

# *Dermatology*



# DIALOGUES

Gaining and Maintaining Flare Control in  
Moderate-to-Severe Atopic Dermatitis:  
Enhancing Patient Quality of Life





Part 1: M-S AD Disease Burden, Disease Progression, and Treatment Challenges

Part 2: Current and Developing Systemic Agents for Treating M-S AD in Accordance with Clinical Guidelines

Part 3: Utilizing QOL and PRO Assessment to Enhance Clinical Outcomes in M-S AD Management

Part 4: Incorporating Shared Decision-Making in All Facets of Treatment Selection to Address QOL



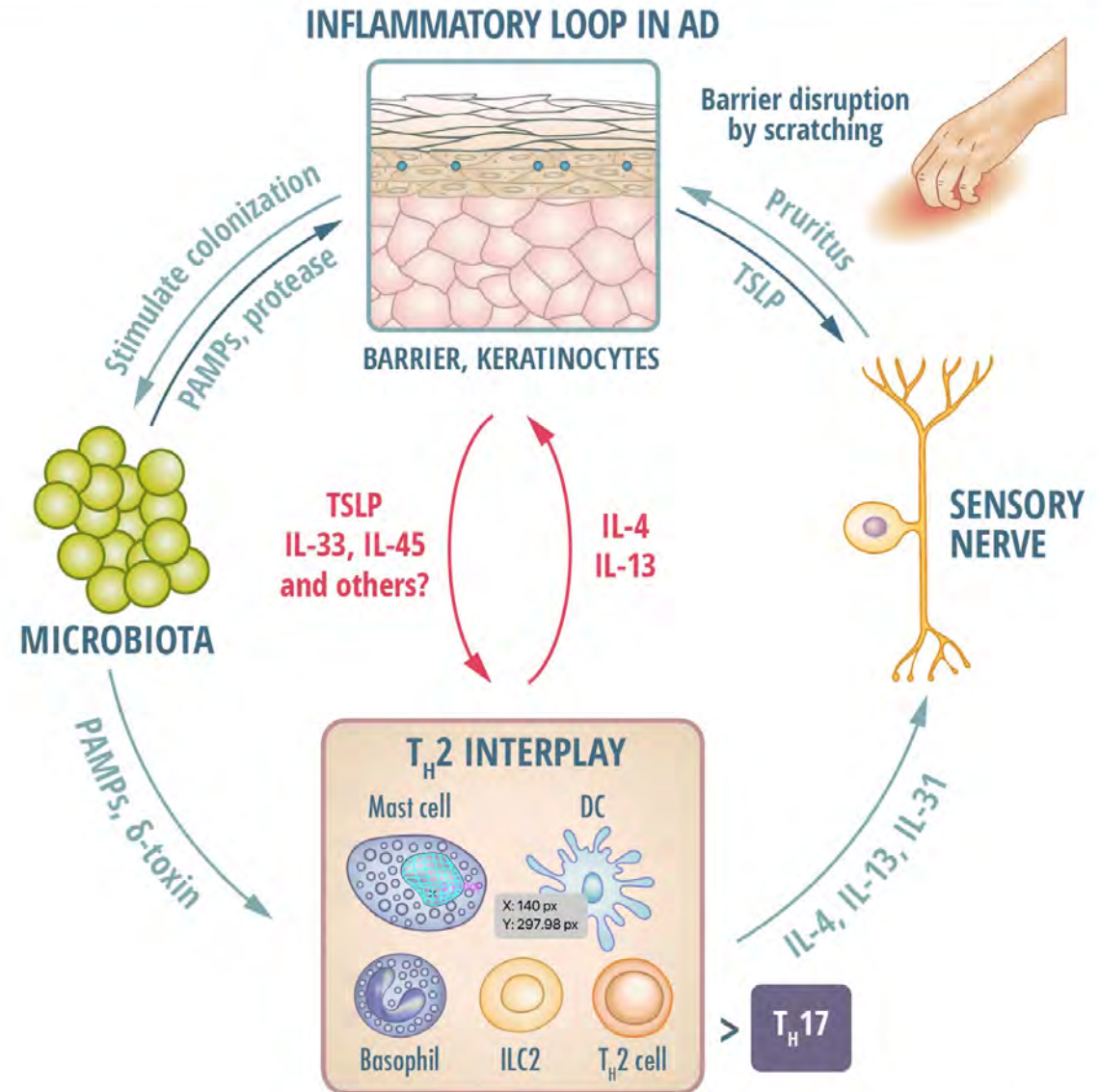


# Educational Objectives



1. Accurately assess dermatology-specific quality of life factors when choosing and managing treatments throughout the progression of M-S AD to align with clinical guidelines
2. Select appropriate treatments by considering distinctions among drug mechanisms of action, efficacy, and safety data of both approved options and emerging biologic agents for M-S AD
3. Consistently apply shared decision-making in all patient discussions concerning treatment selection, modification, or intensification while accounting for quality of life through patient-reported outcome assessments

- Epidermal barrier dysfunction and type 2 dominated immune responses
- Type 2 inflammation plays a key role in both acute and chronic phases of the disease







# Unmet Needs in Atopic Dermatitis



AD affects nearly 10 million children and over 16 million adults in the US

Prevalence of childhood AD has increased from 8% in 1997 to ~12% in 2017

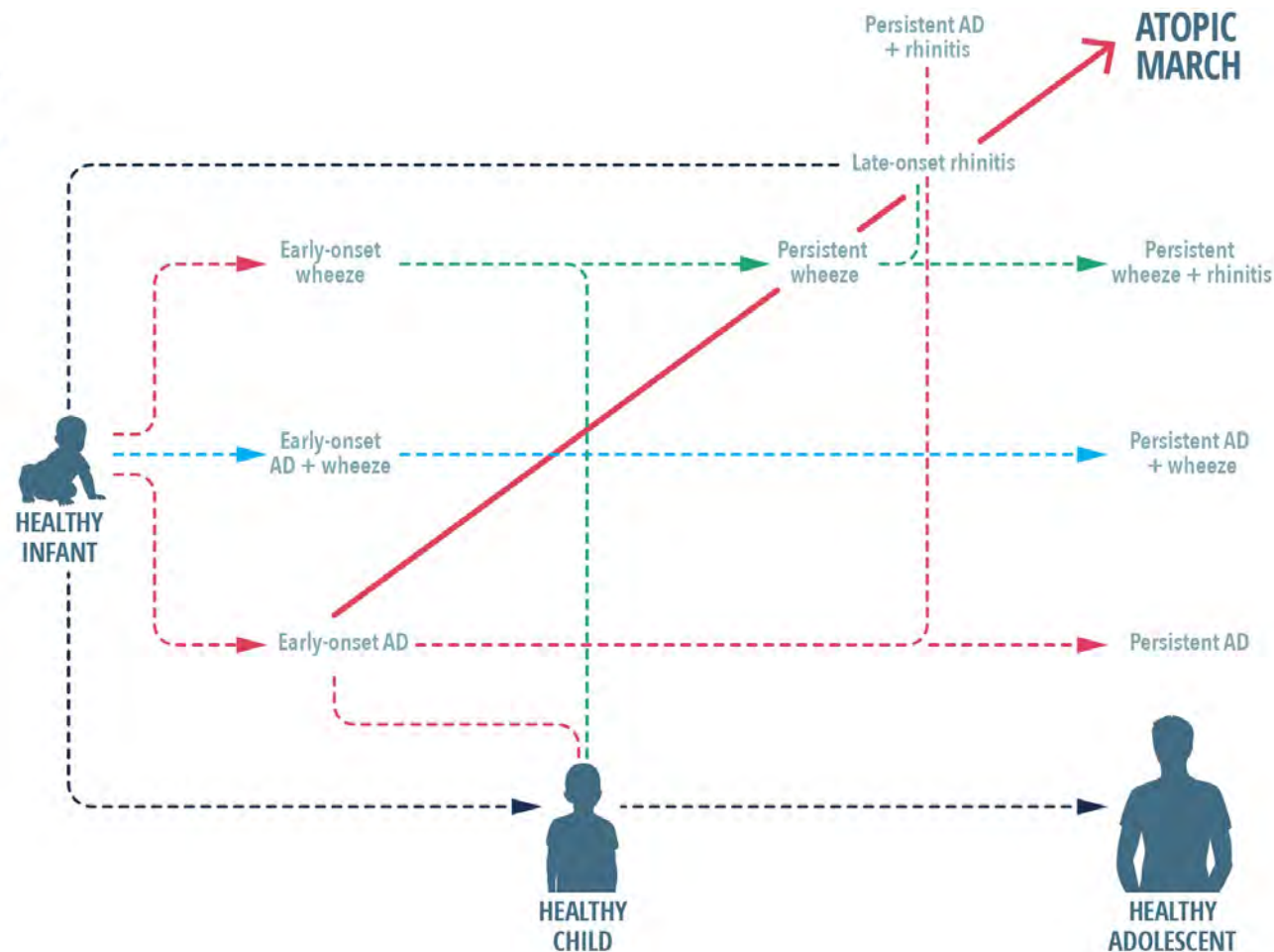
Adult patients with AD reported a substantial disease burden, suggesting an unmet need for more effective AD treatment options

Annual economic burden of AD has been conservatively estimated at \$5.3 billion in 2017

Pathophysiology is complex and new insights have led to the new FDA-approved systemic agents for AD

Most adults with moderate-to-severe AD report inadequate disease control

- The complex pathophysiology of AD translates into a heterogeneous clinical presentation and trajectories of disease progression
  - A significant proportion will develop persistent AD and/or other atopic conditions
- Atopic march:
  - **Younger onset of AD**
  - Family history of AD
  - **Greater early severe AD**
  - Filaggrin mutation
  - Urban environment
  - Polysensitization



Could early use of emollients attenuate the atopic march?



## Essential Features

*Must be present*

- Pruritus
- Eczema (acute, subacute, chronic)
  - Typical morphology and age-specific patterns<sup>†</sup>
  - Chronic or relapsing history

<sup>†</sup>Patterns include:

- Facial, neck, and extensor involvement in infants and children
- Current or prior flexural lesions in any age group
- Sparing of groin and axillary regions

## Important Features

Seen in most cases, adding support to the diagnosis

- Early age of onset
- Atopy
  - Personal and/or family history
  - IgE reactivity
- Xerosis

## Associated Features

Suggests the diagnosis of AD but are too non-specific to be used for defining/detecting AD for research and epidemiology studies

- Atypical vascular responses
- Keratosis pilaris, pityriasis alba, hyperlinear palms, ichthyosis
- Ocular, periorbital changes
- Other regional findings
- Perifollicular accentuation, lichenification, prurigo lesions



## Infants and up to 2-years-old

- Most common symptom is scaly eczematous patches, excoriations, oozing erosions, and/or lichenified plaques
  - Face
  - Scalp
  - Extensors

\*20% of children are affected

## 2-years-old to puberty

- Most common symptom is red thick rash, which may ooze or bleed when scratched
  - Extensors or flexural areas
  - Cervical region
  - Talocrural region

## Teens and adults

- Most common symptom is red to dark brown scaly rash, which may bleed and crust when scratched
  - Hands
  - Cervical region
  - Extensors or flexural areas
  - Periorbital skin
  - Talocrural region and feet

\*2% to 8% of adults are affected

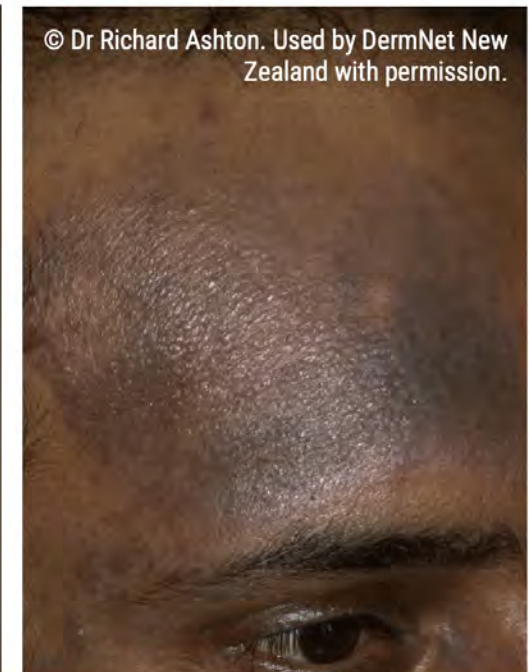


## Lighter skin types:

- Erythematous patches and plaques affecting flexor surfaces

## Darker skin types:

- Greater propensity for papulation, lichenification, and pigmentary changes
- Favors extensor surfaces in skin of color
- Erythema in darker skin types often presents as a violaceous hue, an ashen gray or darker brown color
  - Clinicians can mistakenly minimize disease severity in patients of color with AD since erythema is more difficult to detect
- Black/African patients have an increased tendency for hyperlinearity of the palms, periorbital dark circles, Dennie-Morgan lines, and prurigo nodularis
- Asian patient often has psoriasiform features, with lesions having more well-defined borders with increased scaling and lichenification





## Differential Diagnoses

This list is not comprehensive and may include other conditions

- Chronic hand eczema (excluding contact dermatitis)
- Nummular eczema
- Follicular eczema
- Lichenoid eczema
- Dyshidrosis
- Prurigo nodularis
- Lichen simplex chronicus
- Nipple eczema
- Asteatotic eczema
- Gestational eczema
- Eczema of older adults or atopic dermatitis of the elderly (excluding mycosis fungoides)
- Eyelid dermatitis (excluding contact dermatitis)



## Atopic Dermatitis Comorbidities

This list is not comprehensive and may include other conditions

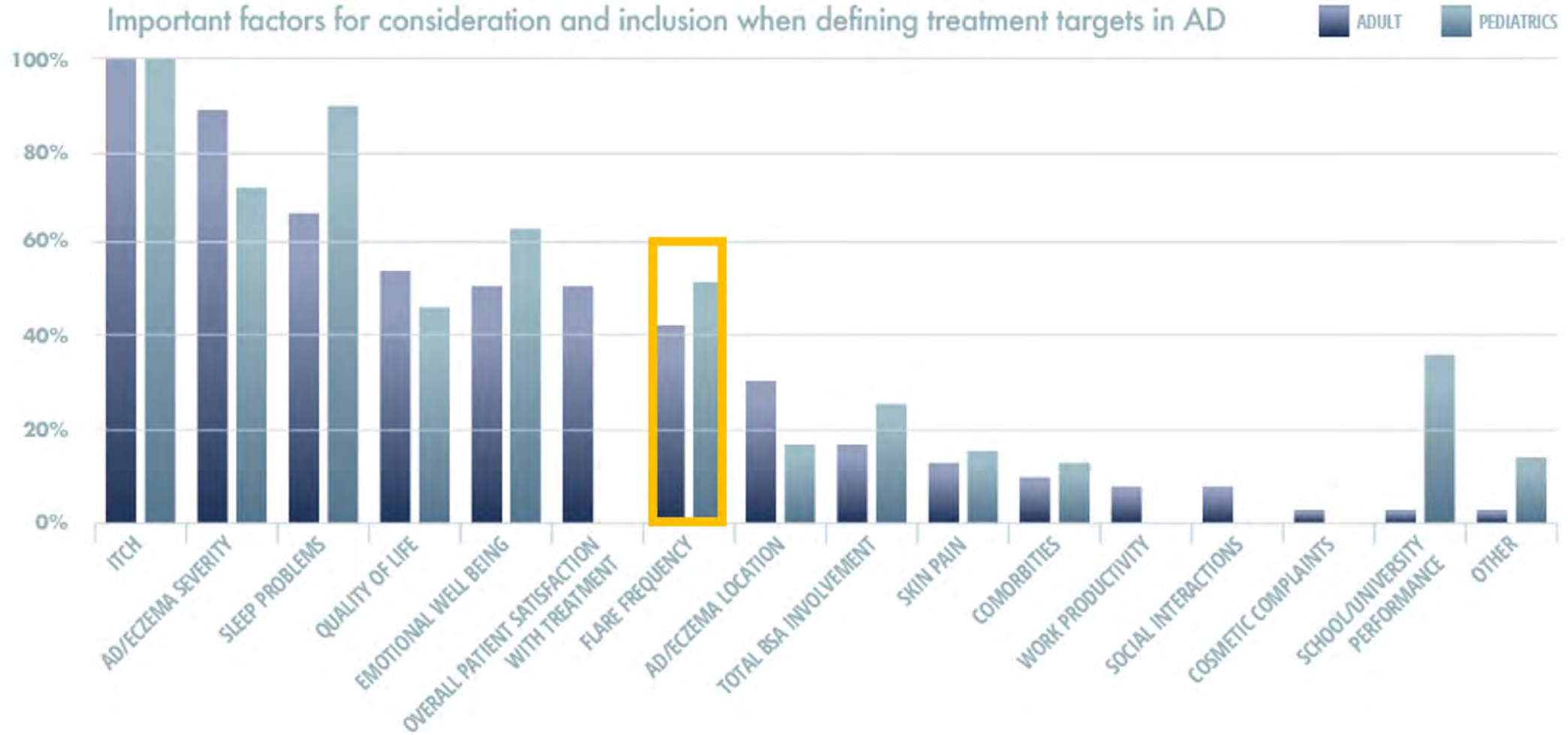
- Asthma
- Food allergies
- Environmental allergies
- Eosinophilic esophagitis
- Sleep disturbances
- Cardiovascular diseases
- Depression, anxiety, suicidal ideation
- Increased risk of infection
- Obesity
- Autoimmune disease

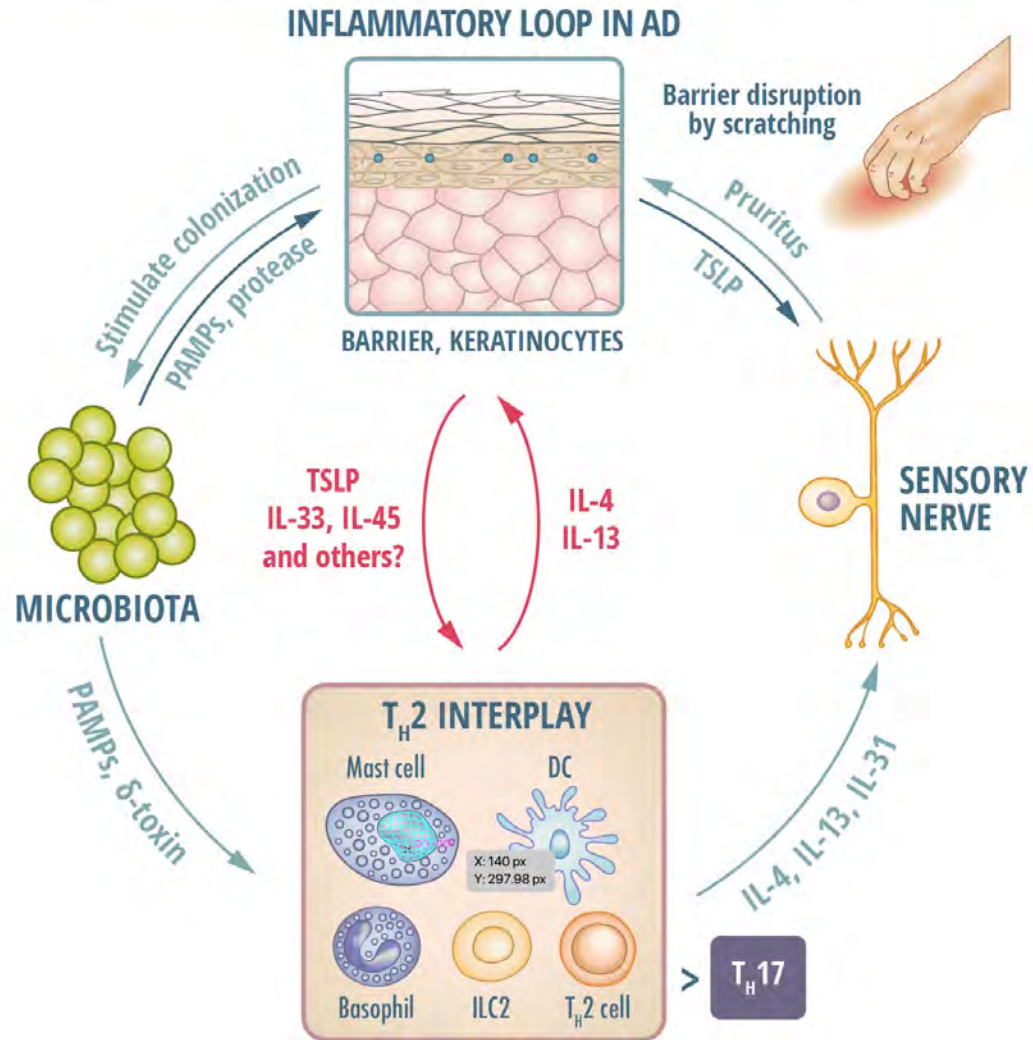
## Flare events indicate A-D worsening and require treatment escalation and/or intensification

- Flare events can vary by patient with minimal changes over time, while the clinical course can fluctuate with periods of remission interrupted by acute exacerbations
- Flares cause a substantial impact on psychosocial functionality, patient quality of life, and an economic burden
- Flares have been viewed as an aside to a chronic disease rather than an urgent condition

**Flare management is imperative for long-term disease control**







**GET PATIENT CLEAR**



**SAFELY KEEP PATIENT CLEAR**

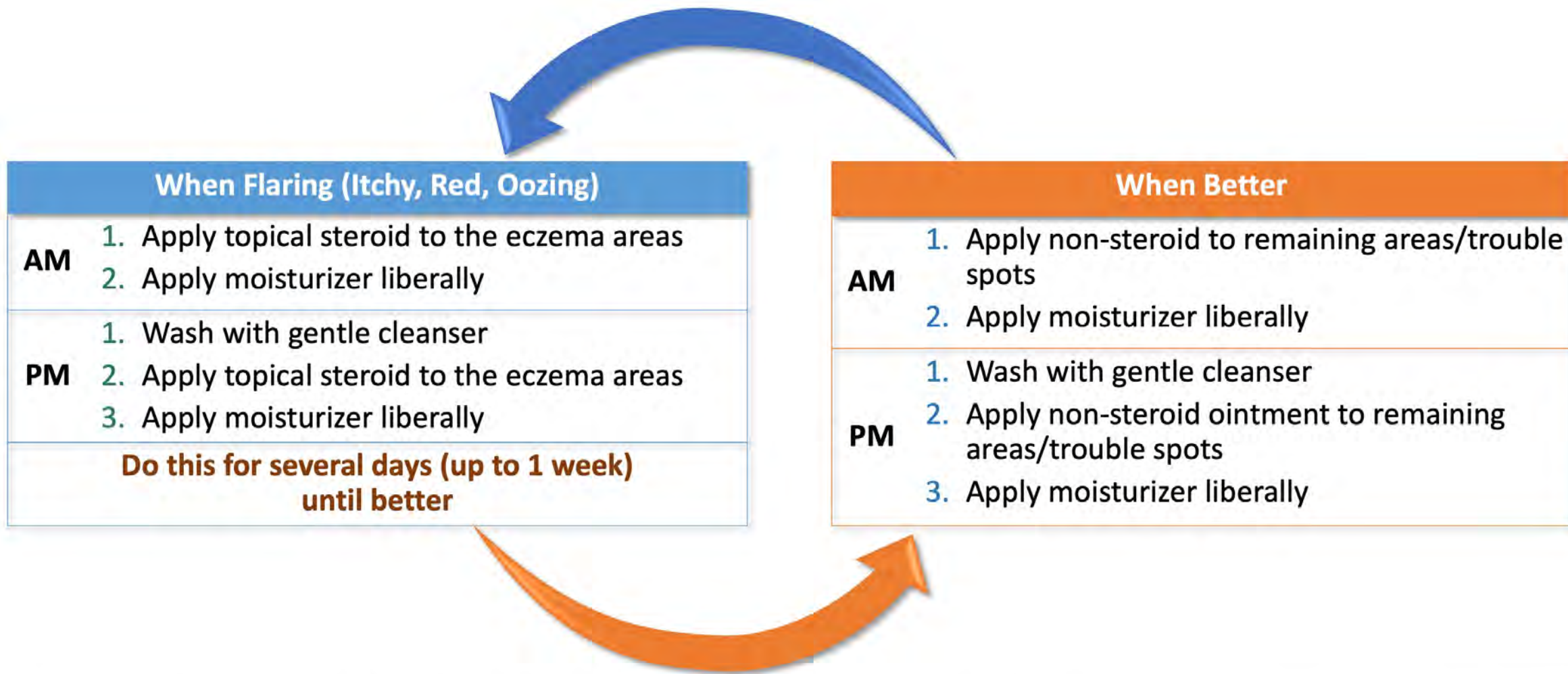


**MAINTAIN PATIENT BEING CLEAR**



**FLARE CHASING AND DOSE ESCALATING**









# Inadequate M-S AD Flare Prevention is an Unmet Need for Patients with Refractory Disease

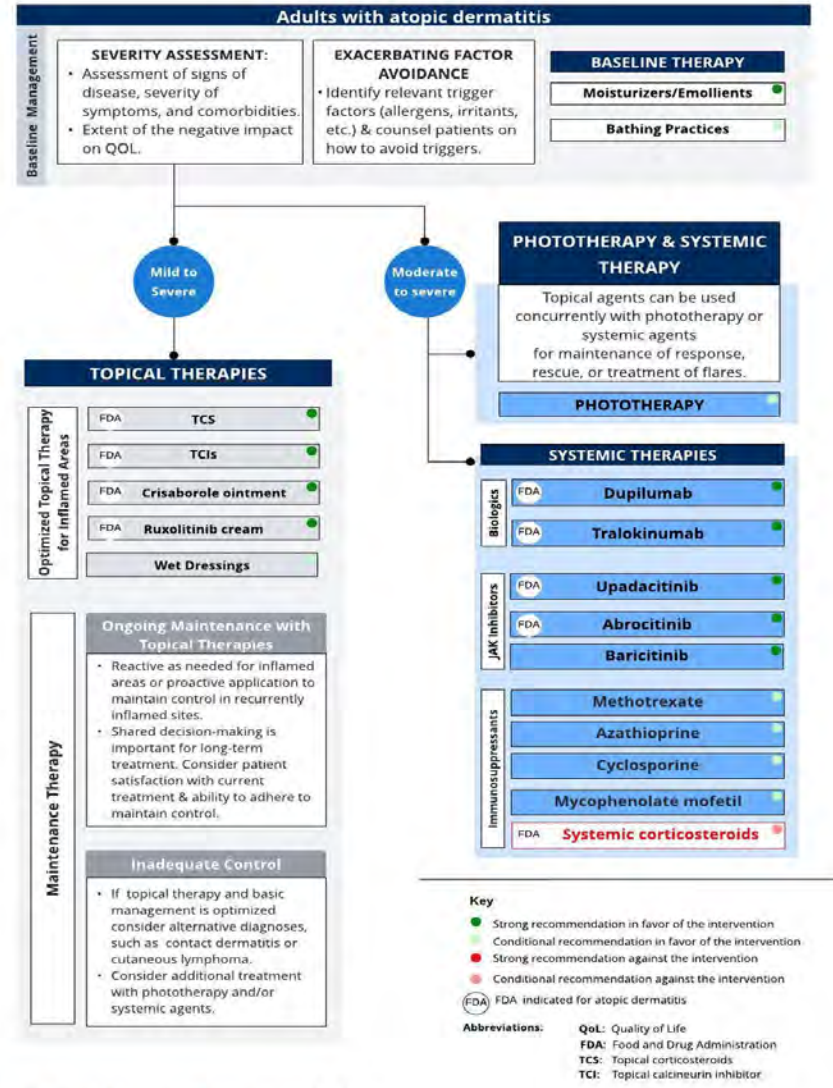


In an international survey of patients with M-S AD, 75% of patients and caregivers stated that effective disease control would be the single most important contribution to QoL

- Avoidance of triggers that cause flare events is a major consideration among patients with M-S AD and has a substantial impact on daily life decisions
- Caregivers are also impacted by flare events, especially in low-income households
- Total household expenses are influenced by flare events as caregivers must spend time addressing patients' needs and forgoing ability to work/generate income
- Patients in underserved communities can often misunderstand the severity of flare events and care may be delayed causing exacerbation of M-S AD



- The Academy published a series of updates to the AD guidelines, which were originally published in 2014
- Patients with more severe or widespread AD, with substantially impaired quality of life, and whose AD is refractory to optimized topical therapy may consider the use of phototherapy or systemic therapies to improve disease control and quality of life



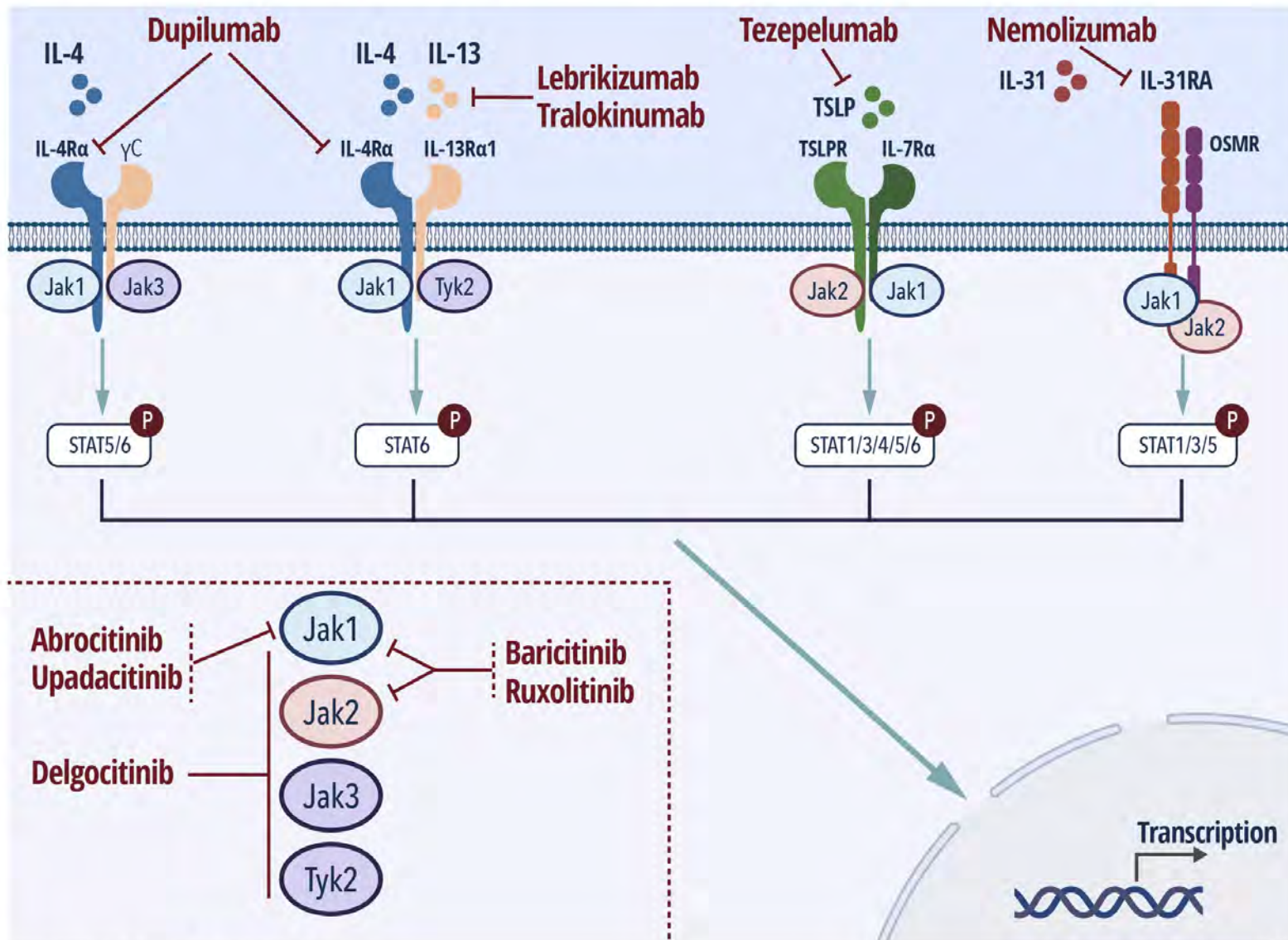


- Treatment that is almost no longer used/prescribed
- Might be used in short courses to control very severe flares of eczema
- Long-term side effects are associated with prolonged use



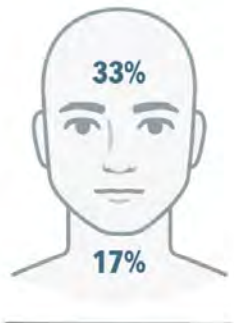


# Targeted Pathways for M-S AD Treatment Options to Prevent Flare Events



**BSA score: 1 (1%–9%), 2 (10%–29%), 3 (30%–49%), 4 (50%–69%), 5 (70%–89%), and 6 (90%–100%)**

## HEAD & NECK



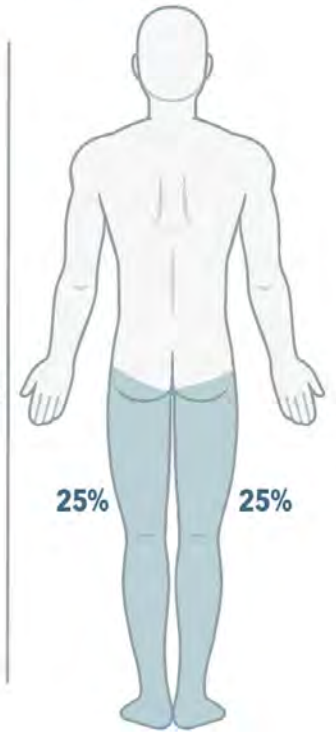
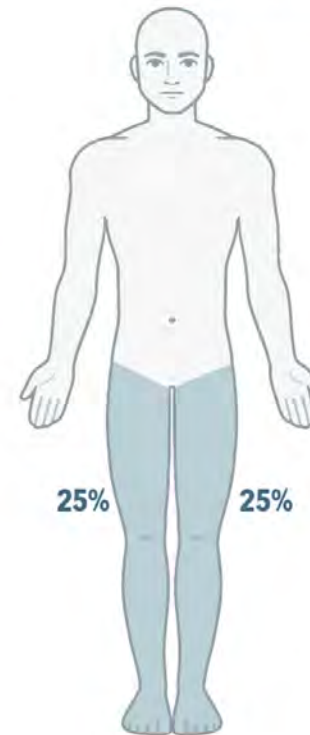
## TRUNK



## UPPER EXTREMITIES



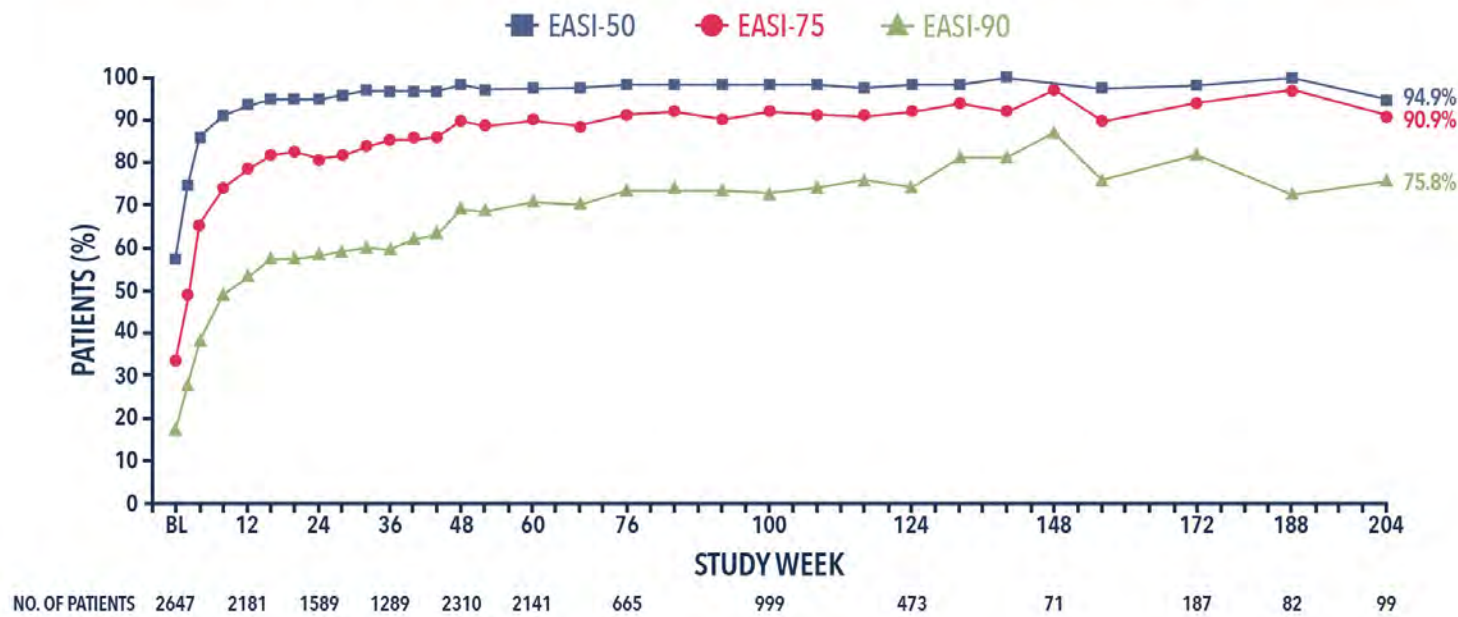
## LOWER EXTREMITIES





## Open label up to 4-years, 52-week trial CHRONOS in adult patients with M-S AD

Percentage of patients achieving  $\geq 50\%$ ,  $\geq 75\%$ , and  $\geq 90\%$  improvement in Eczema Area and Severity Index (EASI-50, EASI-75 and EASI-90, respectively) over time

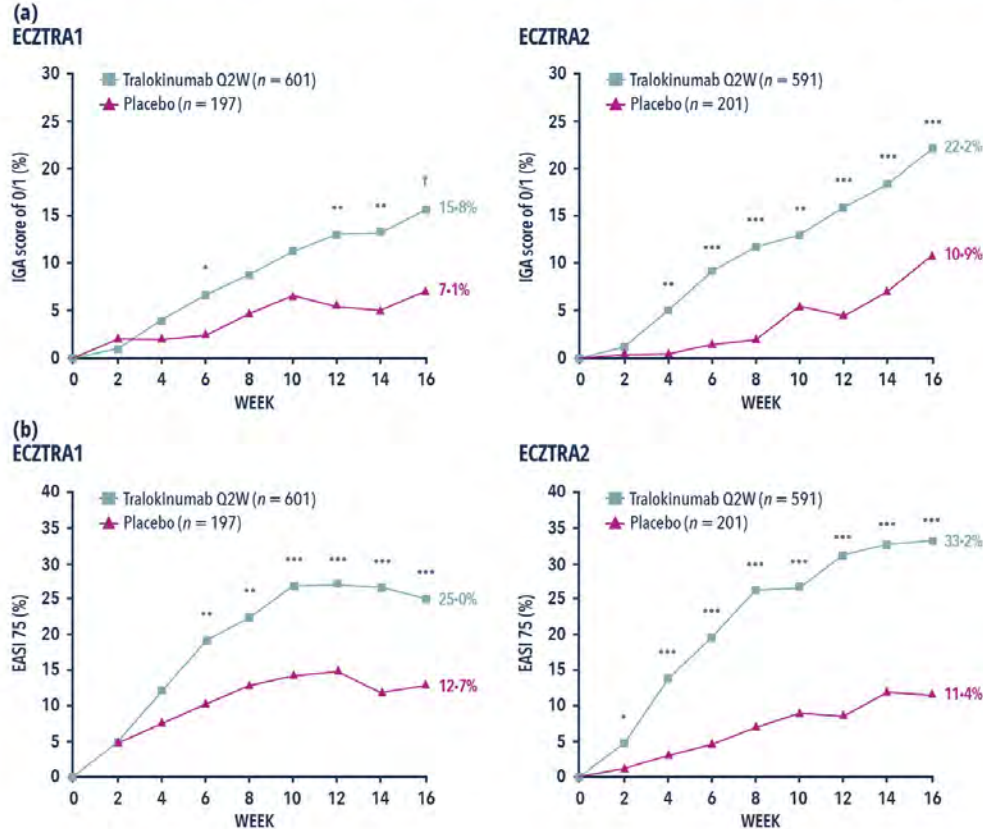


- Primary endpoint: incidence and rate (events per patient-year [PY]) of TEAEs
- Common treatment-emergent adverse events ( $\geq 5\%$ ) included: nasopharyngitis, AD, upper respiratory tract infection, oral herpes, conjunctivitis, injection-site reaction, and headache



## Phase III, 52-week trials ECZTRA1 and ECZTRA2 in adult patients with M-S AD

Achievement of (a) Investigator's Global Assessment (IGA) score of 0 or 1 and (b)  $\geq 75\%$  improvement in Eczema Area and Severity Index (EASI 75) in the 16-week initial treatment period in ECZTRA 1 and ECZTRA 2



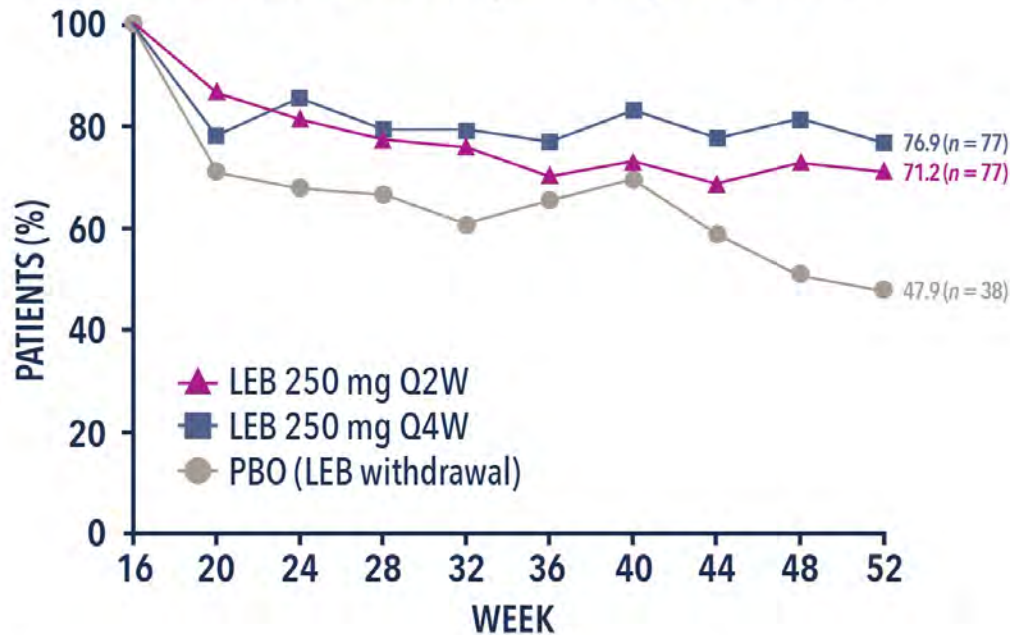
- Primary endpoints: Investigator's Global Assessment (IGA) score of 0 (clear skin) or 1 (almost clear skin) at week 16 and EASI 75 at week 16
- Common treatment-emergent adverse events ( $\geq 5\%$ ) included: upper respiratory tract infection (mainly reported as common cold) and conjunctivitis occurred more frequently with tralokinumab than with placebo, and dermatitis atopic and skin infection occurred more frequently with placebo



## Phase III, 52-week study in ADvocate1 and ADvocate2 in adolescent and adults patients with M-S AD

### Maintenance of response over time in lebrikizumab (LEB) responders re-randomized at week 16

#### IGA (0, 1) and $\geq 2$ -point Improvement

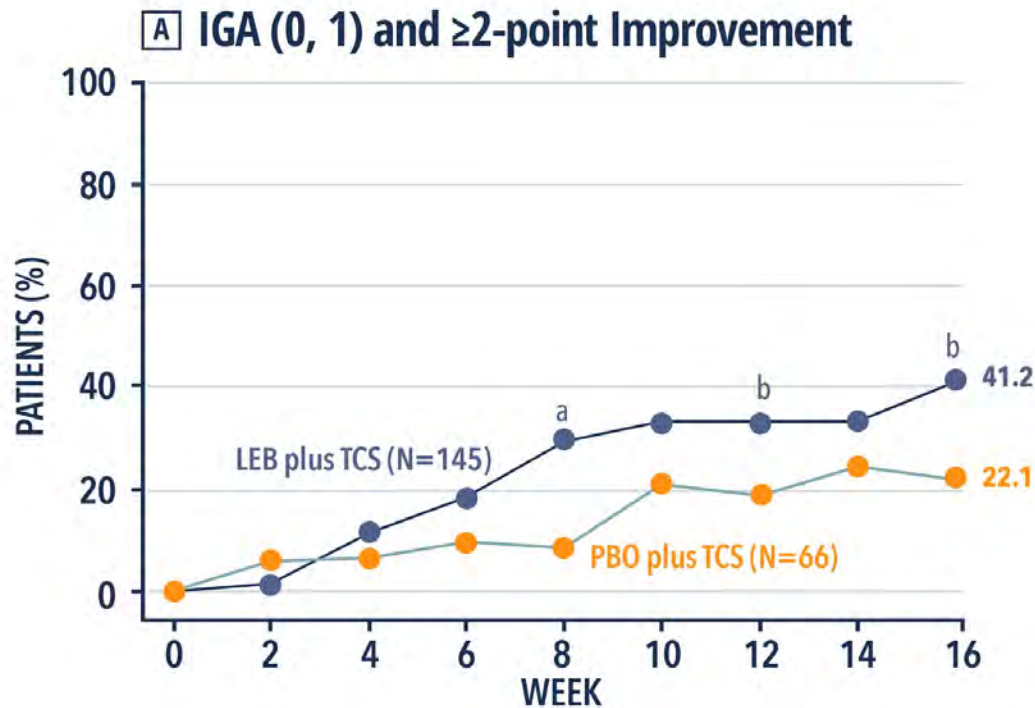


- Primary endpoint: Investigator’s Global Assessment (IGA) score of 0 (clear skin) or 1 (almost clear skin); range, 0 to 4 [severe disease] with a reduction (indicating improvement) of at least 2 points from baseline at week 16
- Common treatment-emergent adverse events ( $\geq 5\%$ ) included: AD (8.9%), conjunctivitis (8.2%), nasopharyngitis (8.2%) and allergic conjunctivitis (6.0%)



## Phase III, 16-week study in ADhere in adolescent and adult patients with M-S AD

### Time-Course Response for the Clinical Outcomes (Primary End Point)



- Primary outcome: percentage of patients with an IGA score of 0 (clear skin) or 1 (almost clear skin), and a 2 or more point improvement from baseline at week 16
- TEAEs frequently reported included: Conjunctivitis (7 [4.8%]), headache (7 [4.8%]), hypertension (4 [2.8%]), injection site reactions (4 [2.8%]), herpes infection (5 [3.4%])

IGA, investigator's global assessment; LEB, lebrikizumab; PBO, placebo; TCS, topical corticosteroids; TEAEs, treatment-emergent adverse events.

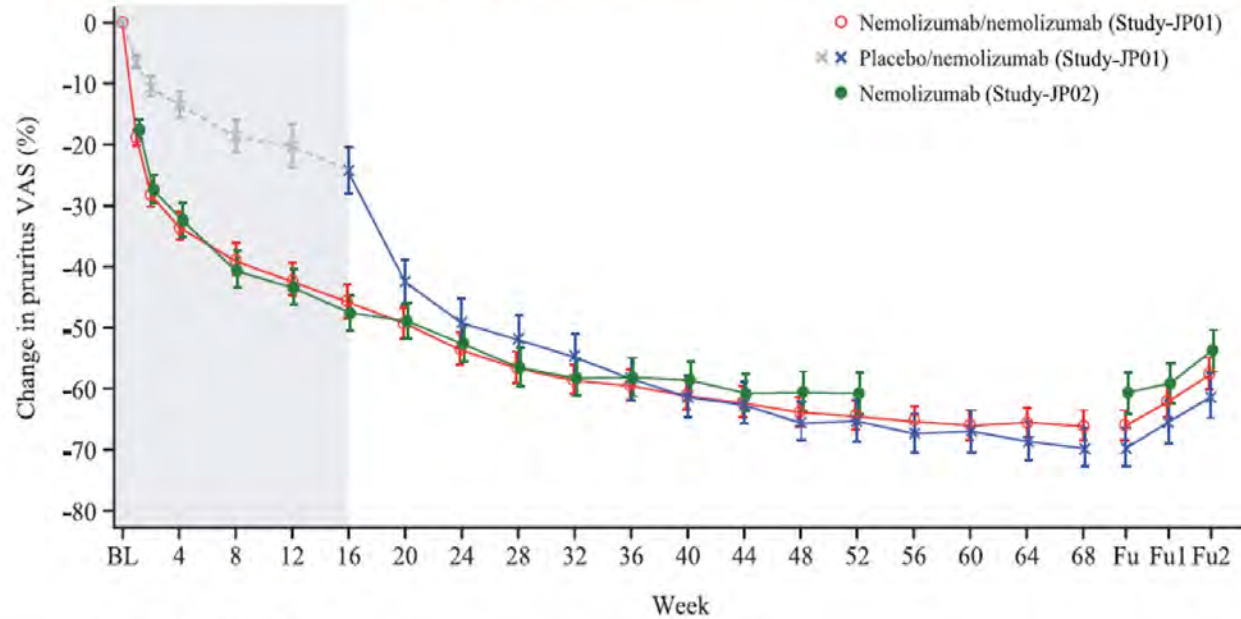
<sup>a</sup>P < .001. <sup>b</sup>P < .05. <sup>c</sup>P < .01.

Simpson EL et al. JAMA Dermatol. 2023 Feb 1;159(2):182-191.



## Phase III, long-term, 68-week studies in adolescent and adult patients with M-S AD and pruritus

### Time-Course Response for the Clinical Outcomes (Primary End Point)



- Primary outcomes: percent change in the weekly mean pruritus VAS score from baseline to week 16
- Most common TEAEs included: nasopharyngitis (33.9%) and AD (25.2%)

Number of patients

Nemolizumab/nemolizumab (Study-JP01)	143	136	126	117	116	115	114	114	114	113	113	113	112	112	111	111	109	106	107	
Placebo/nemolizumab (Study-JP01)	72	69	66	60	55	55	55	55	55	54	54	54	53	52	52	52	52	52	51	
Nemolizumab (Study-JP02)	88	88	88	87	87	85	83	82	82	80	79	79	78	78					78	78

Fu1 and Fu2 denote 4 and 8 weeks after the end of the treatment period, respectively. Error bars denote standard error of the mean. Study-JP01 was double-blind until week 16 (denoted by shaded area).

BL, baseline; Fu, follow-up; VAS, visual analogue scale.

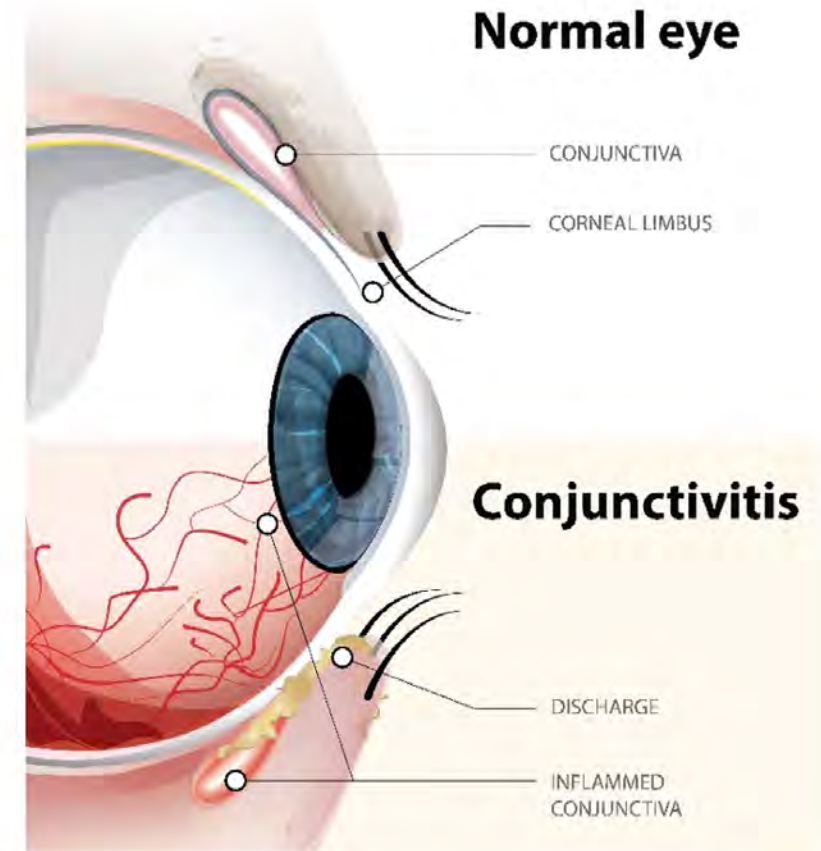
Kabashima K et al. Br J Dermatol. 2022 Apr;186(4):642-651.



Ocular surface disease is the most common adverse event from clinical trials and real-world experience

Symptoms can vary depending on etiology, including redness, itching, burning, discharge, and eyelid edema

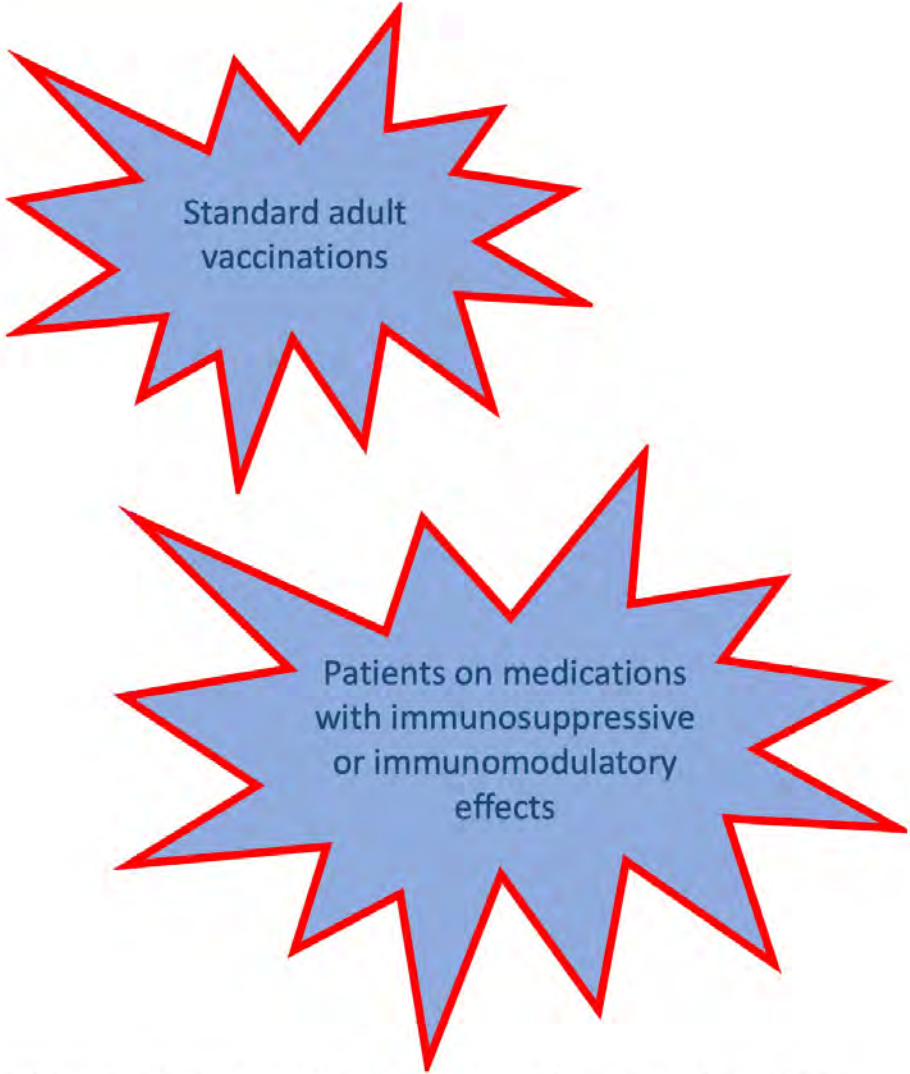
- Patients should be counseled about the incidence of conjunctivitis and its occurrence with newer biologic agents but that ocular symptoms typically are mild and resolve over time
- Clinicians providing atopic dermatitis care should establish a relationship with an eye care specialist so patients can be referred as necessary





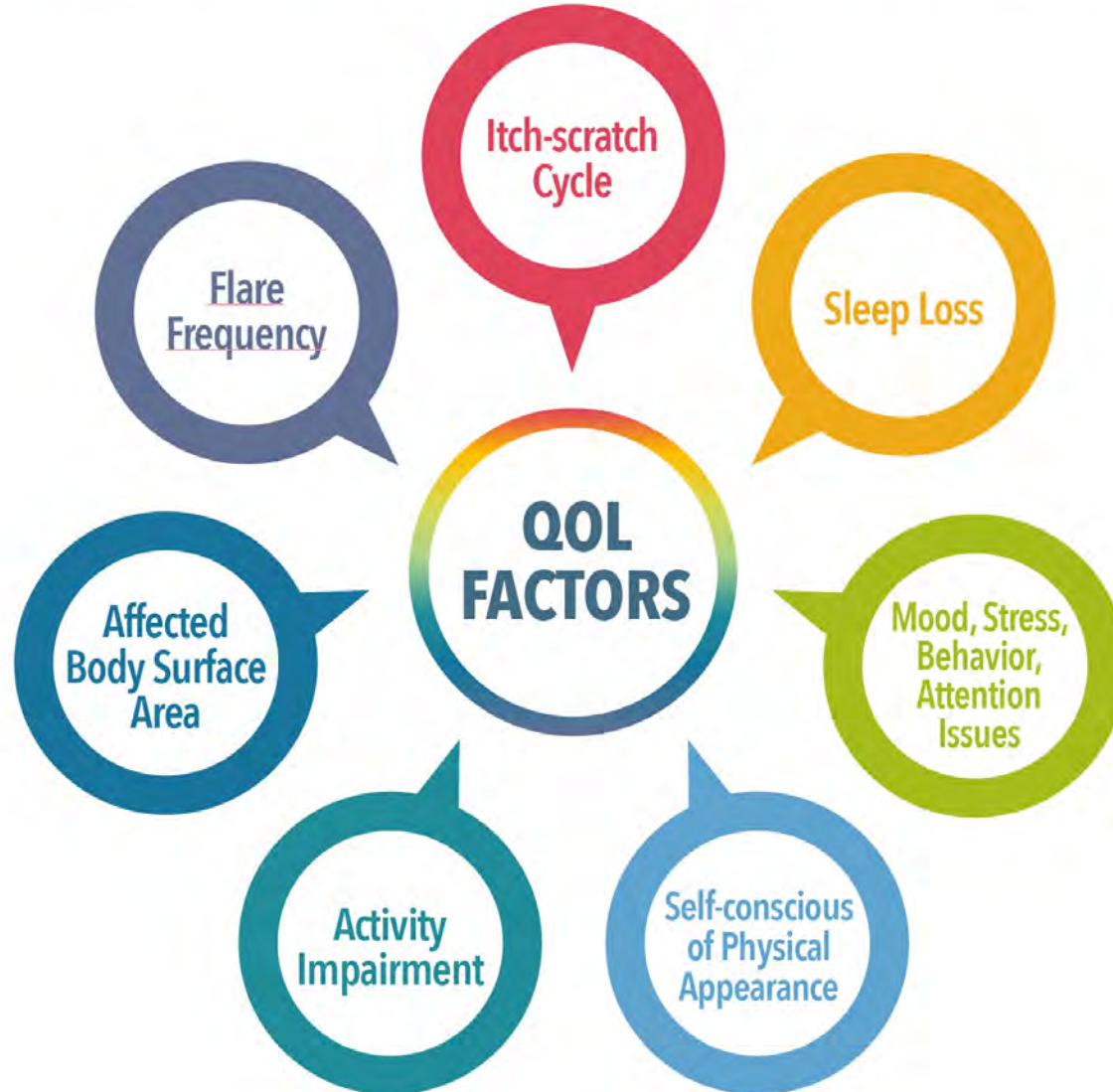


# Recommendations for Patients Receiving Biologic Therapies and Vaccinations



- Pneumococcal<sup>a</sup>
- Inactivated influenza<sup>a</sup>
- Recombinant zoster<sup>a</sup>
- Other inactivated<sup>a</sup>
- COVID-19<sup>a</sup>
- COVID-19 booster<sup>a</sup>
- Live attenuated<sup>b</sup>

<sup>a</sup>Indicated for administration. <sup>b</sup>Not indicated for administration while concurrently on therapy  
Fan R, et al. Yale J Biol Med. 2022 Jun 30;95(2):249-255.







# Unmet Needs for Patients with Diverse Skin Tones and M-S AD



Implicit bias, which is stereotypes and attitudes that we develop toward certain groups of people, affecting patient relationships and care decisions

Patients with diverse skin tones are more likely to experience morbidities associated with M-S AD

- Use the educate, expose, and approach strategy to address implicit bias
- Engage patients in meaningful, empathic communication
- Review literature to stay up to date on research involving patients with diverse skin tones and to also be cognizant of resources that addresses certain patient populations
- Collaborate with larger healthcare systems to help close the divide between clinical practice and social determinants of health

**Journaling**



**Listing symptoms**



**Diet tracker**



**Listing medications**



Traditional tracking methods can be helpful to understand what patients experience when they are not presenting with a flare in clinic; however, there are additional tools that can be used to assess disease temporality and patient quality of life...



## EASI

Severity Score Grade each sign on a scale:	Area Score							
	% Involvement	0	1-9%	10-29%	30-49%	50-69%	70-89%	90-100%
0=clear/none 1=mild 2=moderate 3=severe	Area Score	0	1	2	3	4	5	6

Clear	Almost Clear	Mild	Moderate	Severe	Very Severe
0	0.1-1.0	1.1-7.0	7.1-21.0	21.1-50.0	50.1-72.0

Body Region	Erythema (0-3)	Edema/Papulation (0-3)	Excoriation (0-3)	Lichenification (0-3)	Area Score (0-6)	Multiplier	Score
Head/Neck	( ) +	( ) +	( ) +	( )	( ) x	x 0.1	
Trunk	( ) +	( ) +	( ) +	( )	( ) x	x 0.3	
Upper Extremities	( ) +	( ) +	( ) +	( )	( ) x	x 0.2	
Lower Extremities	( ) +	( ) +	( ) +	( )	( ) x	x 0.4	

The final EASI score is the sum of the 4 region scores (0-72): \_\_\_\_\_

## IGA

Score	Morphological Description
0 - Clear	No inflammatory signs of atopic dermatitis (no erythema, no induration/papulation, no lichenification, no oozing/crusting). Post-inflammatory hyperpigmentation and/or hypopigmentation may be present.
1 - Almost clear	Barely perceptible erythema, barely perceptible induration/papulation, and/or minimal lichenification. No oozing or crusting.
2 - Mild	Slight but definite erythema (pink), slight but definite induration/papulation, and/or slight but definite lichenification. No oozing or crusting.
3 - Moderate	Clearly perceptible erythema (dull red), clearly perceptible induration/papulation, and/or clearly perceptible lichenification. Oozing and crusting may be present.
4 - Severe	Marked erythema (deep or bright red), marked induration/papulation, and/or marked lichenification. Disease is widespread in extent. Oozing or crusting may be present.

## POEM

**Patient-Oriented Eczema Measure**

Please circle one response for each of the seven questions below. Young children should complete the questionnaire with the help of their parents. Please leave blank any questions you feel unable to answer.

- Over the last week, on how many days has your/your child's skin been itchy because of the eczema?  
No Days    1-2 Days    3-4 Days    5-6 Days    Every Day
- Over the last week, on how many nights has your/your child's sleep been disturbed because of the eczema?  
No Days    1-2 Days    3-4 Days    5-6 Days    Every Day
- Over the last week, on how many days has your/your child's skin been bleeding because of the eczema?  
No Days    1-2 Days    3-4 Days    5-6 Days    Every Day
- Over the last week, on how many days has your/your child's skin been weeping or oozing clear fluid because of the eczema?  
No Days    1-2 Days    3-4 Days    5-6 Days    Every Day
- Over the last week, on how many days has your/your child's skin been cracked because of the eczema?  
No Days    1-2 Days    3-4 Days    5-6 Days    Every Day
- Over the last week, on how many days has your/your child's skin been flaking off because of the eczema?  
No Days    1-2 Days    3-4 Days    5-6 Days    Every Day
- Over the last week, on how many days has your/your child's skin felt dry or rough because of the eczema?  
No Days    1-2 Days    3-4 Days    5-6 Days    Every Day

Total Score (maximum 28) \_\_\_\_\_

## SCORAD

**SCORAD INDEX**  
EUROPEAN TASK FORCE ON ATOPIC DERMATITIS

Last Name: \_\_\_\_\_ First Name: \_\_\_\_\_  
Date of Birth: \_\_\_\_\_ DD/MM/YY  
Date of Visit: \_\_\_\_\_

Figures in parentheses for children under two years

A: EXTENT Please indicate the area involved: \_\_\_\_\_  
B: INTENSITY \_\_\_\_\_  
C: SUBJECTIVE SYMPTOMS PRURITUS + SLEEP LOSS \_\_\_\_\_

**A/5 + 7B/2 + C**

CRITERIA	INTENSITY
Erythema	
Oedema/Papulation	
Oozing/Crust	
Excoriation	
Lichenification	
Dryness	

\* Dryness is evaluated on uninvolved areas

Visual analog scale (average for the last 3 days or nights)  
PRURITUS (0 to 10): \_\_\_\_\_  
SLEEP LOSS (0 to 10): \_\_\_\_\_

**MEANS OF CALCULATION**  
INTENSITY ITEMS (average representative area)  
0 = absence  
1 = mild  
2 = moderate  
3 = severe

**10**





# Patient-Reported Outcomes to Assess M-S AD Burden and Quality of Life



Any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else.

**HEALTH-RELATED QOL**

**SELF-EFFICACY**

**SYMPTOM INDICES**

**WILLINGNESS TO CHANGE**

**ADHERENCE TO MEDICATIONS**

**SATISFACTION OF CARE**

**SOCIAL HEALTH**

**VALUE OF TREATMENT**



7-item PRO measure scored over the patient's past week involving: itch, sleep, bleeding, weeping/oozing, cracking, flaking, and dryness/roughness

Demonstrated: \_\_\_\_\_



Valid

POEM Scoring	
No days	0
1 – 2 days	1
3 – 4 days	2
5 – 6 days	3
Every day	4

POEM Interpretation	
0 to 2	Clear or almost clear
3 to 7	Mild eczema
8 to 16	Moderate eczema
17 to 24	Severe eczema
25 to 28	Very severe eczema

25-item PRO measure to identify mental and emotional stimulation, physical and emotional stability, security, sharing and belonging, self-esteem, personal development, and fulfillment

Demonstrated:

- ✓ Valid
- ✓ Consistent

QoLIAD Scoring	
Applies	1
Does not apply	0
High scores indicates low quality of life	

I can't wear the clothes I want to wear.

I don't want people to see my skin.

I am embarrassed about my appearance.





# Strategies to Collecting Quality of Life Data in Clinical Practice



- Use tablet computers to use in collecting and scoring patient-reported outcomes while patients wait to see the provider
- Allow patients to collect outcomes from home before or after an office visit can streamline the process
- Computer adaptive testing can address logistical challenges because it reduces time spent collecting non-applicable data
- Maximize data collection via electronic health records with downloadable reports





# Multidisciplinary Team Approach to Flare Event Prevention



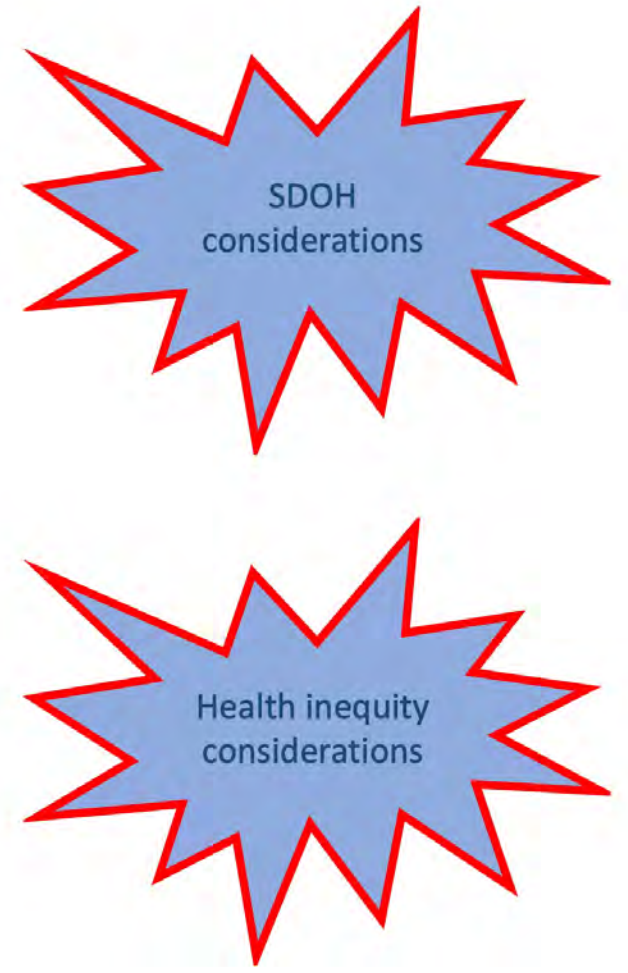
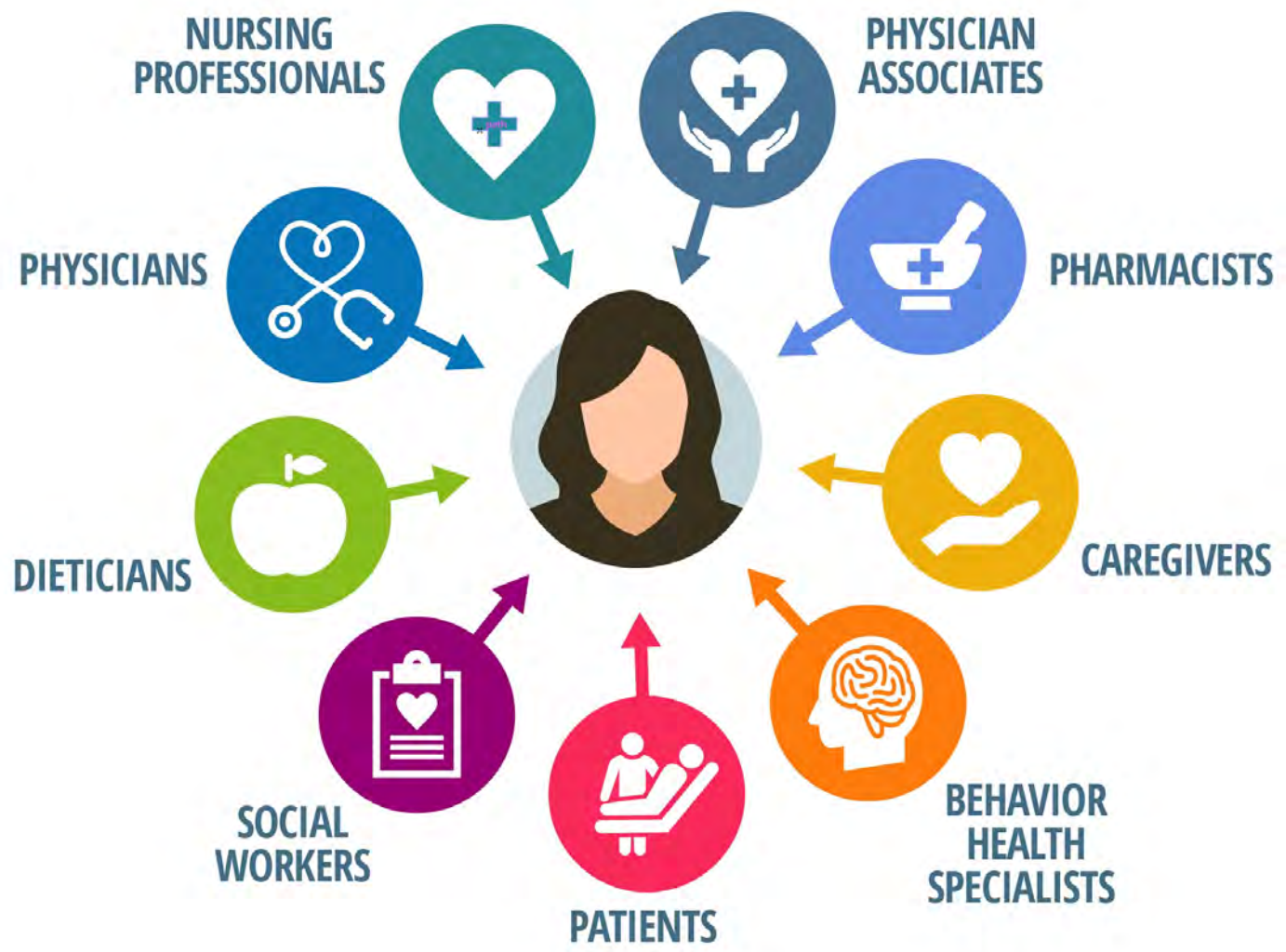
- Flares vary depending on the individual, frequency, severity, and sites of disease and can be either reactive or proactive
- Flares can be associated with secondary skin infections, which may require additional treatment

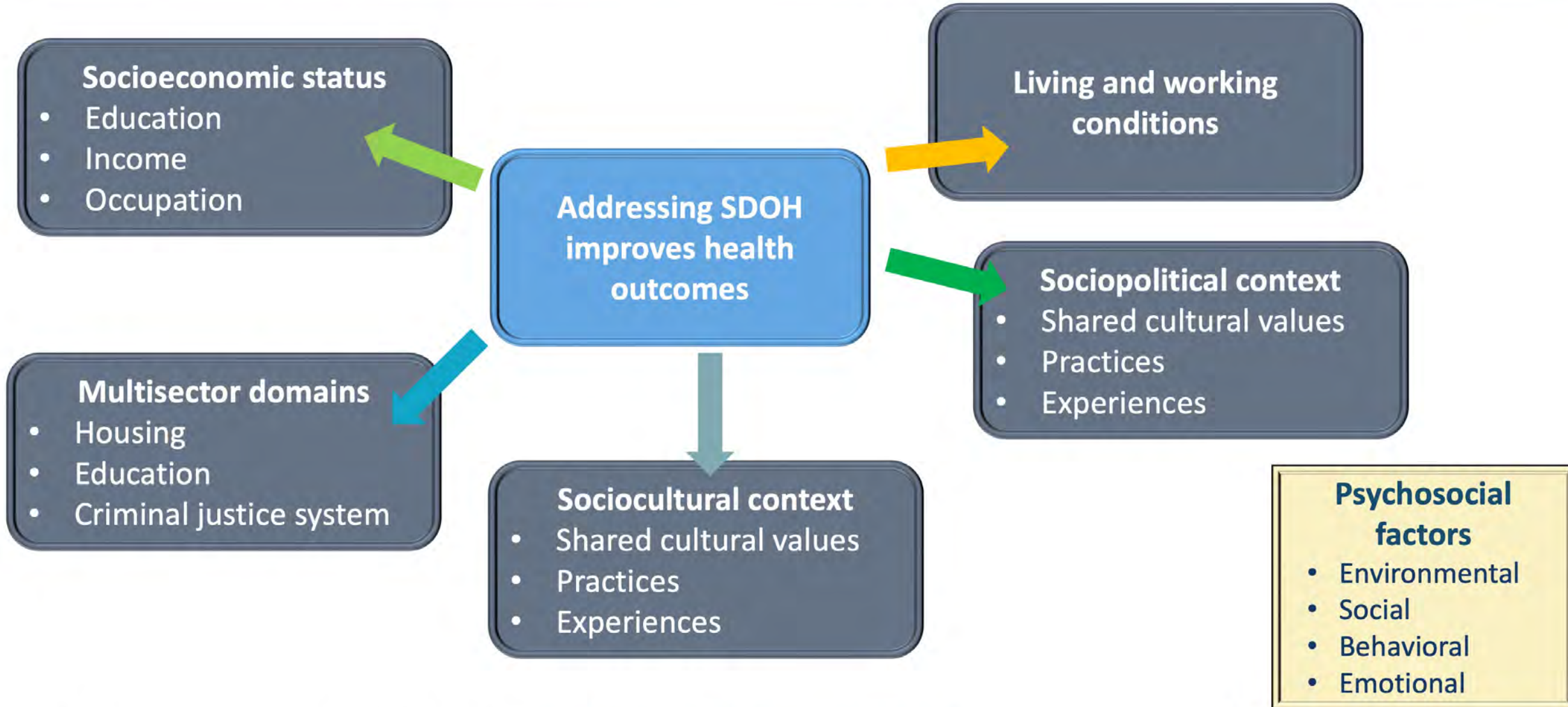
Providing structured educational programs for both patients and caregivers can help to facilitate an understanding of M-S AD treatment and management goals, including the appropriate use of therapies, and improve treatment adherence and reduce misconceptions





# Multidisciplinary Teams in the Management of M-S AD to Address QOL Factors







Joint process between healthcare providers and patients based on evidence-based information and a patient's preferences, beliefs, and values

- > Outcomes
- > Benefits
- > Risks
- > Uncertainties

Empowers patients to make decisions about the treatment and care that is right for them at that time, including choosing to continue with their current treatment or choosing no treatment at all

**E**

**EFFICACY**

Speed, depth,  
duration,  
remission?

**A**

**ACCESSIBILITY**

Cost, route,  
time

**S**

**SAFETY**

Adverse events  
that impact  
health

**T**

**TOLERABILITY**

Adverse events,  
important but not  
dangerous

**E**

**EFFICACY**

Speed, depth,  
duration,  
remission?

**S**

**SAFETY**

Adverse events  
that impact  
health

**T**

**TOLERABILITY**

Adverse events,  
important but not  
dangerous

**A**

**ACCESSIBILITY**

Cost, route,  
time

**R**

**REMISSION**

Stopping  
medication or  
lowering dose or  
frequency





# Enhancing Patient Engagement in the Treatment and Management of M-S AD



Lack of diversity is a barrier to the interpretation of safety and efficacy data across population subgroups, which is imperative in reducing disparities and advancing health equity

## Barriers

- Medical mistrust
- Lack of representation among clinical trials
- Patient access and insurance coverage
- Negative beliefs, norms, and attitudes

## Solutions

- Provide patient education to increase interest in decision-making
- Encourage participations in clinical trials
- Improve representation among investigators and clinical research staff





# Health Equity in the Treatment and Management of M-S AD



Shift in focus on quality of care should yield:

Achieved patient goals and clinical effectiveness

Perceived enhancement in care received

Improved physical, mental, and emotional well-being

Better understanding of patient  
experience and health outcomes

Make informed, appropriate  
treatment decisions





# VIBE Framework to Make Equitable Decisions with Patients



## Views

- Is the patient view being considered?

## Inclusion

- Has the necessary time been taken to hear concerns and needs of the patient?

## Benefits and Burdens

- How will the patient benefit from this decision?
- What harm may be done by this decision?

## Equity

- Does the decision lead to an equitable situation for the patient?

The VIBE framework provides questions that should be asked throughout conversations with patients to make equitable decisions regarding treatment and management choices



- Systemic biologic therapy options are an effective and safe option for patients with M-S AD for preventing flare events and provide long-term disease maintenance
- Prevention and control of flare events can have a substantial impact on patient quality of life and relieving the M-S AD burden
- Shared decision-making is a beneficial tool to address treatment selection, modifications, or intensification in conjunction with the needs of the patient



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