Music City SCALE
Symposium for Cosmetic Advances & Laser Education
An HMP Global Company

OPTIMIZING OUTCOMES IN CHRONIC HAND ECZEMA

Navigating Diagnosis, Treatment, and Long-Term Care

Supported by an educational grant from LEO Pharma, Inc.

Disclosures

- **Christopher G. Bunick, MD, PhD:** Investigator – AbbVie, Almirall, Apogee, Daiichi Sankyo, LEO Pharma, Ortho Dermatologics, Palvella, Sun Pharma, Takeda, Timber, Triveni; Consultant – AbbVie, AbSci, Almirall, Amgen, Apogee, Arcutis, Botanix, Castle Biosciences, Connect BioPharma, Dermavant, Disc Medicine, Eli Lilly, EPI Health/Novan, Galderma, Highlight Therapeutics, Incyte, LEO Pharma, Novartis, Ortho Dermatologics, Pfizer, Priovant, Regeneron, Sanofi, South Beach Symposium, Sun Pharma, Takeda, Teladoc, Triveni, UCB, Veradermics

- **Emma Guttman-Yassky, MD, PhD:** Research Support, Consulting, or Lecture Fees – AbbVie, Almirall, Amgen, Anacor, AnaptysBio, Arena, Asana Biosciences, Boehringer, Botanix, Cara Therapeutics, Celgene, Concert, Dermavant, Dermira, DS Biopharma, Eli Lilly, Escalier, FLX Bio, Galderma, Gilead, Glenmark, GSK, Immune, Incyte, Innovaderm, Janssen, Kiniksa, Kyowa Kirin, LEO Pharma, MedImmune, Mitsubishi Tanabe, Novartis, Pfizer, Ralexar, Regeneron, Sanofi, Sienna, Sun Pharma, Target, UCB, Union Therapeutics, Vitae

Learning Objectives

- Apply evidence-based approaches to diagnose and evaluate CHE, taking into account etiologic subtypes and underlying pathogenic mechanisms
- Evaluate current safety/efficacy data for newer and emerging CHE therapies to guide appropriate patient selection and treatment
- Implement individualized treatment plans for patients with CHE that consider topical, phototherapy, systemic, and over-the-counter management strategies
- Outline evidence-informed CHE prevention strategies using practical clinical tools to improve patient outcomes

CHE = chronic hand eczema.

CHE Pathogenesis and Therapeutic Implications

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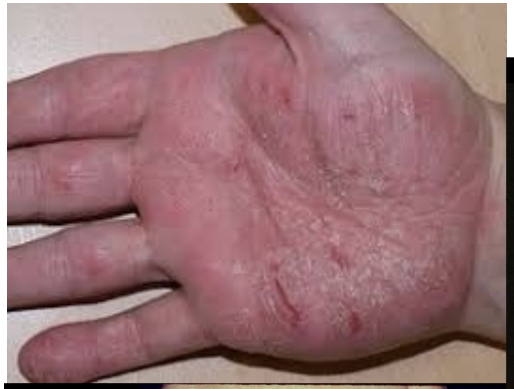
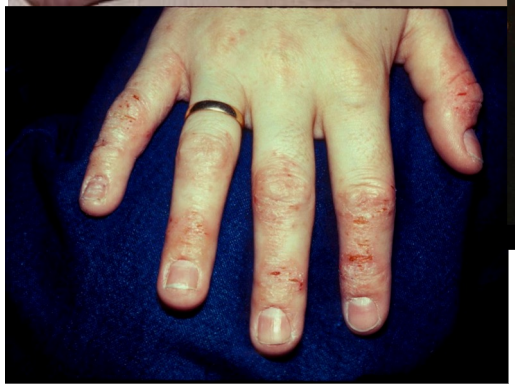
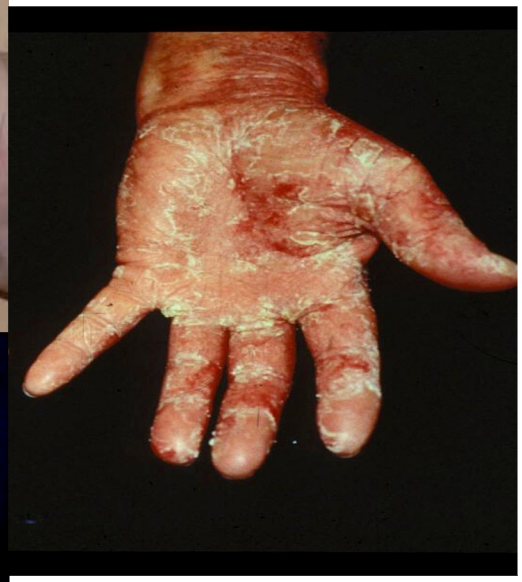
New York, NY

Chronic Hand Eczema







- Up to 10% of population
- Most common occupational disease
- Recurrent, chronic disease
- Hybrid eczema (50% ICD, 15% ACD, 50-80% have atopy)
- ~1/3 have a history of AD
- More than 1/3 have moderate-to-severe disease
- Huge unmet need for better treatments for long-term disease control

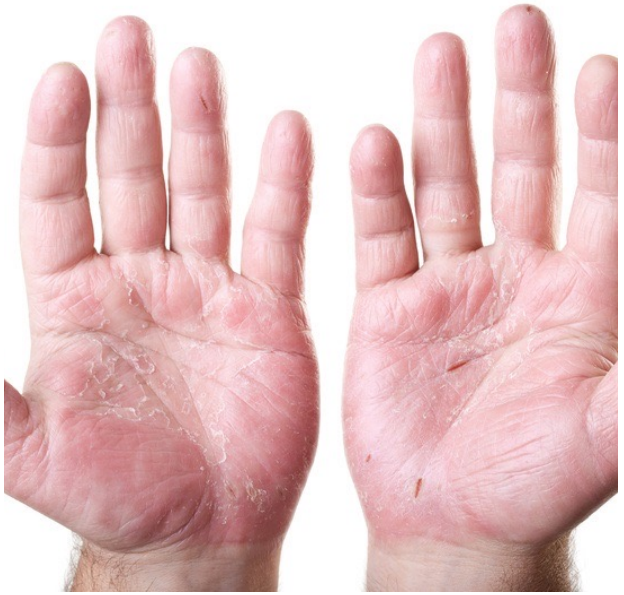
Delgocitinib 2% cream is the first FDA-approved treatment for CHE

ICD = irritant contact dermatitis; ACD = allergic contact dermatitis; AD = atopic dermatitis.

Patruno C, et al. *Dermatitis*. 2026 [Epub ahead of print]. Molin S, Guttman-Yassky E, et al. *Acta Derm Venereol*. 2025;105:adv42596.

Chronic Hand and Feet Eczema

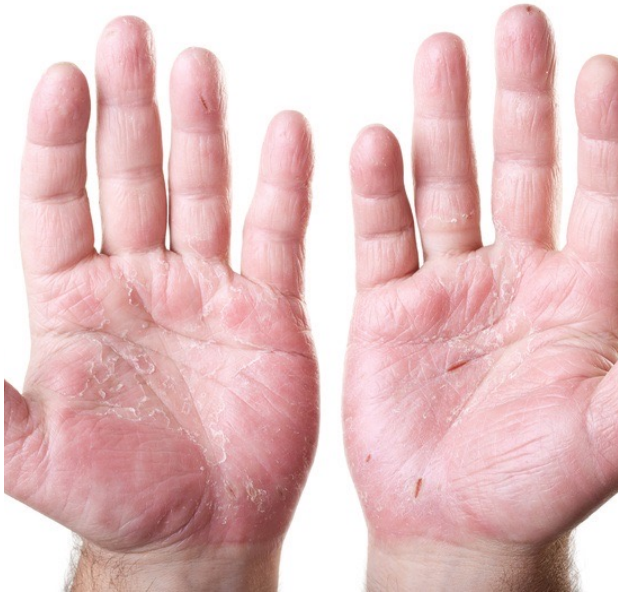
- Often chronic
- Irritant
- Allergic (less than 20% patch test positive)
- Atopic
- Nummular
- Vesicular
- Frictional (psoriasiform or hyperkeratotic)



Patruno C, et al. *Dermatitis*. 2026 [Epub ahead of print]. Molin S, Guttman-Yassky E, et al. *Acta Derm Venereol*. 2025;105:adv42596.

Atopy

- Atopic dermatitis is the most important risk factor for CHE
- Between 33-50% of all patients with CHE are atopic (existing AD, asthma, allergic rhinitis, increased IgEs)



Molin S, et al. *Clin Exp Dermatol*. 2011;36(6):595-601.

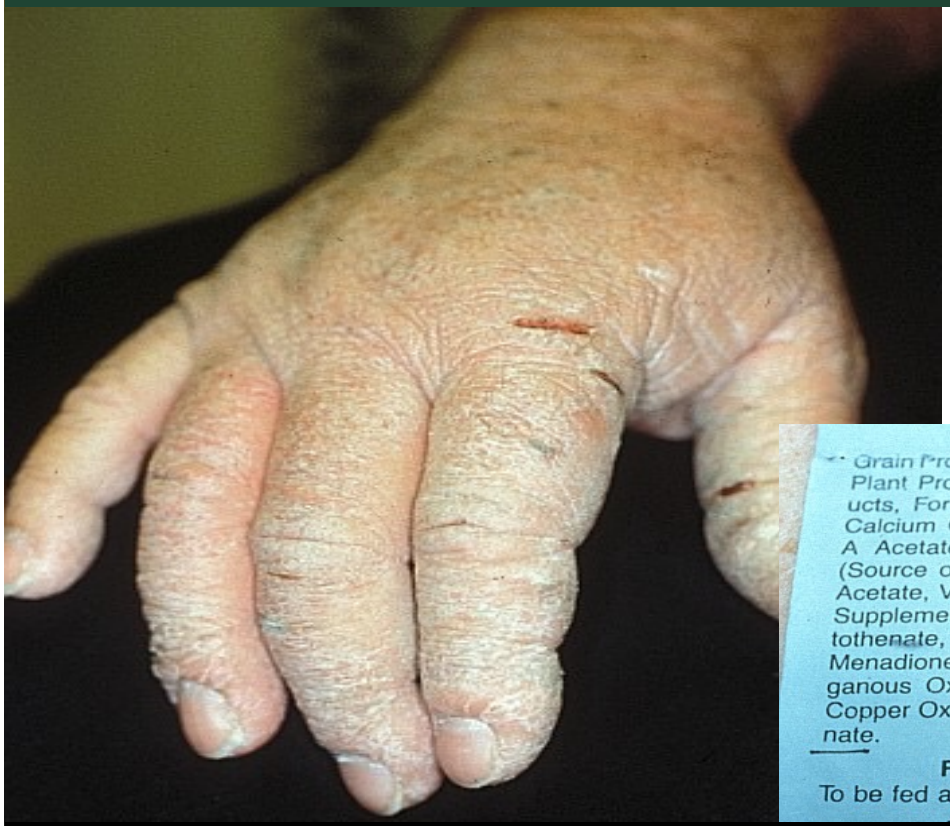
Relevant Allergens for CHE

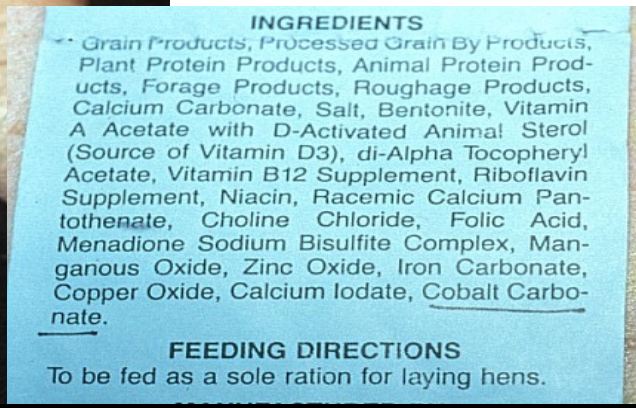
- Metals
- Rubbers and glues
- Preservatives
- Dyes or plant allergens that can penetrate the skin

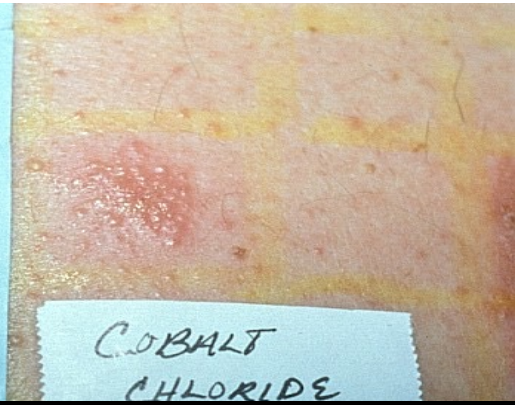
Metals

- Nickel sulfate
- Cobalt chloride
- Potassium dichromate
- Sodium gold thiosulfate

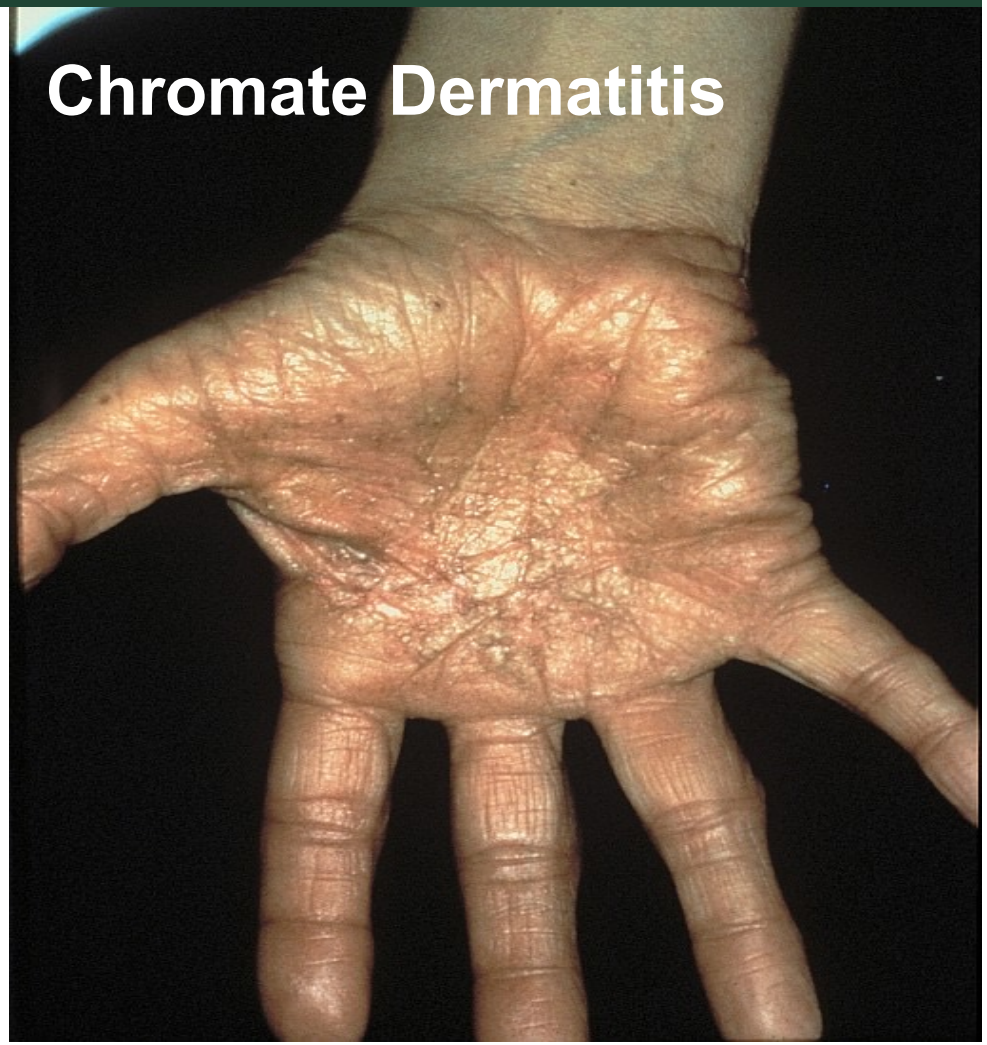
Cobalt Allergy







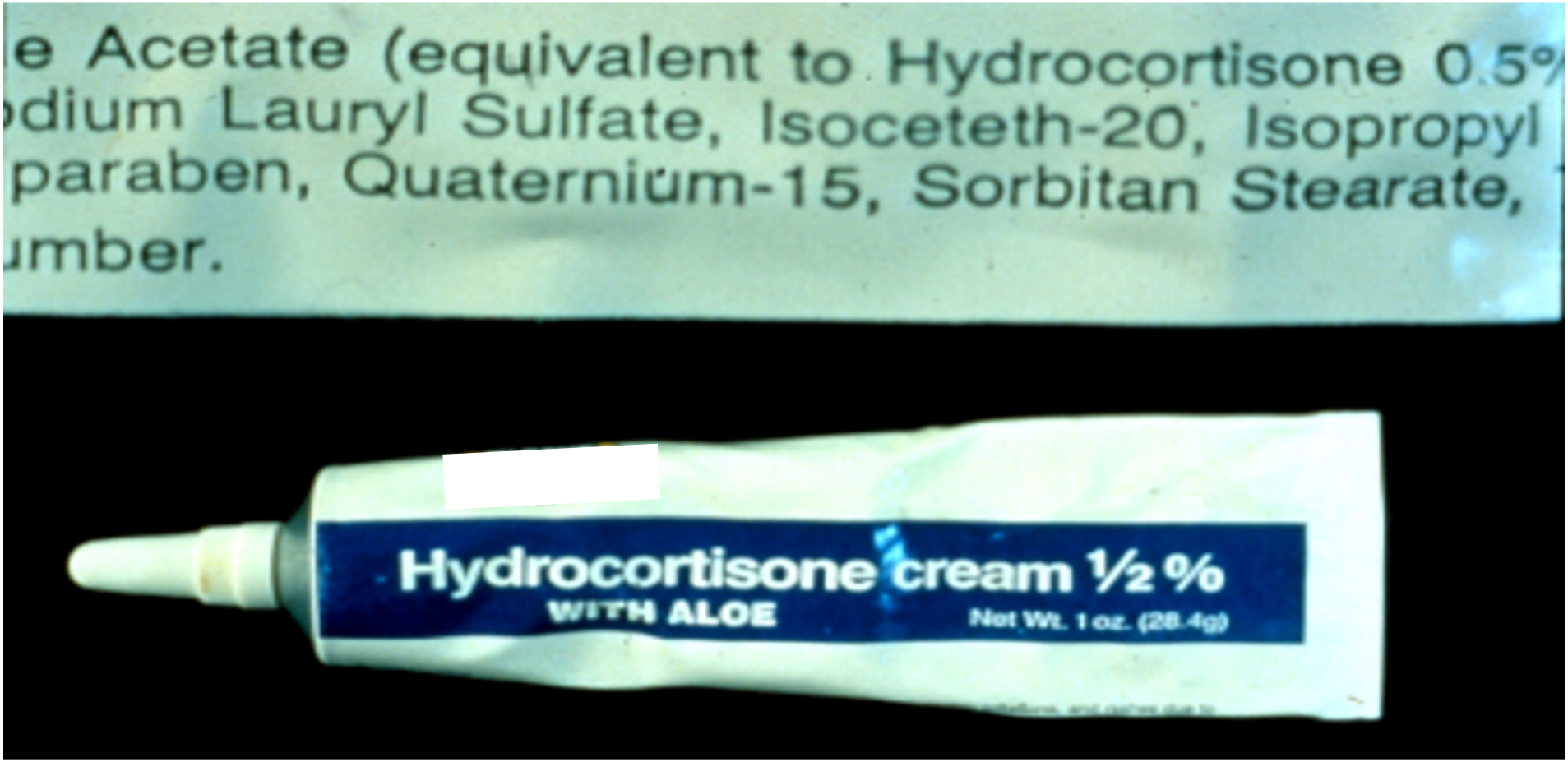

RUBBER LUBRICANT
triple duty
1 MOUNT & DEMOUNT TIRES
2 LUBRICATE RUBBER PARTS
3 CLEAN & DRESS UP RUBBER
HARMLESS TO NATURAL AND SYNTHETIC RUBBER
FIVE GALLONS


Chromate Dermatitis

Preservatives

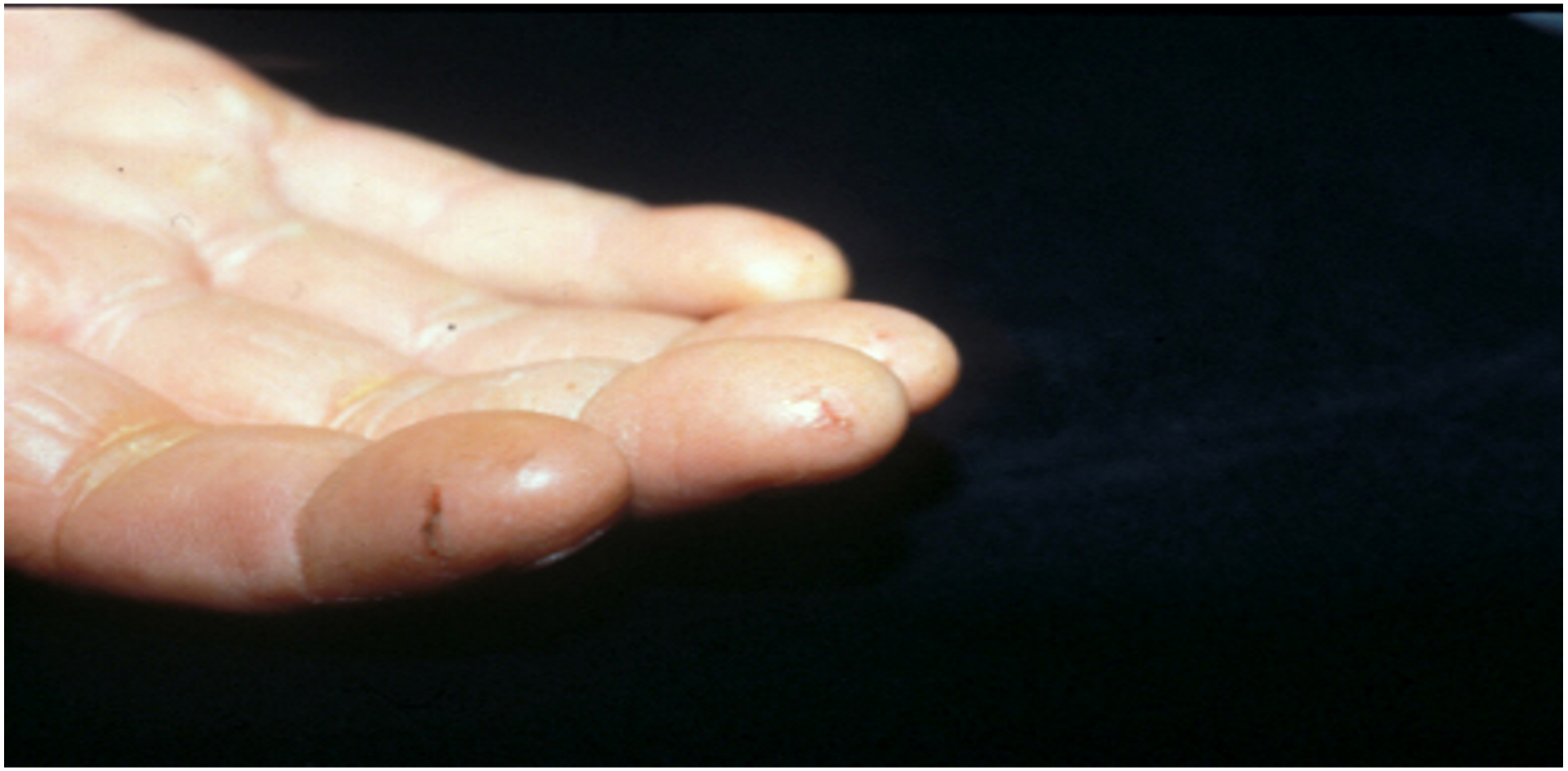
- Formaldehyde

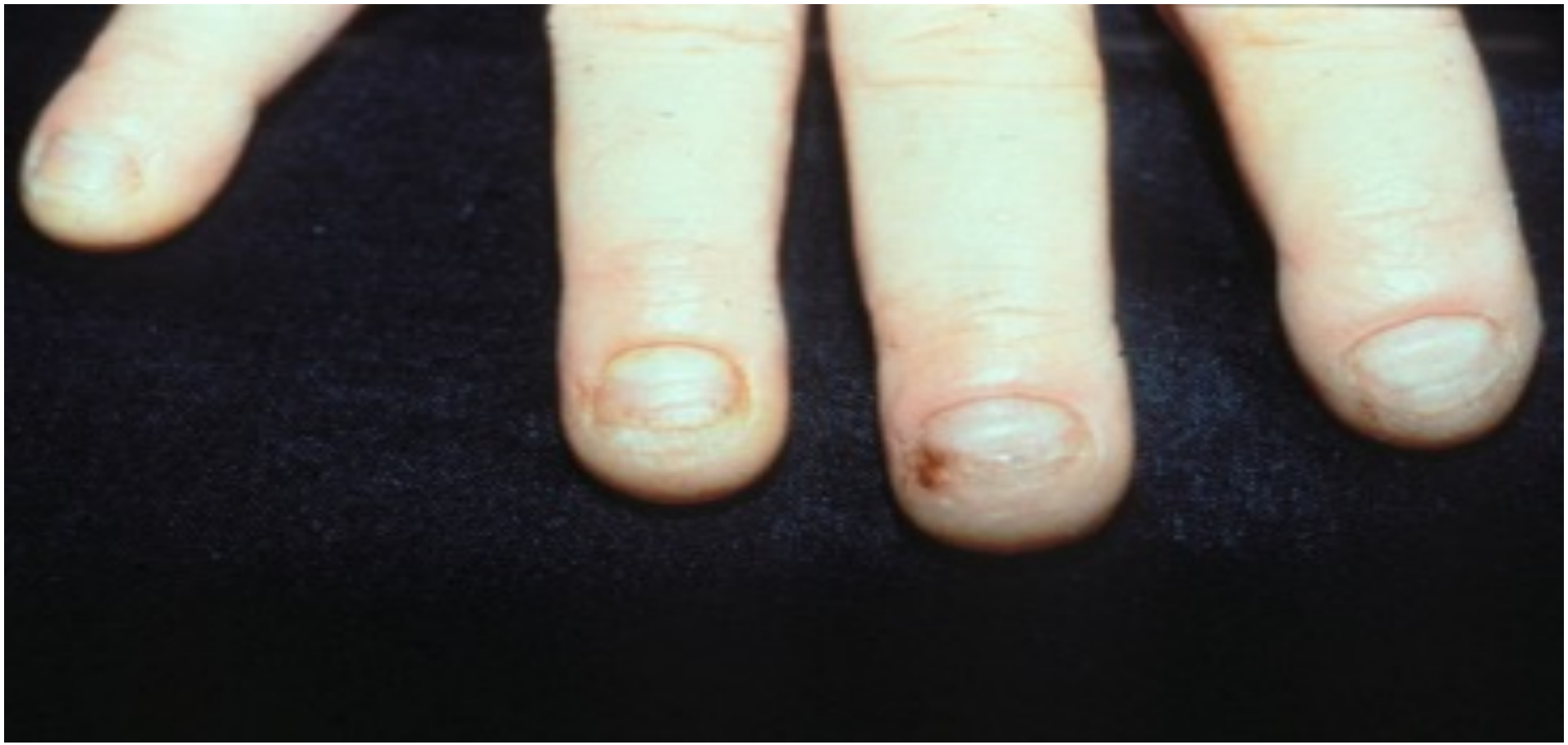
- Formaldehyde releasers
  - **Quarternium-15**
  - *Diazolidinyl urea*
  - *Imidazolidinyl urea*
  - *Bronopol*
  - *DMDM hydantoin*


e Acetate (equivalent to Hydrocortisone 0.5%
odium Lauryl Sulfate, Isoceteth-20, Isopropyl
paraben, Quaternium-15, Sorbitan Stearate,
umber.
Hydrocortisone cream ½ %
WITH ALOE
Net Wt. 1 oz. (28.4g)

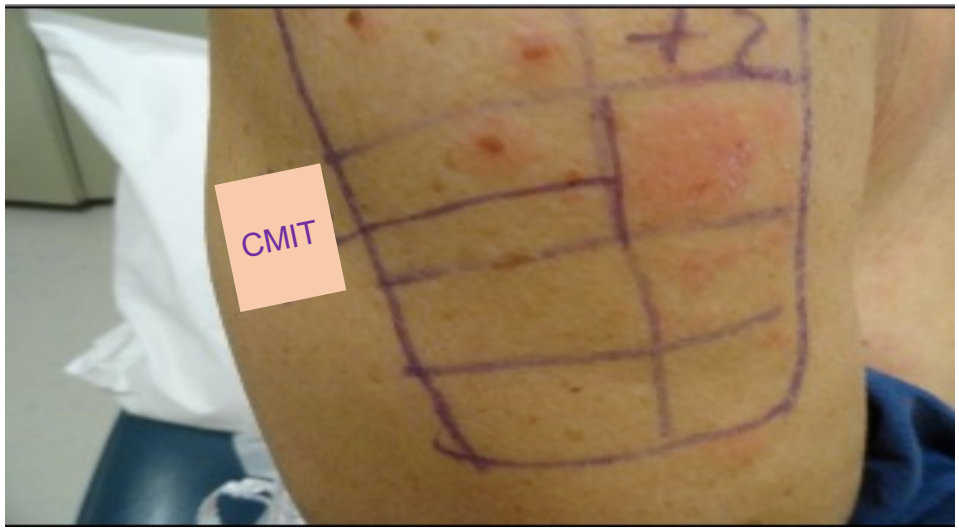
Non-Formaldehyde-Releasing Preservatives

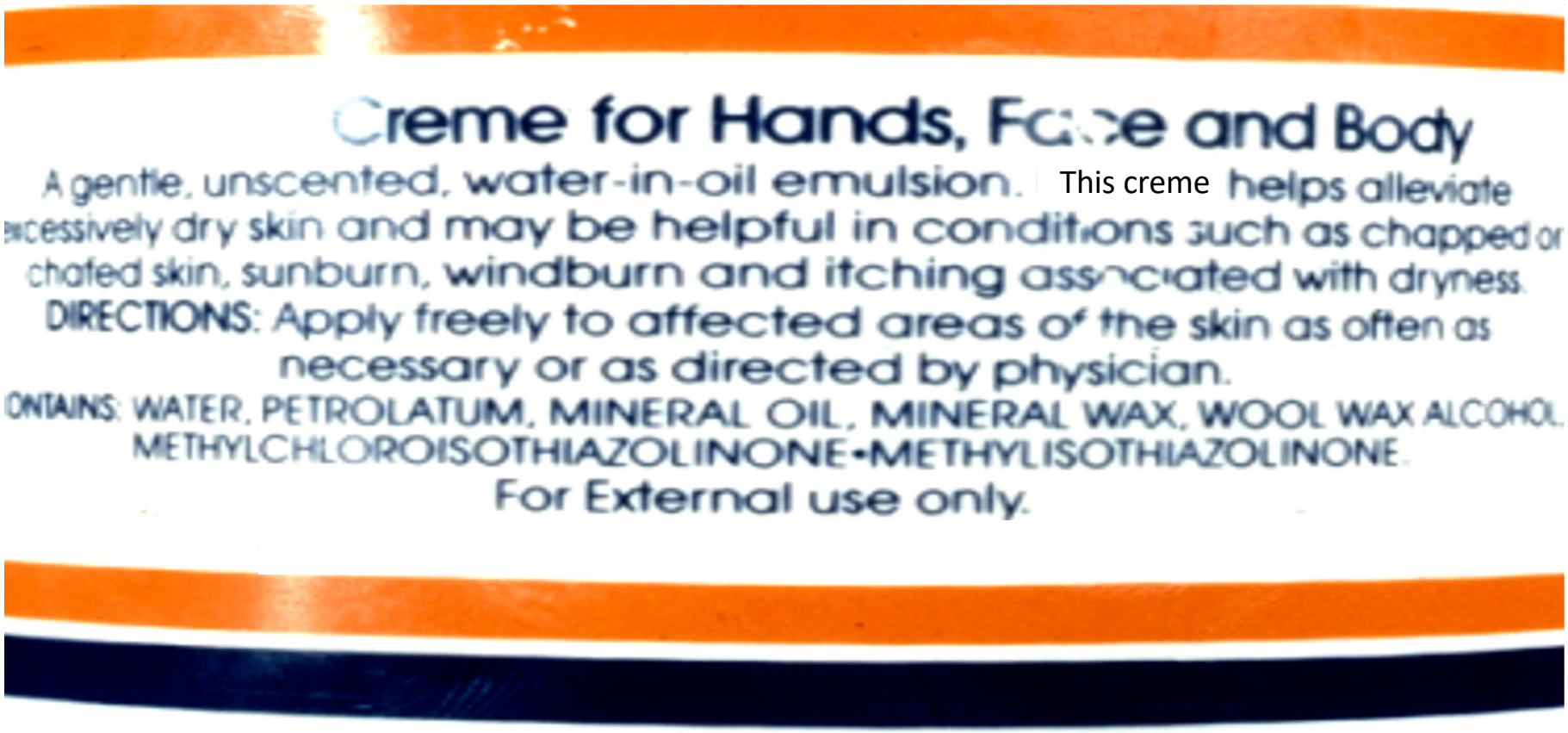
- Methylchloroisothiazolinone (CMIT)
- Propylene glycol
- Parabens
- Glutaraldehyde
- Methyldibromo glutaronitrile/phenoxyethanol

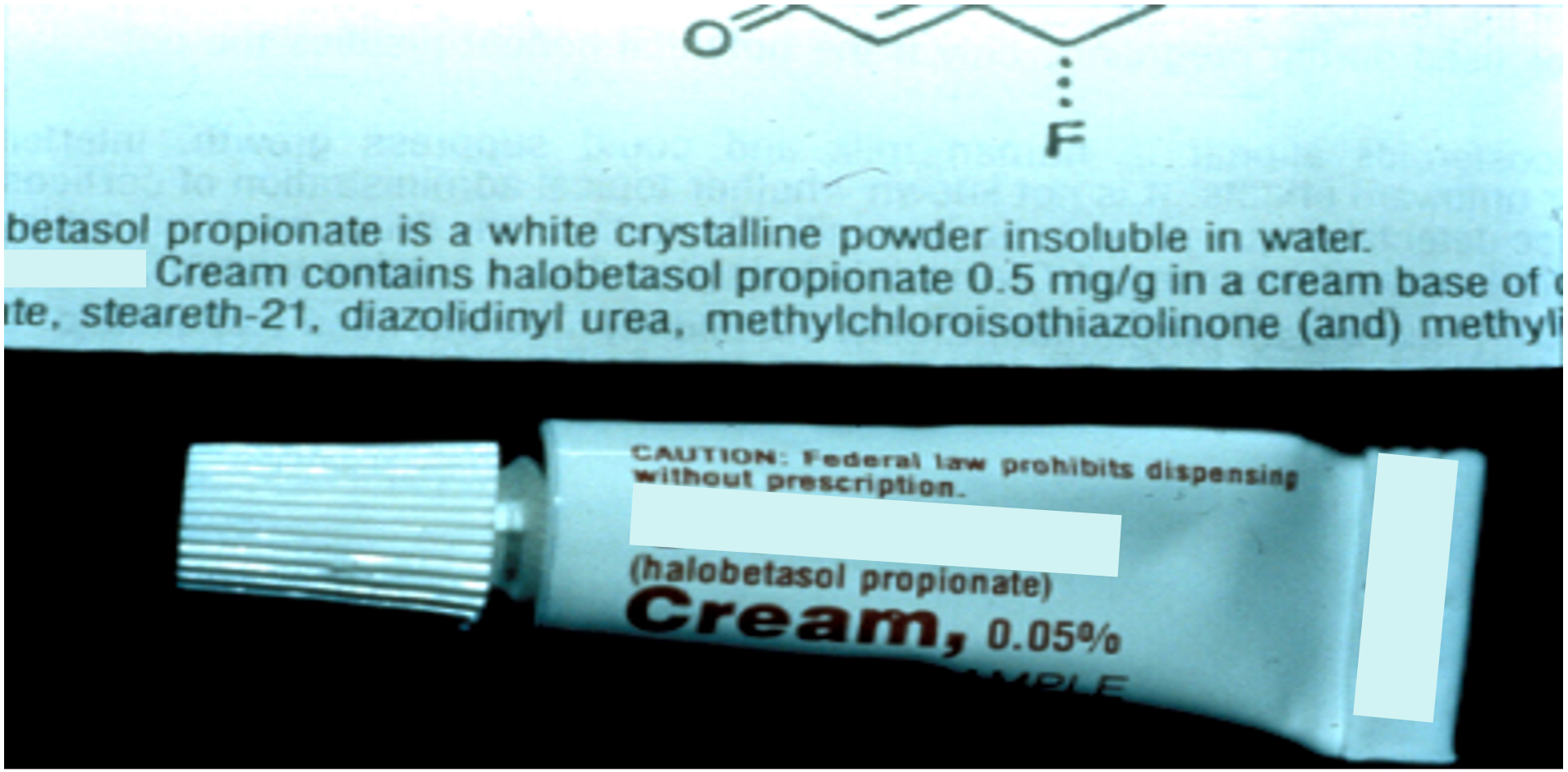




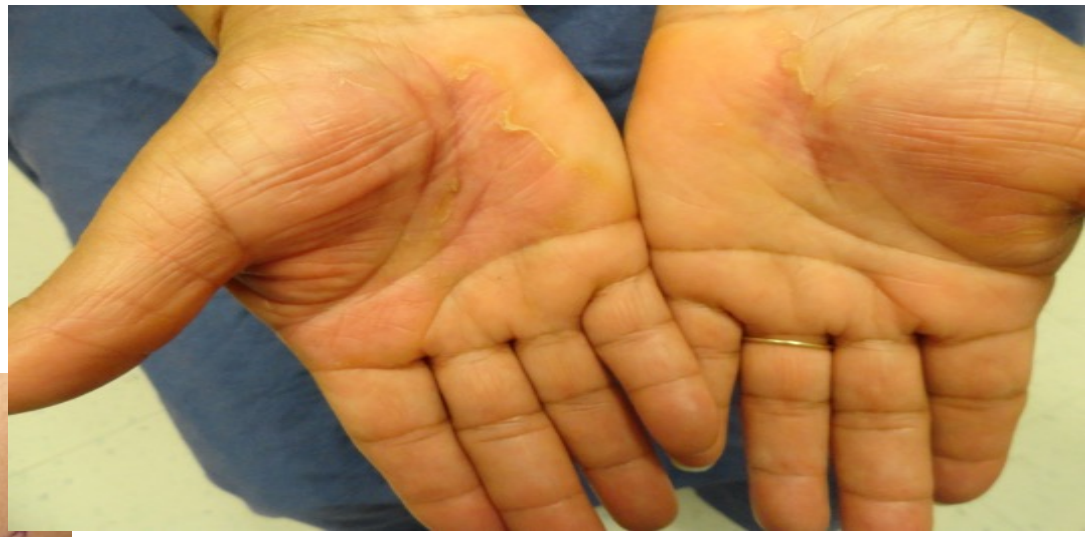
CMIT

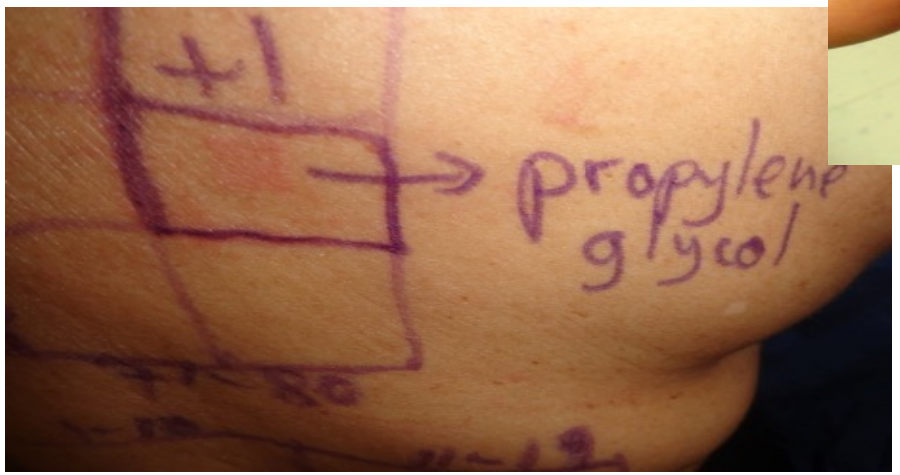



Creme for Hands, Face and Body
A gentle, unscented, water-in-oil emulsion. This creme helps alleviate
excessively dry skin and may be helpful in conditions such as chapped or
chafed skin, sunburn, windburn and itching associated with dryness.
DIRECTIONS: Apply freely to affected areas of the skin as often as
necessary or as directed by physician.
CONTAINS: WATER, PETROLATUM, MINERAL OIL, MINERAL WAX, WOOL WAX ALCOHOL,
METHYLCHLOROISOTHIAZOLINONE-METHYLISOTHIAZOLINONE.
For External use only.


O
F
betasol propionate is a white crystalline powder insoluble in water.
Cream contains halobetasol propionate 0.5 mg/g in a cream base of
te, steareth-21, diazolidinyl urea, methylchloroisothiazolinone (and) methyl
CAUTION: Federal law prohibits dispensing without prescription.
(halobetasol propionate)
Cream, 0.05%

Propylene Glycol





IMPORTANT PRESERVATIVE IN STEROIDAL CREAMS – need to consider if patient not responding to treatment

Prognosis

- Moderate-to-severe CHE is the strongest risk factor for disease persistence

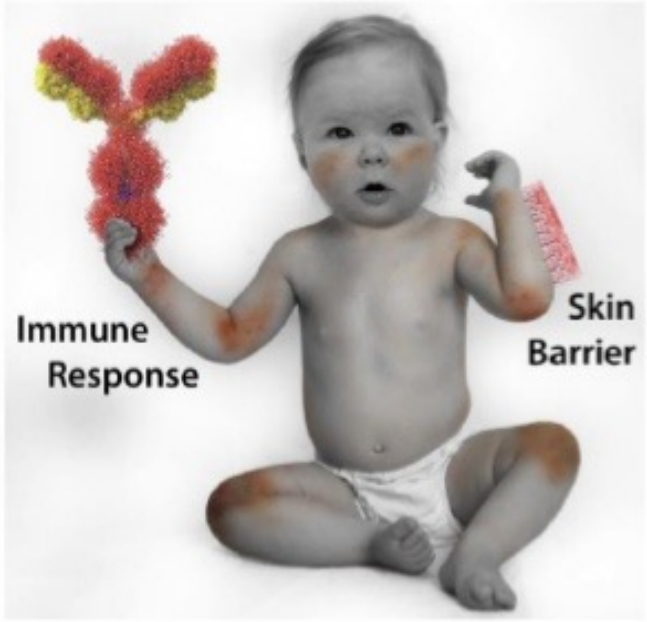
- Other factors contributing to disease persistence: Childhood eczema, and early onset before the age of 20

Thyssen JP, et al. *Contact Dermatitis*. 2010;62(2):75-87.

AD Is Characterized by Barrier and Immune Abnormalities

IL-4
IL-13
IL-31
IL-22

Inside - out



Irritants,
allergens,
and microbes

Outside - in

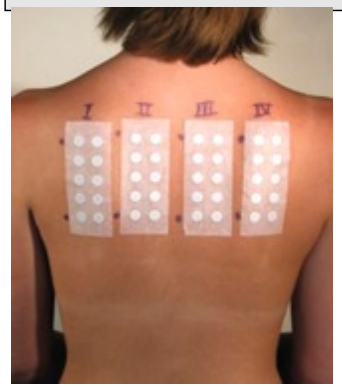
FLG
LOR
Lipids

IL = interleukin; FLG = filaggrin; LOR = loricrin.
Leung DYM, et al. *J Allergy Clin Immunol*. 2014;134(4):769-779.

Defining the Phenotype of ACD

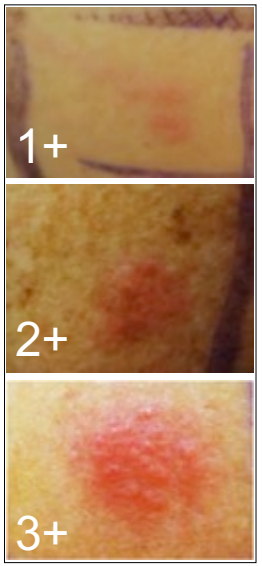
- 30 patients patch-tested to the 15 most common NACDG allergens
- Petrolatum occlusion as control

→ 24 patients had positive reactions at 72h, scored as 1+, 2+, or 3+



Adapted from Lindberg M, Matura M. "Patch Testing". In: *Contact Dermatitis*. 5th ed. Springer; 2011.

Reaction Intensity	Nickel	Rubber	Fragrance	Other metals
3+	2	0	0	0
2+	7	4	2	0
1+	1	3	1	4
n total	10	7	3	4



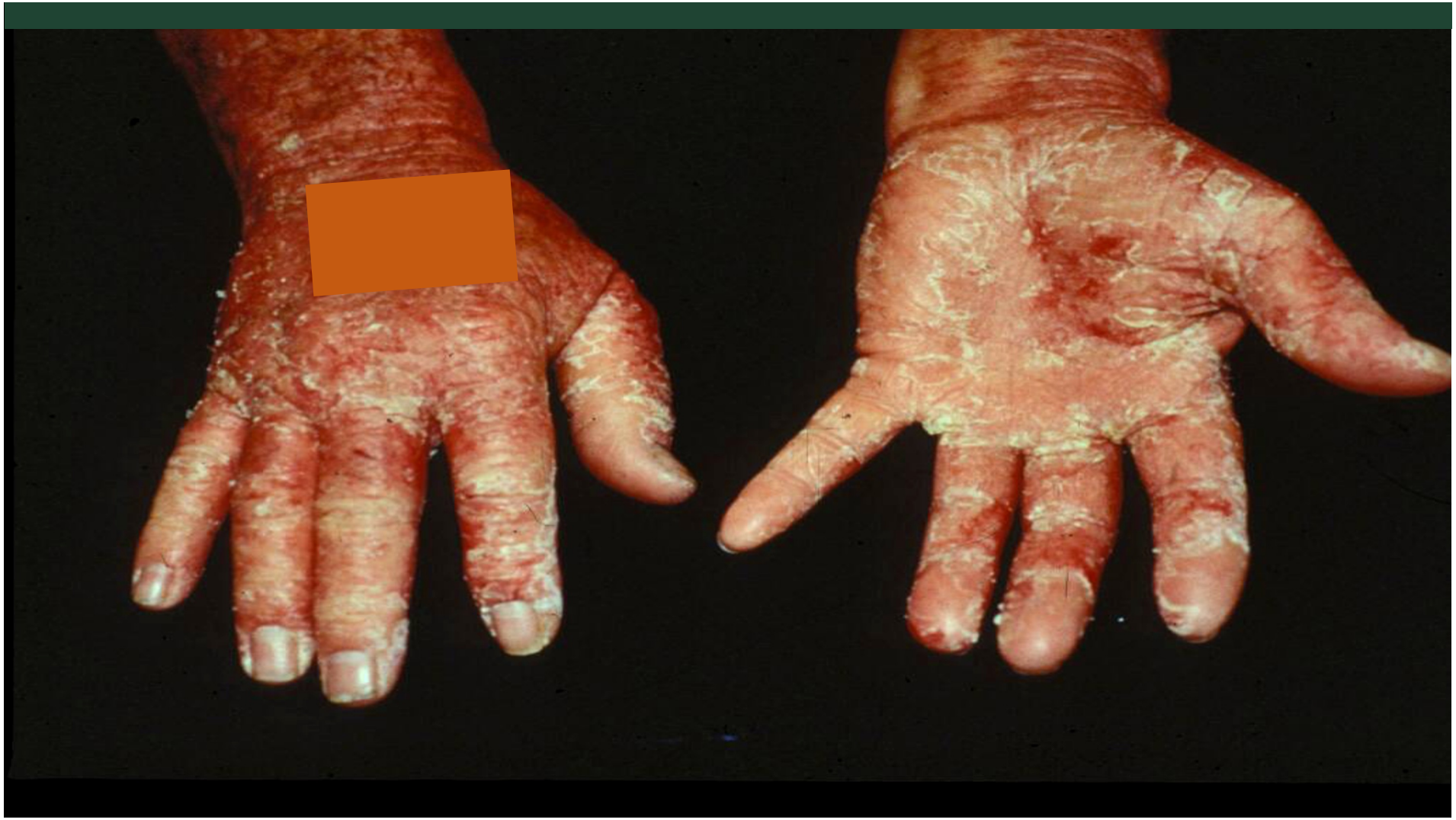
- Immunohistochemistry
- Immunofluorescence
- Real-time PCR
- Gene microarrays

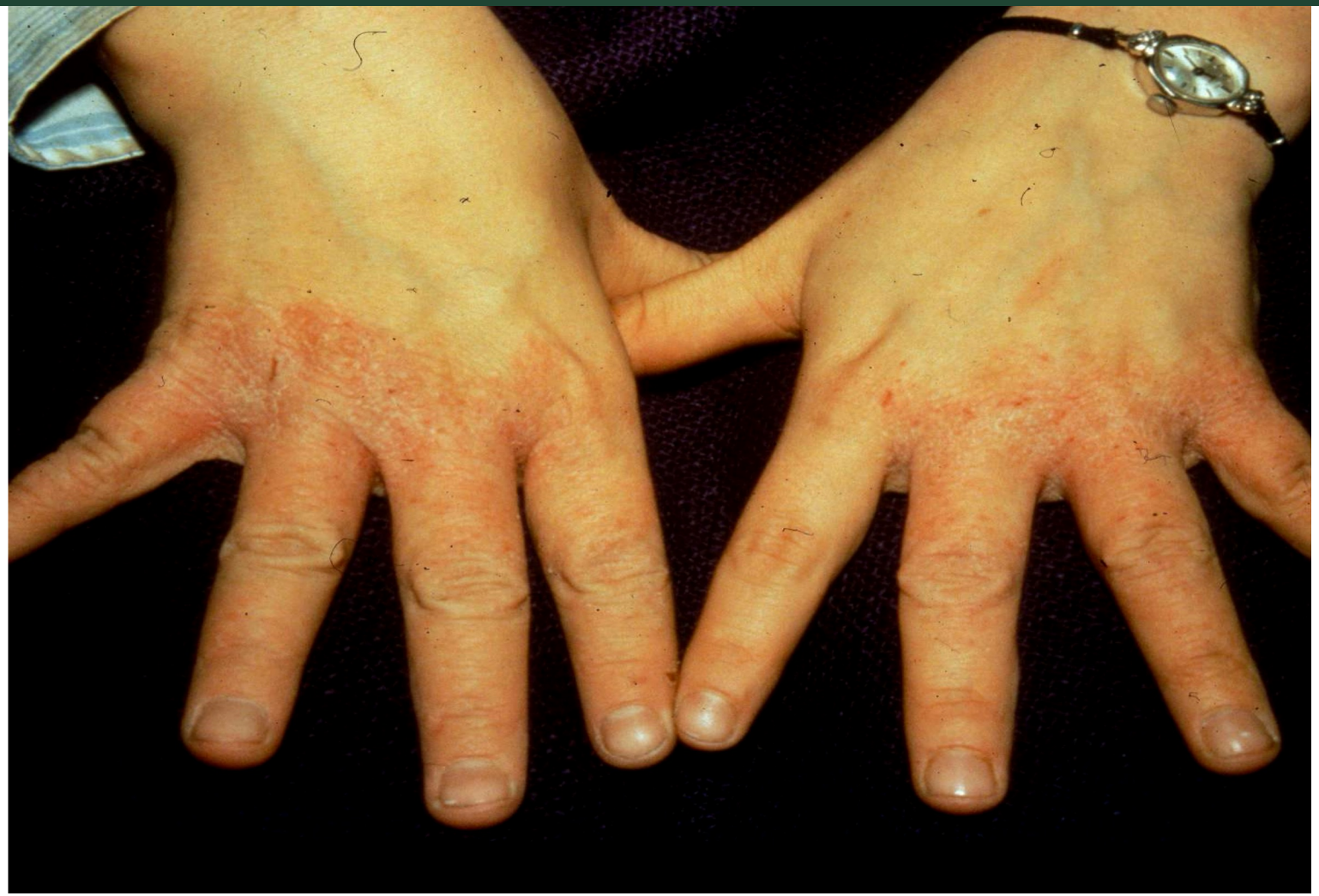
NACDG = North American Contact Dermatitis Group;
PCR = polymerase chain reaction.
Dhingra N, et al. *J Allergy Clin Immunol*. 2014;134(2):362-372.

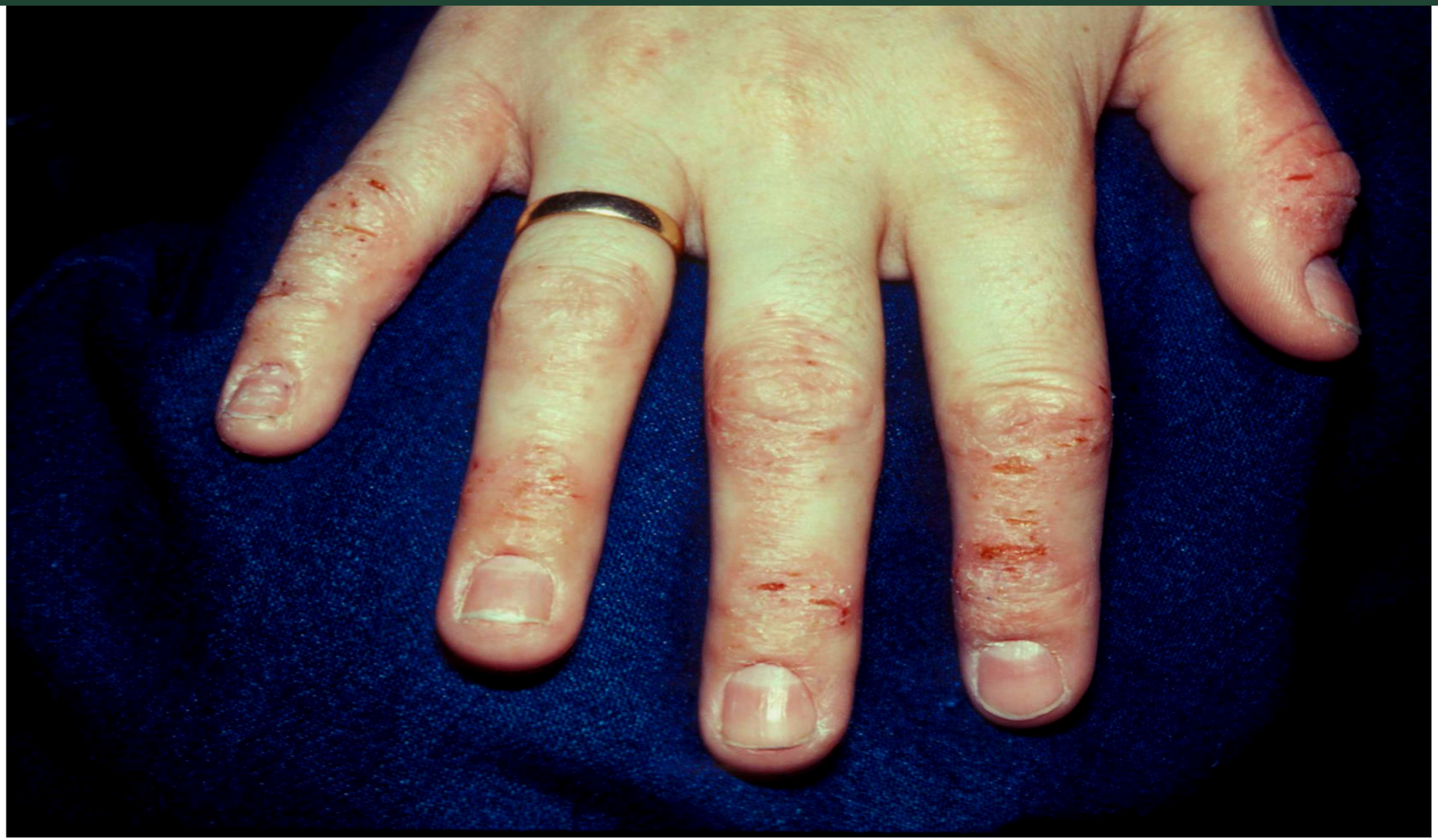
Different Allergens Show Distinct Immune Polarizations

- Different allergens induce differential T-cell polarization
  - Nickel: Th1/interferon/Th17 immune polarization
  - Fragrance and rubber: Th2/Th22 immune polarization
- These data may help to explain recent observations linking ACD and atopic dermatitis

IFN = interferon; GSVA = gene-set variation analysis.
Dhingra N, et al. *J Allergy Clin Immunol*. 2014;134(2):362-372.

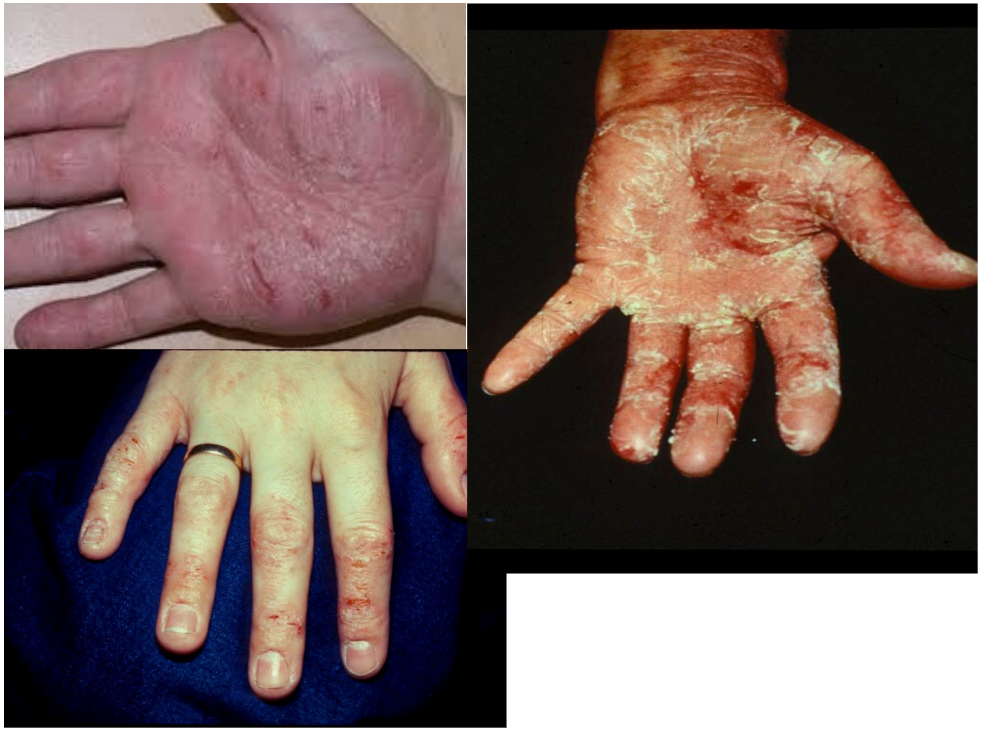






CHE Has a Variable Pathogenesis (Dependent on Primary Condition and Allergen)

- ICD presents a Th1/Th17 immune profile
- ACD presents a Th1/Th17 profile for metals, and Th2/Th22 for rubber and fragrance
- AD presents a Th2/Th22 profile



Ideally, treatments should be directed toward primary abnormalities

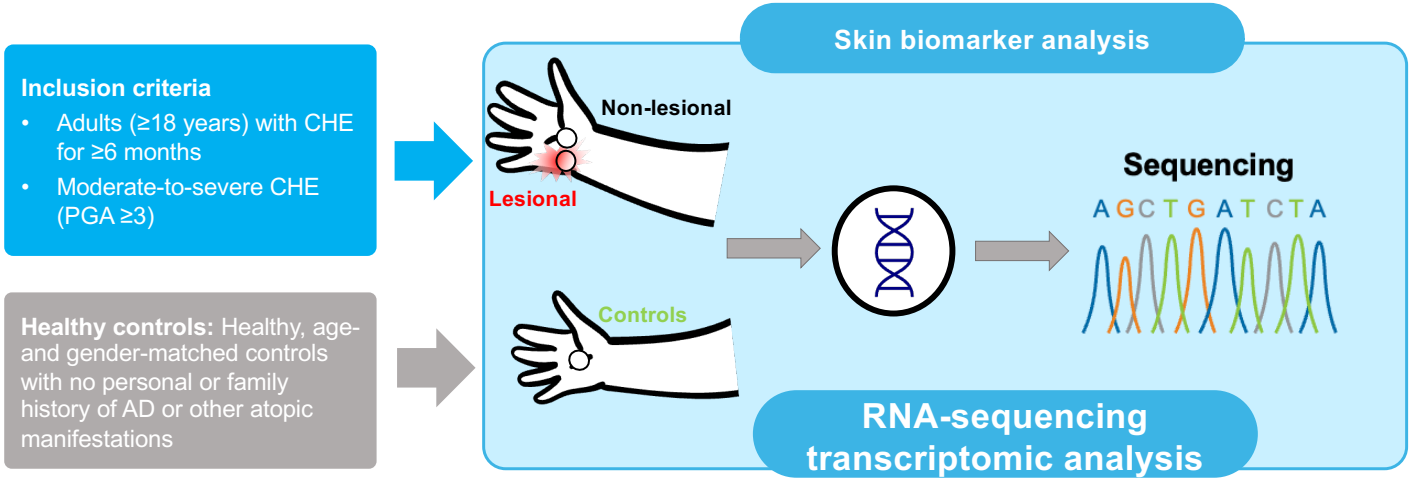
How Did We Get to This Point in AD (and Psoriasis)?

Biomarker studies in hand eczema are needed to help therapeutic development for various types of CHE (irritant CD/AD, allergic CD)

Both successes and failures have helped to frame pathogenic concepts and therapeutic directions

Defining the Phenotype of CHE with and without AD

- Tape strips were collected from lesional and adjacent non-lesional skin of patients with CHE (n=95) and healthy control skin (n=20)
- 20 tape strips performed on each site
- Samples analyzed with RNA sequencing
- Biomarkers were correlated with clinical severity scores



PGA = Physician Global Assessment.

Bar J, et al. Presented at: European Academy of Dermatology and Venereology (EADV) Congress; October 11-14, 2023; Berlin, Germany. Late-breaking abstract. Bar J, et al. *Allergy*. 2025;80(8):2271-2285.

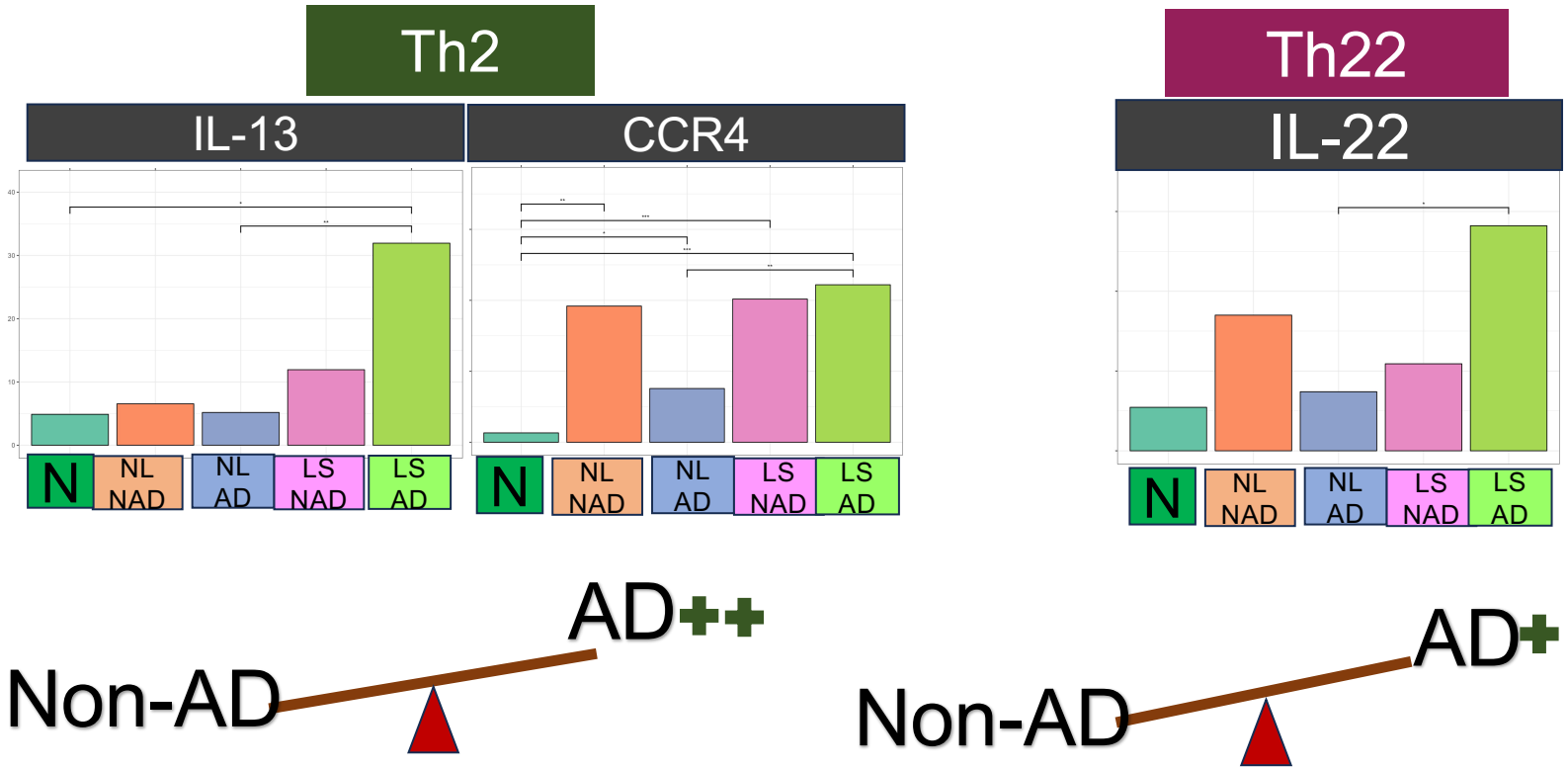
Study Population

	Chronic Hand Eczema with AD (n=45)	Chronic Hand Eczema without AD (n=50)	Healthy Controls (n=20)	*P*-Value
Age (y), mean (SD)	41.4 (16.6)	46.7 (16.5)	41 (10.7)	0.18
Sex (male/female),	15/30	15/35	11/9	0.14
Race, no (%)				
White	34 (76%)	46 (92%)	17	0.14
Black	6 (13%)	3 (6%)	3	
Asian	4 (9%)	1 (2%)	*NA*	
Other	1 (2%)	NA		
CHE subtypes, no (%)				
Dyshidrotic/pompholyx	12 (26%)	17 (34%)		0.5
Foot eczema involvement	11 (24%)	12 (24%)		1
Clinical Severity Scores, mean (range)				
mTLSS	13.6 (5-20)	12.9 (6-19)	*NA*	0.25
HECSI	68.4 (10-149)	58.1 (10-235)		0.22
DLQI	12.5 (2-26)	10.9 (1-30)		0.24
Pain VAS	5.1 (0-10)	4.3 (0-10)		0.2
PGA Feet	2.5 (1-3)	2.1 (0-4)		0.14
PGA Hand	3.7 (3-4)	3.5 (3-4)		0.5
BSA	3.1 (0-14)	*NA*		*NA*
IGA	2 (0-4)	*NA*		*NA*

SD = standard deviation; mTLSS = modified Total Lesion Symptom Score; HECSI = Hand Eczema Severity Index; DLQI = Dermatology Life Quality Index; VAS = Visual Analog Scale; BSA = body surface area; IGA = Investigator Global Assessment.

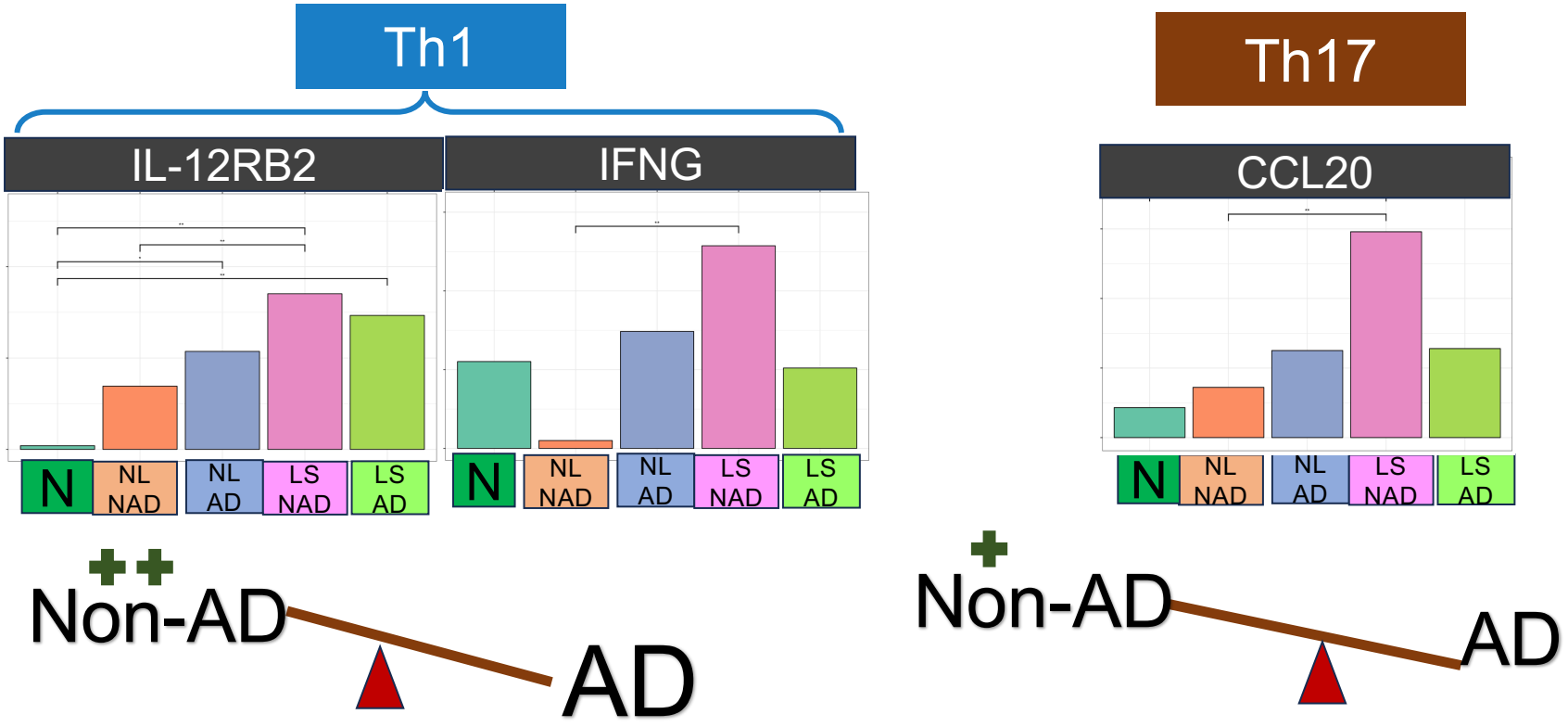
Bar J, et al. Presented at: EADV Congress; October 11-14, 2023; Berlin, Germany. Late-breaking abstract. Bar J, et al. *Allergy*. 2025;80(8):2271-2285.

CHE in Patients with AD Shows Stronger Th2/Th22 Skewing (vs Non-AD)



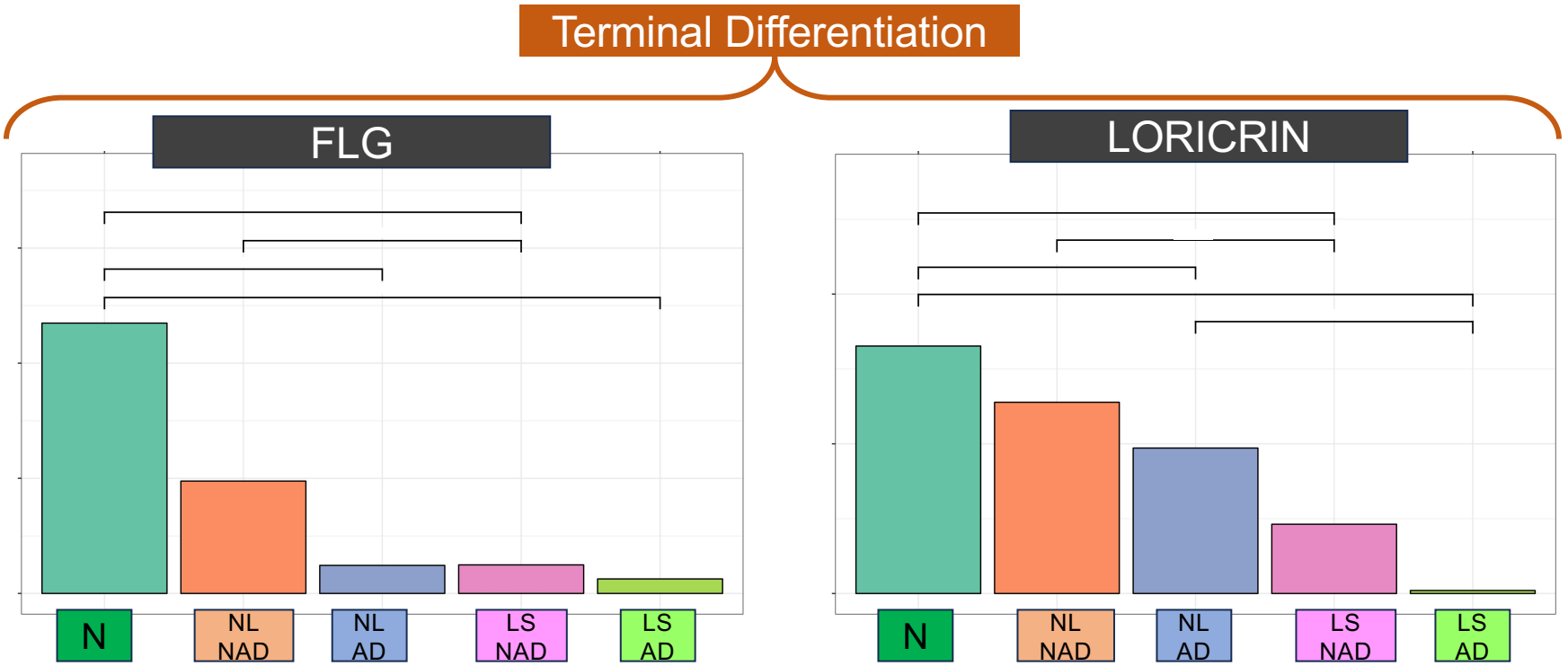
Bar J, et al. Presented at: EADV Congress; October 11-14, 2023; Berlin, Germany. Late-breaking abstract.

Non-AD CHE Shows Stronger Th1/Th17 Skewing (vs AD)



Bar J, et al. Presented at: EADV Congress; October 11-14, 2023; Berlin, Germany. Late-breaking abstract.

CHE Has Terminal Differentiation Abnormalities Regardless of AD Status



Bar J, et al. Presented at: EADV Congress; October 11-14, 2023; Berlin, Germany. Late-breaking abstract.

Multiple Biomarkers Are Correlated with CHE Severity

mTLSS

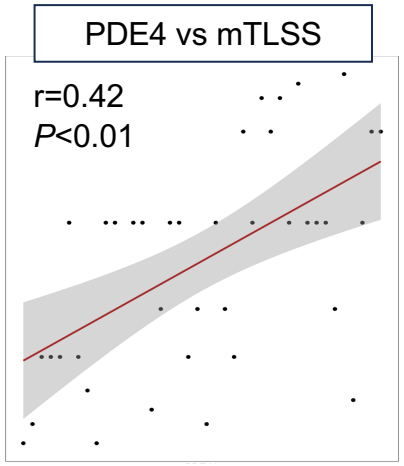
CHE with AD						CHE with No AD					
LESIONAL			NON-LESIONAL			LESIONAL			NON-LESIONAL		
Marker	R	*P*-value	Marker	R	*P*-value	Marker	R	*P*-value	Marker	R	*P*-value
CCL17	0.52	0.002	CCL11	0.52	0.002	ANXA9	-0.41	0.016	CDH10	-0.57	0.000
CD4	0.48	0.004	IGDCC4	0.46	0.007	IL37	-0.45	0.007	CLDN12	-0.61	0.000
CD69	0.40	0.019	IL4	0.45	0.009						
CD8A	0.42	0.013	LORICRIN	0.44	0.011						
GZMB	0.59	0.000	PDE3A	0.46	0.008						
IL1R2	0.40	0.019	PTGIS	0.43	0.013						
ITGB2	0.46	0.006									
PDE4A	0.42	0.013									
SOCS2	0.49	0.003									
XCL1	0.51	0.002									
XCL2	0.58	0.000									
TCHH	-0.58	0.000									
GAL	-0.49	0.003									

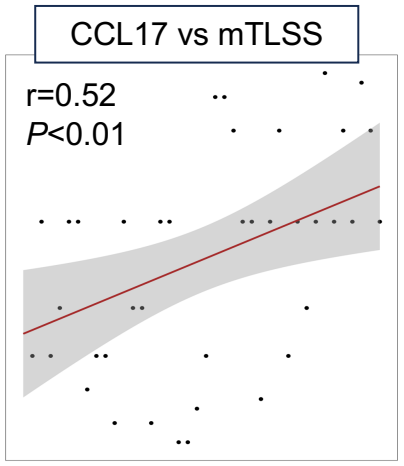
Pain VAS

CHE with No AD		
LESIONAL		
Marker	R	*P*-value
IL23A	0.42	0.013

HECSI

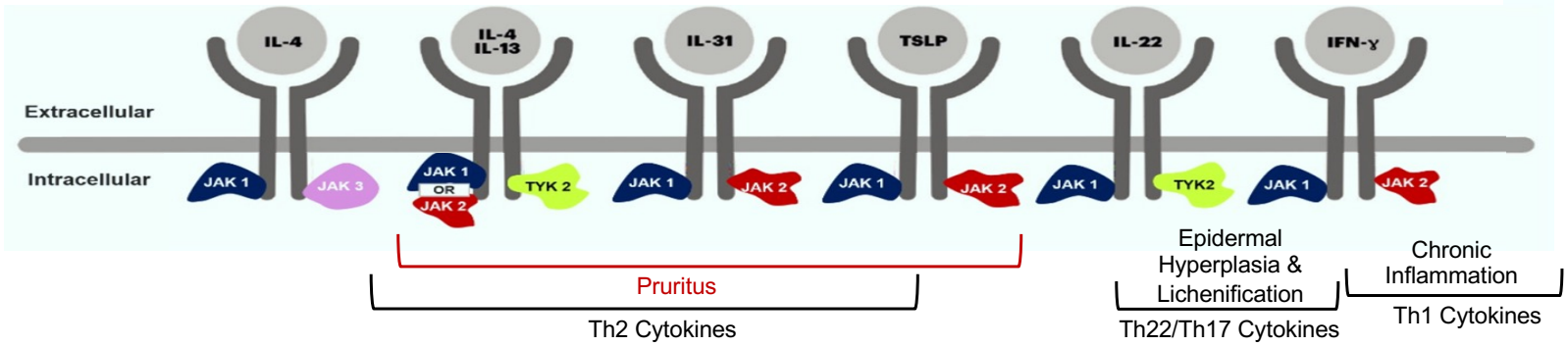
CHE with AD						CHE with No AD					
LESIONAL			NON-LESIONAL			LESIONAL			NON-LESIONAL		
Marker	R	*P*-value	Marker	R	*P*-value	Marker	R	*P*-value	Marker	R	*P*-value
FLG	-0.42	0.016				ANXA9	-0.47	0.005	JAK1	0.56	0.001
SPTLC1	-0.42	0.015							CDH22	-0.49	0.003
TGFB3	-0.42	0.016							CLDN12	-0.47	0.005
									IL17RC	-0.56	0.001





Bar J, et al. Presented at: EADV Congress; October 11-14, 2023; Berlin, Germany. Late-breaking abstract.

JAK Inhibitors Modulate Several Inflammatory Cytokines Relevant to Chronic Hand Eczema



TSLP = thymic stromal lymphopoietin.

Cartron AM, et al. *Clin Exp Dermatol*. 2021;46(5):820-824. Huang IH, et al. *Front Immunol*. 2022;13:1068260.

Clinical Scores of CHE: PGA/IGA (Physician/Investigator Global Assessment)

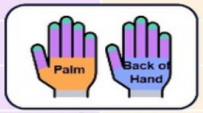
Scale used for alitretinoin in phase 3

PGA severity	Features	Intensity	Area involved
Severe	E, S, H/L V, O, F, P/P	At least one moderate or severe At least one severe	> 30% of affected hand surface
Moderate	E, S, H/L V, O, F, P/P	At least one mild or moderate At least one moderate	10%-30% of affected hand surface
Mild	E, S, H/L V, O, F, P/P	At least one mild At least one mild	Less than 10% of affected hand surface
Almost clear	E, S, H/L V, O, F, P/P	At least one mild Absent	Less than 10% of affected hand surface
Clear	E, S, H/L V, O, F, P/P	Absent Absent	Not detectable

E=Erythema, S=Scaling, H/L=Hyperkeratosis/Lichenification, V=Vesiculation, O=Oedema, F=Fissures, P/P=Pruritus/Pain

Bissonnette R, et al. Presented at: IEC Symposium at American Academy of Dermatology (AAD) Annual Meeting; March 2021.

Clinical Scores of CHE: HECSI (Hand Eczema Severity Index)

Clinical Signs	Fingertips	Fingers (except tips)	Palm of Hand	Back of Hand	Wrist
Erythema	 **Intensity scores** 0 – No skin changes 1 – Mild disease 2 – Moderate disease 3 – Severe disease				
Infiltration/Papulation					
Vesicles					
Fissures					
Scaling					
Oedema					
Sum of Intensity Scores					
Extent		**Extent Score (% of area affected)**	0 – 0% 1 – 1 to 25% 2 – 26 to 50% 3 – 51 to 75% 4 – 76 to 100%		
HECSI scores	**Sum of Intensity Scores x Extent Score**				

Total HECSI Score (Sum of HECSI scores):	**Score of 0-360**
HECSI Score	**Severity**
0	Clear
1 to 16	Almost Clear
17 to 37	Moderate
38 to 116	Severe
≥ 117	Very Severe

Simpson EL, et al. *J Eur Acad Dermatol Venereol*. 2023;37(9):1863-1870.

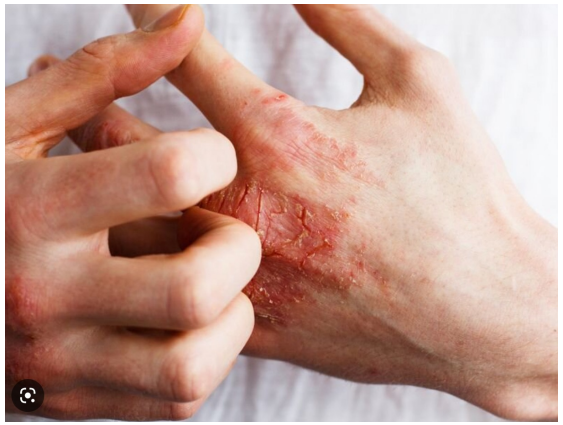
Clinical Scores of CHE: mTLSS (Modified Total Lesion Symptom Score)

Parameter	Description of Severity
Erythema	0 = Absent 1 = Faint erythema 2 = Prominent redness 3 = Deep intense red coloring
Scaling	0 = Absent 1 = Slight flaking over limited areas, mostly fine scales 2 = Flaking over widespread area(s), coarser scales 3 = Desquamation covering >30% of the hand with coarse thick scales
Lichenification (hyperkeratosis)	0 = Absent 1 = Mild thickening with exaggerated skin lines over limited areas 2 = Palpable thickening over widespread area(s) 3 = Prominent thickening over widespread area(s) with exaggeration of normal skin markings
Vesicles	0 = Absent 1 = Scattered vesicles affecting up to 10% of hand, without erosion 2 = Scattered or clustered vesicles affecting up to 30% of hand, without visible erosion or excoriation 3 = High density of vesicles extending over large area(s), or with erosion or excoriation
Oedema	0 = Absent 1 = Dermal swelling over less than 10% of hands 2 = Definite dermal swelling over more than 10% of hands 3 = Dermal swelling with skin infiltration over widespread area(s)
Fissures	0 = Absent 1 = Cracked skin affecting a small area of the hand 2 = Cracked skin affecting multiple areas of the hand and causing pain 3 = One or more deep fissures with bleeding or severe pain
Pruritus / pain	0 = Absent 1 = Occasional, slight discomfort a few times per day 2 = Intermittent, causing discomfort frequently during the day 3 = Persistent or interfering with sleep
0 = absent, 1 = mild, 2 = moderate, 3 = severe	

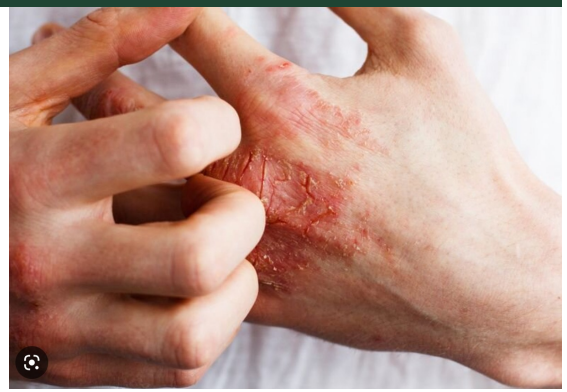
Ruzicka T, et al. *Br J Dermatol*. 2008;158(4):808-817.

Future Directions for Hand Eczema

- Need to incorporate non-invasive biomarkers – tape strips in the study of chronic hand eczema phenotypes (ICD/ACD/AD) and their different response to treatments in clinical trials



Thank You



We are now beginning an exciting medical and scientific path for a new treatment paradigm for our patients with CHE

Emma.Guttman@mountsinai.org

Current and Emerging Management Strategies for CHE

Christopher G. Bunick, MD, PhD
Associate Professor of Dermatology
Program in Translational Biomedicine
Yale Institute of Global Health
Yale School of Medicine

Treatment Approach for CHE: Delgocitinib Is the Only Treatment FDA-Approved for CHE

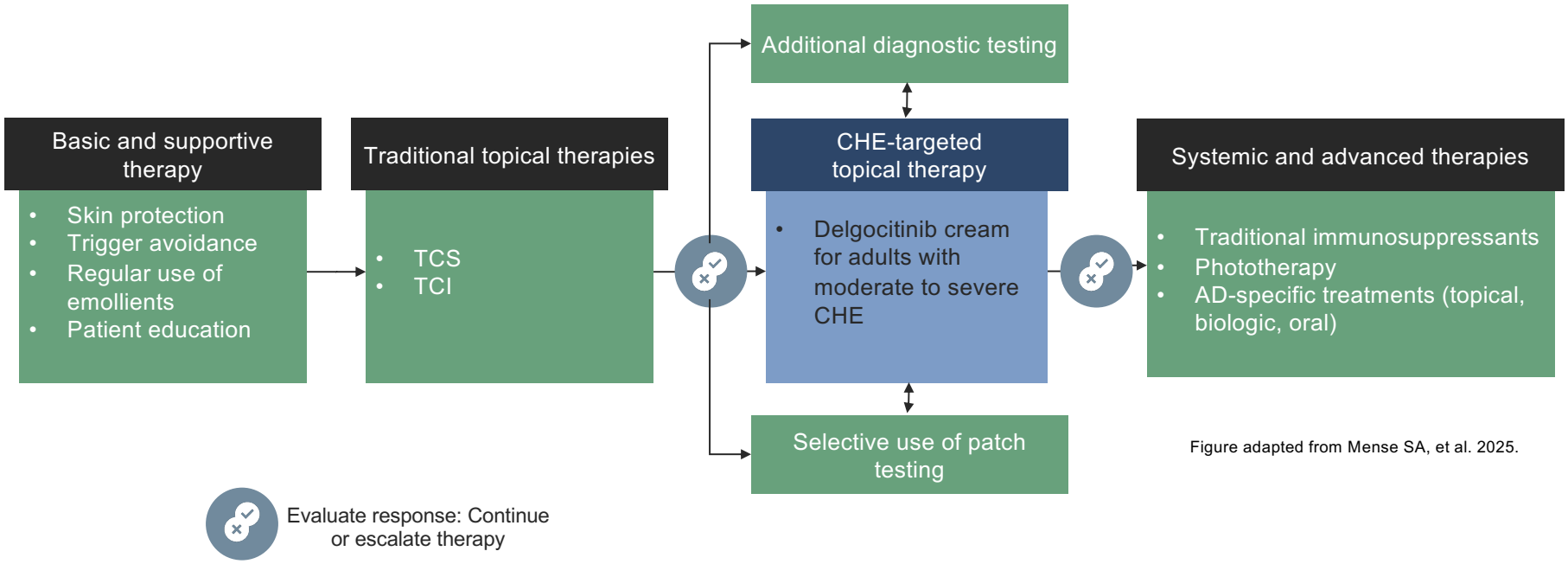


Figure adapted from Mense SA, et al. 2025.

TCI = topical calcineurin inhibitor; TCS = topical corticosteroid.

Mense SA, et al. *Dermatol Ther* (Heidlb). 2025;15(7):1953-1971.

Topical Corticosteroids Can Harm the Skin Barrier

The effect of tacrolimus compared with betamethasone valerate on the skin barrier in volunteers with quiescent atopic dermatitis*

S.G. Danby,[1] J. Chittock,[1] K. Brown,[1] L.H. Albenali[1,2,3] and M.J. Cork[1,3]

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[2]Kuwait Ministry of Health, Kuwait City, Kuwait
[3]The Paediatric Dermatology Clinic, Sheffield Children's Hospital, Sheffield, U.K.

CONCLUSION

- In pts with quiescent AD, 4-wk course of betamethasone (BID) reduced skin barrier function, stratum corneum integrity, and NMF levels towards the level of the subclinical barrier defect observed in active disease at non-lesional sites

Novel biophysical skin biomarkers discriminate topical anti-inflammatory treatments based on their potential for local adverse effects

Simon G. Danby[1] | Stephen Matcher[2] | Robert Byers[1] | Rosie Taylor[3] | Sura Sahib[1,4,5] | Paul Andrew[1] | Kirsty Brown[1] | Linda Kay[1] | Carl Wright[1] | Abi Pinnock[1] | John Chittock[1] | Mengqiu Duan[2] | Amy Cha[6] | Roni Adiri[7] | Chuanbo Zang[8] | John Werth[8] | Michael J. Cork[1,4,5]

CONCLUSION

- In pts with AD, the application of betamethasone BID for 2 wks to areas of skin without visible signs of inflammation led to substantial thinning of the epidermis (by ~30%)
- Thinning of the epidermis was accompanied by concordant changes in vascular structure
- The effects on the skin were transient, but evidence of epidermal thinning persisted in the areas treated with betamethasone

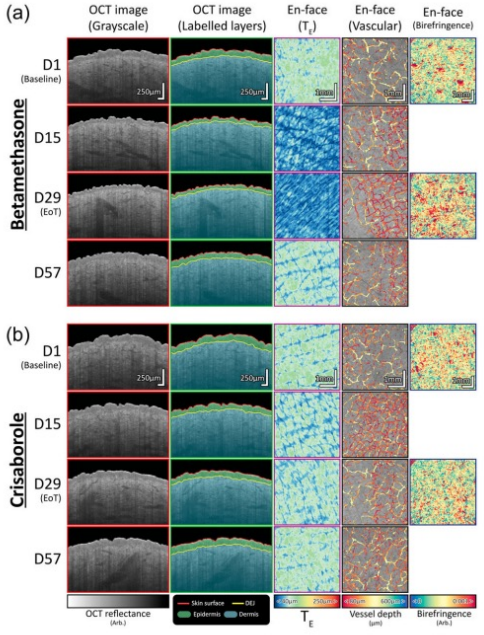
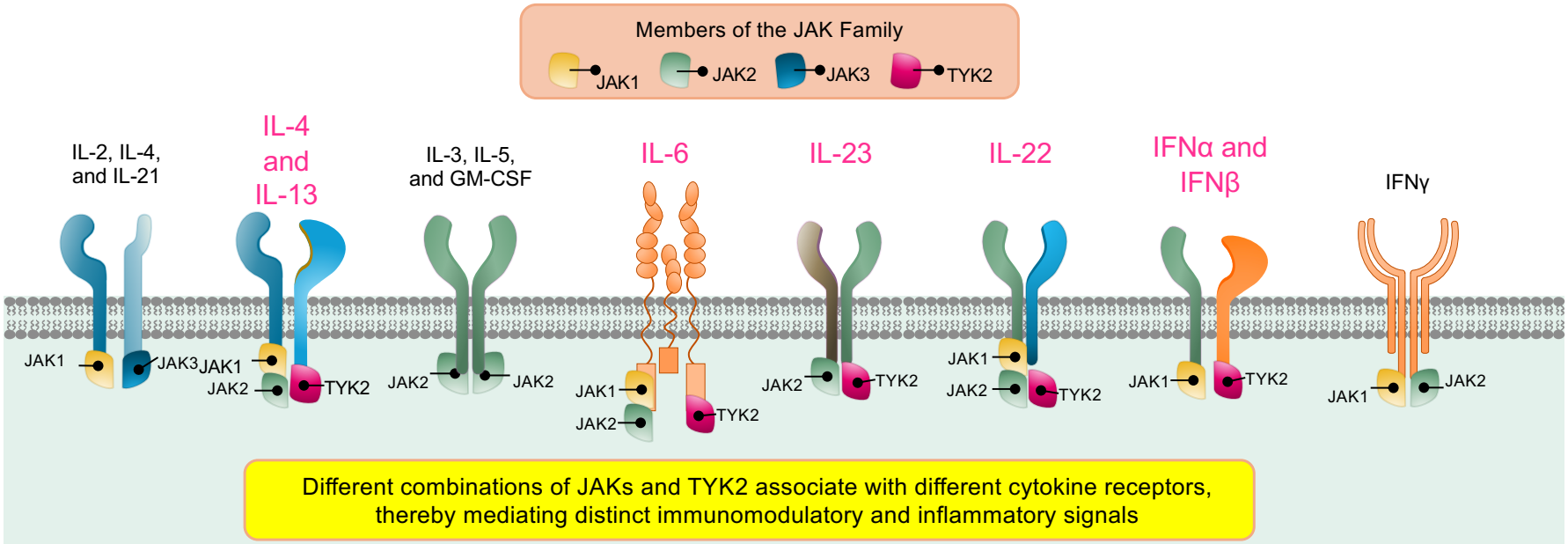


FIGURE 2 Representative OCT and PS-OCT data. Taken from areas treated with betamethasone (a) and crisaborole (b). The first column shows cross-sectional OCT B-scans for each of the study visits. The second column shows these same B-scans with the skin

Ways TCS harm the skin barrier:
Epidermal thinning (~30% in 28d)
↓ NMF → ↓ PCA/UCA → ↓ carboxyl groups
↑ pH → overactive proteases (KLK5/7)
Loss of superficial vascular plexus depth
Altered collagen density and organization
Altered lipid organization
↑ TEWL

NMF = natural moisturizing factor; PCA = pyrrolidone carboxylic acid; UCA = urocanic acid; TEWL = transepidermal water loss.
Danby SG, et al. *Br J Dermatol*. 2014;170(4):914-921. Danby SG, et al. *JEAVD Clin Pract*. 2025;4(1);103-116.

Extracellular Cytokine Signaling Is Linked to Intracellular JAK/STAT Signaling



The JAK-STAT pathway is implicated in the activation of keratinocytes and immune cells. This may lead to increased cytokine secretion, which in turn promotes further inflammation and amplifies the immune response.

GM-CSF = granulocyte-macrophage colony-stimulating factor; TYK = tyrosine kinase.

Adapted from Schwartz DM, et al. *Nat Rev Drug Discov*. 2017;16(12):843-862. Lee GR, et al. *Dermatol Ther*. 2019;32(3):e12840. Tanimoto A, et al. *Inflamm Res*. 2015;64(1):41-51. Dubin C, et al. *Ther Clin Risk Manag*. 2020;16:1319-1332. Erratum in: *Ther Clin Risk Manag*. 2021;17:233. Virtanen AT, et al. *BioDrugs*. 2019;33(1):15-32. Junttila IS. *Front Immunol*. 2018;9:888. Weidinger S, et al. *Nat Rev Dis Primers*. 2018;4(1):1. Gittler JK, et al. *J Allergy Clin Immunol*. 2013;131(2):300-313.

DELTA 1 & 2: Trial Designs

Primary endpoint: IGA-CHE treatment success (0/1) at Week 16

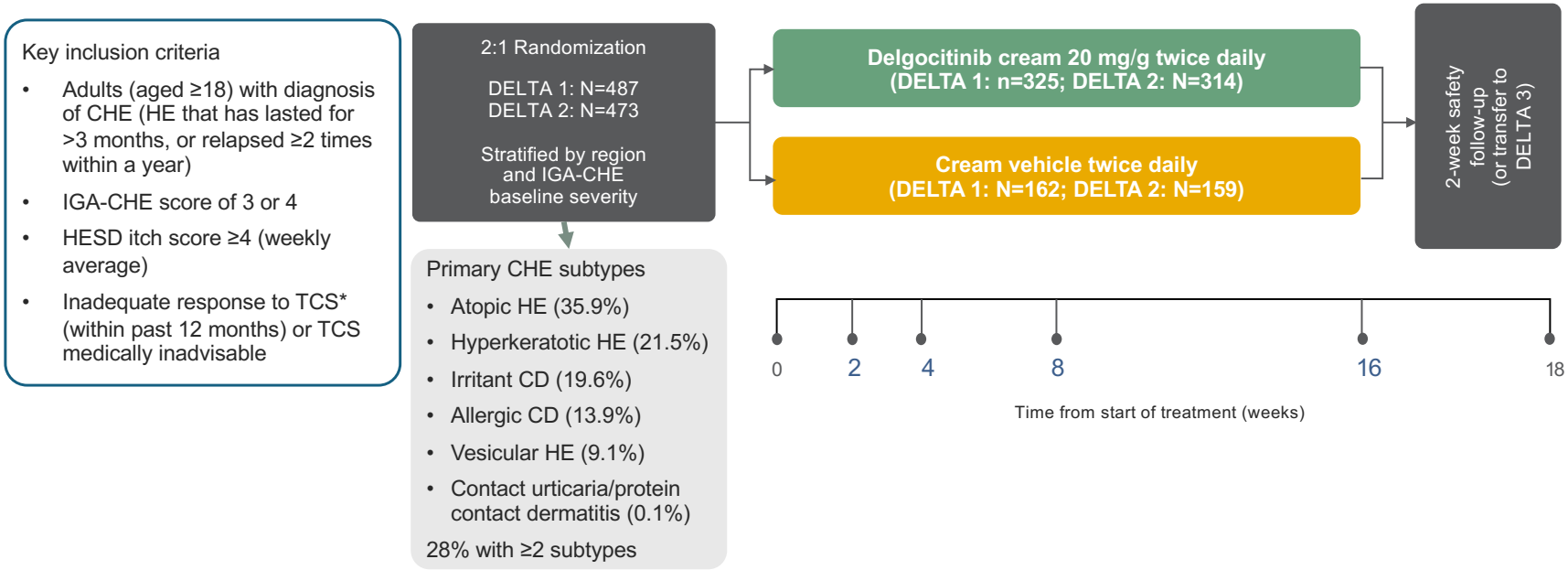


Figure adapted from Bissonnette R, et al. 2024.

***Failure of potent or very potent TCS.**
HESD = hand eczema symptom diary; LTE = long-term extension.
FDA. Accessed May 12, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219155s000lbl.pdf.
Bissonnette R, et al. *Lancet*. 2024;404(10451):461-473.

DELTA 1 & 2: Key Inclusion/Exclusion Criteria

Inclusion criteria

- Age of ≥18 years at screening
- Diagnosis of CHE: Hand eczema that has persisted for >3 months or returned at least twice within the last 12 months
- Moderate-to-severe disease severity at screening and baseline (IGA-CHE score of 3 or 4)
- HESD itch score (weekly average) of ≥4 points at baseline
- Documented recent history of inadequate response to treatment with TCS (within the last year) or TCS otherwise medically inadvisable
- Adherence to standard non-medicated skin care, including avoidance of known and relevant irritants and allergens
- A woman of childbearing potential must use an acceptable method of birth control throughout the trial up until the end-of-treatment/early termination visit

Exclusion criteria*

- Concurrent skin diseases or clinically significant infection on the hands
- Active AD requiring medical treatment in regions other than the hands and feet
- Active psoriasis on any part of the body
- Hyperkeratotic hand eczema in combination with a history of psoriasis on any part of the body
- Previous/current treatment with systemic/topical JAK inhibitors (including delgocitinib)
- Clinically significant infection within 28 days prior to baseline
- History of any known primary immunodeficiency disorder

***Please note that this is not an exhaustive list; the full exclusion criteria can be viewed in: Supplement to Bissonnette R, et al. *Lancet.* 2024;404(10451):461-473.**

DELTA 1 & 2: Demographics and Baseline Characteristics

	DELTA 1			DELTA 2		
	Total (N=487)	Delgocitinib cream 20 mg/g (n=325)	Cream vehicle (n=162)	Total (N=473)	Delgocitinib cream 20 mg/g (n=314)	Cream vehicle (n=159)
Age, median years (IQR)	44.0 (32.0–55.0)	45.0 (32.0–55.0)	42.5 (30.0–55.0)	44.0 (33.0–56.0)	46.0 (34.0–57.0)	42.0 (31.0–54.0)
Sex, n (%) Male Female	 181 (37) 306 (63)	 123 (38) 202 (62)	 58 (36) 104 (64)	 161 (34) 312 (66)	 110 (35) 204 (65)	 51 (32) 108 (68)
Race, n (%) White Black or African American Asian Other/Not reported	 427 (88) 4 (1) 19 (4) 37 (8)	 283 (87) 3 (1) 14 (4) 25 (8)	 144 (89) 1 (1) 5 (3) 12 (7)	 441 (93) 3 (1) 15 (3) 14 (3)	 295 (94) 2 (1) 8 (3) 9 (3)	 146 (92) 1 (1) 7 (4) 5 (3)
Age at onset of CHE, median years (IQR)	32.0 (20.0–47.0)	33.0 (21.0–47.0)	30.0 (20.0–46.0)	34.0 (22.0–48.0)	35.0 (24.0–49.0)	32.0 (21.0–46.0)
Duration of CHE, median years (IQR)	6.0 (2.0–15.0)	6.0 (2.0–15.0)	5.5 (2.0–15.0)	5.0 (2.0–11.0)	4.0 (2.0–11.0)	5.0 (2.0–12.0)
IGA-CHE, n (%) Moderate Severe	 327 (67) 160 (33)	 218 (67) 107 (33)	 109 (67) 53 (33)	 360 (76) 113 (24)	 239 (76) 75 (24)	 121 (76) 38 (24)
HECSI, median (IQR)	n=487 65.0 (42.0–99.0)	n=325 66.0 (43.0–98.0)	n=162 61.5 (38.0–105.0)	n=472 59.0 (38.5–83.5)	n=313 59.0 (38.0–82.0)	n=159 59.0 (40.0–90.0)
DLQI Median (IQR) ≥4, n (%)	n=479 12.0 (8.0–17.0) 453 (95)	n=321 12.0 (9.0–17.0) 305 (95)	n=158 12.0 (7.0–18.0) 148 (94)	n=469 11.0 (7.0–17.0) 452 (96)	n=310 11.0 (7.0–17.0) 299 (97)	n=159 11.0 (7.0–17.0) 153 (96)

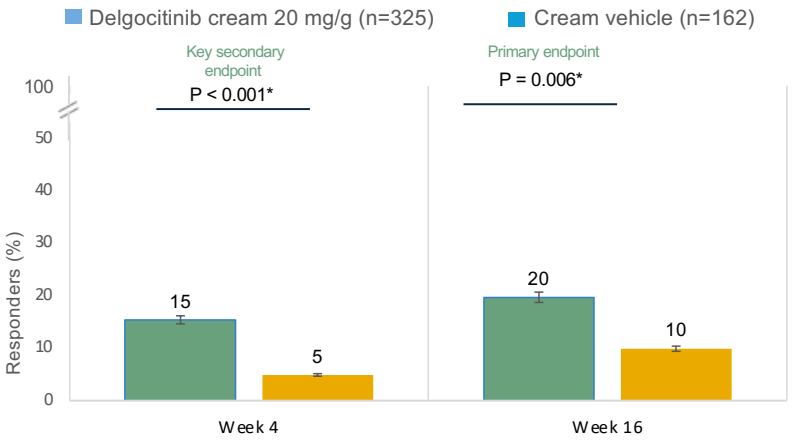
Table adapted from Bissonnette R, et al. 2024.

IQR = interquartile range.

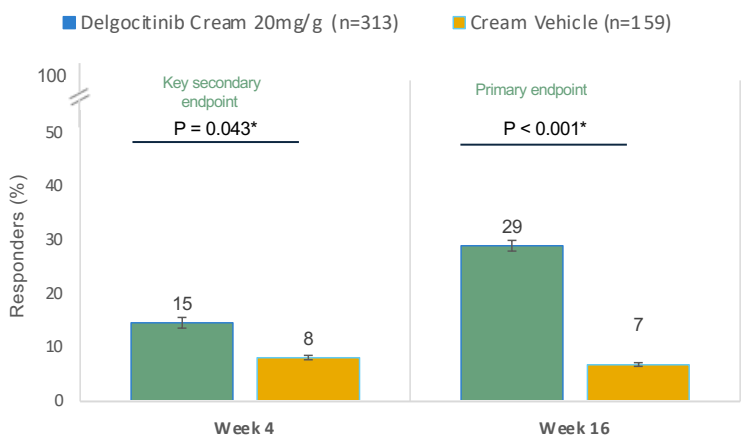
Bissonnette R, et al. *Lancet*. 2024;404(10451):461-473.

Treatment Success Was Defined as Achieving Clear Skin or Barely Perceptible Erythema

DELTA 1: IGA-CHE treatment success



DELTA 2: IGA-CHE treatment success



Figures adapted from Bissonnette R, et al. 2024. Delgocitinib Prescribing Information.

- Delgocitinib achieved statistically significant improvements over cream vehicle in the primary and all key secondary endpoints at all prespecified timepoints
- Week 8 IGA-CHE treatment success
  - DELTA 1: 23% Delgocitinib cream vs 11% cream vehicle (P = 0.0010)
  - DELTA 2: 32% Delgocitinib cream vs 9% cream vehicle (P < 0.0001)

IGA-CHE assessment scale

Score	Severity	Erythema	+	No signs of
0	Clear			Scaling Hyperkeratosis/lichenification Vesiculation Edema Fissures
1	Almost clear	barely perceptible		

***Significant according to prespecified testing procedure.**

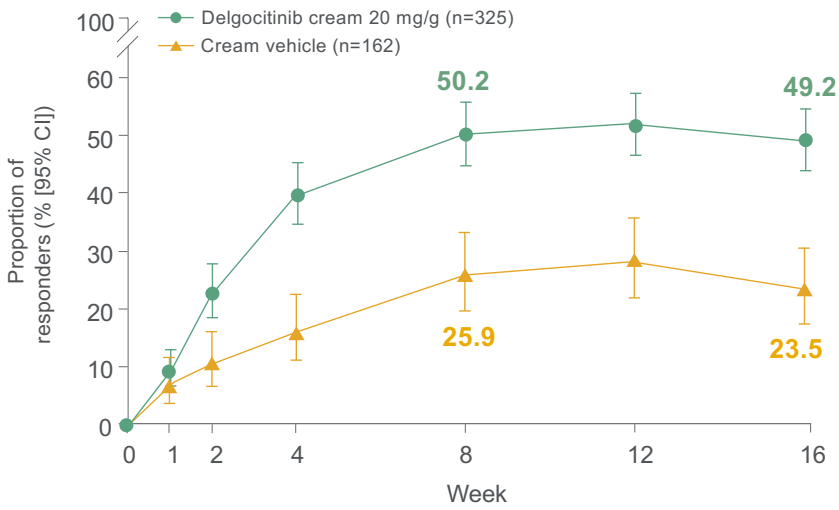
Bissonnette R, et al. *Lancet*. 2024;404(10451):461-473. FDA. Accessed May 12, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219155s000lbl.pdf. Silverberg JI, et al. *Arch Dermatol Res*. 2024;316(4):110.

DELTA 1 & 2: HECSI-75 (FAS, NRI)*

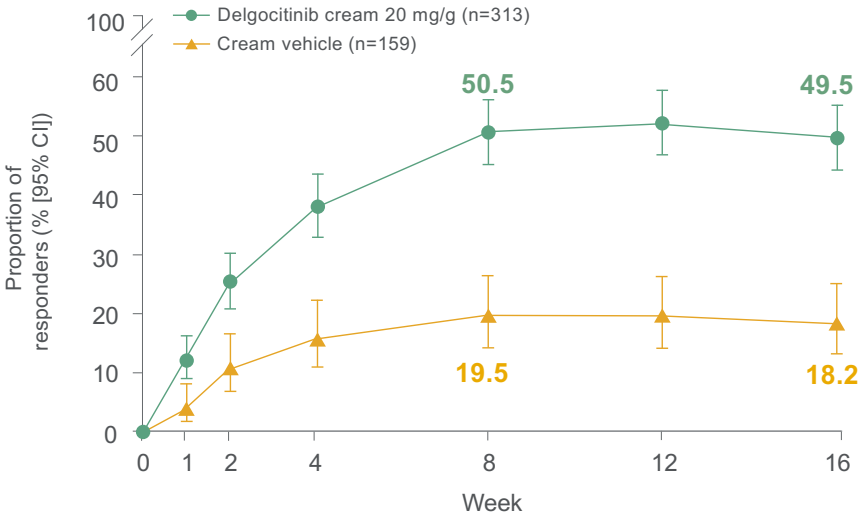
HECSI-75, which measures ≥75% improvement in HECSI, was shown to be appropriate for defining clinically meaningful change.
A score of 0–16 equates to clear (0) or almost clear (1–16).

Limitation: HECSI was not included in the USPI because it is not fit for purpose for efficacy labeling claims, as it is not clearly interpretable (eg, HECSI: under- and over-represents signs/symptoms and has weak scoring algorithm evidence).

DELTA 1



DELTA 2



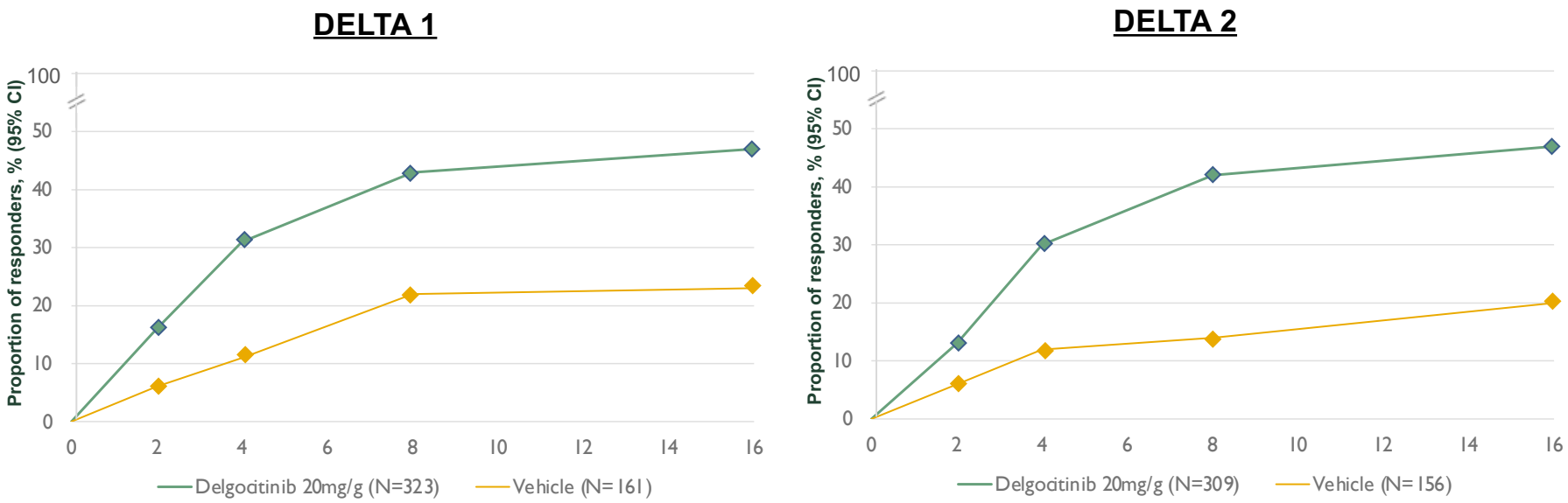
Figures adapted from Bissonnette R, et al. 2024.

***HECSI-75 at Weeks 8 and 16 were key secondary endpoints. Differences between the two treatment groups at Week 8 and 16 were significant (*P*<0.0001) in both trials. Primary analysis of the composite estimand.**
Data considered non-response if observed after initiation of rescue treatment or after permanent discontinuation of trial drug. Missing data imputed as non-response.
USPI = United States Prescribing Information; CI = confidence interval; FAS = full analysis set; NRI = non-responder imputation.

Bissonnette R, et al. *Lancet*. 2024;404(10451):461-473. Yüksel YT, et al. *Contact Dermatitis*. 2025;92(1):51-60.

DELTA 1 and DELTA 2: HESD Itch ≥4-Point Reduction by Week 16

DELTA 1 and DELTA 2 HESD itch ≥4-point reduction by week among patients with ≥4-points baseline itch score to 16 weeks (FAS, NRI)

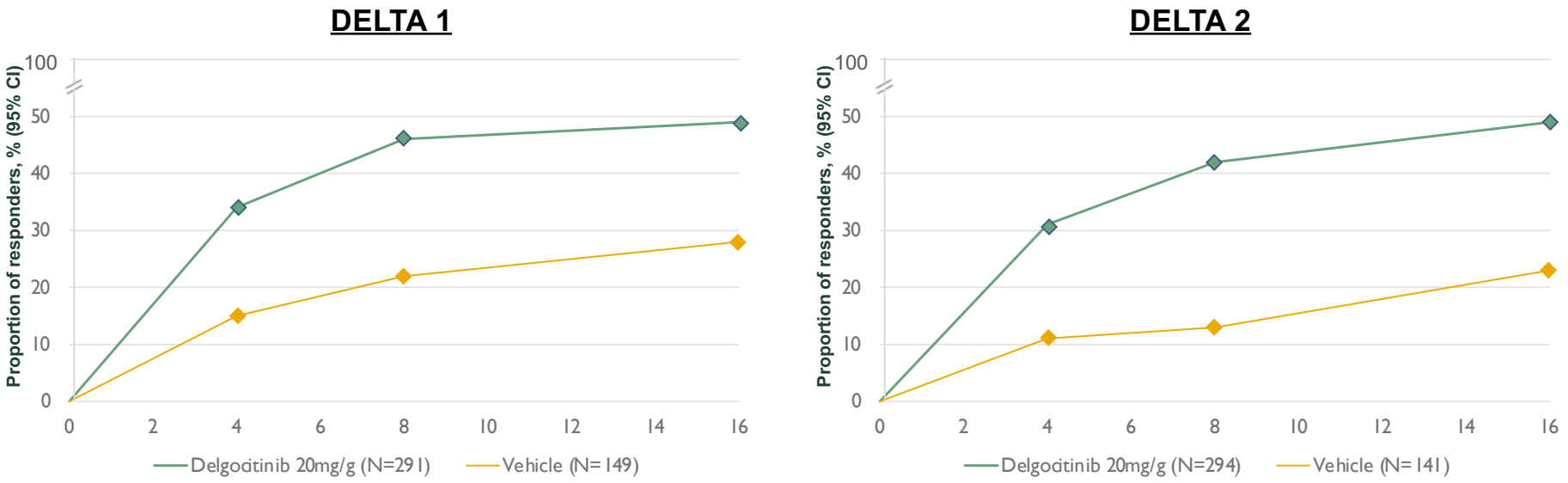


Daily HESD itch/pain scored from 0–10 (no symptom to severe symptom) alongside 5 other domains. The weekly score was averaged.

FDA. Accessed May 12, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219155s000lbl.pdf.

DELTA 1 and DELTA 2: HESD Pain ≥4-Point Reduction by Week 16

DELTA 1 and DELTA 2 HESD pain ≥4-point reduction by week among patients with ≥4-points baseline pain score to 16 weeks (FAS, NRI)

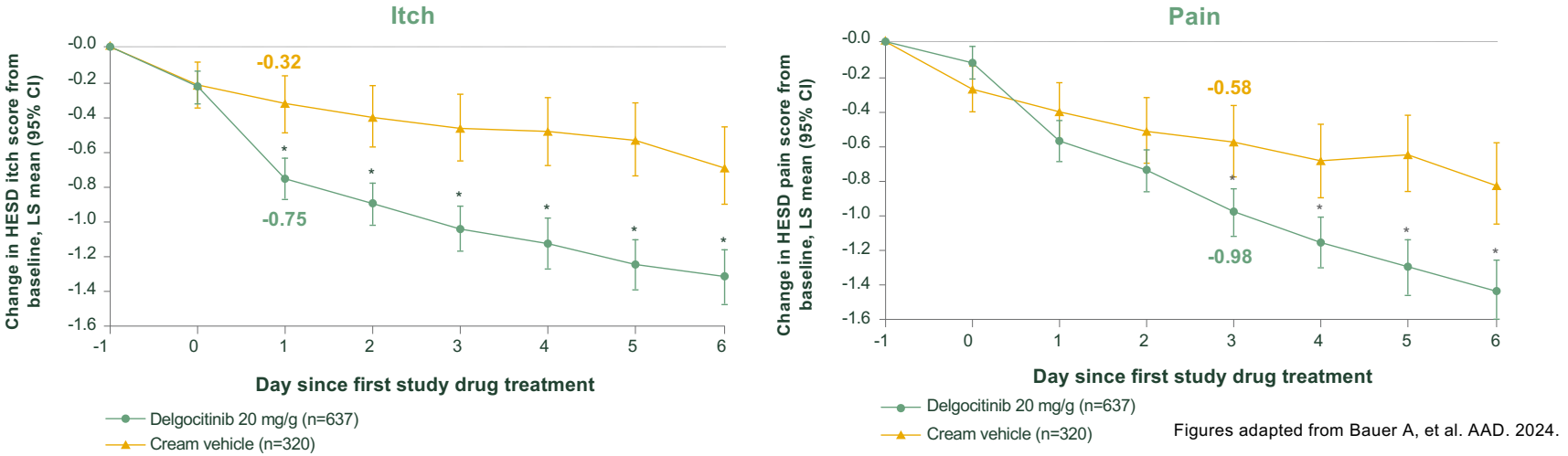


Daily HESD itch/pain scored from 0–10 (no symptom to severe symptom) alongside 5 other domains. The weekly score was averaged.

FDA. Accessed May 12, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219155s000lbl.pdf.

Change in Daily HESD Itch and Pain Scores

DELTA 1 and 2: Change in daily HESD score for itch and pain from baseline to Day 6 (FAS, WOCF)



Figures adapted from Bauer A, et al. AAD. 2024.

- **Mean change in daily itch score shows significance from day 1 compared to vehicle**
- **Mean change in daily pain score shows significance from day 3 compared to vehicle**

Analyses were pre-specified in the SAP. Data is pooled and imputed as non-response by using WOCF (including baseline value) after initiation of rescue treatment, or after permanent discontinuation of IMP. Missing data are imputed with WOCF (including the baseline value).

***P*<0.001 vs cream vehicle.**
ANCOVA model: Change in HESD itch/pain score from baseline = treatment + trial ID + region + baseline IGA-CHE score + baseline HESD itch/pain score.
FAS = full analysis set; WOCF = worst observation carried forward; LS = least square; SAP = statistical analysis plan; IMP = investigational medicinal product.
Bauer A, et al. Presented at: American Academy of Dermatology (AAD) Annual Meeting; March 8-12, 2024; San Diego, CA. Poster 53696.

DELTA 1 & 2 Pooled Data: Summary of AEs

	DELTA 1 and DELTA 2, Pooled	
	Delgocitinib Cream N=638, PYO=196.71	Vehicle Cream N=321, PYO=93.91
All events, n (%)	291 (45.6%)	153 (47.7%)
Serious AEs, n (%)	11* (1.7%)	6 (1.9%)
Fatal events, n (%)	0 (0%)	0 (0%)
Severity, n (%)		
Mild	223 (35.0%)	120 (37.4%)
Moderate	118 (18.5%)	60 (18.7%)
Severe	15 (2.4%)	9 (2.8%)
Possibly or probably study drug-related AEs, n (%)	34 (5.3%)	24 (7.5%)
AEs leading to permanent discontinuation of study drug, n (%)	3^ (0.5%)	11 (3.4%)

Table adapted from Bissonnette R, et al. AAD. 2024.

In DELTA 1 and DELTA 2, adverse reactions that were reported in ≤1% of participants in the DELGO group were application site pain, paresthesia, pruritus, erythema, and bacterial skin infections, including finger cellulitis, paronychia, other skin infections, leukopenia, and neutropenia.

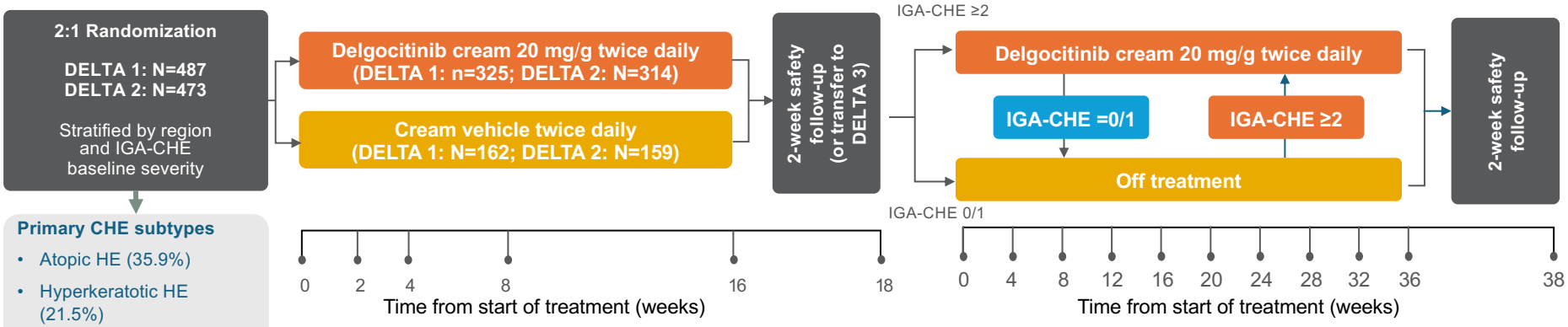
***SAEs:** N=11, E=12: **No serious AEs were related to delgocitinib cream treatment.** The events were 1 each of: COVID-19 pneumonia, bacterial keratitis, peritonsillar abscess, tonsillitis, hand dermatitis, epilepsy, generalized tonic-clonic seizure, migraine, intervertebral disc protrusion, inguinal hernia, post-procedural haemorrhage, gallbladder adenocarcinoma.

^Discontinuation of IMP: N=3, E=3: Events were 1 each of: Contact dermatitis, eczema, skin bacterial infection.

AEs = adverse events; PYO = patient-years of observation.

FDA. Accessed May 12, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219155s000lbl.pdf. Bissonnette R, et al. Presented at: AAD Annual Meeting; March 8-12, 2024; San Diego, CA. Bissonnette R, et al. *Lancet.* 2024;404(10451):461-473.

DELTA 1, 2, & 3: Trial Designs



Participants were advised to apply the cream to the affected area of the hands and wrists, continuing to treat these areas throughout the study. Treatment should also be applied to any new areas that develop.

DELTA 3 — Open-label, LTE

Primary endpoint: Number of treatment-emergent adverse events from baseline up to Week 38

Key inclusion criteria: Participants must have met the eligibility criteria at screening and baseline, and have completed the treatment period in DELTA 1 or DELTA 2

Figures adapted from Gooderham M, et al. 2024.

***Failure of potent or very potent TCS.**

FDA. Accessed May 12, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219155s000lbl.pdf. Gooderham M, et al. Presented at: AAD Annual Meeting; March 8-12, 2024; San Diego, CA. Bissonnette R, et al. *Lancet*. 2024;404(10451):461-473.

DELTA 3: Overall Safety Summary in Phase 3 Open-Label Study

Overall summary of adverse events seen within DELTA 3

	Total DELTA-3 Population (n=801, PYO=535.65)		
	n (%)	E	R
All events	495 (61.8)	1238	231.12
Serious events	27 (3.4)	36	6.72
Fatal events	3 (0.4)*	3	0.56
Severity			
Mild	390 (48.7)	771	143.94
Moderate	242 (30.2)	429	80.09
Severe	28 (3.5)	38	7.09
Probably or possibly related to IMP	27 (3.4)	31	5.79
AEs leading to permanent discontinuation of IMP	7 (0.9)	8	1.49

The majority of AEs up to 52 weeks of treatment were of mild or moderate severity, and assessed as not related to delgocitinib cream

No SAEs were considered to be related to delgocitinib cream

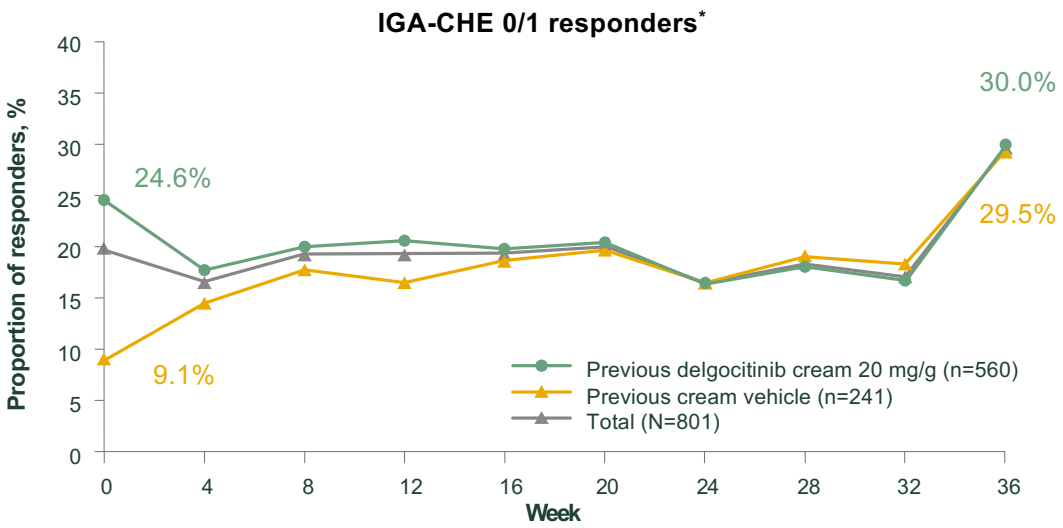
*3 deaths were reported during the trial, none were assessed as related to IMP: 1 patient had metastatic esophageal cancer reported on the day of first IMP dose; 1 death of unknown cause 17 days into an off-treatment period in a patient with multiple comorbidities admitted with fall, thought to be metastasis from a pre-existing renal cell carcinoma; 1 myocardial infarction 7 months after last dose.

In an open-label extension trial (DELTA 3), 801 subjects were treated for up to an additional 36 weeks after completing DELTA 1 or DELTA 2. A total of 198 subjects received continuous treatment with delgocitinib for 52 weeks. Eczema herpeticum was observed in one subject, and herpes zoster was observed in two subjects treated with delgocitinib.

AESI = adverse event of special interest; SAE = serious adverse event.

FDA. Accessed May 12, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219155s000lbl.pdf.
Gooderham M, et al. *J Am Acad Dermatol*. 2025;93(1):95-103.

Maintenance of Efficacy



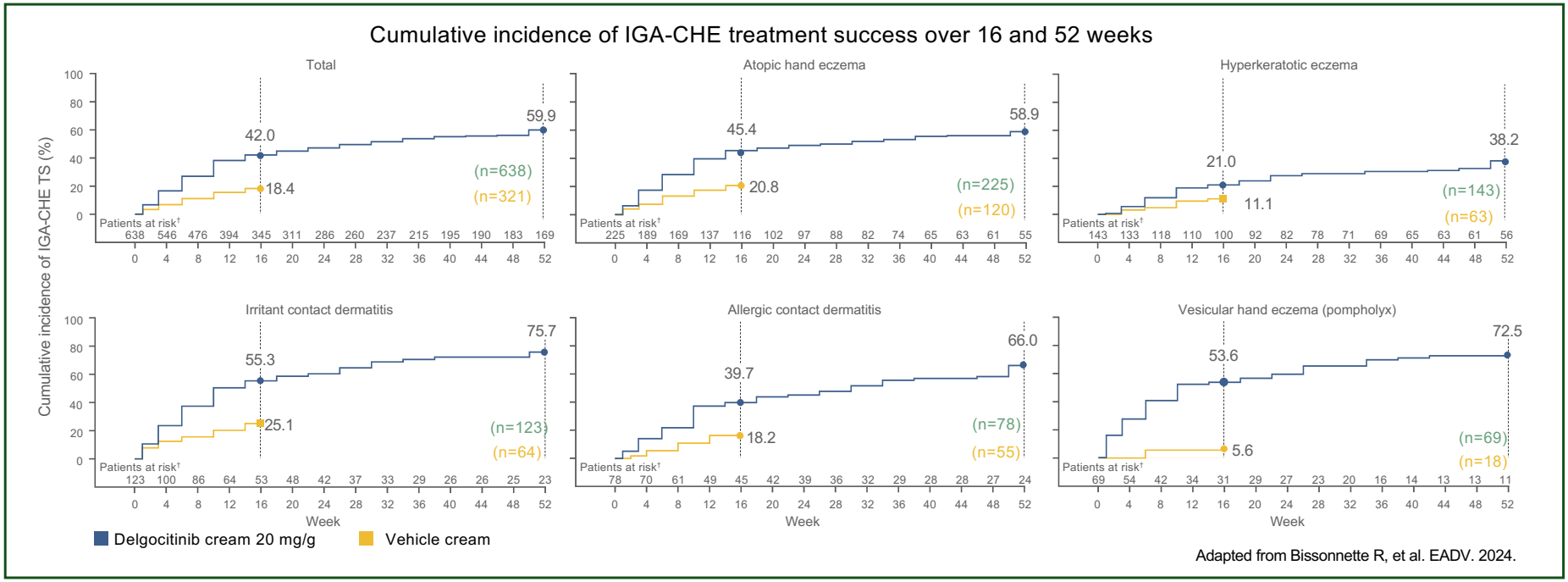
- **Re-capture: Loss of response on stopping delgocitinib can be regained upon treatment re-initiation**
- **Long-term safety: 198 subjects received continuous treatment for 52 weeks** through DELTA 1/2 and 3

Among subjects treated with delgocitinib in DELTA 1/2, IGA-CHE 0/1 was generally maintained throughout DELTA 3, while among subjects treated with cream vehicle in DELTA 1/2, IGA-CHE 0/1 response rate improved over the extension trial

The primary endpoint was the number of treatment-emergent AEs from baseline up to the end of the safety follow-up period at week 38. Proportions of patients in DELTA 3 achieving IGA-CHE 0/1, baseline to week 36 (safety analysis set). IGA-CHE ranges from 0 to 4 (clear to severe). Subjects experiencing discontinuation of IMP, initiation of rescue treatment, withdrawal from trial, or have missing data due to other reasons are imputed as non-responders.
***Subjects experiencing discontinuation of IMP, initiation of rescue treatment, withdrawal from trial, or have missing data due to other reasons are imputed as non-responders.**
FDA. Accessed May 12, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219155s000lbl.pdf. Gooderham M, et al. Presented at: AAD Annual Meeting; March 8-12, 2024; San Diego, CA.

IGA-CHE Treatment Success across CHE Subtypes*

Limitation: This post-hoc analysis (not-prespecified) of pooled data from DELTA 1 and DELTA 2 included patients who continued to participate in DELTA 3. Limitations and context associated with the open-label study design include decreasing sample size, potential continued involvement of responders, and attrition of non-responders. Data presented are descriptive in nature. Conclusions should be made with caution.

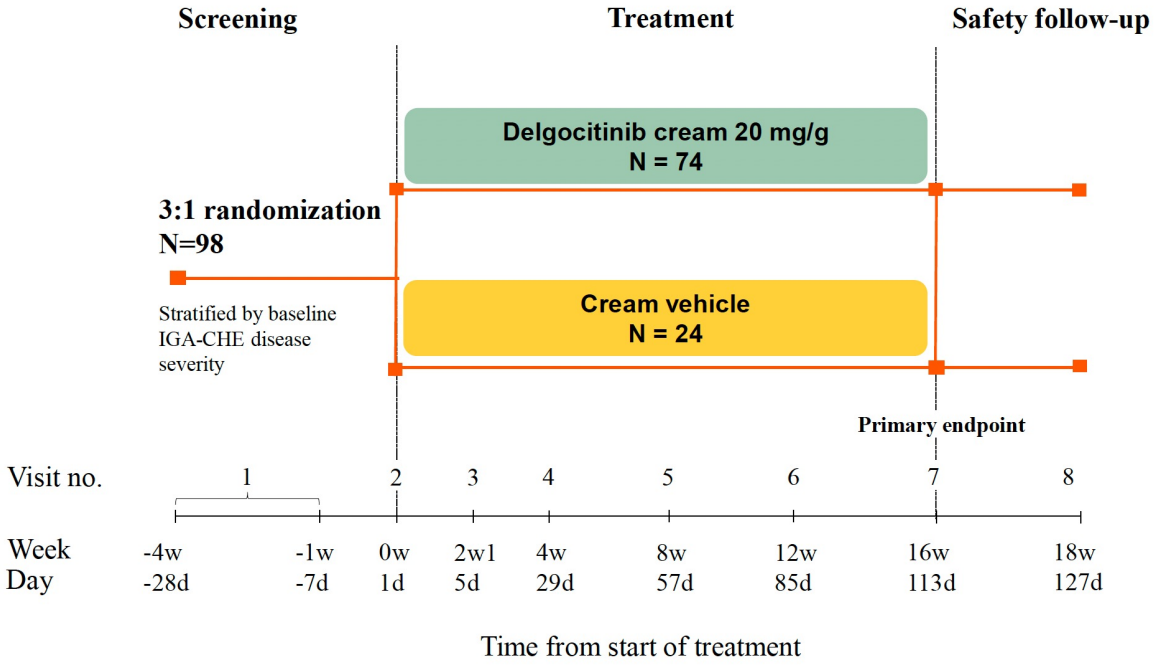


***Subtypes were defined according to the 2015 European Society of Contact Dermatitis (ESCD) guidelines. Contact urticaria/protein contact dermatitis was reported in one patient in the cream vehicle group and none in the delgocitinib group; †Patients treated with delgocitinib cream 20 mg/g in DELTA 1 or DELTA 2 and DELTA 3.**

Bissonnette R, et al. Presented at: EADV Congress; September 25-28, 2024; Amsterdam, Netherlands. Diepgen TL, et al. *J Dtsch Dermatol Ges*. 2015;13(1):e1-e22.

Pan-JAK Inhibitor Delgocitinib in Chronic Hand Eczema Trial – DELTA TEEN

Goal: To evaluate the efficacy and safety of twice-daily applications of delgocitinib cream compared with cream vehicle for a 16-week treatment period in adolescents with moderate to severe CHE



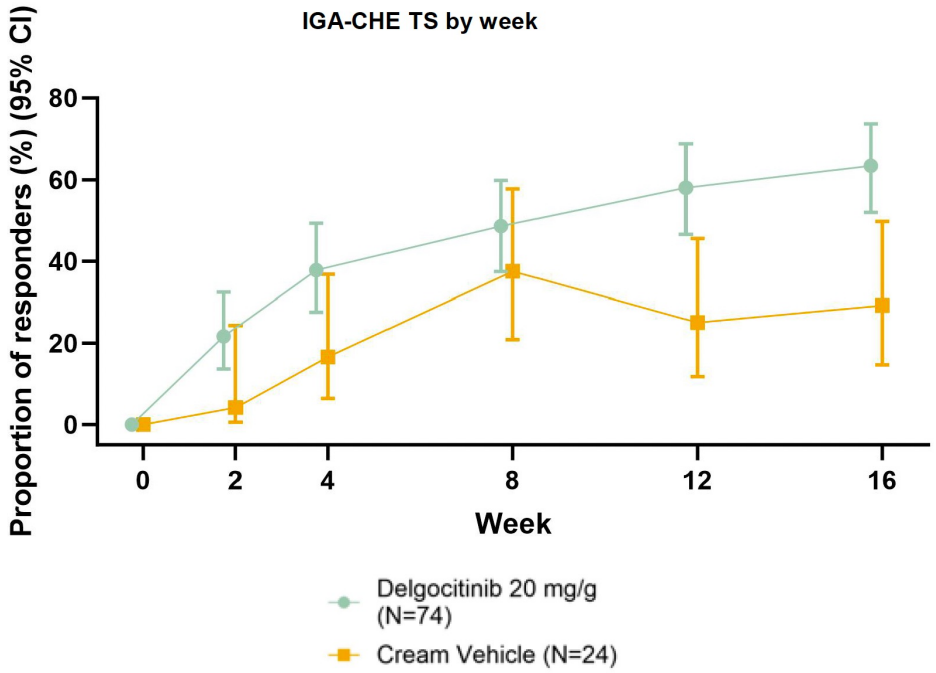
Key inclusion criteria

- Age 12 to 17 years at screening and baseline.
- Disease severity graded as moderate to severe (i.e. an IGA-CHE score of 3 or 4).
- Inadequate response to TCS, or TCS medically inadvisable.

Molin S, et al. Presented at: EADV Congress; September 17-20, 2025; Paris, France.

Pan-JAK Inhibitor Delgocitinib in Chronic Hand Eczema Trial – DELTA TEEN

Delgocitinib cream is superior to cream vehicle for the primary endpoint (IGA-CHE TS at Week 16): IGA-CHE score of 0/1 (clear/almost clear) with a ≥2 step improvement from baseline



Delgocitinib cream N=74 Responders (%)	Cream vehicle N=24 Responders (%)	Difference (95% credibility interval)[a]	Probability[b]
47 (63.5%)	7 (29.2%)	37.9% (13.5% to 58.2%)	0.999

a = The 95% credibility interval is generated as the 2.5% and 97.5% quantiles of the difference in posterior distributions. Delgocitinib cream 20 mg/g is considered superior to cream vehicle if the 2.5% percentile of the posterior distribution of the treatment difference is ≥0.

b = Probability that the difference in posterior distributions between delgocitinib cream 20 mg/g minus cream vehicle is larger than zero.

Molin S, et al. Presented at: EADV Congress; September 17-20, 2025; Paris, France.

Pan-JAK Inhibitor Delgocitinib in Chronic Hand Eczema Trial – DELTA TEEN

Delgocitinib cream is superior to cream vehicle for all key secondary endpoints

	Key secondary endpoint	Delgocitinib cream N=74 Responders (%)	Cream vehicle N=24 Responders (%)	Difference (95% credibility interval)[a]	Probability[b]
	HECSI-90 at Week 16	**53 (71.6%)**	**9 (37.5%)**	36.4% (12.3% to 59.9%)	0.999
ITCH	≥4 points reduction of HESD itch score at Week 16[c]	**35 (64.8%)**	**7 (36.8%)**	31.7% (5.6% to 51.1%)	0.989
PAIN	≥4 points reduction of HESD pain score at Week 16[c]	**31 (63.3%)**	**5 (33.3%)**	31.2% (8.7% to 49.4%)	0.994
	≥4 points reduction of HESD score at Week 16[c]	**30 (55.6%)**	**5 (31.3%)**	25.1% (3.9% to 42.3%)	0.986

a = The 95% credibility interval is generated as the 2.5% and 97.5% quantiles of the difference in posterior distributions. Delgocitinib cream 20 mg/g is considered superior to cream vehicle if the 2.5% percentile of the posterior distribution of the treatment difference is ≥0. **b** = Probability that the difference in posterior distributions between delgocitinib cream 20 mg/g minus cream vehicle is larger than zero. **c** = Reduction of the score (weekly average) of ≥4 points from baseline to Week 16 among subjects with a baseline score (weekly average) ≥4 points.

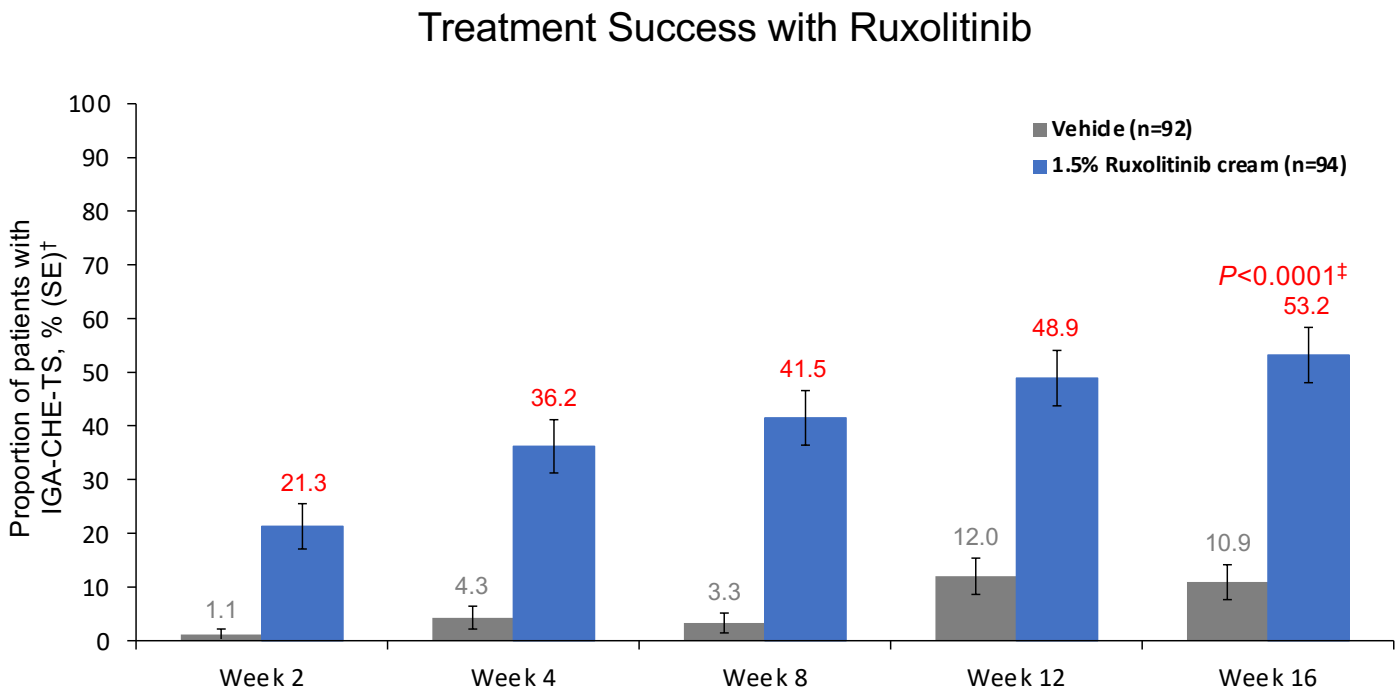
Molin S, et al. Presented at: EADV Congress; September 17-20, 2025; Paris, France.

Baseline Characteristics: Phase 2 Study of Ruxolitinib Cream

Characteristic	Total (N=186)
CHE subtype, n (%)†	
Irritant contact dermatitis	51 (27.4)
Allergic contact dermatitis	30 (16.1)
Vesicular hand eczema (pompholyx)	28 (15.1)
Hyperkeratotic eczema	26 (14.0)
Contact urticaria/protein contact dermatitis	1 (0.5)
Unclassified‡	60 (32.3)
IGA-CHE score, n (%)	
3 (moderate)	135 (72.6)
4 (severe)	51 (27.4)
Itch NRS score, median (range)	6.6 (2.1−10)
Skin pain NRS score, median (range)	6.3 (0.6−10)
Time since initial CHE diagnosis, median (range), y	6.0 (0.6−54.0)

†More than 1 CHE subtype could be selected; ‡Defined by investigators as a CHE type that is not atopic hand eczema (exclusion criteria for the study) and does not fit other listed types.
NRS = numerical rating scale.
Zirwas M, et al. Presented at: Fall Clinical Dermatology Conference; October 24-27, 2024; Las Vegas, NV.

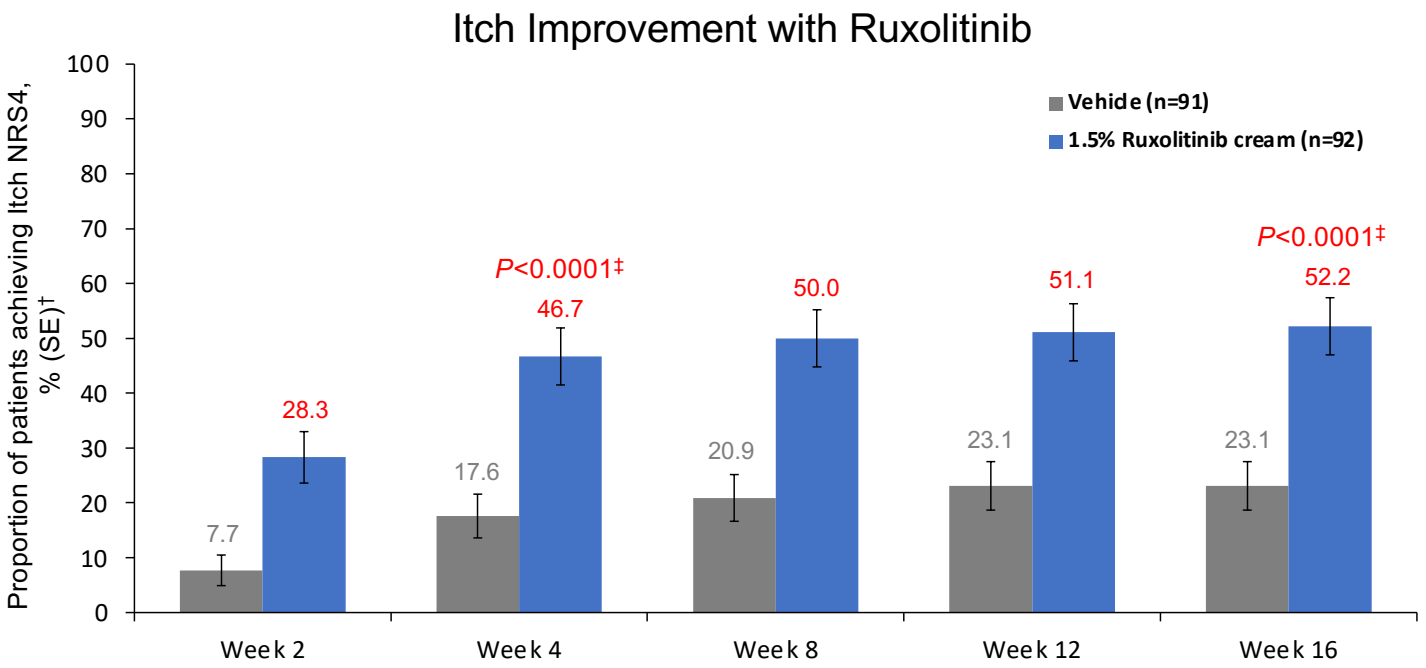
Phase 2 Study: IGA-CHE-TS with Ruxolitinib



IGA-CHE-TS, IGA-CHE score of 0 or 1 with ≥2-grade improvement from baseline. †Patients with missing post-baseline values were imputed as nonresponders; ‡*P*-value was calculated for Week 16 only, using the Cochran–Mantel–Haenszel test with stratification for IGA-CHE score of (3 or 4) and region (North America or outside of North America).

Zirwas M, et al. Presented at: Fall Clinical Dermatology Conference; October 24-27, 2024; Las Vegas, NV.

Phase 2 Study: Itch NRS4 with Ruxolitinib



Itch NRS4, ≥4-point improvement in CHE-related Itch NRS score from baseline. †Patients with Itch NRS score ≥4 at baseline were included in this analysis. Patients with missing post-baseline values on Days 1−7 were imputed using multiple imputation; ‡*P*-value was calculated for Day 7 only, using the Cochran–Mantel–Haenszel test with stratification for IGA-CHE score (3 or 4) and region (North America or outside of North America).

NRS4 = Numerical Rating Scale 4.

Zirwas M, et al. Presented at: Fall Clinical Dermatology Conference; October 24-27, 2024; Las Vegas, NV.

Phase 2 Study: Treatment-Related Adverse Events with Ruxolitinib

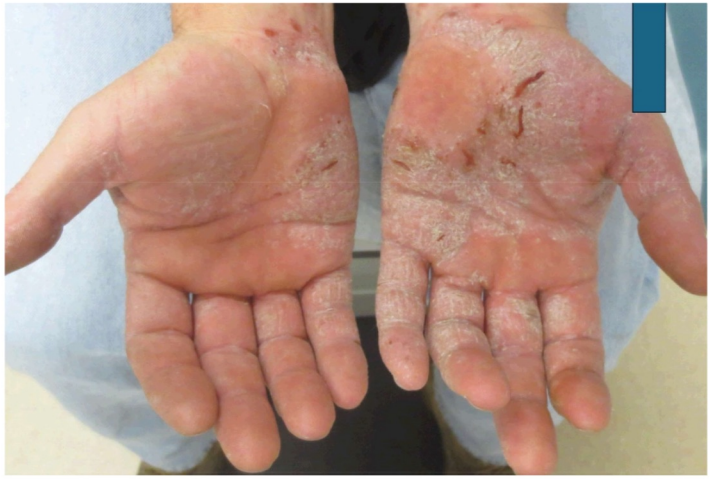
n (%)	Vehicle (n=92)	1.5% Ruxolitinib Cream (n=94)
Application site pain	1 (1.1)	1 (1.1)
Application site paresthesia	0	1 (1.1)
Application site reaction	0	1 (1.1)
Arthralgia	1 (1.1)	0
Drug hypersensitivity	1 (1.1)	0
Eczema	0	1 (1.1)
Hand dermatitis	1 (1.1)	0 (0.0)
Skin papilloma	0	1 (1.1)
Upper respiratory tract infection	0	1 (1.1)

- **No serious infections, MACE, malignancies, or thromboses were observed**
- **No new safety signals emerged**

MACE = major adverse cardiovascular event.
Zirwas M, et al. Presented at: Fall Clinical Dermatology Conference; October 24-27, 2024; Las Vegas, NV.

Case Study: 26-Year-Old Floral Shop Employee with Chronic Hand Eczema

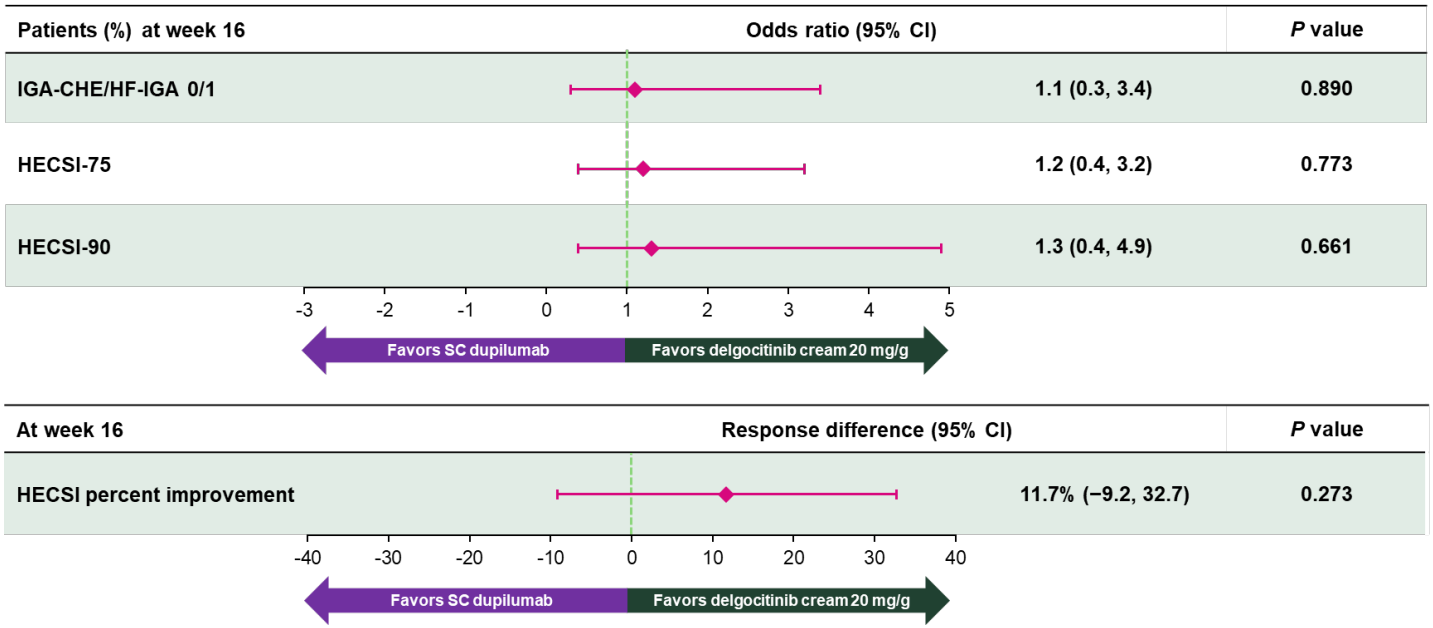
- Presented with severe hand eczema
- Patch testing: Positive for sesquiterpene lactone*
  - Able to avoid plants containing this compound → led to some symptom improvement
- Persistent atopic dermatitis on the hands still requires management



*Sesquiterpene lactones are a group of over 5000 secondary metabolites found across the plant kingdom, including the Cactaceae, Solanaceae, Araceae, and Euphorbiaceae families

Image courtesy of Christopher Bunick, MD, PhD.

Delgocitinib vs Dupilumab for Atopic Hand Eczema at 16 Weeks

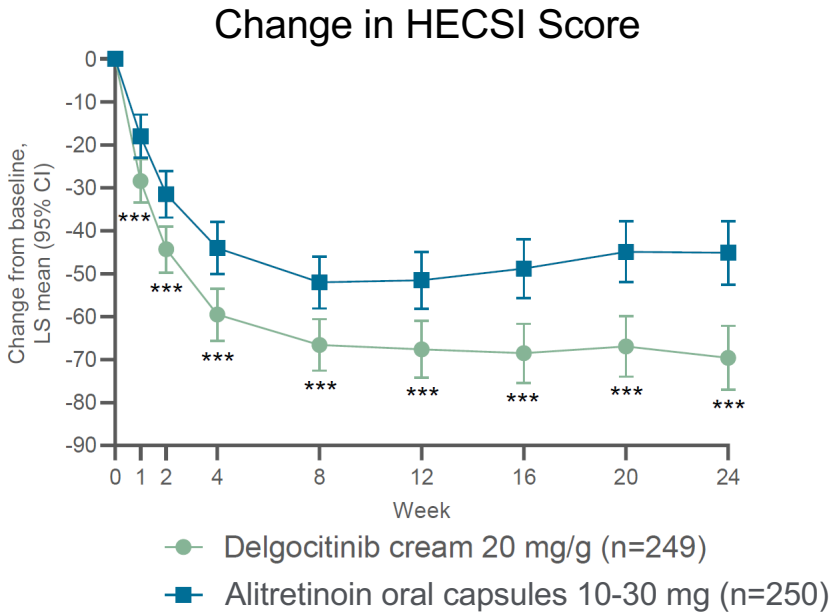


There was comparable efficacy of SC dupilumab and topical delgocitinib at 16 weeks

HF-IGA = Hand and Foot Investigator Global Assessment.

Cohen D, et al. Presented at: Fall Clinical Dermatology Conference; October 24-27, 2024; Las Vegas, NV.

DELTA FORCE: Delgocitinib vs Alitretinoin for Chronic Hand Eczema at 26 Weeks



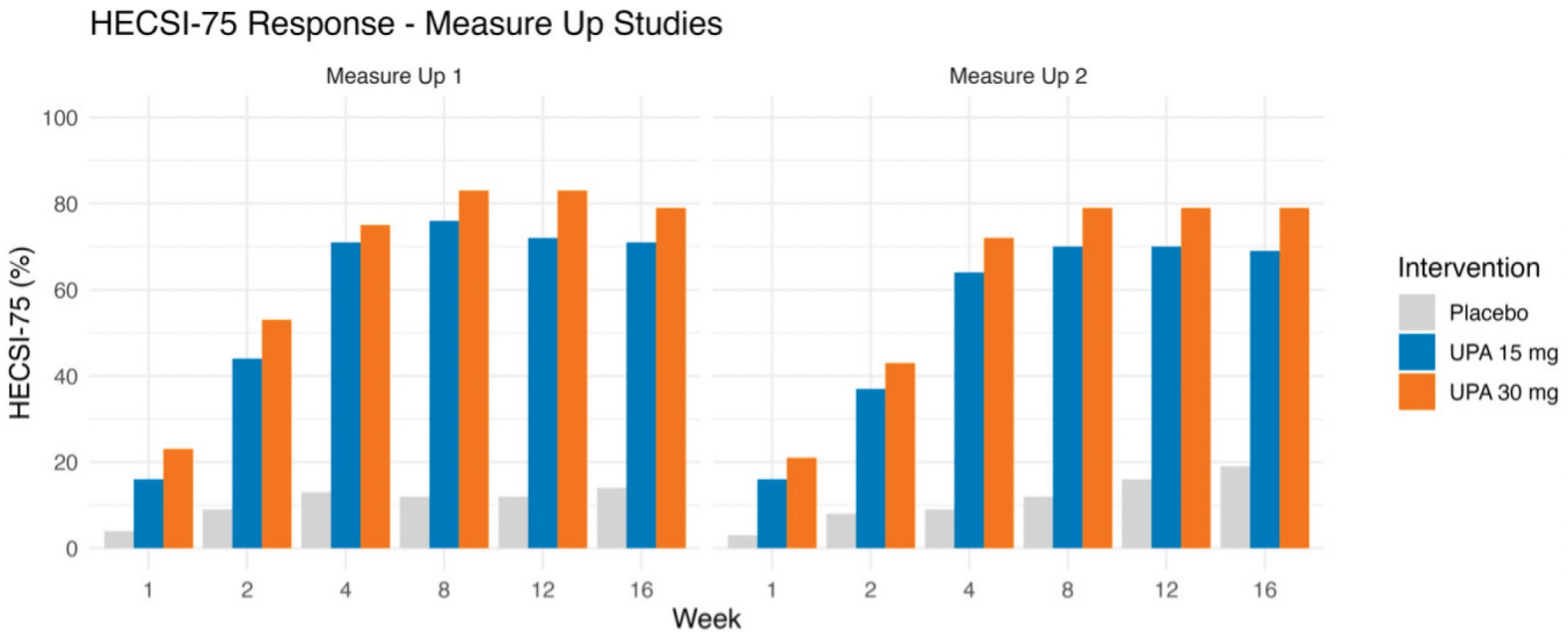
In DELTA FORCE, topical delgocitinib was more effective than oral alitretinoin, with differences between treatment groups observed from Week 1

Delgocitinib was well-tolerated, with fewer AEs than the alitretinoin group

***$P \leq 0.001$; **$P < 0.01$; *$P < 0.05$.

Giménez-Arnau AM, et al. Presented at: Fall Clinical Dermatology Conference; October 24-27, 2024; Las Vegas, NV.

Oral JAKi in CHE: Upadacitinib Effective for Treatment of CHE Due to Atopic Dermatitis



Alani O, et al. *J Drugs Dermatol*. 2025;24(7):702-707.

Oral abrocitinib phase 2 trial for CHE at 16 weeks

- Abrocitinib overall demonstrated 81% (200 mg dose) and 78.1% (100 mg dose) reductions in modified Total Lesion Symptom Score (mTLSS) (vs 46.5% PBO, Δ=31.6-34.5%) at week 16.
- Similar results were obtained for atopic and non-atopic CHE subtypes.
- IGA 0/1 plus 2 grade improvement was observed in 55.6% (200 mg) and 44.4% (100 mg) of patients (vs 18.5% PBO, Δ=25.9-37.1%); marked improvements in itch and pain were also observed.

Bissonnette R. Efficacy and safety of abrocitinib in patients with chronic hand eczema: a randomized, double-blind, multicenter, placebo-controlled trial. Presented at: 2026 American Academy of Dermatology Annual Meeting; March 27-31, 2026; Denver, CO.

See related article on pg 1559

Demystifying Hand Eczema

Ayman Grada[1] and Christopher G. Bunick[2,3]

Journal of Investigative Dermatology (2023) **143,** 1338–1339; doi:10.1016/j.jid.2023.03.1666

The central dogma of molecular biology states that genetic information flows from DNA to RNA to protein, with DNA replication (DNA copied to DNA), transcription (DNA to RNA), and ribosomal translation (RNA to protein) comprising the key biological processes regulating this information. Advances in biomedical research techniques over the past 1-2 decades have progressively enabled the ability to use these biological processes to understand disease pathogenesis, clinical diagnosis, and disease-specific treatments. In particular, whole-genome sequencing (genomics), RNA sequencing (transcriptomics), and protein expression analysis (proteomics) are revolutionizing at a rapid pace the integration of cell and/or tissue analysis with clinical management decisions, making personalized or precision medicine a greater reality for patients. In "the proteome of hand eczema assessed by tape stripping," Sølberg et al. used protein expression analysis to evaluate a common clinical problem in dermatology (Sølberg et al., 2023).

One of the challenges to advancing personalized medicine is reducing a common phenotype (e.g., rash on the hands) into distinct molecular endotypes (e.g., different pathogenic etiologies driving atopic dermatitis (AD), irritant contact dermatitis (ICD), allergic contact dermatitis (ACD), psoriasis, etc.) that may share a common phenotypic presentation. Dermatologists know that patients with a chronic hand rash can be challenging to treat because the precise diagnosis is not always apparent from clinical morphology alone. Shave or punch skin biopsies are routinely used to narrow down a differential diagnosis, but biopsies on acral sites are more difficult, with pain, bleeding, and loss of function being potential adverse events. Because hand rashes comprise a very heterogeneous group of skin disorders, there is an unmet need in dermatology for a simple, non- to minimally invasive technique to endotype or stratify patients into the correct diagnostic and treatment groups.

In Sølberg et al., directly tackle this unmet need for chronic hand eczema (CHE) by using tape stripping to characterize the proteome of patients with CHE (with and without AD) using lesional, non-lesional, and healthy skin samples. Tape stripping is a practical method to obtaining superficial skin tissue samples. This technique involves applying adhesive tape to the affected skin and then removing it, along with the top dead layers of the skin (i.e., the stratum corneum). The stratum corneum samples are then evaluated using a variety of devices depending on the purpose; in Sølberg et al., that technique was liquid chromatography-mass spectrometry. Tape strips have been used to broadly characterize immune and epidermal barrier biomarkers of the lesional and nonlesional skin of AD and psoriasis, providing a useful approach not only for clinical trials and longitudinal studies but potentially for routine clinical practice.

According to transcriptome analysis in The Human Protein Atlas, 71% of the human proteome is expressed in the skin; 612 of these genes showed elevated protein expression in the skin compared to other tissue types (2022). This supports the use of tape stripping to generate a molecular signature or fingerprint of corneocytes and establish disease-specific stratum corneum protein signatures for the dorsal and palmar skin of the hands. However, a question Sølberg et al. address is whether proteomic analysis of stratum corneum can accurately differentiate the immunology of CHE subtypes. Although CHE is a common inflammatory dermatosis, it is an umbrella term that is often used to encompass AD, ICD, and ACD, yet these disorders can be driven by different immune responses. Moreover, hand rashes that mimic CHE, such as tinea manuum, psoriasis, and more rarely cutaneous T-cell lymphoma, can be mislabeled as CHE (Yumeen et al., 2020). Previous studies investigating the immunology of hand rashes have shown that AD-related CHE presents with a T helper (Th) type Th2/Th22 immune profile. ACD, depending on the allergen, can be driven by the Th2/Th22 response for rubber and fragrance or Th1/Th17 response for metals (nickel). ICD presents with a Th1/Th17 immune profile and is mainly driven by an innate immune response (IL-1α, IL-1β, TNF-α, GM-CSF, and IL-8) (Lee et al., 2013; Ungar et al., 2017). ICD reactions are often the first step in the activation process in ACD (Leonard and Guttman-Yassky, 2019).

Importantly, the authors found that the proteomic differences between CHE subtypes were restricted to lesional skin areas and, indeed, there were differences in the immune-related proteome. Compared to healthy skin, the lesional samples from patients with CHE exhibited increased expression of immune-related markers and a decreased expression of structural barrier proteins. In agreement with previous studies, the pro-inflammatory cytokine IL-34 was highly expressed in non-lesional CHE skin (regardless of etiology) than in healthy skin. IL-34 is an epidermal negative immune regulator cytokine and has been considered the best single-gene classifier, discriminating non-lesional from lesional skin in patients with AD with almost 100% accuracy (Guttman-Yassky et al., 2019).

In total, the authors identified 908 differentially expressed proteins (DEPs) between lesional and healthy skin. Key elevated DEPs included several pro-inflammatory signatures: skin alarmins (keratins 6a, 16, and 17), CD44 (associated with activation of dendritic cells and has been shown to be increased in contact dermatitis) (Lugović-Mihić et al., 2020), complement proteins C3 and C5, IL-18 (migration of antigen-presenting cells and production of antigen-specific T-cells), fibrinogen A and G (which help form protective biofilms following skin wounding), and nicotinamide phosphoribosyltransferase. Increased expression of chaperonin subunits belonging to the T-complex protein Ring Complex suggests misfolded cytoskeleton proteins in CHE lesional skin. In contrast, lower expression of structural proteins (filaggrin 2, loricrin), antimicrobial peptides (dermcidin), complement pathway inhibitors (CD55, CD59), and anti-inflammatory cytokines (IL-37) depict CHE as an inflammatory process with compromised barrier integrity and reduced ability to combat microbial infection or dysbiosis.

How soon will dermatologists use tape stripping in their clinic? Although not implemented routinely for hand rashes yet, adhesive technologies exist and are used to evaluate the need to biopsy a nevus (melanoma test evaluating LINC and PRAME expression levels and TERT DNA mutations) (Ferris et al., 2017), classify melanoma risk (for the need for sentinel lymph node biopsy and subsequent level of clinical surveillance) (Jarell et al., 2022), and aid the selection of biologic therapy categories for patients with plaque psoriasis (transcriptomic analysis on ~ 7,000 RNAs isolated from stratum corneum) (Bagel et al., 2021). The work by Sølberg et al. represents another significant effort to use tape stripping and proteomics to advance our scientific understanding of CHE. This work begins the important and much-needed differentiation of hand rash (labeled as CHE) based on pathobiology. Ultimately, tape stripping appears to be a viable tool not only for research purposes but also for point-of-care diagnostics in dermatology patients.

Clinical Implications

- Heterogeneity of chronic hand eczema (CHE) poses a diagnostic and therapeutic challenge.
- Tape stripping is a minimally invasive technique to obtain skin tissue samples from acral sites.
- Proteomic analysis revealed molecular differences in underlying CHE etiologies.

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CONFLICT OF INTEREST

AG declares no relevant conflict of interest. CGB has served as an investigator for Almirall, Timber, and Palvella and a consultant for AbbVie, Almirall, Arcutis, Eli Lilly, EPI Health, LEO Pharma, Novartis, Pfizer, Sanofi-Regeneron, and UCB.

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Sølberg JBK, Quaade AS, Drici L, Sulek K, Ulrich NH, Løvendorf MB, et al. The proteome of hand eczema assessed by tape stripping. J Invest Dermatol 2023;143:1559–68.e5.

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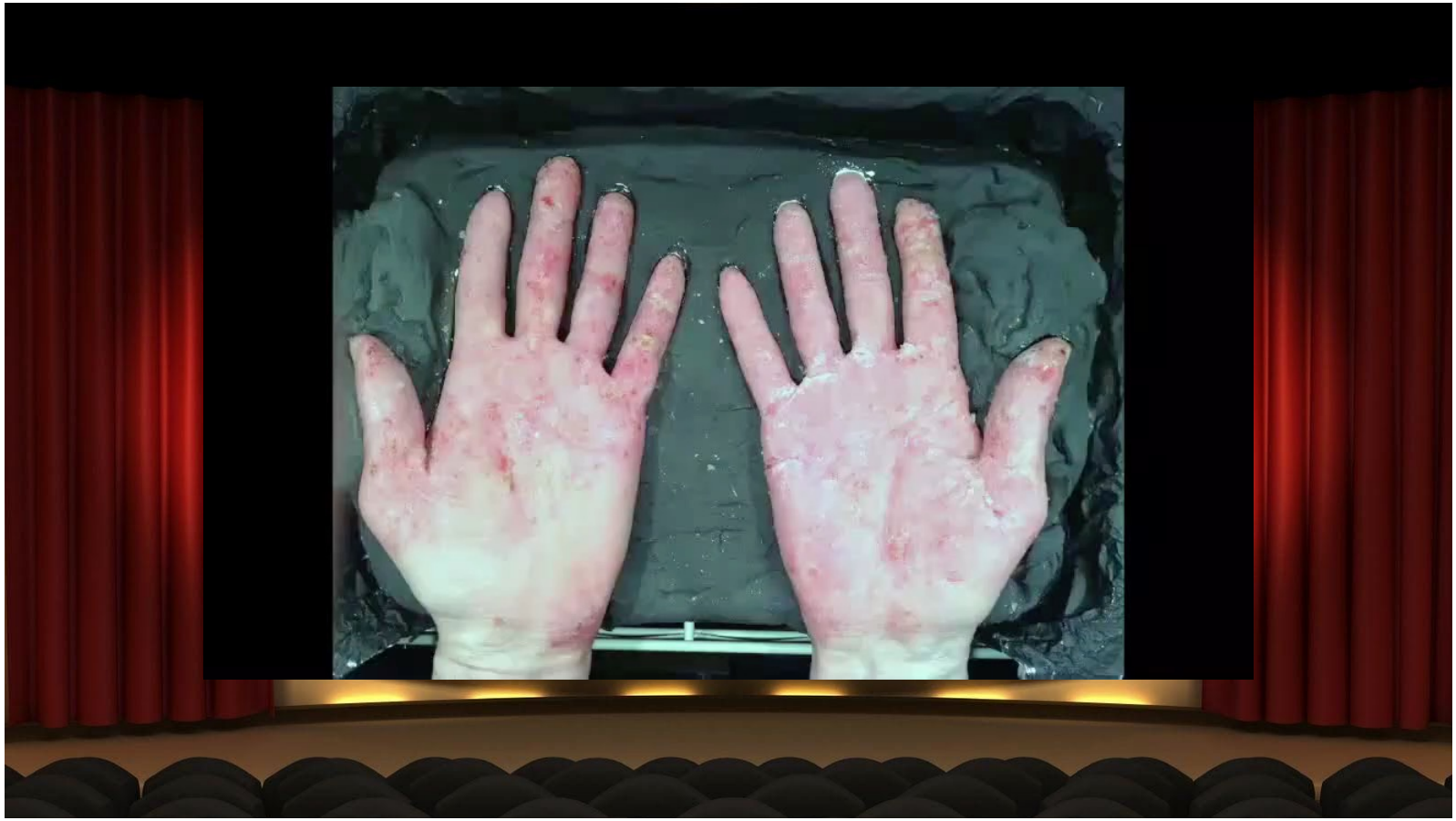
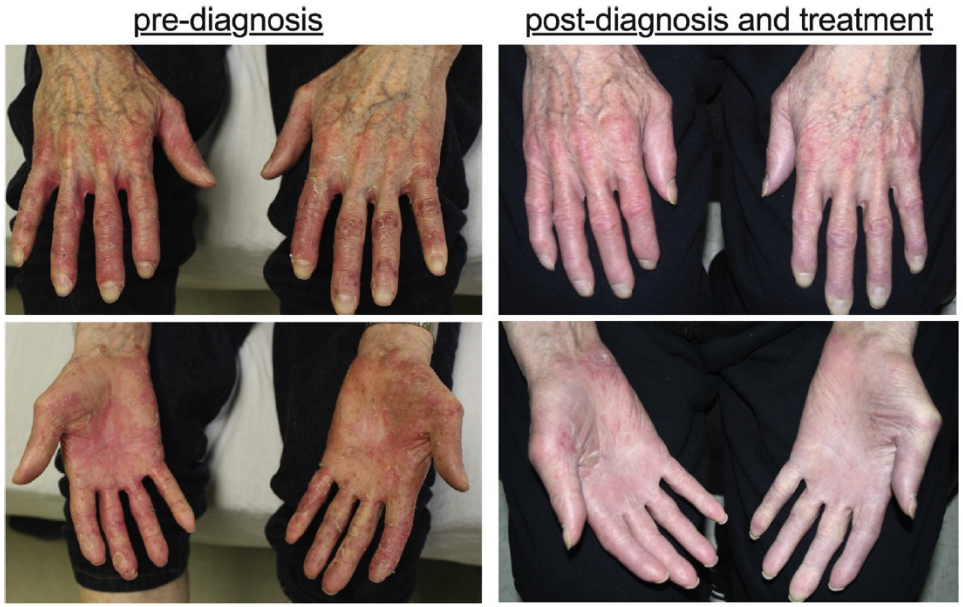
Yumeen S, Mirza FN, Lewis JM, Carlson KR, King B, Cowper S, et al. CD8+ mycosis fungoides palmaris et plantaris with peripheral blood involvement. JAAD Case Rep 2020;6:434–7.

Grada A, Bunick CG. *J Invest Dermatol*. 2023;143(8):1338-1339.

Chronic Hand Eczema Theater



Yumeen S, et al. *JAAD Case Rep*. 2020;6(5):434-437.



When in doubt, or treatment response is not making sense, get a skin biopsy!

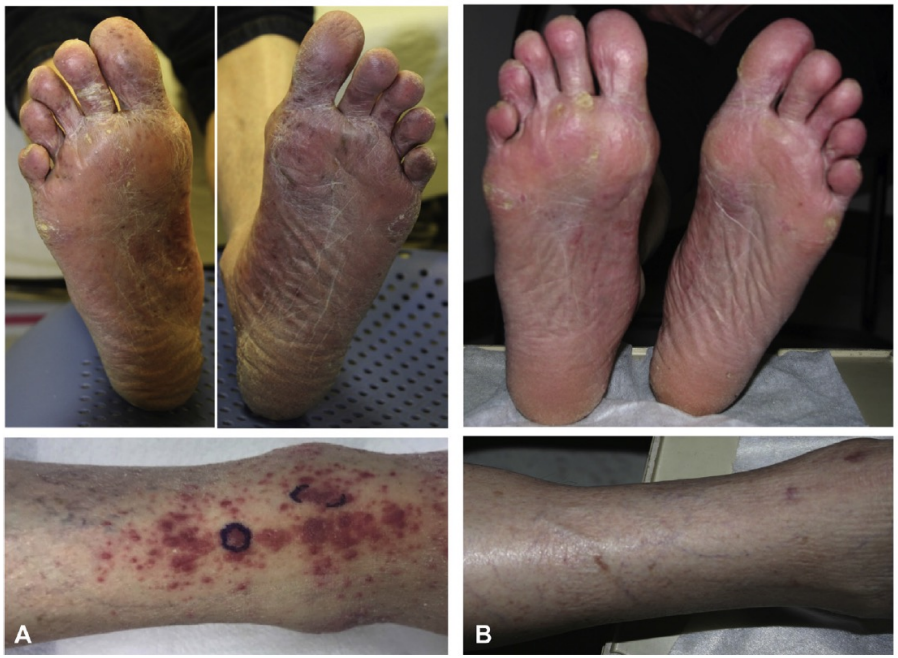


Fig 1. Mycosis fungoides palmaris et plantaris with peripheral blood involvement. Clinical images of hands, ankle, and soles (**A**) before diagnosis and treatment, and (**B**) 5 months after treatment with extracorporeal photophoresis, bexarotene, and spot electron-beam therapy to the palms.

Yumeen S, et al. *JAAD Case Rep*. 2020;6(5):434-437.

Key Learning Points

- CHE has multiple etiologic subtypes, and patients may have more than 1 subtype
- Underlying pathogenic mechanisms of CHE involve JAK/STAT signaling
- Evaluation of patients with CHE should consider the role of potential allergens and whether patch testing is appropriate
- New and emerging CHE therapies are improving patient treatment through targeted topical, oral, and biologic approaches
- Individualized treatment plans for patients with CHE should consider topical, phototherapy, systemic, and over-the-counter management strategies
- Chronic topical corticosteroid use should be avoided in patients with CHE