite existing therapies, most adults with DM and PM experienced at least one disease flare in the past year**

**72%**
(N=378)



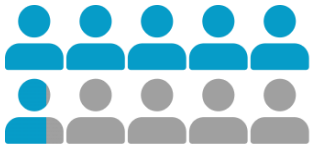
**Among patients experiencing at least one disease flare, most were hospitalized**

**97%**
(N=183)



**Nearly all patients with DM report experiencing pain attributed to their myositis**

**57%**
(N=183)

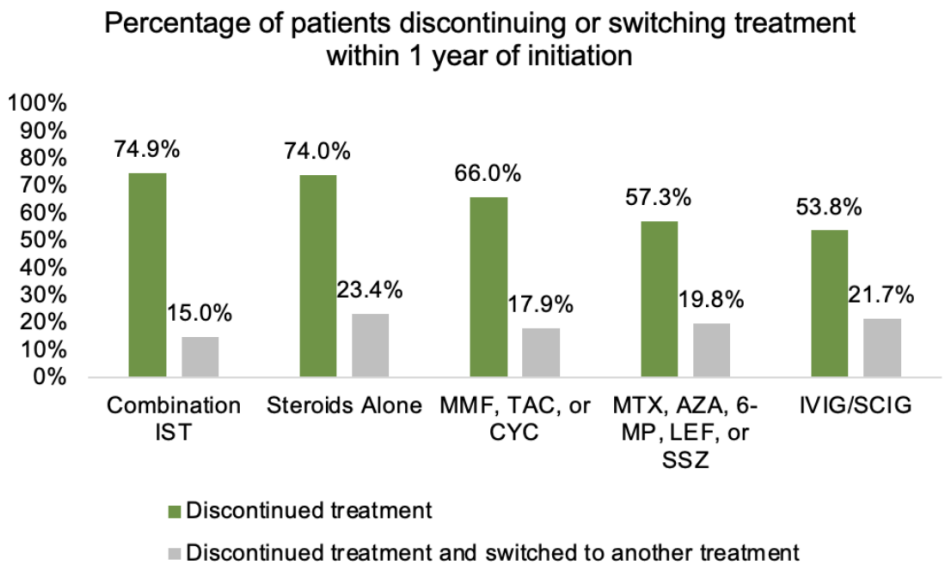


**% of patients with DM who use opioids to manage DM-associated pain**

Christopher-Stine L, et al. *J Manag Care Spec Pharm*. 2020;26(11):1424-1433. Bhashyam A, et al. *Rheumatology (Oxford)*. 2022;62(1):264-269.

# Pts with DM Frequently Discontinue Tx with Steroids, DMARDs, IVIG, Reflecting Dissatisfaction of Current Tx

**Real-world data (N = 2,022) reveal frequent treatment discontinuation and persistent corticosteroid dependence, highlighting the need for more effective, durable, and steroid-sparing options in DM**




- >60% of patients with DM discontinue their initial therapy within the first year of initiation, indicating limited durability of current regimens
  - Discontinuation rates range from 54-75% across treatment classes, highest among those on combination ISTs and monotherapy corticosteroids
  - >50% of patients discontinue IVIG within one year of starting therapy
- Among patients who switch to non-steroidal options, ~40-50% receive concomitant corticosteroids

**IST = immunosuppressive therapy, MMF = mycophenolate mofetil, TAC = tacrolimus, CYC = cyclosporine, MTX = methotrexate, AZA = azathioprine, 6-MP = 6-mercaptopurine, LEF = leflunomide, SSZ = sulfasalazine, IVIG/SCIG = intravenous or subcutaneous immunoglobulin**

**Bensimon A, et al. Presented at: ACR Convergence 2022; November 14, 2022; Philadelphia, PA. 1838.**

# Despite These Risks, Corticosteroids Remain the Cornerstone of DM Therapy, Reflecting the Inadequacies of Current Steroid-Sparing Options

- **Standard-of-care in DM remains largely unchanged since the 1980s**, relying on combinations of corticosteroids and off-label ISTs
  - These conventional therapies, in addition to IVIg, **are not uniformly effective in pts with DM**

- Even among patients treated with IVIg or off-label targeted therapies, chronic high-dose steroid use remains high, **with most requiring doses ≥10 mg/day for ≥100 days/year**

- Expert consensus now supports minimizing steroid duration **of any dose**: Thus, **new agents capable of achieving steroid-sparing efficacy would represent a major step forward in addressing this therapeutic gap**

# Historical Approach to Treating Dermatomyositis

- **Unmet needs**
  - Many patients achieve partial but not durable remission, particularly of skin activity despite systemic immunosuppression
  - Pruritus, dyspigmentation, calcinosis, and scarring remain poorly responsive to available therapies
  - Discordance between muscle and skin response complicates treatment selection and trial design
  - Reliance on broad immunosuppression (steroids, MTX, MMF) with toxicity and variable efficacy
  - Care is fragmented across dermatology, rheumatology, pulmonology, and oncology

# Limitations of Trial Design

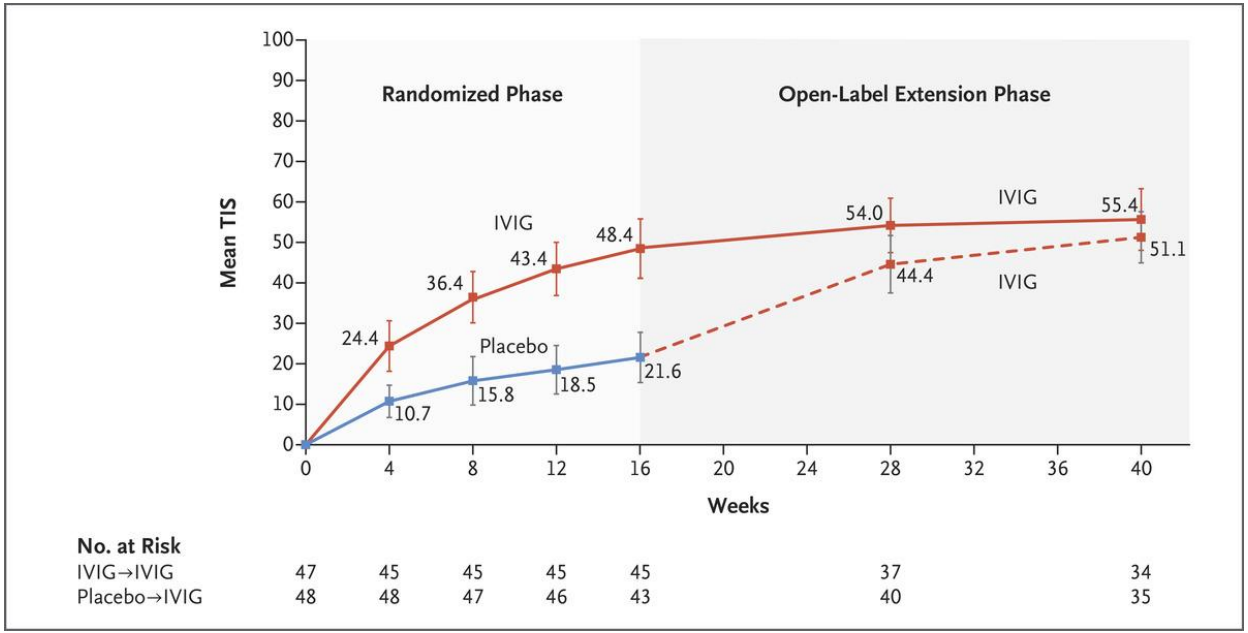
- Dominance of composite endpoints in DM trials
- Limited use of skin-specific primary endpoints
- Absence of trials in skin-predominant DM

# Where We've Been

- **Medications that failed to meet DM endpoints**
  - Lenabasum (cannabinoid agonist)
    - Failed to meet TIS, but of note, had skin efficacy
  - Tocilizumab (IL-6 antagonist)
  - Ustekinumab (IL12/23 antagonist)
  - IMO-8400 (TLR7/8/9 antagonist)
    - CDASI as primary endpoint
  - Zetomipzomib / KZR-616 (immunoproteasome inhibitor)
  - Abatacept (CTLA-4–Ig; T-cell co-stimulation modulator)
  - Ravulizumab (C5 complement inhibitor)
  - **And more…**

# Where We've Been

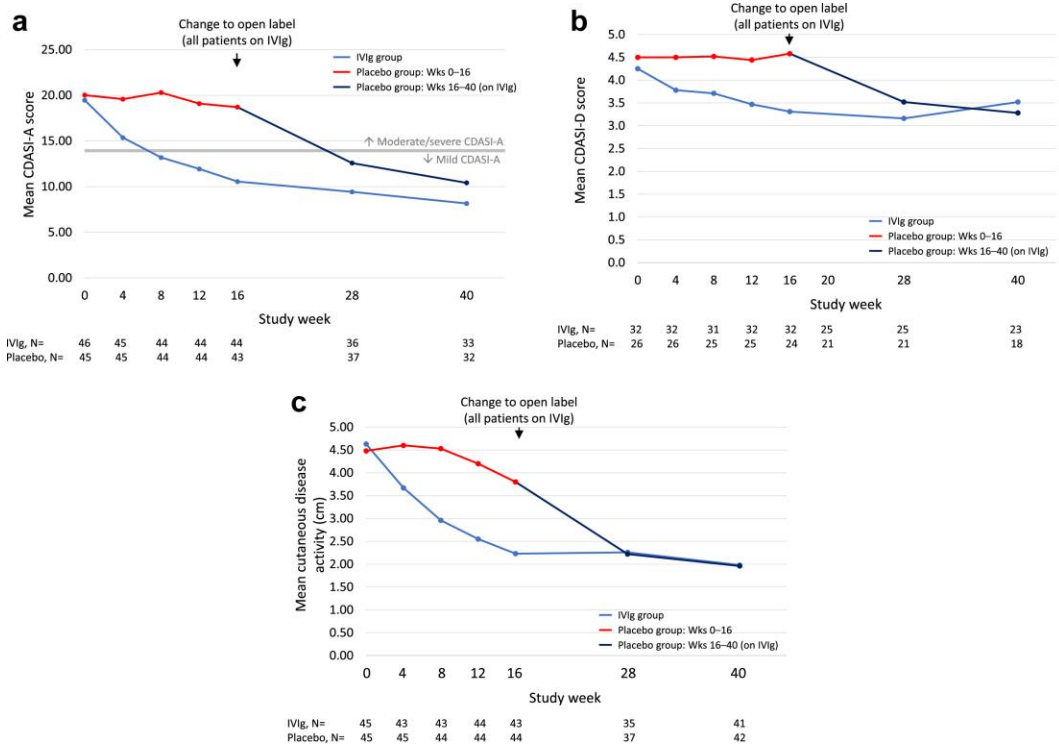
- **Medications that met DM endpoints**
  - IVIG (FDA approval 2021)




Aggarwal R, et al. *N Engl J Med.* 2022;387(14):1264-1278.

# IVIG for Cutaneous Disease in DM

- **Post-hoc analysis**
  - After 28 weeks, more than 70% of patients experienced > 35% improvement in CDASI-A (clinically meaningful)
  - Dermatologic scores did not plateau at week 40
  - Strong correlation between DM outcomes, suggesting that myopathic and cutaneous aspects of DM improve similarly with IVIG




Werth VP, et al. *EClinicalMedicine*. 2023;64:102234.

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# The Road Ahead

# Dermatomyositis Inflammatory Pathways

- **Key pathogenic mechanisms**
  - **Type I interferon pathway activation** (central driver)
  - Autoantibody production (myositis-specific antibodies)
  - Complement-mediated vascular injury
  - Cytokine dysregulation (IFN-α, IFN-β, TNF-α)
  - Pruritus mediated by IL-31

**IFN = interferon; IL = interleukin.**
**Kamperman RG, et al. *Int J Mol Sci*. 2022;23(8):4301.**

# JAK/STAT Pathway and TYK2

- **JAK/STAT signaling in dermatomyositis**
  - Type I interferons bind cell surface receptors
  - Activate **JAK-STAT signaling pathway**
  - Lead to expression of interferon-inducible genes
  - Result in inflammation and tissue damage

- **Therapeutic implications**
  - JAK inhibitors target this pathway
  - Show promise in refractory dermatomyositis
  - Blood-based biomarkers (eg. Siglec-1) for monitoring
  - TYK2 inhibition: Emerging therapeutic target

**JAK = Janus kinase; STAT = signal transducers and activators of transcription.**
**Kamperman RG, et al. *Int J Mol Sci*. 2022;23(8):4301.**

# What’s Coming

- Anti-interferon therapies (dazukibart, anifrolumab)
- JAK/TK2
- FcRN inhibitors (efgartigimod alfa-fcab)

# Anifrolumab in recalcitrant cutaneous dermatomyositis: A multicenter retrospective cohort study

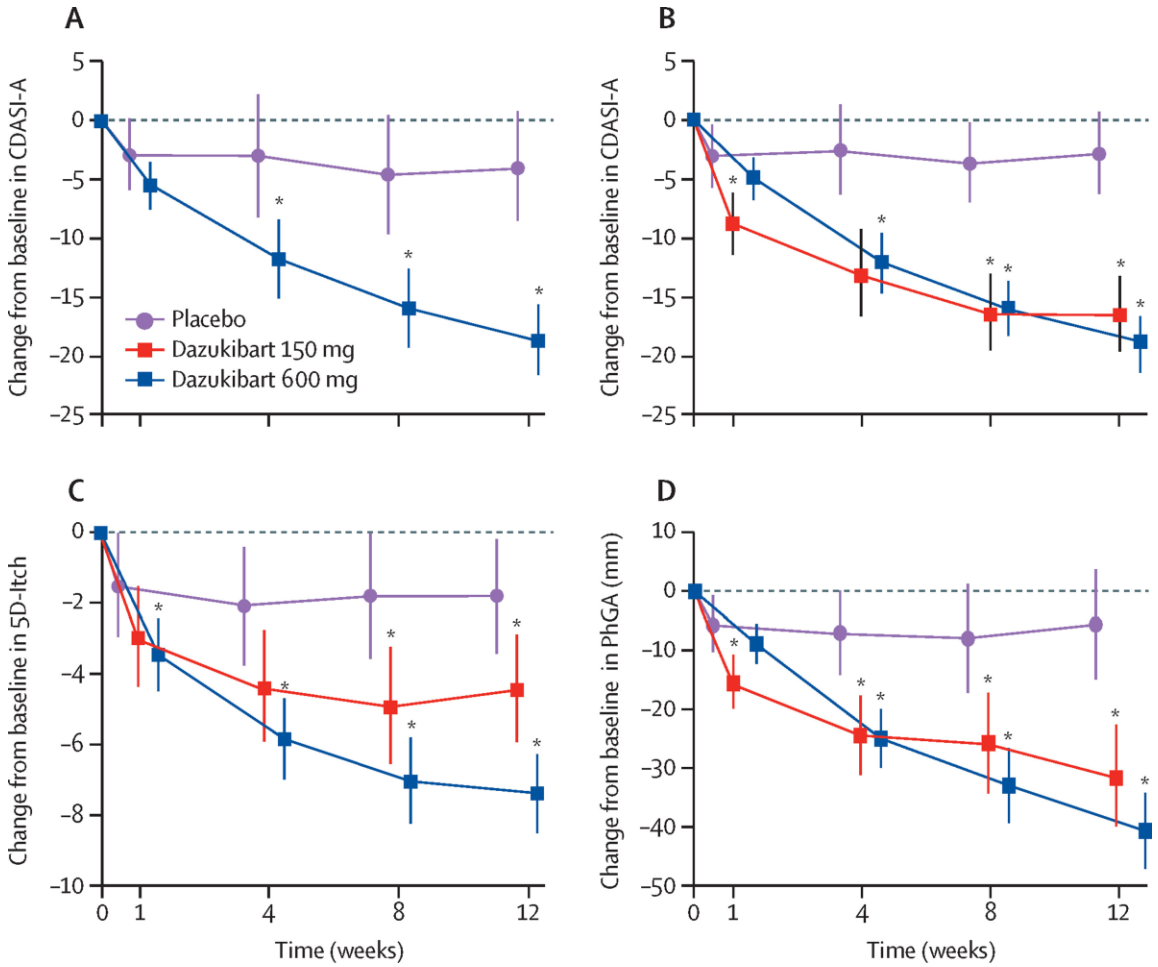
Katharina S. Shaw MD [a b], Kimberly B. Hashemi MD [c d], Rochelle L. Castillo MD, MS [c d], Elizabeth Rainone ALB [c], Allen W. Ho MD [c], Philip J. Kahn MD [e], Vikash S. Oza MD [e f], Alisa Femia MD [f], Ruth Ann Vleugels MD, MPH, MBA [c d]

**Shaw KS, et al. *J Am Acad Dermatol*. 2024;91(6):1217-1219.**

# Efficacy, safety, and target engagement of dazukibart, an IFNβ specific monoclonal antibody, in adults with dermatomyositis: a multicentre, double-blind, randomised, placebo-controlled, phase 2 trial

David Fiorentino [1], Aaron R Mangold [2], Victoria P Werth [3], Lisa Christopher-Stine [4], Alisa Femia [5], Myron Chu [6], Amy C M Musiek [7], Jason C Sluzevich [8], Lauren V Graham [9], Anthony P Fernandez [10], Rohit Aggarwal [11], Kerri Rieger [1], Karen M Page [12], Xingpeng Li [12], Craig Hyde [13], Natalie Rath [6], Abigail Sloan [12], Barry Oemar [12], Anindita Banerjee [12], Mikhail Salganik [12], Christopher Banfield [12], Srividya Neelakantan [12], Jean S Beebe [12], Michael S Vincent [12], Elena Peeva [12], Ruth Ann Vleugels [14]

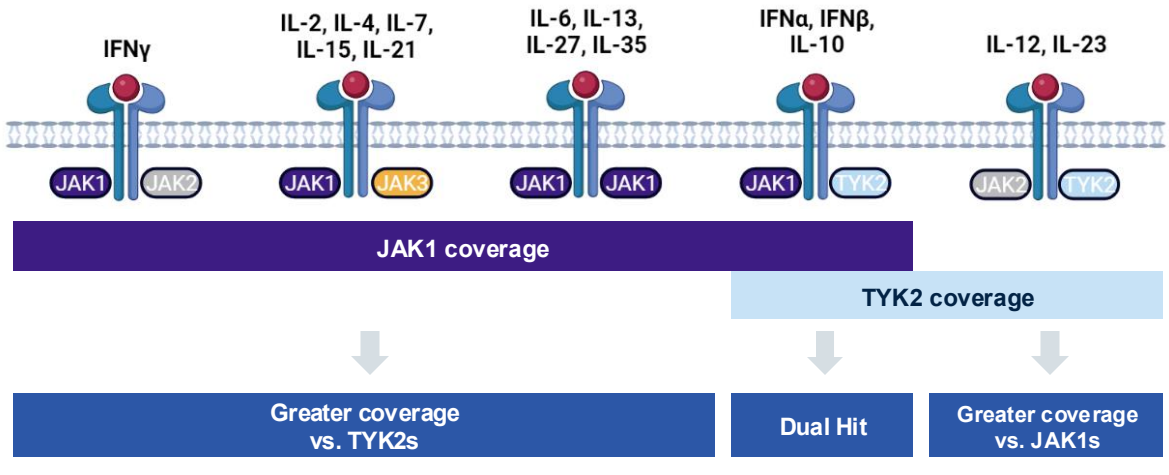
Fiorentino D, et al. *Lancet*. 2025;405(10473):137-146.




Fiorentino D, et al. *Lancet*. 2025;405(10473):137-146.

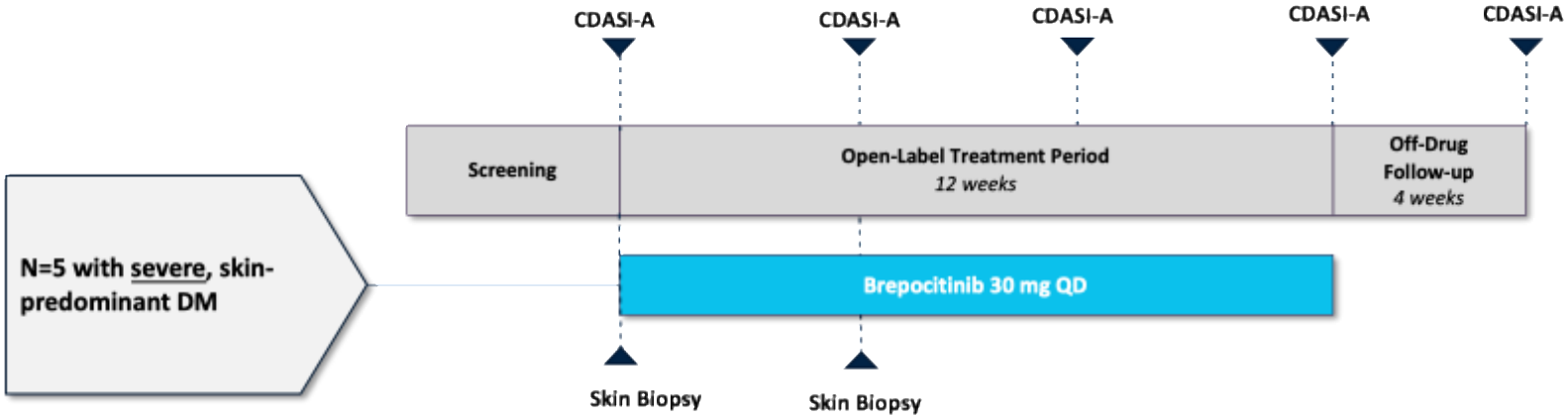
# More Is Coming

**Different diseases are driven by different combinations of cytokines, requiring inhibition of specific JAK isoforms to treat distinct indications most effectively**




Paik JJ, et al. *Clin Exp Rheumatol*. 2025;43(2):354-363. Zhu C, et al. *Arthritis Rheumatol*. 2025;77(6):750-764.

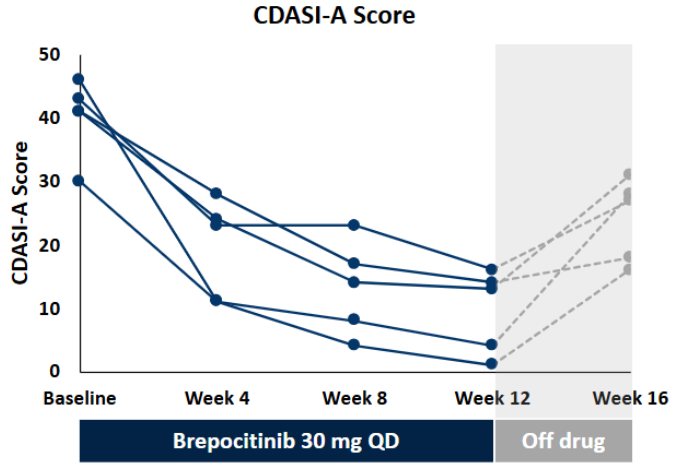
# Phase 2 Open-Label Trial Was Designed to Provide Mechanistic Insights into Early Clinical Responses to Brepocitinib in Patients with Severe Skin-Predominant DM

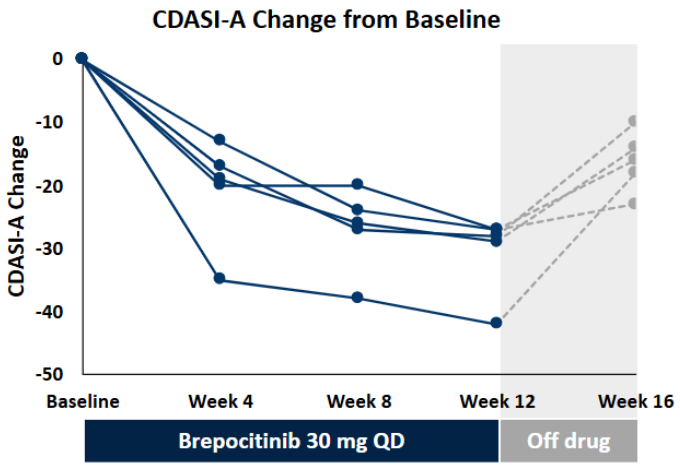



- Primary efficacy endpoint: CDASI-A
- Integrated translational analyses: Single-cell and spatial transcriptomic profiling performed on paired lesional and non-lesional DM skin biopsies at week 0 and week 4
  - Single-cell RNA sequencing (scRNA-seq): Characterizes gene expression at the level of individual cells, enabling the identification of key transcriptional changes in distinct cell subpopulations
  - Spatial transcriptomics (ST): Maps gene expression while preserving tissue architecture, allowing visualization of cell location, cellular niches, and cell-cell proximity

**Paik JJ, et al. *Clin Exp Rheumatol*. 2025;43(2):354-363. Mangold A, et al. Presented at: ARD Society Meeting; October 25, 2025; Chicago, IL.**

# All Participants Exhibited Rapid and Clinically Meaningful Reductions in Skin Disease Activity

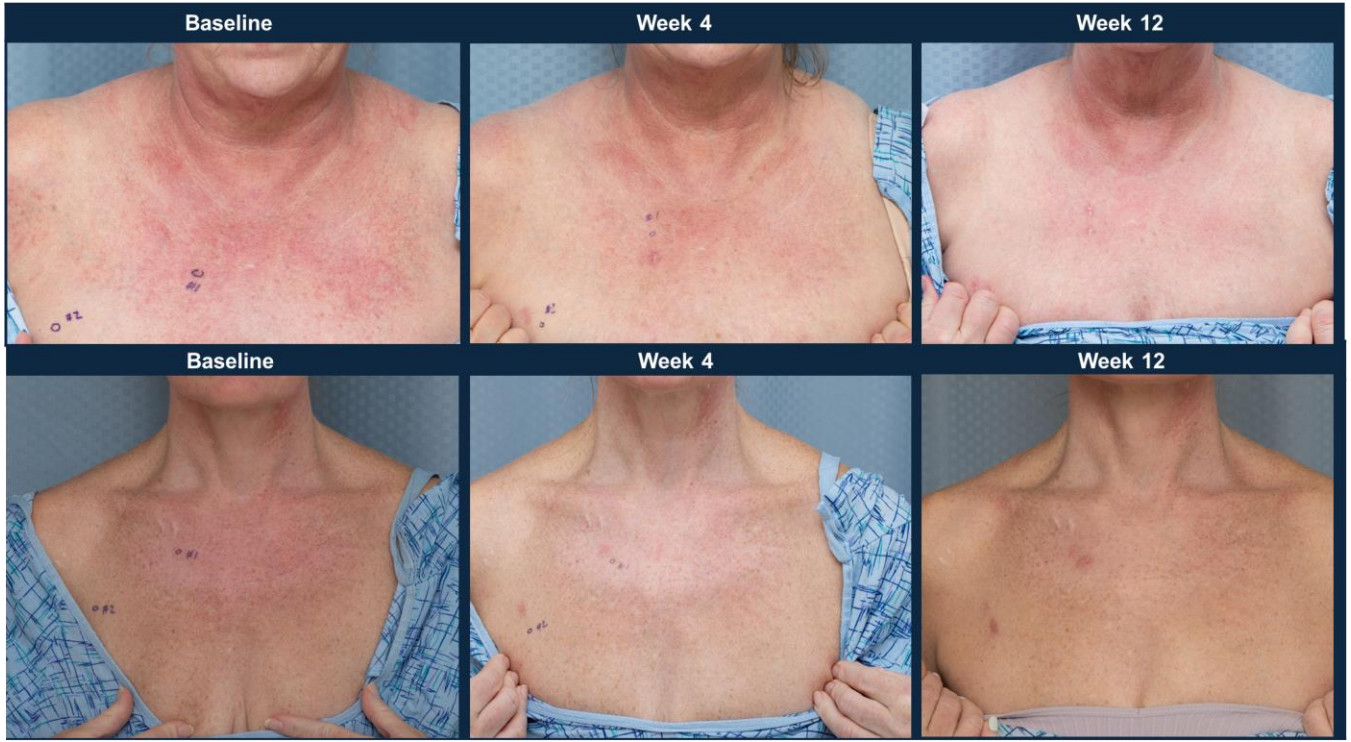



- All study participants had CDASI-A improvement exceeding the published MCIDs (≥40% decrease1 and ≥4-point2)
- Onset of efficacy was rapid, with median 19-point (47%) reduction from baseline to Week 4
- Two participants (40%) achieved CDASI-A ≤ 5 at Week 12, indicating functional remission of skin disease
- All study participants worsened by ≥4-points after brepocitinib was discontinued

**Paik JJ, et al. *Clin Exp Rheumatol*. 2025;43(2):354-363. Mangold A, et al. Presented at: ARD Society Meeting; October 25, 2025; Chicago, IL.**

# Representative Patient Photos Show Rapid Clinical Improvement at Week 4 with Continued Benefit through Week 12




Mangold A, et al. Presented at: ARD Society Meeting; October 25, 2025; Chicago, IL.

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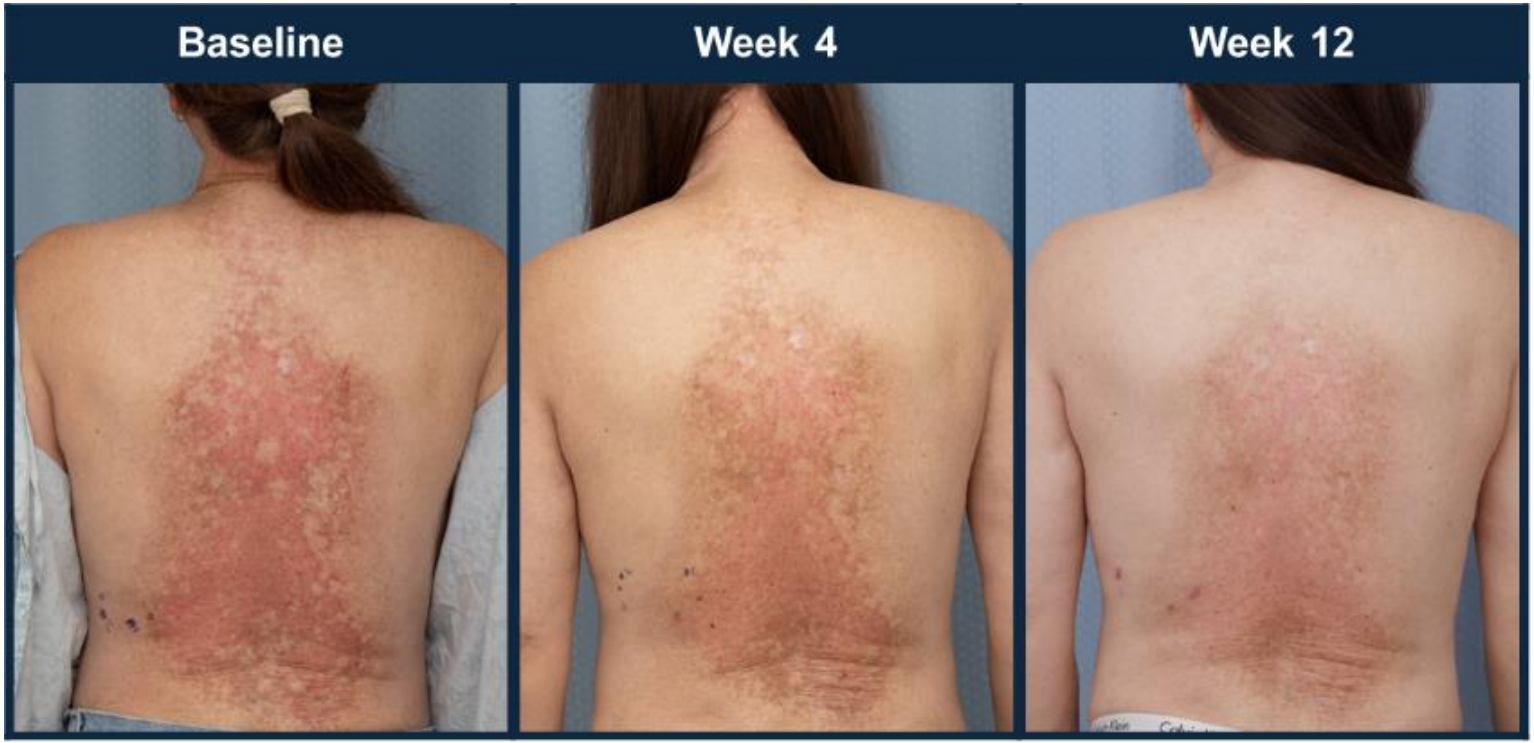


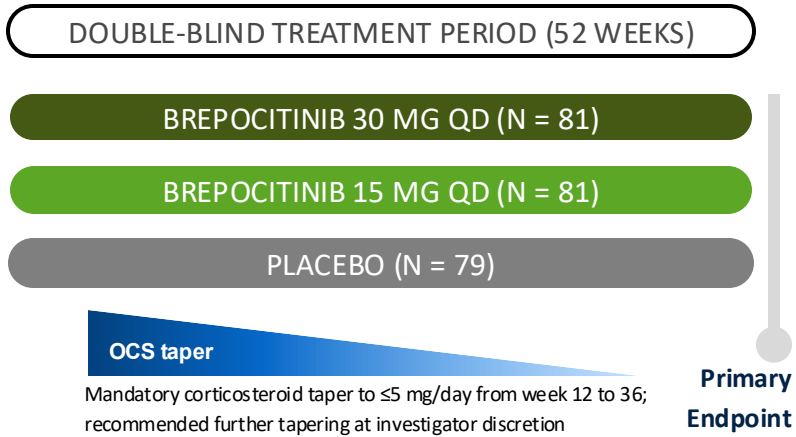

Mangold A, et al. Presented at: ARD Society Meeting; October 25, 2025; Chicago, IL.

# VALOR Phase 3 Study Design

- Distinguished by a 52-week endpoint, protocol-defined steroid taper, and inclusion of patients with active skin and muscle disease

**N=241 adults with dermatomyositis**

Randomized 1:1:1
by PhGA-VAS




**Eligible patients**

- Definite or probable dermatomyositis (2017 EULAR/ACR criteria)
- Skin and muscle disease activity
- Refractory or intolerant to SOC therapy

**Permitted Background Therapy**

- Oral IST, antimalarial, and/or OCS

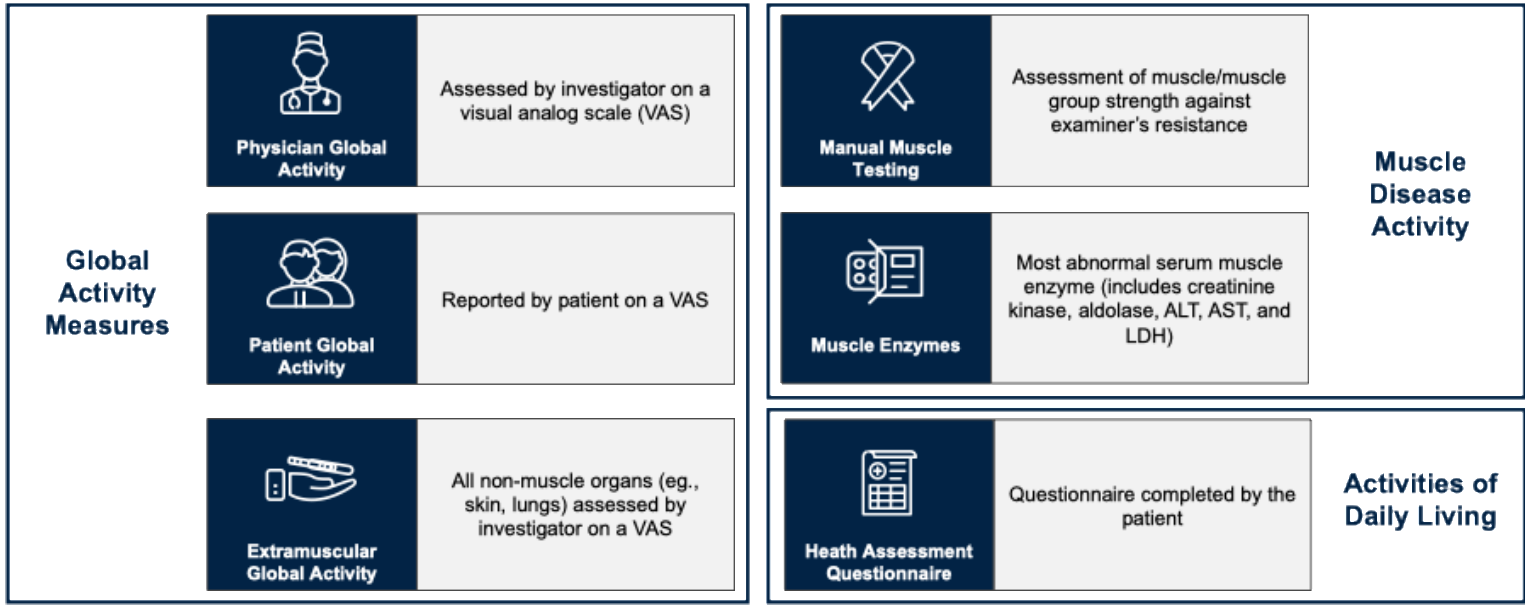
**Primary Endpoint**

- Mean Total Improvement Score at Week 52 (brepocitinib 30mg versus placebo)

**Paik JJ, et al. *J Invest Dermatol.* 2025;145(Suppl 11):E89. Mangold A, et al. Presented at: Annual Rheumatology Dermatology (ARD) Society Meeting; October 25, 2025; Chicago, IL.**

# Total Improvement Score (TIS)

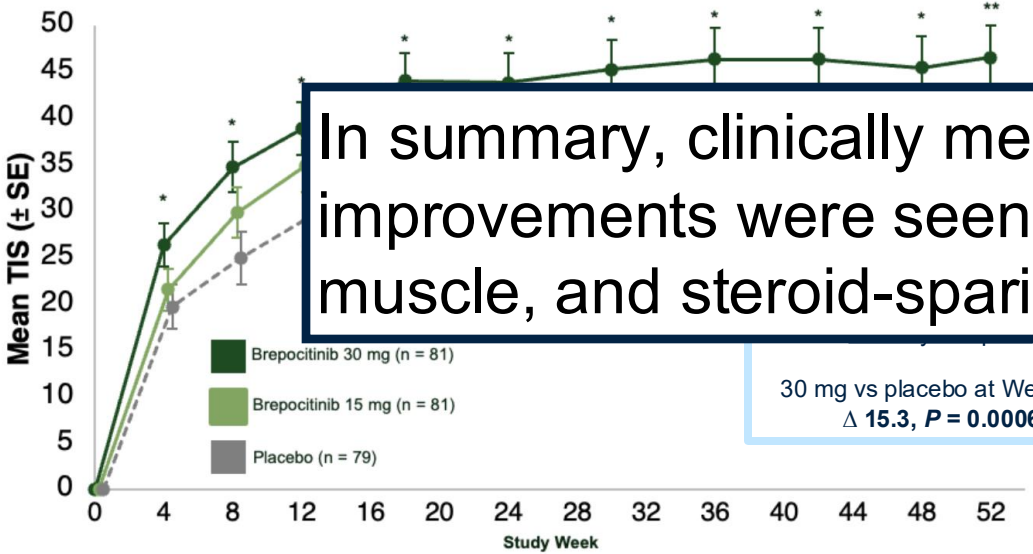
- The TIS reflects improvement from baseline in 6 core set measures (CSMs), including 3 global measures that capture disease activity across organ systems, 2 muscle-specific measures, and a commonly used measure for ADLs




Aggarwal R, et al. *Ann Rheum Dis*. 2017;76(5):792-801.

# Brepocitinib (Dual JAK1/TYK2 Inhibitor)

Primary endpoint met with clinically-meaningful and consistent efficacy despite greater steroid tapering




**In summary, clinically meaningful improvements were seen across skin, muscle, and steroid-sparing endpoints**

reduction among
on background OCS

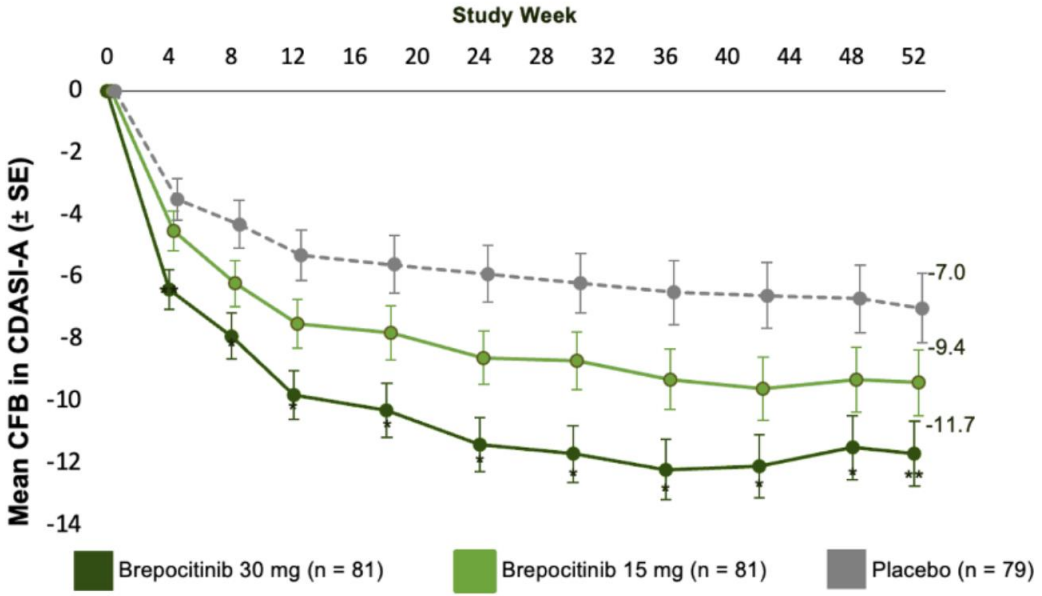
| | Brepocitinib 30mg | Placebo |
|---|---|---|
| baseline (mg) | 12.2 | 11.3 |
| ≤2.5 mg at month 12 | **62%** | **34%** |
| Off steroids at month 12 | **42%** | **23%** |

***Nominal *P* < 0.05; ****P* < 0.001. The definition of rescue medication was prespecified. This included initiation or clinically-meaningful increase in intensity of one or more systemic therapies given for treatment of DM. The robustness of the primary endpoint result with brepocitinib 30 mg was confirmed with multiple prespecified sensitivity analyses, including a treatment policy analysis and tipping point analysis.**

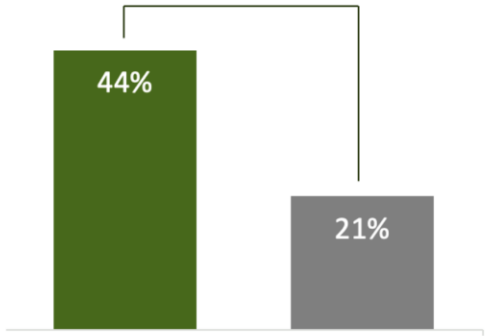
**Paik JJ, et al. *J Invest Dermatol.* 2025;145(Suppl 11):E89. Mangold A, et al. Presented at: ARD Society Meeting; October 25, 2025; Chicago, IL.**

# Brepocitinib Time Course of CDASI-Activity Change from Baseline

Statistically significant reduction in CDASI-A observed as early as Week 4 and maintained through Week 52, even with substantial corticosteroid tapering




30 mg vs. Placebo: Δ **26.6%; *P*=0.0060***




**Portion of Patients Achieving Cutaneous Clinical Remission by Week 52 (CDASI-A ≤ 5)**

Subjects with baseline CDASI-A > 14

***Nominal *P* < 0.05; ** *P* < 0.001**

**Paik JJ, et al. *J Invest Dermatol.* 2025;145(11 suppl):E89. Mangold A, et al. Presented at: ARD Society Meeting; October 25, 2025; Chicago, IL.**

# Measurements of skin disease, muscle disease, rapidity of onset, and steroid sparing; consistent dose response was also seen across endpoints

| Key Endpoint | Important Features | Brepocitinib 30mg (n=81) | Placebo (n=79) | P-Value |
|---|---|---|---|---|
| Mean TIS (Primary) | Composite endpoint, focus on **muscle disease** and **global** benefit | 46.5 | 31.2 | **0.0006** |
| CDASI-A change from baseline at Week 52 | Improvement in **skin disease** activity | -11.7 | -7.0 | **0.0006** |
| DMOMS at Week 52 | DM-specific **muscle and skin** composite measure of benefit | 57.9 | 40.5 | **0.0014** |
| TIS40 Response at Week 52 | Moderate TIS response (focus on **global benefit / muscle**) | 67.9% | 44.3% | **0.0040** |
| Time to Consecutive TIS40 Response by Week 52 | **Time to onset of sustained benefit** (particularly high bar) | 85 days | 168 days | **0.0155** |
| Patients achieving TIS40 Response + ≤2.5 mg OCS at Week 52 | Achievement of clinical response and **steroid reduction** | 54.3% | 26.6% | **0.0006** |
| CDASI-A 40% Response with ≥4-point improvement at Week 52 | Clinically meaningful **skin response** | 61.7% | 44.3% | **0.0357** |
| TIS60 Response at Week 52 | Major TIS response – **Highest TIS response threshold** | 46.1% | 26.4% | **0.0126** |
| Change from baseline in HAQ-DI at Week 52 | Improvement in physical and functional disability and daily living activities related to **muscle** strength | -0.337 | -0.042 | **0.0035** |
| Change from baseline in CDASI-A at Week 4 | **Rapid onset** of skin response | -6.4 | -3.5 | **0.0003** |

**Paik JJ, et al. *J Invest Dermatol.* 2025;145(11 suppl):E89. Mangold A, et al. Presented at: ARD Society Meeting; October 25, 2025; Chicago, IL.**

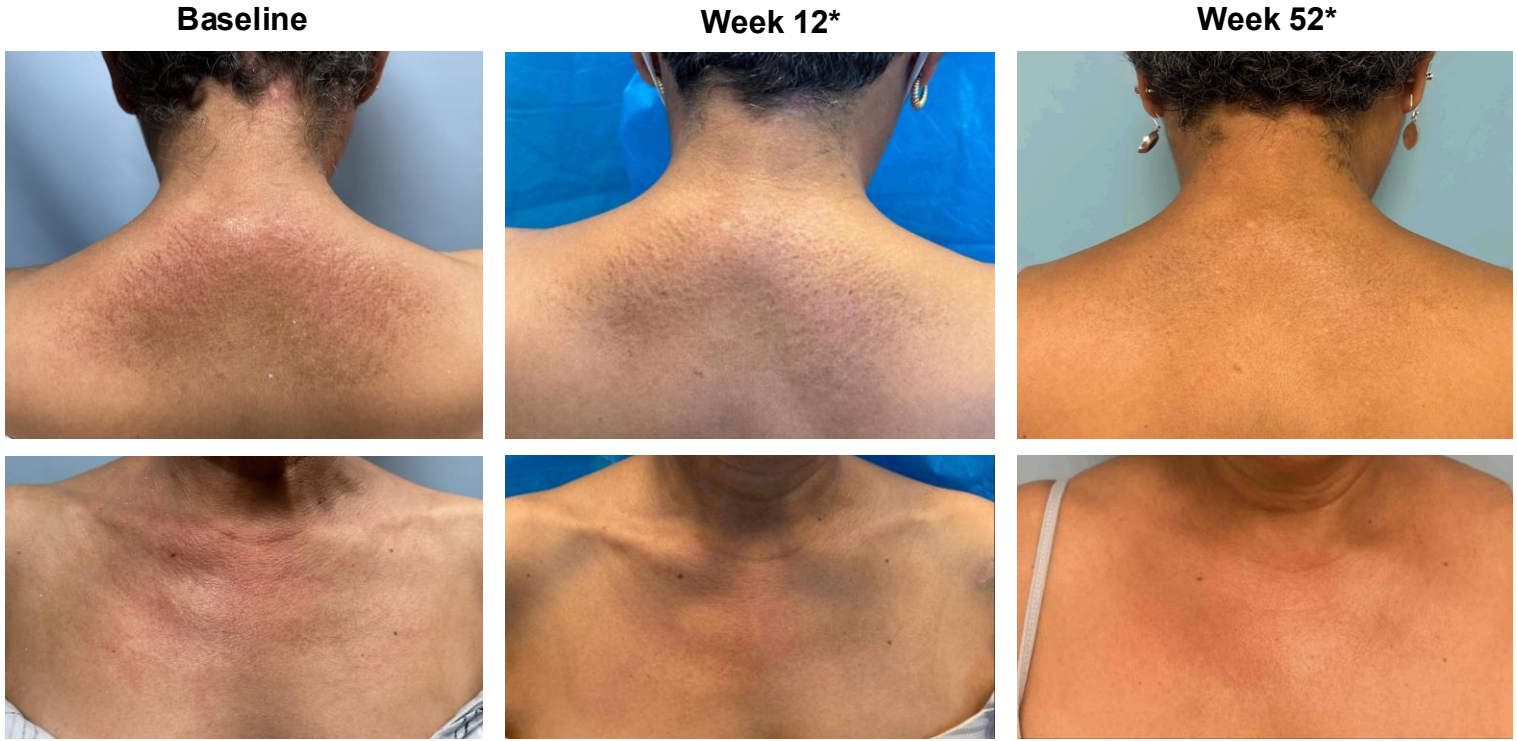
# AESIs Occurred at Similar Frequencies across Groups

Only two malignancies were observed, both in placebo group; only one thromboembolic event was observed, also in placebo group; other AESIs were observed in both brepocitinib 30mg and placebo groups at similar frequencies

| | Brepocitinib 30 mg QD (N=81) | Brepocitinib 15 mg QD (N=81) | Placebo (N=79) |
|---|---|---|---|
| **Participants with** | | | |
| AEs | 73 (90%) | 70 (86%) | 72 (91%) |
| Death | 0 | 0 | 0 |
| SAEs | 13 (16%) | 7 (9%) | 10 (13%) |
| Infection SAEs | 8 (10%) | 2 (3%) | 1 (1%) |
| AEs leading to treatment discontinuation | 5 (6%) | 6 (7%) | 9 (11%) |
| AEs leading to study discontinuation | 3 (4%) | 4 (5%) | 3 (4%) |
| **Adverse Events of Special Interest:** | | | |
| Cardiovascular events | 1 (1%) | 0 | 2 (3%) |
| Thromboembolic events | 0 | 0 | 1 (1%) |
| Viral reactivation | 4 (5%) | 2 (2%) | 4 (5%) |
| Opportunistic infections | 0 | 0 | 0 |
| New or recurrent diagnoses of malignancy | 0 | 0 | 2 (3%) |
| Increase in ALT or AST | 1 (1%) | 2 (2%) | 1 (1%) |

**Note: Percentages are based on the number of unique participants with an event out of the column total. Treatment-emergent AEs are reported.**
**AE = adverse event, ALT = alanine aminotransferase, AST = aspartate aminotransferase, SAE = serious adverse event.**
**Paik JJ, et al. *J Invest Dermatol.* 2025;145(11 suppl):E89. Mangold A, et al. Presented at: ARD Society Meeting; October 25, 2025; Chicago, IL.**

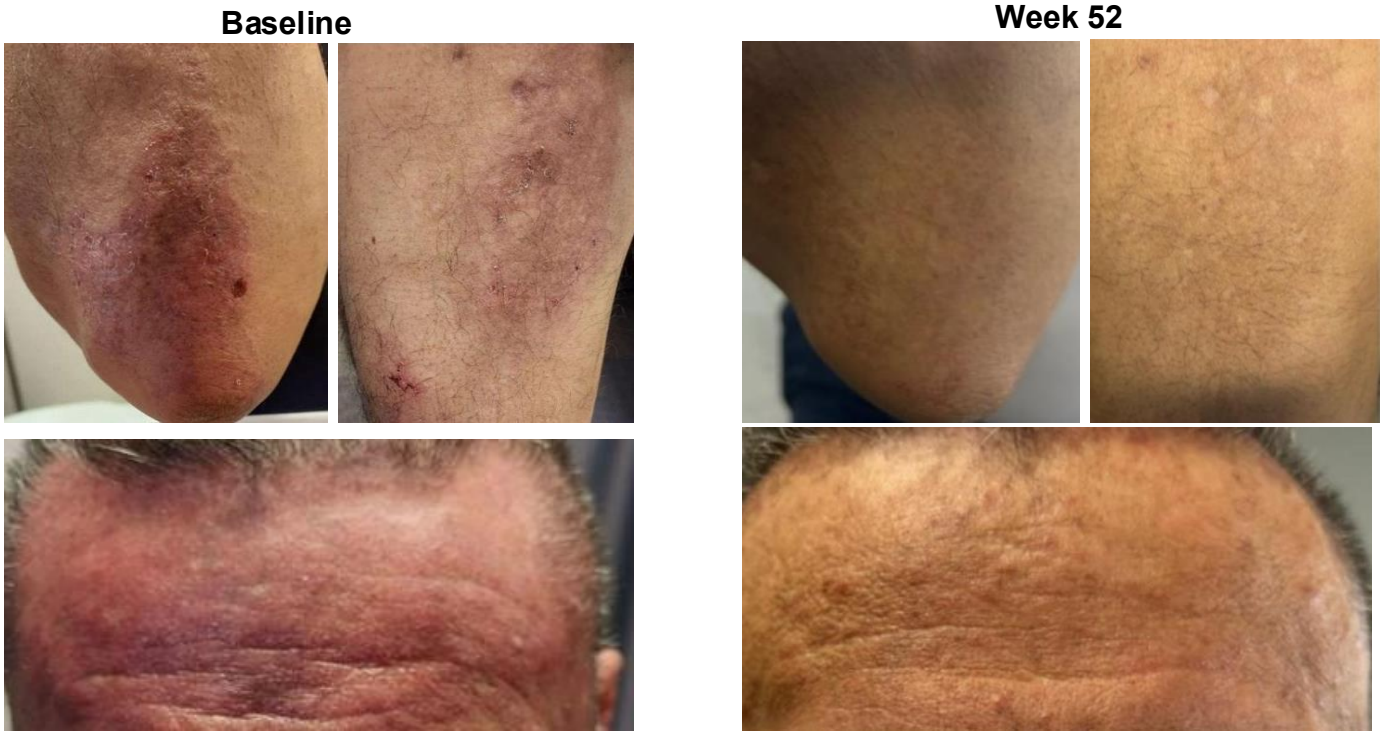
# Representative Patient Photos Show Clinical Improvement at Week 12 with Continued Benefit through Week 52




*Patient received brepocitinib 15 mg daily.

Paik JJ, et al. *J Invest Dermatol.* 2025;145(11 suppl):E89. Mangold A, et al. Presented at: ARD Society Meeting; October 25, 2025; Chicago, IL.

# Representative Photos Demonstrate Resolution of Severe and Ulcerative Skin Disease by Week 52




Paik JJ, et al. *J Invest Dermatol.* 2025;145(11 suppl):E89. Mangold A, et al. Presented at: ARD Society Meeting; October 25, 2025; Chicago, IL.

# Key Learning Points

- Conventional immunosuppressive therapies provide incomplete, slow, and often non-durable control, with persistent corticosteroid dependence, treatment toxicity, and high discontinuation rates highlighting major unmet clinical needs
- Advances in disease biology, especially the central role of type I interferon signaling and JAK/STAT pathway activation, are enabling a transition toward mechanism-targeted and steroid-sparing therapies with rapid cutaneous improvement
- IVIG demonstrates clinically meaningful improvement in validated skin outcomes, and emerging targeted therapy with brepocitinib shows robust efficacy across skin activity, muscle disease, and corticosteroid tapering endpoints, supporting a new era of disease-modifying treatment

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# The Importance of Interdisciplinary Care in Dermatomyositis

**Victoria Werth, MD**

*Professor of Dermatology*
*University of Pennsylvania*

# Multiple Disciplines See Patients with DM

- There are patients with skin-predominant disease and those with systemic disease and minimal or no skin findings
- The identification of patients with primarily skin autoimmune disease frequently requires collaboration between dermatologists and rheumatologists
- Often, patients who present to dermatologists have somewhat different manifestations than those seeing rheumatologists
  - Only when both fields work together does the bigger picture of the disease emerge

# Diagnostic Criteria for DM (Bohan and Peter's)

- Symmetric proximal weakness with or without dysphagia or respiratory muscle involvement
- Abnormal muscle biopsy specimen
- Elevation of skeletal muscle-derived enzymes
- Abnormal electromyogram
- Typical skin rash
  - Definite DM: Rash and 3 or 4 criteria
  - Probable DM: Rash and 2 criteria
  - Possible DM: Rash and 1 criterion

**Bohan A, Peter JB. *N Engl J Med.* 1975;292(8):403-407.**

# Presentation of DM at Large Tertiary Medical Center (3 Years)

| | Dermatology # patients | Rheumatology # patients |
|---|---|---|
| Classic DM | 27 (32.5%) | 24 (88.9%) |
| Amyopathic DM | 33 (39.8%) | 1 (3.7%) |
| Hypomyopathic DM | 23 (27.7%) | 2 (7.4%) |

Klein RQ ... Werth VP, et al. *J Am Acad Dermatol.* 2007;57(6):937-943.

# ILD in DM at Large Tertiary Medical Center (3 Years)

| ILD | Classic DM | Amyopathic DM | Hypomyopathic DM |
|---|---|---|---|
| Present | 23 (40%) | 9 (26%) | 11 (44%) |
| Absent | 35 (60%) | 26 (74%) | 14 (56%) |

***P* = 0.27**

Klein RQ ... Werth VP, et al. *J Am Acad Dermatol.* 2007;57(6):937-943.

# Multiple Disciplines See Patients with DM

- These collaborations allow for the optimal development of disease diagnostic and classification criteria, agreement on how to measure outcomes, as well as the design, performance, and interpretation of clinical studies

- In the clinical arena assist in the diagnosis and management of various disease manifestations

- The clinic and education, as well as the basic, translational, and clinical research needs in these multisystem diseases, benefit from close communication and collaboration

# Typical Patient with DM

- Rash
- Muscle weakness
- Inflammatory arthritis
- 25% of CADM have interstitial lung disease
- Need to rule out malignancy
- Diarrhea (possible lymphocytic colitis)
- Peripheral neuropathy

# DM Specialists

- Rheumatology
- Dermatology
- Pulmonary
- Neurology
- Oncology
- Gastroenterology

# Interdisciplinary Care

- Treatment and involvement of other disciplines depends on which organs are involved, how severe or refractory the patient is
  - Ex. Patient with DM presents with worsening muscle weakness, dyspnea, persistent cutaneous disease: Refer to pulmonology and coordinate care with rheumatology
- There are rheum-derm experts in many academic centers that care for patients with systemic aspects of the disease and are doing clinical studies
- Not every patient necessarily needs to see another specialist
  - Rheumatologic Dermatology Society

# Key Learning Points

- Dermatomyositis is a multisystem disease involving skin, muscle, lungs, joints, nerves, GI, and oncology in the case of paraneoplastic dermatomyositis
- It is important to examine the patient carefully to determine the organs that are involved
- The approach depends on which organs are involved and the severity and responsiveness to treatment
- For significant organ involvement beyond the skin, refer and collaborate with the relevant specialties