



New Topical and Systemic Treatments for CHE

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Disclosures

- Research support, consulting or lecture fees on atopic dermatitis from Regeneron, Sanofi, Pfizer, Galderma, Celgene, Leo Pharma, Janssen, Medimmune, Dermira, Anacor, AnaptysBio, Glenmark, Novartis, Abbvie, GSK, Sun Pharma, Mitsubishi Tanabe, Vitae, Almirall, Asana Biosciences, Amgen, Immune, Gilead, Concert, Kyowa Kirin, DS Biopharma, Ralexar, Eli Lilly, UCB, Escalier, Boehringer, Botanix, Incyte, Sienna, Innovaderm, Cara Therapeutics, Dermavant, Union Therapeutics, Kiniksa, Arena, FLX Bio, Target
- No patents, ownership, or financial gain from any atopic dermatitis drug



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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)

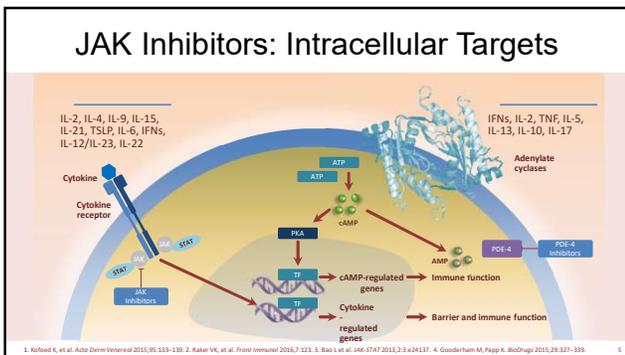
Multiple cycles → Therapeutic Generations

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

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Emerging Topical and Systemic Treatments for CHE

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JAK Inhibition Targets Key Cytokines in CHE

- Chronic Hand Eczema involves several cytokine pathways, including Th1, Th2, and Th17
- Thus, for effective therapeutic response in majority of patients more than one cytokine pathway needs to be targeted

Cytokines	JAK1	JAK2	JAK3	TYK2
IL-23, IL-17		2		T2
IL-12		2		T2
IL-13	1			T2
IL-22	1	2		T2
IL-20	1	2		T2
IL-5	1	2		
IFN-γ	1	2		
IL-21	1		3	
TSLP	1	2		
IL-4	1		3	
IL-31	1	2		T2

Gadina M et al. Rheumatology 2019

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Phase 2a, randomized, vehicle-controlled, double-blind, proof-of-concept trial of topical delgocitinib for adults with chronic hand eczema

Background

- Delgocitinib is a pan JAK, that inhibits JAK1/2/3 and TYK2
- The immune abnormalities of chronic hand eczema involve Th1/Th17 (irritant contact dermatitis), Th1/Th17/Th2/Th22 (allergic contact dermatitis, depending on allergen), and Th2/Th22 (atopic hand eczema)¹
- Thus, a JAK inhibitor may be beneficial in treatment of all forms of chronic hand eczema since

Key inclusion criteria:

- 18-65 years old
- Chronic hand eczema of at least mild severity (based on PGA)

Primary endpoint: PGA success at Week 8^a

Secondary endpoints:

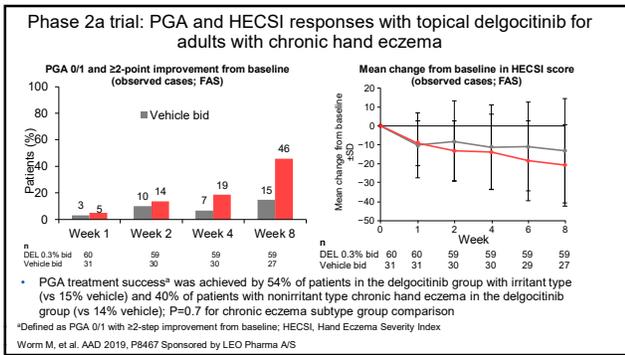
- Differences in mean HECSI score at Week 8
- PaGA success at Week 8

Baseline demographics and characteristics

	Delgocitinib 0.3% bid (n=60)	Vehicle bid (n=31)
Age, years	43.8 ±13.0	40.8 ±12.5
Male:Female	18:42 (30:70)	11:20 (35:65)
Race		
White:Other	59:1 (98:2)	30:1 (97:3)
Predominant chronic hand eczema subtype		
Irritant:Nonirritant	25:35 (42:58)	13:18 (42:58)
PGA		
Mild	13 (22)	5 (16)
Moderate	36 (60)	17 (55)
Severe	11 (18)	9 (29)
HECSI score	32.6 ±21.5	40.5 ±34.3

1. Dhirga N, et al. J Allergy Clin Immunol 2014;134:362-72
^aDefined as PGA 0/1 with ≥2-step improvement from baseline; HECSI, Hand Eczema Severity Index; PaGA, Patients Global Assessment of Disease Severity; Worm M, et al. AAD 2019, P6467. Sponsored by LEO Pharma A/S

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Phase 2a trial: Safety of topical delgocitinib in adults with CHE

n (%)	Delgocitinib 0.3% bid (N=60)	Vehicle bid (N=31)
Any AE	34 (57)	14 (45)
Treatment-related AEs	3 (5)	8 (26)
Most common AEs (≥5% of patients)		
Nasopharyngitis	15 (25)	4 (13)
Postoperative wound infection ^a	4 (7)	2 (6)
Hand dermatitis (worsening)	3 (5)	9 (29)
Headache	4 (7)	1 (3)
Creatine phosphokinase increased	0	2 (6)

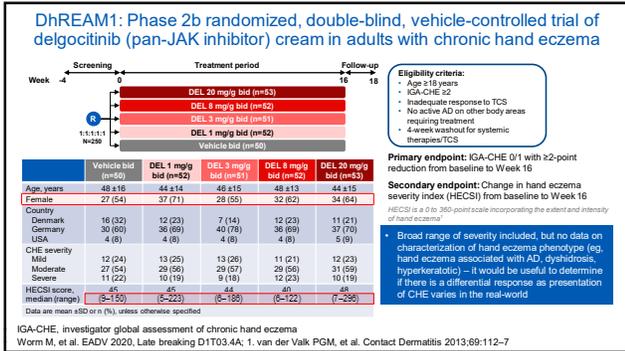
- There was 1 serious AE in the delgocitinib group (back pain, unrelated to treatment)
- No AE led to study discontinuation in the delgocitinib group
- No clinically relevant changes in vital signs or lab values in either group

• Patients with irritant chronic hand eczema had numerically greater improvements than patients with nonirritant chronic hand eczema, but the difference was not significant

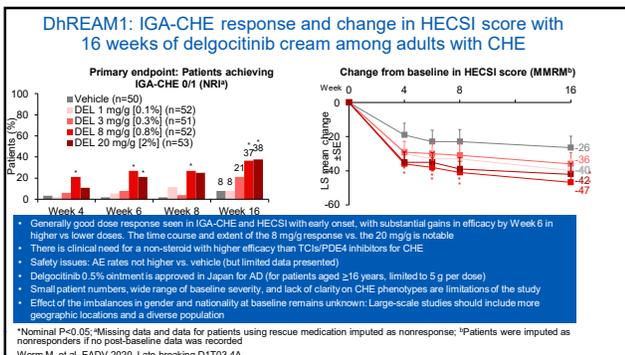
• PGA responses were significantly different from vehicle, but HECSI responses were not

- It is important to standardize scores for chronic hand eczema (US studies use PGA and mTLSS)
- HECSI is controversial and doesn't seem to yield good data

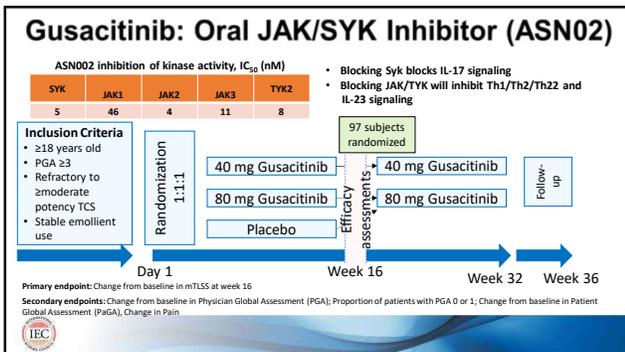
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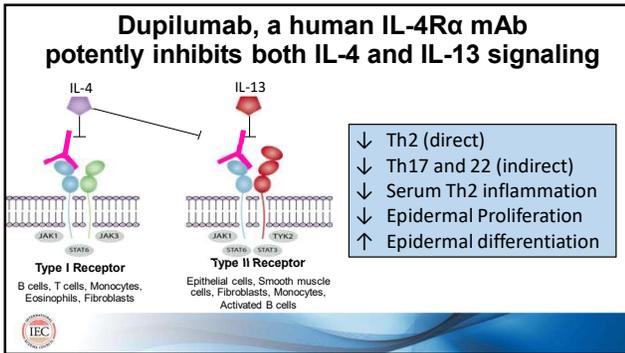
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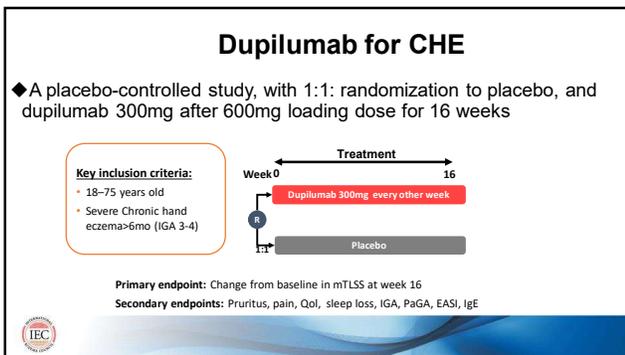
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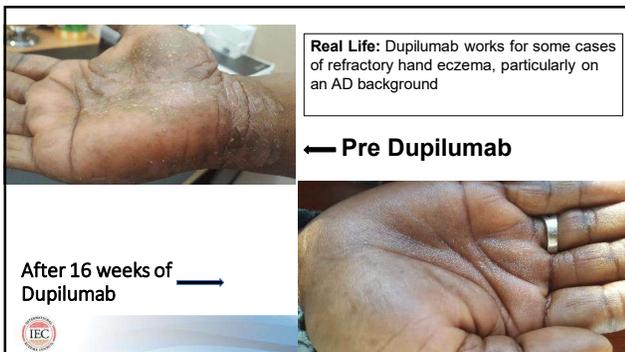
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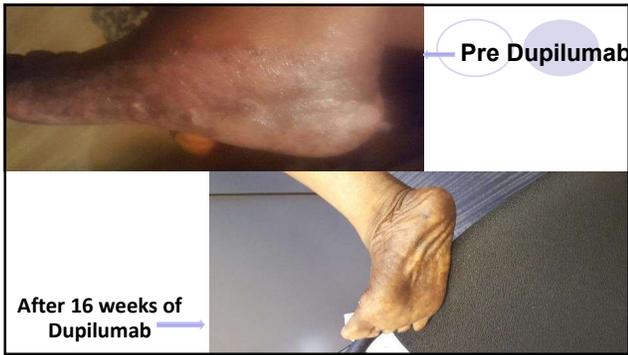
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Apremilast for CHE

◆ A pilot study of 10 patients with CHE to be treated with Apremilast 30mg BID as a single arm for 6 months

Key inclusion criteria:

- 18-75 years old
- Severe Chronic hand eczema > 6mo (IGA 3-4)

Week 0 → Treatment → 24 weeks

Ⓡ Apremilast 30mg BID

Study terminated after enrolling one patient as PI (Dr Erlich) left GW

Primary endpoint: Change from baseline in PGA at 6 months
Secondary endpoints: mTLSS, DLQI, Safety, time to response

Off label use: some efficacy in certain patient population (particularly those with irritant or allergic contact dermatitis where Th17/Th1 are involved)

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Future Directions for hand eczema

- Need to incorporate non invasive biomarkers—tape strips in the clinical trials to help shed light into the phenotypes of the different CHE phenotypes (ICD/ACD/AD)

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