

HIGHLIGHTS

# AEDV

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## D atópica

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## POSTERS

### A TOPIC LABIAL PIGMENTATION: A NEW DIAGNOSTIC FEATURE IN ASIAN PATIENTS WITH A TOPIC DERMATITIS

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#### INTRODUCTION

**Atopic dermatitis (AD)**

- A chronically relapsing inflammatory skin disease
- Recently, the diagnostic significance of minor features has been shown to vary according to race and age, but minor features and other stigmata provide important clues for the diagnosis of AD

**Pigmented lesions on the lips**

- Caused by physiological or pathological factors, along with exogenous or endogenous factors
- Many patients with AD and labial pigmented macules or patches are seen in clinical practice
- To our knowledge, there was only one report on the association of labial pigmentation and atopic dermatitis

#### Results

**Clinical features of labial pigmentation in patients with and without AD**

	Patients with AD	Patients without AD	p-value
Number of patients with pigmentation	41 of 175 (24.27%)	27 of 176 (15.34%)	<0.001*
Number of macules or patches (mean ± SE)	3.40 ± 0.33	1.07 ± 0.71	<0.001*
Location of pigmentation (most common site)	middle side of upper lip	middle side of lower lip	
Age at onset	unknown, in most cases	unknown, in most cases	
Distribution			
Focal	9 of 41 (21.71%)	24 of 27 (88.89%)	<0.001*
Multifocal	47 of 61 (80.29%)	3 of 27 (11.11%)	
Diffuse	11 of 61 (18.03%)	0 of 27 (0%)	

AD, Atopic dermatitis; SE, standard error  
\*Difference between groups is statistically significant (P<0.05)

**Comparison of clinical characteristics of patients with and without atopic labial pigmentation**

	AD patients with labial pigmentation (n=41)	AD patients without labial pigmentation (n=135)	p-value
Age at AD (mean ± SE)	22.84 ± 1.52	21.76 ± 1.07	0.278
Sex			
Female	30 (73.17%)	82 (60.37%)	0.529
Male	11 (26.83%)	53 (39.63%)	
Age at onset of AD (mean ± SE)	5.46 ± 1.03	11.26 ± 1.04	0.019*
Family history of AD	16 (39.02%)	34 (24.81%)	0.173
Allergic disorder	39 (95.12%)	31 (22.52%)	0.000*
Urticaria (n=136)	36 of 46 (77.17%)	47 of 66 (71.21%)	0.019*
Sensitivity to AD			
None	2 (4.88%)	6 (4.39%)	0.263
Moderate	36 (87.80%)	61 (44.81%)	
Severe	3 (7.32%)	41 (29.80%)	

AD, Atopic dermatitis; SE, standard error  
\*Difference between groups is statistically significant (P<0.05)

**Stigmata in the AD patient group with atopic labial pigmentation**

- Most patients had facial and neck lesions, various cheilitis, and ichthyosis on the pruritus were observed in more than half of the patients, and we observed a difference in severity among the patients
- Many patients also had Dennie-Morgan folds, anterior neck folds, orbital darkening, facial erythema/paronychia, and hand-foot eczema
- Some patients showed Heiligenthal's sign, nipple eczema, white dermographism, and a tendency toward colostrum infections
- In 100% cases, we observed food intolerance, recurrent conjunctivitis, and vitiligo
- Notably, ichthyosis on the pruritus was observed in many patients with labial pigmentation, which differs from patients with general AD

#### Discussion

**In our study**

- Labial pigmentations were more frequent in the AD patient group than in the control patient group, tended to appear as several macules or patches, and were most common in the middle section of the upper lip
- As opposed to the focal distribution of labial pigmentation within the control patient group, multifocal distribution of labial pigmentation was most common in the AD patient group
- Previous reports about melanotic lesions of the lip
- Lesions were most often found on the lower lip of young adult women
- The middle section of the lower lip was the most common area for labial pigmentation in the control patient group without AD, which was consistent with previous studies. However, in the AD group, there was a significant difference in the prevalence, number, location and distribution of pigmented lesions.

**The etiology of labial pigmentation**

- Physiological or pathological and result from exogenous or endogenous causes
- "Atopic labial pigmentation": the macules or patches associated with AD
- Ichikawa et al.
- 59 of 136 patients (58%) had a combination of labial melanotic macules and AD
- 1/3 of AD patients were markedly dry and scaly and proposed that the mucous membrane was damaged as the lips were rubbed together, which presumably caused the pigmentation.
- Long-standing inflammation and friction contribute to the development of atopic labial pigmentation.
- Application of topical corticosteroids induce melanocyte activation, both directly and by its immunosuppressive activity.


**Pigmentary lesions in patients with AD**

- Atopic dermatitis
- Atopic dermatitis that predominantly affects the anterolateral aspects of the neck in patients with AD
- An epidemiological and clinical study of atopic dermatitis from the National Skin Centre in Singapore
- 14.7% of AD patients and was more common in Asian patients
- Atopic labial hyperpigmentation was more common in AD than in atopic dermatitis
- The pathology is thought to be due to melanin melanocytes and post-inflammatory hyperpigmentation, similar to atopic labial hyperpigmentation


**Limitation**

- A small sample size and selection bias
- A bias toward patients with moderate or severe AD
- We performed chart reviews of medical history, physical examinations, photographic records, and dermoscopic images as needed, but did not perform histopathologic studies

#### Distribution of labial pigmentation



(A) Focal macules in one section of the lip  
(B) Multifocal macules on two or more sections of the lip  
(C) Diffuse macules or patches with irregular edges and widely distributed in multiple sections of the lip



## Upadacitinib Improved Patient-Reported Pruritus in Moderate-to-Severe Atopic Dermatitis: Results From a Phase 2b Randomized, Placebo-Controlled Trial

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### INTRODUCTION

- Atopic dermatitis (AD) is a chronic, itchy, inflammatory skin disease, characterized by eczematous lesions and pruritus, and is associated with considerable morbidity<sup>1</sup> (the effects of up to 50% of children and 50% of adults experience<sup>2</sup>).
- The American Academy of Dermatology treatment guidelines recommend systemic immunomodulatory agents for patients with moderate to severe disease for whom optimized topical regimens and/or phototherapy do not adequately control AD.<sup>3</sup>
- This treatment of AD via the JAK-STAT signaling pathway is AD suggests that inhibition of JAK 1 – mediated pathway could be a promising approach to the treatment of moderate to severe AD<sup>4</sup> by interfering with JAK 1-mediated cytokines such as IL-2, IL-3, IL-4, IL-6, IL-9, and IL-12.<sup>5</sup>
- Upadacitinib (UPA) is a novel, oral, daily, and JAK 1-selective inhibitor that is being investigated for treatment of AD and other inflammatory diseases (rheumatoid arthritis, psoriasis arthritis, and psoriasis erythrodermia, Crohn's disease, graft vs host disease, and ulcerative colitis).

### OBJECTIVE

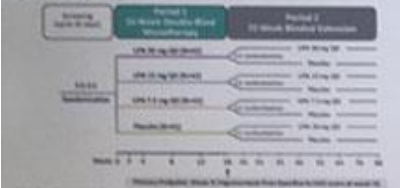
- Evaluate patient-reported pruritus following UPA treatment, from the initial 16-week, double-blind portion of the 56-week phase 2b trial in patients with moderate to severe AD.

### KEY POINTS

#### STUDY DESIGN

- Background:** Adults aged 18 to 67 years with a confirmed diagnosis of AD, onset of symptoms at least 5 years before baseline, moderate to severe AD (Eczema Area and Severity Index [EASI]) 16, affected body surface area (BSA) 10, and Investigator Global Assessment (IGA) 3 or 4 at baseline. Patients had an inadequate response to treatment with topical corticosteroids (TCS) or topical calcineurin inhibitors (TCI), or topical treatments were inadequately maintained. Patients used an additive free, bland emollient twice daily for 2 days before baseline. Treatment with TCS, TCI, or prescription medications with additive was not allowed within 10 days before baseline.
- Methods:** Patients were randomized 1:1:1:1:1 to UPA 1.5 mg, UPA 3 mg, UPA 12 mg, UPA 30 mg, or matching placebo (PBO), double-blind daily for 16 weeks. Randomization was stratified by geographic region (USA, Europe, Asia/Oceania, Latin America, South America).

#### Figure 1. Study Design



#### STATISTICAL ANALYSIS AND ASSESSMENTS

- Primary Endpoints: Itching Score (NRS) (itch during previous 24 hours), range 0-10.
- Secondary Endpoints: Patient-Reported Pruritus (PRP) (itch during previous 24 hours), range 0-10.
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- Secondary Endpoints: Patient-Reported Pruritus (PRP) (itch during previous 24 hours), range 0-10.

### RESULTS

- All primary and secondary endpoints were met and have been previously reported, and no new safety signal was identified.
- Mean % improvement from baseline in EASI score at week 16 (primary endpoint) was achieved by 78.8% UPA 30 mg, 62.7% UPA 12 mg, and 35.6% UPA 3 mg vs 23.0% placebo (P<0.001 for UPA 30 mg and 12 mg; P=0.05 for UPA 3 mg).
- Overall, the baseline characteristics were well-balanced across treatment groups (Table 1). The majority were male, white, and from the USA/Europe/Asia/Oceania region.

#### Table 1. Patient Characteristics at Baseline

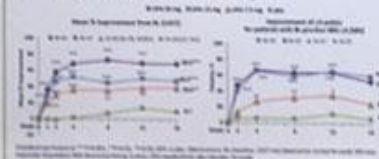
	UPA 1.5 mg	UPA 3 mg	UPA 12 mg	UPA 30 mg	PBO
<b>Age</b>					
Mean	39.9	39.9	39.9	39.9	39.9
SD	12.9	12.9	12.9	12.9	12.9
<b>Sex</b>					
Male	38.8	38.8	38.8	38.8	38.8
Female	61.2	61.2	61.2	61.2	61.2
<b>Race</b>					
White	87.8	87.8	87.8	87.8	87.8
Black	12.2	12.2	12.2	12.2	12.2
Other	0	0	0	0	0
<b>Region</b>					
USA	39.9	39.9	39.9	39.9	39.9
Europe	39.9	39.9	39.9	39.9	39.9
Asia/Oceania	39.9	39.9	39.9	39.9	39.9
Latin America	39.9	39.9	39.9	39.9	39.9
South America	39.9	39.9	39.9	39.9	39.9

	UPA 1.5 mg	UPA 3 mg	UPA 12 mg	UPA 30 mg	PBO
<b>Age</b>					
Mean	39.9	39.9	39.9	39.9	39.9
SD	12.9	12.9	12.9	12.9	12.9
<b>Sex</b>					
Male	38.8	38.8	38.8	38.8	38.8
Female	61.2	61.2	61.2	61.2	61.2
<b>Race</b>					
White	87.8	87.8	87.8	87.8	87.8
Black	12.2	12.2	12.2	12.2	12.2
Other	0	0	0	0	0
<b>Region</b>					
USA	39.9	39.9	39.9	39.9	39.9
Europe	39.9	39.9	39.9	39.9	39.9
Asia/Oceania	39.9	39.9	39.9	39.9	39.9
Latin America	39.9	39.9	39.9	39.9	39.9
South America	39.9	39.9	39.9	39.9	39.9

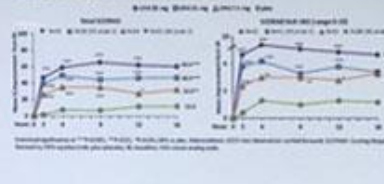
### EFFICACY

- Significant improvement from baseline at week 16 in the UPA 30 mg group for all efficacy measures. Significant improvements were also observed for the other UPA groups in Patient-Reported Pruritus (PRP) (Figure 2), SCORAD-Itch (Figure 3), POEM-Itch (Figure 4), and AdEm-SS Itch Items (Figure 5).

#### Figure 2. Improvement in Pruritus NRS Endpoints

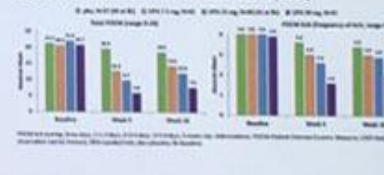


#### Figure 3. Improvement in SCORAD (Itch)

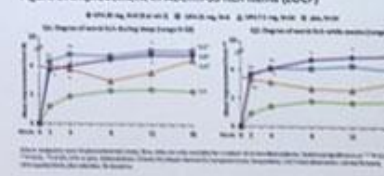


- Absolute POEM scores are illustrated in Figure 4. Mean improvement from baseline to Week 16 for POEM (statistical significance at \*\*\*\*P<0.001, \*\*\*P<0.01, \*\*P<0.05, UPA vs PBO was: Overall (range 0-10) 5.5\* UPA 1.5 mg, 6.4\*\*\* UPA 3 mg, and 12.3\*\*\* UPA 30 mg vs 1.4 placebo.
- XOEM (itch frequency of itch, range 0-4) 1.2 UPA 1.5 mg, 1.1 UPA 3 mg, and 2.0\*\*\* UPA 30 mg vs 0.4 placebo.

#### Figure 4. Improvement in Mean POEM Scores (Itch)



#### Figure 5. Improvement in AdEm-SS Itch Items (Itch)



### SAFETY

- Treatment-emergent adverse events (AEs) are shown in Table 2. There were no deaths or events of serious, CV events (defibrillator), deep vein thrombosis/pulmonary embolism, gastrointestinal perforation, herpes zoster, malignancy, opportunistic infection, renal dysfunction, or tuberculoses.

#### Table 2. Treatment-Emergent Adverse Events (AEs) During Initial 16 Weeks

Adverse Event	UPA 1.5 mg	UPA 3 mg	UPA 12 mg	UPA 30 mg	PBO
Death	0	0	0	0	0
CV events	0	0	0	0	0
Defibrillator	0	0	0	0	0
Deep vein thrombosis/pulmonary embolism	0	0	0	0	0
Gastrointestinal perforation	0	0	0	0	0
Herpes zoster	0	0	0	0	0
Malignancy	0	0	0	0	0
Opportunistic infection	0	0	0	0	0
Renal dysfunction	0	0	0	0	0
Tuberculosis	0	0	0	0	0

### CONCLUSIONS

- UPA treatment for 16 weeks resulted in significant improvements in multiple pruritus-related endpoints.
- The positive benefit-risk profile of UPA supports proceeding to phase 3 trials in AD.

### REFERENCES

1. Williams HC, et al. *J Am Acad Dermatol*. 2012;67:404-414. 2. Han J, et al. *Br J Dermatol*. 2012;167:108-115. 3. Han J, et al. *Br J Dermatol*. 2012;167:108-115. 4. Han J, et al. *Br J Dermatol*. 2012;167:108-115. 5. Han J, et al. *Br J Dermatol*. 2012;167:108-115.

### DISCLOSURES AND ACKNOWLEDGMENTS

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## SPIN 2019

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PARIS - FRANCE

**Background:** In Atopic Dermatitis (AD), the Harmonizing Outcome Measures for Eczema (HOME) initiative has selected the Eczema Area and Severity Index (EASI) as the core instrument for assessing the clinical findings, and the Patient Oriented Eczema Measure (POEM) as the most appropriate tool for evaluating patient-reported symptoms. In adult patients with AD, the Dermatology Life Quality Index (DLQI) and the Quality of Life Index for Atopic Dermatitis (QoLIAD) have shown test-retest reliability, internal consistency, and construct validity. They have the potential for being recommended as QoL instruments in adult patients with AD, but validation studies are missing. In the QoLIAD banding has not been established.

**Objective:** To find which score (DLQI, POEM, and QoLIAD) is better for assessing QoL affection in adult patients with AD through correlation with EASI, and to determine QoLIAD banding for mild, moderate, and severe QoL affection in AD.

**Methods:** Patients >18-years-old with AD that agreed to fill the DLQI, POEM, and QoLIAD questionnaires; and to undergo a physical examination which was classified according to the EASI. Age, gender, profession, personal or familiar atopic history, AD evolution, previous and current treatments were registered.

The POEM score was the only following a normal distribution, for that reason we estimated the Pearson Correlation Coefficient for determining its correlation with EASI. The Spearman Correlation Coefficient was estimated for correlating DLQI and QoLIAD with EASI as they did not follow a normal distribution. We adjusted three robust simple linear regression models, in order to quantify the association between EASI and DLQI, POEM, and QoLIAD. A p-value lower than 0.05 was considered as statistical significant.



**Results:** A total of 72 patients were registered. 55% were women and 45% were men. As it is shown in Table 1, with the correlation coefficient there is a linear relation within the three scores and the EASI

	CORRELATION COEFFICIENT	REGRESSION COEFFICIENT	P-VALUE	PSEUDO R <sup>2</sup>	FORMULA
POEM	0.4444	0.234	0.0000	0.1106	POEM=9.9+0.234(EASI)
DLQI	0.4915	0.219	0.0000	0.1492	DLQI=7.48+0.219(EASI)
QoLIAD	0.4307	0.252	0.003	0.0951	QoLIAD=5.89+0.252(EASI)

Table 1

According to the Pseudo-R<sup>2</sup> value the DLQI has the strongest correlation with EASI. Using the obtained value in the regression coefficient we developed three formulas that are able to estimate POEM, DLQI, and QoLIAD. by using the EASI. With the QoLIAD's formula we established banding for this instrument as shown in Table 2

EASI	POEM	DLQI	QoLIAD
AD severity	Quality of Life affection		
Mild (0-7)	Clear-almost clear (0-2)	No effect (0-1)	Mild (0-7)
	Mild (3-7)	Small effect (2-5)	
Moderate (7.1-21)	Moderate (8-16)	Moderate effect (6-10)	Moderate (8-10)
Severe (21.1-50)	Severe (17-24)	Very large effect (11-20)	Severe (11-18)
Very severe (50.1-72)	Very Severe (25-28)	Extremely large effect (21-30)	Very Severe (19-25)

Table 2

**Conclusion:** In the era where QoL instruments are being more frequently used in AD. The **DLQI stands as the most suitable instrument.** Dermatologists are more familiarized with it and is more practical in the day-to-day practice.



# TREATMENT OUTCOMES AND GOALS IN ATOPIC DERMATITIS”

**Esther Serra Baldrich.**

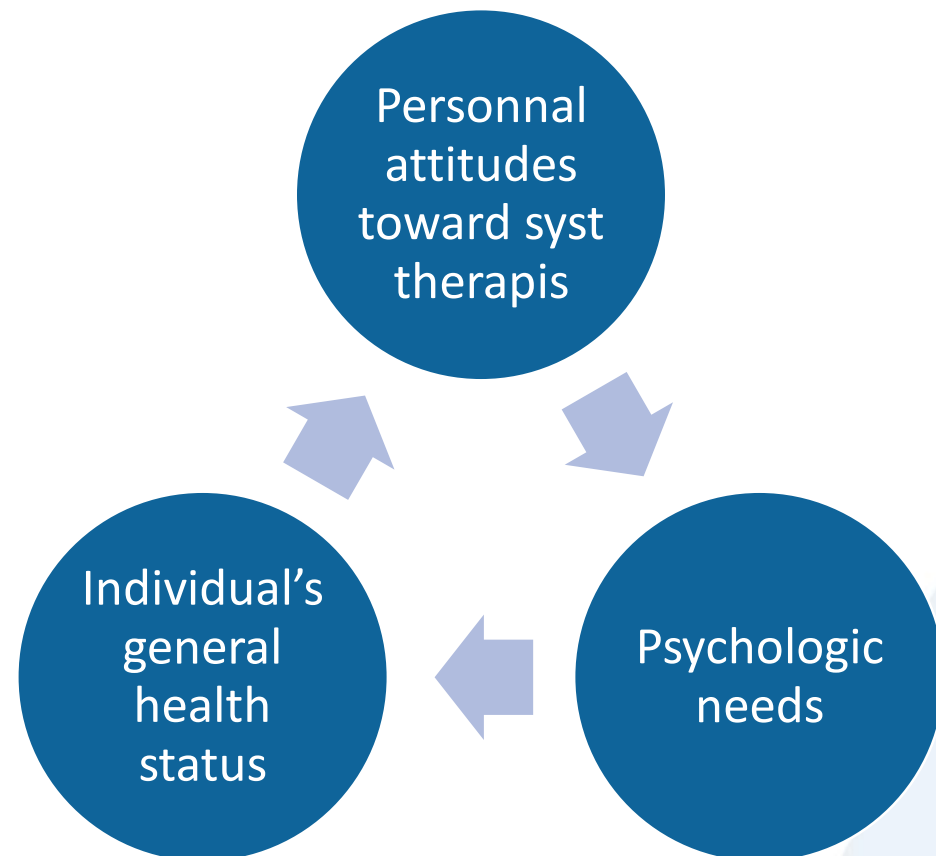
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## FOCUS SESSION 7 TREATMENT OUTCOMES AND GOALS IN ATOPIC DERMATITIS". E Serra Baldrich

- The decision to start systemic medication should include **assessment of severity and quality of life** while considering the



- For an **instrument** to be **useful** to the general dermatologist, it should have demonstrated
  1. validity in clinical practice
  2. require minimal training,
  3. be time-efficient, and
  4. seamlessly integrate into day-to-day practice.



dream\_high

To be “adequate” for use in clinical practice, a severity score should not take longer than 3 minutes



A systematic review of **randomized controlled trials** (RCT) performed in 2016 demonstrated that the **most commonly used severity measures** were

- **SCORAD** ( signs +symptoms)
- **Visual Analogue Scale (VAS)-pruritus** (symptoms)
- **IGA** (signs)
- **and EASI** (signs)

## TO TAKE HOME EASY TOOLS

- APP SCORAD-EASI
- VAS scales /SLEEP
- DLQI only changes Tx
- POEM (PRO) and PO-Scorad



### Itch Measuring Instruments

