2024 Eastern Allergy Conference

Atopic Dermatitis: Best of Guidelines & Yardstick

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Learning Objectives

Upon completion of this learning activity, participants should be able to:

1. Recognize strength and certainty of evidence of treatments for atopic dermatitis from the 2023 Atopic Dermatitis Management AAAAI/ACAAI Joint Task Force on Practice Parameters Guidelines
2. Approach therapy of patients with atopic dermatitis through shared decision making utilizing recommendations from the most recent AAAAI/ACAAI JTF Guidelines
3. Utilize Expert Commentary from the Atopic Dermatitis Yardstick Update to inform and manage patients with atopic dermatitis

Atopic dermatitis

- The most common inflammatory chronic skin disease seen in both developed and developing countries
- Significant impact on QoL of patients and caregivers
- Often associated with both atopic & nonatopic comorbidities
- Not “outgrown” in a significant number of patients

Evolution of our AD Practice Parameter

1997

Disease management of atopic dermatitis: a practice parameter

These parameters were developed by the Joint Task Force on Practice Parameters, representing the American Academy of Allergy, Asthma and Immunology, the American College of Allergy, Asthma and Immunology, and the Joint Council of Allergy, Asthma and Immunology*

The American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI) have jointly accepted responsibility for establishing atopic dermatitis parameters. Because this document incorporated the efforts of many participants, no single individual, including those who served on the Joint Task Force, is authorized to provide an official AAAAI or ACAAI interpretation of these Practice Parameters. Any request for information about or an interpretation of these Practice Parameters by the AAAAI or the ACAAI should be directed to the Executive Offices of the AAAAI, the ACAAI, and the Joint Council of Allergy, Asthma and Immunology.

Expert Opinion

2004

Practice parameter

Disease management of atopic dermatitis: an updated practice parameter

Donald Y. M. Leung, MD*; Richard A. Nicklas, MD†; James T. Li, MD‡; I. Leonard Bernstein, MD§; Joann Blessing-Moore, MD¶; Mark Boguniewicz, MD‖; Jean A. Chapman, MD**; David A. Khan, MD††; David Lang, MD‡‡; Rufus E. Lee, MD§§; Jay M. Portnoy, MD¶¶; Diane E. Schuller, MD‖‖; Sheldon L. Spector, MD***; and Stephen A. Tilles, MD†††

Joint Task Force revised the initial draft into a working draft of the document, which included a review of the medical literature using a variety of search engines such as PubMed. Published clinical studies were rated by category of evidence and used to establish the strength of a clinical recommendation

2012

FEBRUARY 2012

Atopic dermatitis: A practice parameter update 2012

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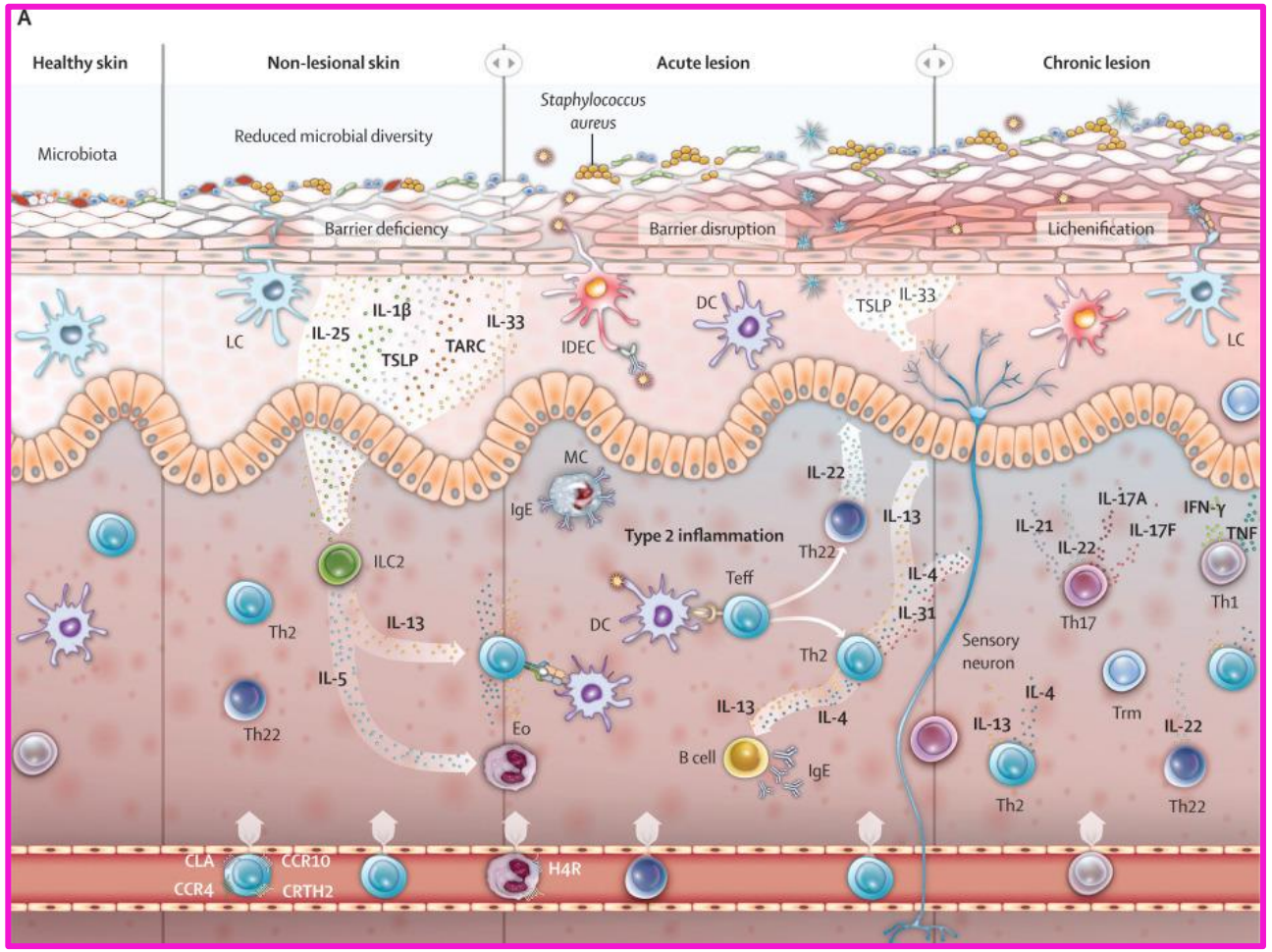
Joint Task Force Contributors: David Bernstein, MD, Joann Blessing-Moore, MD, David Khan, MD, David Lang, MD, Richard Nicklas, MD, John Oppenheimer, MD, Jay Portnoy, MD, Christopher Randolph, MD, Diane Schuller, MD, Sheldon Spector, MD, Stephen Tilles, MD, and Dana Wallace, MD

Included dermatologists (US&EU) & psychologist

Table 1. Classification of Evidence and Recommendations*

Category of evidence	
Ia	Evidence from meta-analysis of randomized controlled trials
Ib	Evidence from at least 1 randomized controlled trial
IIa	Evidence from at least 1 controlled study without randomization
IIb	Evidence from at least 1 other type of quasi-experimental study
III	Evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case-control studies
IV	Evidence from expert committee reports or opinions or clinical experience of respected authorities or both
LB	Evidence from laboratory-based studies†
Strength of recommendation	
A	Directly based on category I evidence
B	Directly based on category II evidence or extrapolated from category I evidence
C	Directly based on category III evidence or extrapolated from category I or II evidence
D	Directly based on category IV evidence or extrapolated from category I, II, or III evidence
E	Directly based on category LB evidence†
F	Based on consensus of the Joint Task Force on Practice Parameters†

Insights into pathophysiology of atopic dermatitis identify therapeutic targets



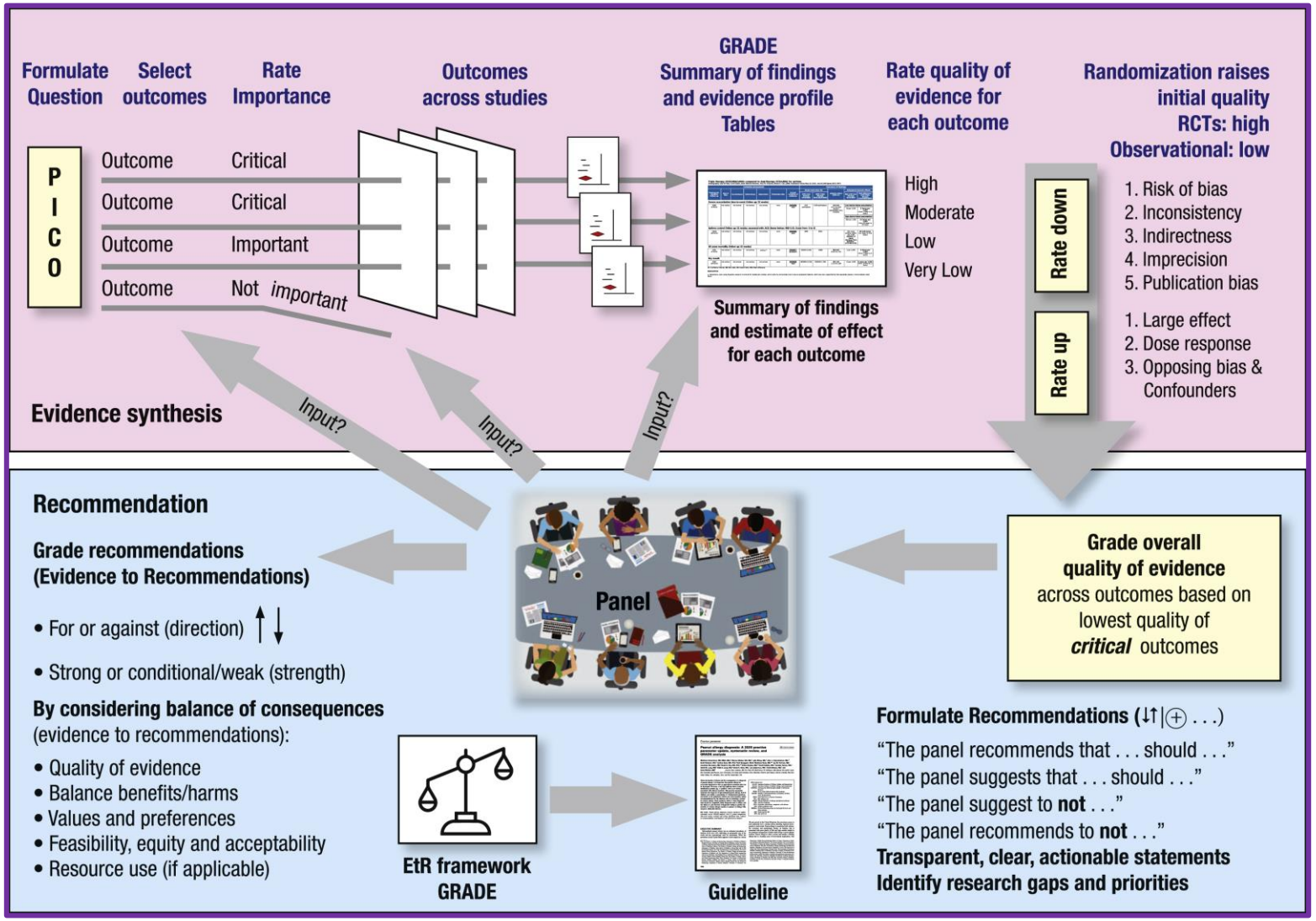
Lancet 2020;396:345-60

Translating evidence to optimize patient care using GRADE

- Optimal evidence-based clinical practice requires systematic summaries of best available evidence, including ratings of quality of that evidence, and is facilitated by availability of trustworthy guidelines
- Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) focuses on systematic summaries of best evidence, systematic reviews and trustworthy guidelines, and emphasizes a structured approach to determining quality (certainty) of bodies of evidence, absolute magnitude of effects of desirable and undesirable consequences (benefits and harms), and use of evidence to develop clinical recommendations
- Adopted by over 110 organizations worldwide… GRADE is foundational to optimal interpretation of research evidence and its application in clinical practice

J Allergy Clin Immunol Pract 2021;9:4221

Schematic view of the GRADE approach to synthesizing evidence and developing recommendations



J Allergy Clin Immunol Pract 2021;9:4221

GRADE for strength of recommendations

Strong recommendation

- Benefits clearly outweigh risks/hassle/cost
- Risk/hassle/cost clearly outweighs benefit

Weak (conditional) recommendation

- Low quality evidence
- Upsides and downsides of management options closely balanced

Additional key considerations: costs, equity, values and preferences

Implications of strong and weak recommendations for different users of guidelines

Meaning	Strong recommendation	Weak (conditional) recommendation
For patients	All or almost all individuals in this situation would want the recommended course of action.	Most individuals in this situation would want the suggested course of action, but many would not.
For clinicians	All or almost all individuals should receive the recommended course of action. Formal decision aids are not likely needed to help individuals make decisions consistent with their values and preferences.	Different choices will be appropriate for different patients, and the clinician must help patients arrive at a management decision consistent with their values and preferences. Decision aids may be useful helping individuals making decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working toward a decision.
For policy-makers	The recommendation can be adapted as policy in most situations, including for use as performance indicators. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Policy-making will require substantial debates and involvement of many stakeholders. Policies are also more likely to vary among regions. Performance indicators would have to focus on the fact that adequate deliberation about the management options has taken place.

J Allergy Clin Immunol Pract 2021;9:4221

AAAAI/ACAAI JTF AD Guidelines 2023

- AAAAI/ACAAI JTF panel - multidisciplinary workgroup (allergists-immunologists, dermatologists, epidemiologists, pediatrician, family medicine, psychologists, pharmacist, physical therapist, research methodologist, patients, caregivers, patient advocates)

- ***AAAAI/ACAAI JTF Atopic Dermatitis Guideline Panel:*** Derek K. Chu MD PhD & Lynda Schneider MD*, Rachel Netahe Asiniwasis MD MSc, Mark Boguniewicz MD, Anna De Benedetto MD, Kathy Ellison M Ed, Winfred T. Frazier MD MPH, Matthew Greenhawt MD MBA MSc, Joey Huynh MPT, Elaine Kim BScPhrm RPh, Jennifer LeBovidge PhD, Mary Laura Lind PhD, Peter Lio MD, Stephen A. Martin MD EdM, Monica O'Brien MBS, Peck Y. Ong MD, Jonathan I. Silverberg MD MPH PhD, Jonathan M. Spergel MD PhD, Julie Wang MD, Kathryn E. Wheeler MD, Gordon H. Guyatt MD MSc OC
  Patient Groups: Global Parents for Eczema Research - Korey Capozza MPH, National Eczema Association - Wendy Smith Begolka MBS
- ***Evidence in Allergy Group:*** Alexandro W. L. Chu BHSc, Irene X. Zhao BHSc, Lina Chen MD, Paul Oykhman MD MSc, Layla Bakaa BSc
- ***AAAAI/ACAAI Joint Task Force on Practice Parameters:*** David Golden MDCM, Marcus Shaker MD MS, Jonathan A. Bernstein MD, Matthew Greenhawt MD MBA MSc, Caroline C. Horner MD MSCI, Jay Lieberman MD, David Stukus MD, Matthew A. Rank, Julie Wang MD, Anne Ellis MD MSc, Derek K. Chu MD PhD, Elissa Abrams, Dennis Ledford MD
- **Collaborators (including patient and caregiver partners):** Teresa Alabata, Julia Baribeau, Kelly Barta, Melissa Cowley, Katherine Ellison, Adrienne Forest, Megan Fritz, Silena Gaines, Beth Ann George, Ashley Nicole Hamlin, Jim Hewlett, Joey Huynh, Stefan Jevtic, Jennifer Larosa, Amanda Isabel Lopez, Andrea Lozada, Harrison Nelson, Monica O'Brien, Jessen Rajan, Justin Ramos, Sashah Sheikh, Harriet Thomas, Marylaura Thomas, Alvin Gutierrez, Jeffrey Pernica, Jasvinder Singh, Allergy & Asthma Network - De De Gardner, Global Allergy & Airways Patient Platform - Tonya A. Winders. Evidence in Allergy group evidence synthesis team members and additional collaborators appear in acknowledgements.

AAAAI/ACAAI JTF AD Guideline 2023 Conflict of Interest

- When panel members had potential conflicts of interest pertaining to specific recommendations, the management process included recusal from decision-making for those recommendations. While they were encouraged to contribute to discussions regarding the scientific evidence summaries, practical issues, and implementation considerations, panel members with a current direct financial interest in a commercial entity with any product that could be affected by the guidelines **and with material intellectual (non-financial) conflicts were recused from making judgments about relevant recommendations.**

Atopic Dermatitis PICO questions: Problem, Intervention, Comparison, Outcome

1. Do bleach baths improve severity of atopic dermatitis?
2. Are elimination diets effective and safe for the treatment of atopic dermatitis?
3. Does allergen immunotherapy improve atopic dermatitis?
4. Are topical calcineurin inhibitors effective and safe for atopic dermatitis when compared to topical steroids?
5. Which systemic immunomodulatory treatments (eg. biologics) should clinicians prescribe to treat atopic dermatitis?

Bleach baths for atopic dermatitis: A systematic review and meta-analysis including unpublished data, Bayesian interpretation and GRADE

- 10 RCTs enrolled 307 pts (median of mean age 7.2 years, EASI baseline mean of means 27.57) for a median of 6 wks (range, 4-10)
- Bleach baths probably improve AD severity (32% improved EASI by 50% vs 22% no bleach; moderate certainty) and may slightly reduce skin S. aureus colonization (low certainty)
- AEs, mostly dry skin and irritation, along with itch, pt-reported disease severity, sleep quality, QoL, and risk of AD flares not clearly different between groups and of low to very low certainty
- In pts with moderate-to-severe AD, bleach baths probably improve clinician-reported severity by a relative 22%.* One in 10 will likely improve severity by 50%

Ann Allergy Asthma Immunol 2022;128:660

* relative decrease of 22% in AD severity provides pt-important relief in those with high disease activity (eg, pt with EASI of 40 might improve by 8.8 points) and likely will be of trivial benefit in pt with low disease activity (eg, pt with EASI of 10 might improve by 2.2 points)

Is there a role for dietary elimination as a treatment for AD?

- Patients with severe AD have a higher risk for food allergies than those without AD
- Food allergy testing and elimination diets are often considered in an effort to improve AD control
- However, recent evidence suggests that oral tolerance to food allergens is promoted through frequent, and perhaps high-dose, oral exposure. Avoidance of food allergens may therefore lead to development of IgE-mediated food allergy

J Allergy Clin Immunol Pract 2022;10:2657

Characteristics of included studies

Study (first author and year)	Type of randomized control trial	n	Mean age, y (SD)	% Female	Mean SCORAD [SD]	% Skin prick test or serum IgE to eliminated food(s)	% Reaction on history or oral food challenge to eliminated food(s)	Excluded foods based on testing or oral food challenge	Intervention	Control	Duration, wk
Neild, 1986[43]	Crossover	53	NR (range, 1-32)	54.7	NR	20	NR	No	CM/egg exclusion plus soy-based milk substitute	Normal diet or CM/egg exclusion plus dried egg and CM	6
Atherton, 1978[52]	Crossover	36	5.5 (1.6)	30	NR	95	20	No	CM/egg exclusion plus soy-based milk substitute	CM/egg exclusion plus dried egg and CM	4
Lever, 1998[46]	Parallel	62	1.2 (0.8)	49.1	12.6 (6.1)*	100	11	Yes	Egg exclusion	Normal diet	4
Mabin, 1995[45]	Parallel	85	4.8 (2.1)	43.5	26.1 (12.2)*	NR	NR	No	Few-foods diet (one meat, rice, potato, one brassica, and one fruit, whey or casein hydrolysate formula)	Normal diet	6
Ridd, 2021[48]	Parallel	84	2.7 (1.2)	47.5	3.5 (3.9)§	14†	NR	Yes	Test-guided elimination (CM, egg, peanut, cashew, cod, and wheat)	Normal diet	2-4‡
Munkvad, 1984[44]	Parallel	33	29 (NR)	65.2	NR	NR	52	No	Elemental diet	Placebo diet (foodstuffs and liquids consumed by inpatients of hospital)	3
Leung, 2004[47]	Crossover	15	1.5 (1.6)	46.7	21.4 (15.7)	33	NR	No	AA-based formula	Preexisting CM or soy formula	6
Isolauri, 1995[51]	Parallel	45	0.5 (0.3)	NR	19.0 (11.0)	51	100	Yes	AA-based formula	Extensively hydrolyzed whey formula	32
Niggemann, 2001[42]	Parallel	73	0.5 (0.1)	32.9	24.6 (19.1)	51	100	Yes	AA-based formula	Extensively hydrolyzed whey formula	24
Jin, 2011[54]	Parallel	113	0.3 (0.1)	27.9	37.6 (10.7)	0	0	No	Partially hydrolyzed CM formula	Regular CM formula	12

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Dietary elimination for the treatment of atopic dermatitis: A systematic review and meta-analysis

- 10 RCT (n = 599); baseline median of study mean age, 1.5 yrs; median of study mean SCORAD 20.7 (3.5-37.6)
- Compared with no dietary elimination, low-certainty evidence showed that dietary elimination may slightly improve eczema severity (50% vs 41% without dietary elimination improved SCORAD by a minimally important difference of 8.7 points
- Dietary elimination may lead to slight, potentially unimportant improvement in eczema severity, pruritus, and sleeplessness in pts with mild to moderate AD. This must be balanced against potential risks for indiscriminate elimination diets including developing IgE-mediated food allergy and withholding more effective treatments for AD

J Allergy Clin Immunol Pract 2022;10:2657

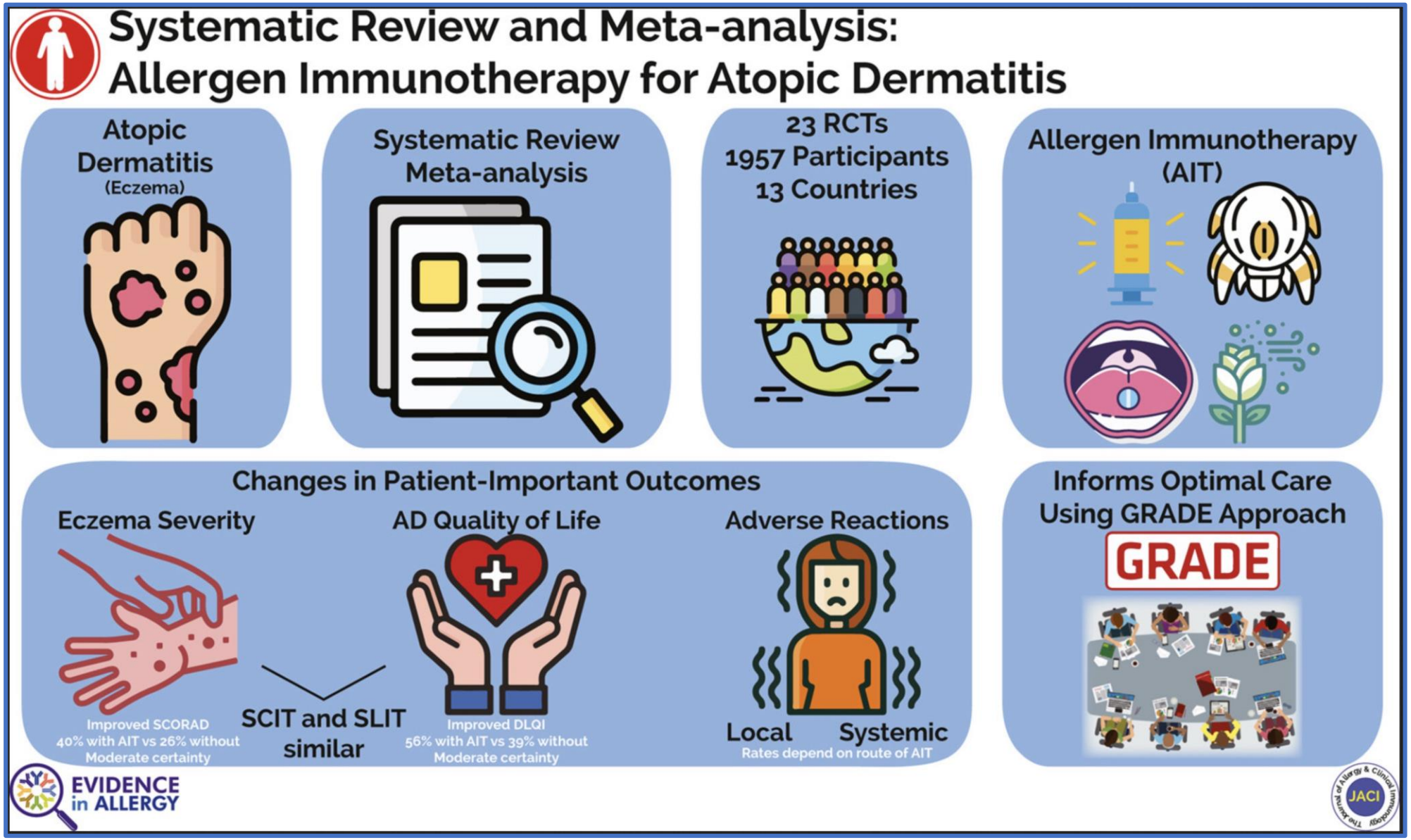
Allergen immunotherapy for atopic dermatitis: A systematic review and meta-analysis of benefits and harms

- Precise role that environmental allergens (e.g. HDM, pollens) play in AD remains unclear
- Previous studies of AIT for AD found mixed results, so the benefits and harms remain uncertain
- Previous practice parameter noted that allergen immunotherapy could be effective for atopic dermatitis

Allergen immunotherapy for atopic dermatitis: A systematic review and meta-analysis of benefits and harms

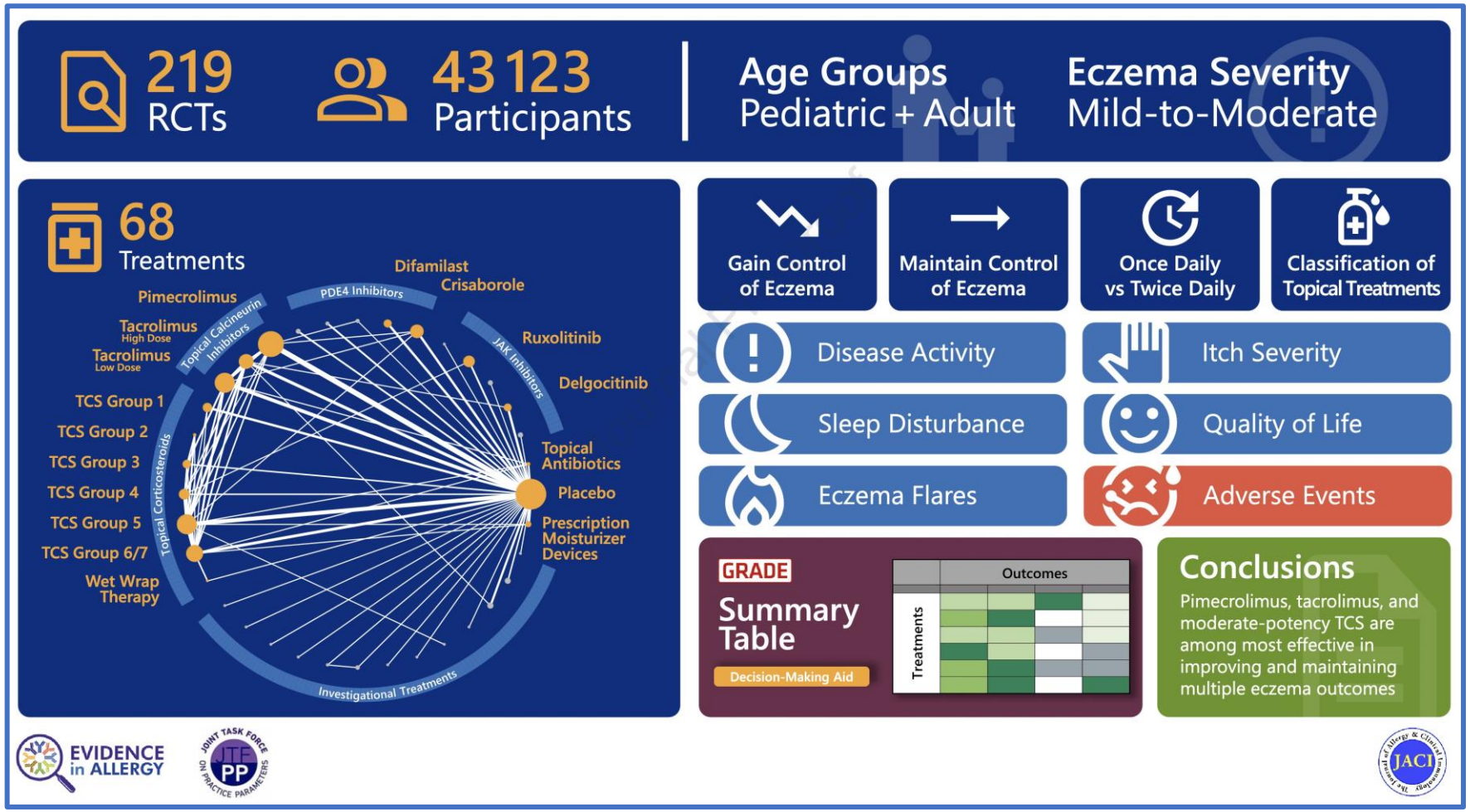
- 23 RCTs including 1957 adult and pediatric patients sensitized primarily to HDM showed that add-on SCIT and SLIT have similar relative and absolute effects and likely result in important improvements in AD severity defined as 50% reduction in SCORAD and QoL defined as improvement in DLQI by 4 points or more
- Both outcomes moderate-certainty
- Relative benefits similar for SCIT & SLIT, for children & adults, and across severities
- Both routes of AIT increased adverse events (SCIT>SLIT)
- Findings support a multidisciplinary and shared-decision making approach to optimally managing AD

J Allergy Clin Immunol 2023;151:147



J Allergy Clin Immunol 2023;151:147

Topical treatments for atopic dermatitis (eczema): systematic review and network meta-analysis of randomized trials



J Allergy Clin Immunol 2023;152:1493

Network meta-analysis—Summary table of comparative effects of topical treatments on patient-important outcomes for controlling atopic dermatitis

		Atopic Dermatitis Severity SCORAD (0–103)	Itch NRS (0–10)	Sleep Disturbance NRS (0–10)	Eczema-Related Quality of Life DLQI (0–30)	Atopic Dermatitis Flare	Any Adverse Event	Discontinuation due to Adverse Event
		MD (95%CrI)	MD (95%CrI)	MD (95%CrI)	MD (95%CrI)	RD (95%CrI)	RD (95%CrI)	RD (95%CrI)
Baseline		25.96	5.40	4.89	9.43	95 per 1000	305 per 1000	28 per 1000
JAK Inhibitors								
Delgocitinib Cream		-5.64 (-8.36 to -2.91)						
Delgocitinib Ointment		-9.98 (-13.81 to -6.15)	-1.47 (-2.17 to -0.77)		-7.41 (-10.16 to -4.66)	-74 (-84 to -51)	-37 (-93 to 25)	-21 (-25 to -15)
Ruxolitinib		-4.82 (-5.65 to -4.00)	-2.11 (-2.96 to -1.26)	-0.57 (-1.15 to 0.02)	-4.82 (-6.35 to -3.44)	-74 (-84 to -51)	-37 (-93 to 25)	-21 (-25 to -15)
PDE4 Inhibitors								
Crisaborole		-4.89 (-8.69 to -1.08)	-0.64 (-1.11 to -0.15)		-1.23 (-2.34 to -0.09)	-59 (-81 to -12)	43 (-32 to 124)	9 (-15 to 58)
Difamilast		-5.41 (-9.12 to -1.68)	-1.26 (-2.09 to -0.42)		-1.55 (-3.00 to -0.03)	-45 (-71 to 2)	-41 (-110 to 39)	-17 (-22 to -9)
Lotamilast		-2.89 (-8.84 to 3.06)	0.04 (-1.53 to 1.62)			-23 (-80 to 196)	6 (-153 to 211)	-10 (-25 to 28)
Roflumilast		-2.15 (-4.20 to -0.12)	-1.55 (-3.39 to 0.29)				177 (-38 to 408)	23 (-27 to 367)
Topical Calcineurin Inhibitors								
Pimecrolimus		-7.23 (-8.76 to -5.72)	-1.61 (-2.00 to -1.21)	-2.13 (-3.15 to -1.01)	-1.44 (-2.38 to -0.62)	-53 (-66 to -39)	21 (-15 to 59)	-11 (-16 to -3)
Tacrolimus 0.1% (High Dose)		-13.05 (-15.15 to -10.95)	-2.27 (-2.84 to -1.70)		-3.65 (-5.59 to -1.83)	-70 (-85 to -41)	29 (-18 to 79)	-15 (-19 to -10)
Tacrolimus 0.03% (Low Dose)		-9.38 (-11.22 to -7.55)	-1.97 (-2.44 to -1.50)	-0.17 (-1.97 to 1.60)	-1.72 (-3.47 to -0.02)	-70 (-85 to -41)	29 (-18 to 79)	-15 (-19 to -10)
Topical Corticosteroids								
Conventional TCS Potency Classification ▲	High	**TCS Group 1**	-17.81 (-21.32 to -14.30)	-2.34 (-4.37 to -0.32)				-96 (-179 to 11)	-25 (-27 to -18)
		TCS Group 2	-13.82 (-18.74 to -8.89)	-3.39 (-5.02 to -1.76)				-16 (-278 to 479)	
	Medium (Moderate or Mid)	**TCS Group 3**	-11.57 (-14.80 to -8.37)	-2.37 (-3.18 to -1.57)	-0.22 (-2.23 to 1.72)	-1.23 (-3.71 to 1.17)	-11 (-83 to 312)	-62 (-138 to 24)	-12 (-23 to 9)
		TCS Group 4	-12.26 (-15.02 to -9.50)	-2.62 (-3.26 to -1.98)		-5.96 (-8.53 to -3.56)	-66 (-92 to 49)	-76 (-142 to -1)	85 (-15 to 381)
		TCS Group 5	-8.46 (-10.90 to -6.03)	-2.09 (-2.54 to -1.64)	-0.92 (-2.57 to 0.71)	-3.82 (-6.21 to -1.44)	-83 (-92 to -57)	-102 (-138 to -63)	-18 (-23 to -12)
	Low	**TCS Group 6/7**	-4.68 (-7.10 to -2.29)	-1.33 (-1.89 to -0.76)	0.32 (-1.51 to 2.10)	-1.48 (-3.38 to 0.34)	-13 (-78 to 234)	-33 (-105 to 47)	-6 (-18 to 13)
Other								
Antibiotic		-1.48 (-6.77 to 3.81)	-0.32 (-2.15 to 1.51)		-1.33 (-3.35 to 0.69)	-56 (-94 to 499)	50 (-153 to 306)	229 (-5 to 834)
Prescription Moisturizers		-1.94 (-4.83 to 0.95)	-1.63 (-2.28 to -0.97)			-60 (-82 to -5)	-8 (-111 to 111)	-10 (-23 to 17)
Tapinarof		-11.26 (-16.55 to -6.03)	-1.93 (-2.99 to -0.89)			-64 (-88 to 20)	155 (19 to 299)	-14 (-23 to 9)

High to moderate certainty evidence	Low to very low certainty evidence
Among the most effective	Possibly among the most effective
Among the intermediate (superior) effective	Possibly among the intermediate (superior) effective
Among the intermediate (inferior) effective	Possibly among the intermediate (inferior) effective
Not clearly different from control	Possibly not clearly different from control

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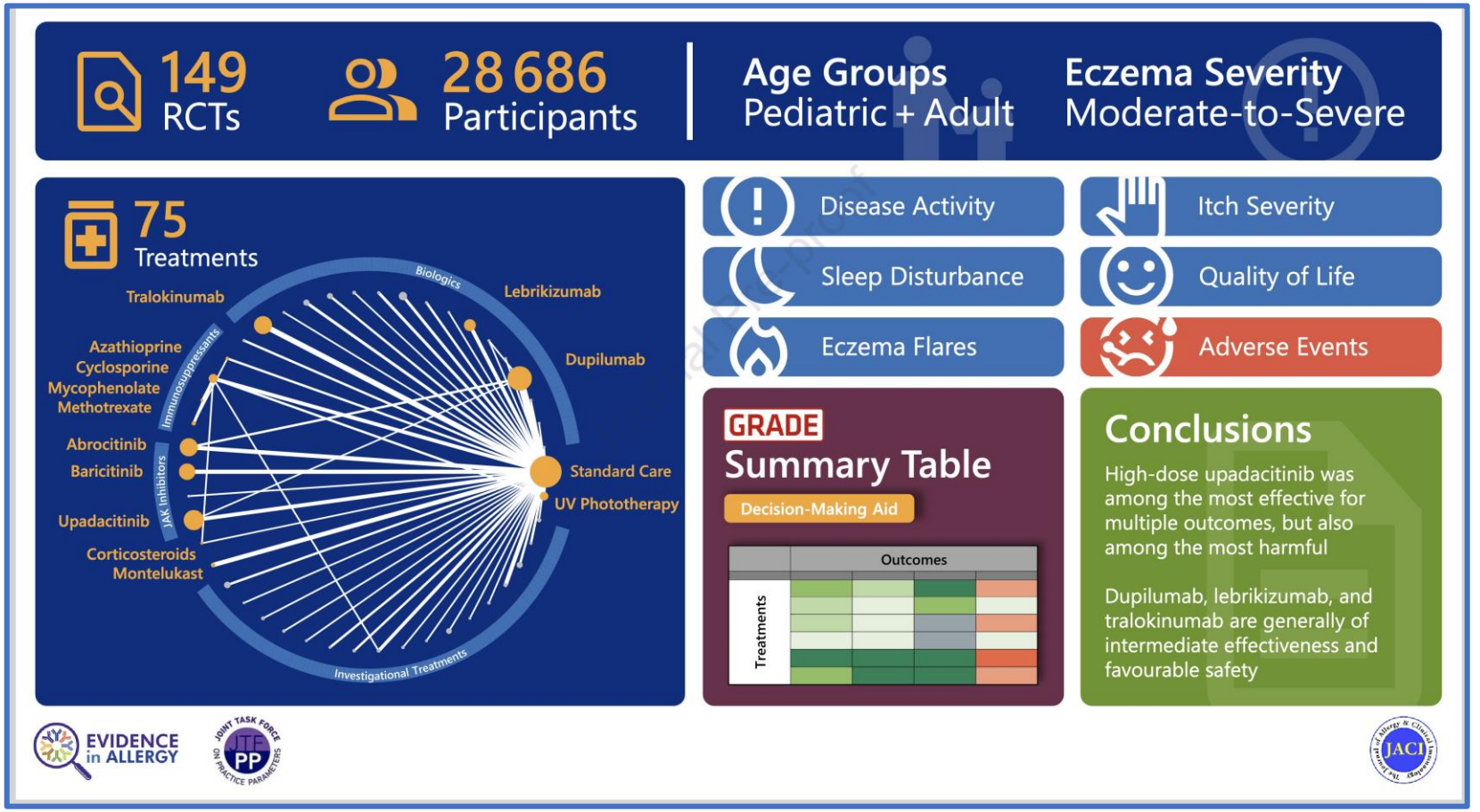
Systemic treatments for atopic dermatitis (eczema): systematic review and network meta-analysis of randomized trials



J Allergy Clin Immunol 2023;152:1470

Summary of comparative effects of systemic treatments on patient-important outcomes for atopic dermatitis (eczema)

	Atopic Dermatitis Severity EASI (0–72)	Patient-Reported AD Severity POEM (0–28)	Itch NRS (0–10)	Sleep Disturbance NRS (0–10)	Eczema-Related Quality of Life DLQI (0–30)	Atopic Dermatitis Flares	Any Adverse Event	Serious Adverse Event
	MD (95%CrI)	MD (95%CrI)	MD (95%CrI)	MD (95%CrI)	MD (95%CrI)	RD (95%CrI)	RD (95%CrI)	RD (95%CrI)
Baseline	29.00	20.87	7.10	5.30	14.74	139 per 1000	592 per 1000	22 per 1000
Cytostatics and Immunophilin Agents								
Azathioprine	-4.95 (-9.70 to -0.22)		-1.41 (-2.75 to -0.06)	-1.30 (-2.88 to 0.28)	-3.05 (-6.30 to 0.19)	-108 (-139 to 644)	193 (-541 to 404)	5 (-21 to 852)
Cyclosporine 4–5mg/kg (High Dose)	-13.38 (-17.01 to -9.83)		-2.05 (-2.79 to -1.33)	-1.45 (-2.37 to -0.58)	-8.34 (-12.54 to -4.11)		215 (22 to 324)	0 (-18 to 87)
Cyclosporine 2–3mg/kg (Low Dose)	-6.73 (-10.96 to -2.52)		-0.96 (-1.81 to -0.14)	-0.12 (-0.97 to 0.68)	-5.93 (-9.81 to -2.07)	0 (-136 to 757)	138 (-106 to 294)	35 (-18 to 516)
Methotrexate	-6.88 (-11.93 to -1.88)		-1.30 (-3.40 to 0.79)	-0.30 (-2.73 to 2.13)	-3.67 (-7.40 to 0.03)	-86 (-138 to 672)	177 (-154 to 343)	7 (-21 to 566)
Mycophenolate	-8.71 (-16.69 to -0.74)							
Monoclonal Antibodies								
Astegolimab	4.47 (-5.17 to 14.10)		0.66 (-1.20 to 2.54)			-64 (-122 to 133)	-169 (-377 to 71)	37 (-19 to 591)
Benralizumab	0.13 (-10.79 to 10.99)							
Dupilumab (Standard Dose)	-10.72 (-12.30 to -9.19)	-7.05 (-7.64 to -6.50)	-2.14 (-2.38 to -1.90)	-1.84 (-2.26 to -1.42)	-4.56 (-5.18 to -3.98)	-74 (-83 to -64)	-20 (-50 to 10)*	-11 (-14 to -7)
Fezakinumab	-4.98 (-13.97 to 4.02)						-52 (-312 to 188)	34 (-19 to 539)
Itepekimab	-3.82 (-11.33 to 3.68)		-1.30 (-2.74 to 0.13)			-55 (-105 to 57)		-13 (-21 to 55)
Lebrikizumab (Standard Dose)	-9.10 (-12.36 to -5.84)	-6.10 (-9.40 to -2.76)	-1.77 (-2.32 to -1.24)	-1.59 (-2.09 to -1.08)	-3.92 (-5.55 to -2.31)	-73 (-124 to 108)	70 (-48 to 171)*	-15 (-20 to 12)
Mepolizumab	-3.48 (-9.89 to 2.93)	-4.21 (-7.30 to -1.13)	-1.30 (-3.03 to 0.41)				-507 (-582 to -124)	-2 (-21 to 489)
Nemolizumab	-3.40 (-7.36 to 0.52)	-4.77 (-7.24 to -2.35)	-2.16 (-2.88 to -1.44)	-1.78 (-2.41 to -1.16)	-1.95 (-3.40 to -0.49)	3 (-42 to 66)	38 (-52 to 121)	4 (-13 to 51)
Omalizumab	0.17 (-6.81 to 7.23)	-0.51 (-3.59 to 2.51)			-4.01 (-6.76 to -1.22)	-20 (-104 to 194)	80 (-317 to 325)	0 (-15 to 45)
Tezepelumab	-2.13 (-6.98 to 2.68)		-0.57 (-1.95 to 0.81)				-66 (-258 to 118)	-8 (-18 to 32)
Tralokinumab (Standard Dose)	-6.45 (-8.67 to -4.27)	-4.47 (-5.37 to -3.58)	-1.08 (-1.51 to -0.65)	-0.93 (-1.36 to -0.49)	-2.36 (-3.21 to -1.51)	-57 (-72 to -40)	-1 (-43 to 40)*	-8 (-13 to 1)
Ustekinumab	1.58 (-5.01 to 8.27)		0.03 (-1.69 to 1.76)		-0.60 (-2.82 to 1.67)	-87 (-121 to 0)	-102 (-337 to 137)	-5 (-21 to 191)
Oral JAK Inhibitors								
Abrocitinib 200mg (High Dose)	-9.44 (-11.90 to -6.98)	-7.38 (-8.23 to -6.51)	-2.22 (-2.62 to -1.83)	-1.74 (-2.17 to -1.29)	-4.56 (-5.39 to -3.71)	-121 (-127 to -114)	85 (45 to 122)†	0 (-10 to 18)‡
Abrocitinib 100mg (Low Dose)	-6.89 (-9.49 to -4.28)	-4.69 (-5.62 to -3.74)	-1.40 (-1.82 to -0.99)	-0.96 (-1.40 to -0.51)	-2.81 (-3.73 to -1.92)	-93 (-105 to -78)	5 (-42 to 51)†	-1 (-11 to 16)‡
Baricitinib 2–4mg (High Dose)	-5.99 (-8.78 to -3.22)	-4.51 (-5.61 to -3.39)	-1.24 (-1.71 to -0.77)	-1.30 (-1.80 to -0.81)	-2.80 (-3.78 to -1.81)	-69 (-114 to 40)	60 (18 to 99)†	-6 (-13 to 6)‡
Baricitinib 1mg (Low Dose)	-3.47 (-6.81 to -0.12)	-2.21 (-3.60 to -0.80)	-0.69 (-1.27 to -0.11)	-0.91 (-1.52 to -0.29)	-1.48 (-2.72 to -0.23)	-34 (-110 to 176)	19 (-36 to 72)†	8 (-6 to 36)‡
Upadacitinib 30mg (High Dose)	-13.99 (-16.62 to -11.37)	-8.26 (-9.41 to -7.20)	-2.91 (-3.35 to -2.49)		-9.76 (-11.23 to -8.28)	-125 (-132 to -111)	108 (72 to 141)†	-4 (-11 to 7)‡
Upadacitinib 15mg (Low Dose)	-11.43 (-14.25 to -8.64)	-6.54 (-7.64 to -5.45)	-1.90 (-2.35 to -1.45)		-8.36 (-9.83 to -6.89)	-115 (-124 to -101)	55 (14 to 95)†	-5 (-12 to 7)‡
UV Light Therapy								
Narrow-Band UVB	-5.45 (-11.68 to 0.77)			-2.50 (-4.06 to -0.93)				
UVA/UVB Therapy	1.90 (-3.42 to 7.07)			-1.60 (-3.25 to 0.04)	-5.60 (-10.19 to -0.96)		-140 (-531 to 321)	36 (-21 to 874)
Other								
Oral Corticosteroid	-4.28 (-14.70 to 6.08)	-3.76 (-10.72 to 3.11)	-0.97 (-2.20 to 0.24)	-0.58 (-1.76 to 0.56)	-4.80 (-9.36 to -0.27)	133 (-134 to 824)		190 (-18 to 930)
Montelukast	-3.45 (-6.50 to -0.44)		0.71 (-0.54 to 1.95)	0.61 (-0.71 to 1.92)			-8 (-515 to 368)	42 (-19 to 614)

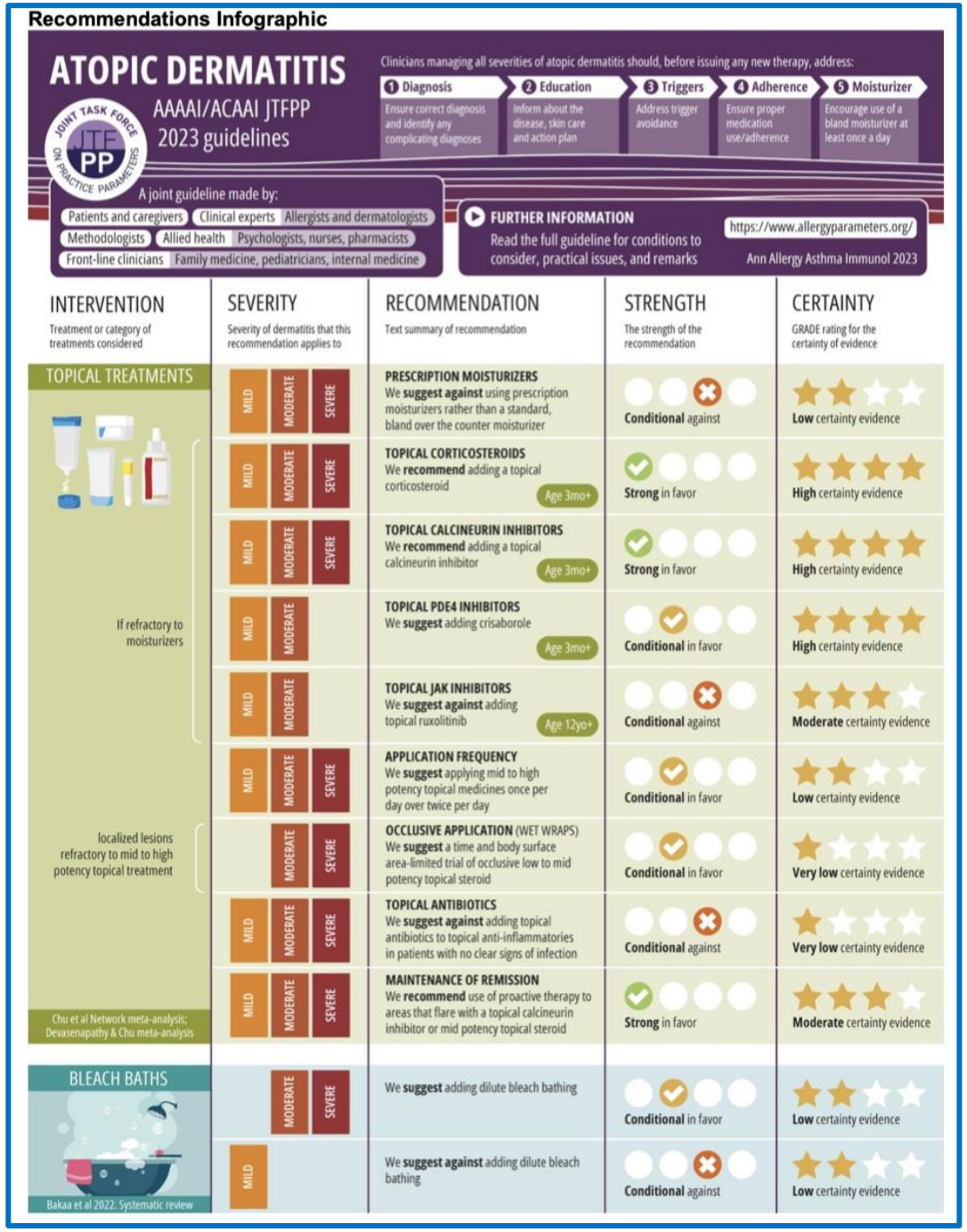
High to moderate certainty evidence	Low to very low certainty evidence
Among the most effective	Possibly among the most effective
Among the intermediate (superior) effective	Possibly among the intermediate (superior) effective
Among the intermediate (inferior) effective	Possibly among the intermediate (inferior) effective
Not clearly different from placebo	Possibly not clearly different from placebo
Among the intermediate harmful	Possibly among the intermediate harmful
Among the most harmful	Possibly among the most harmful

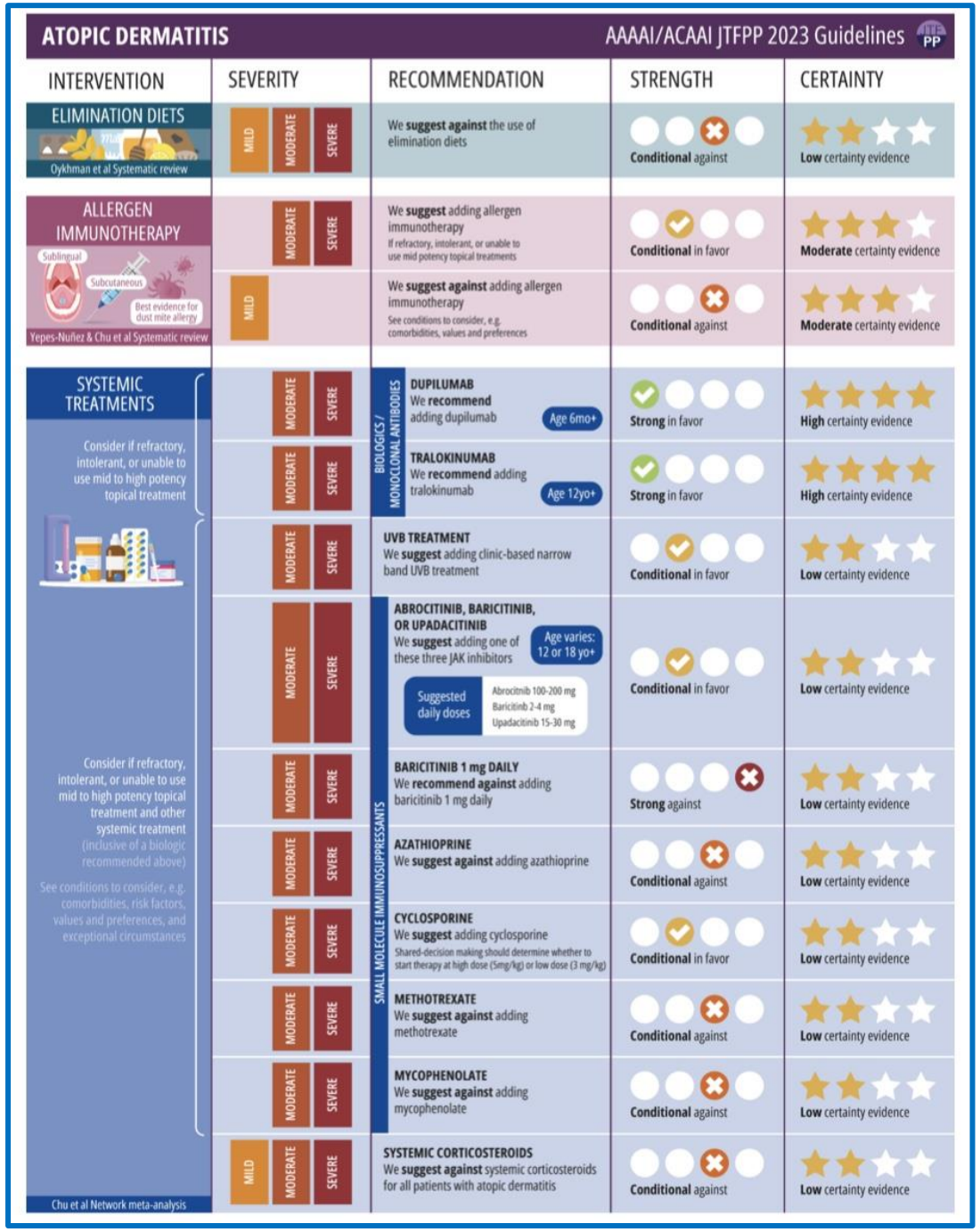
J Allergy Clin Immunol 2023;152:1470

Atopic Dermatitis (eczema) Guidelines: 2023 AAAAI/ACAAI Joint Task Force (JTF) on Practice Parameters GRADE- and Institute of Medicine-based recommendations

- Panel agreed on 25 treatment recommendations to gain and maintain control of AD for patients with mild, moderate, and severe AD
- Strong recommendations:
  - Adding TCS and/or TCI for pts refractory to moisturization alone, and, after initial control of AD is achieved, addressing relapsing disease with continued intermittent (proactive) therapy
  - In pts with moderate-to-severe disease refractory to this, panel recommended adding dupilumab or tralokinumab
- Conditional recommendations:
  - Applying mid-potency topical agents once rather than twice daily, wet wrap therapy or crisaborole if aligned with patient values and preferences, not starting with topical JAK inhibitors as first-line therapy, and, depending on disease severity, adding bleach baths and allergen immunotherapy but not dietary avoidance nor systemic corticosteroids
  - Among pts refractory to topicals and biologics, panel provided multiple conditions to consider for optimal treatment selection, including oral JAK inhibitors, CsA or UV light

Ann Allergy Asthma Immunol 2024;132:274





Ann Allergy Asthma Immunol 2024;132:274

In summary, the JTFPP AD guidelines...

- represent an evolution in trustworthy allergy guidelines distinguished from other guidelines through systematic reviews of the evidence with multidisciplinary panelist engagement, adherence to a rigorous guideline development process, robust use of GRADE that fulfils requirements to report its proper use, core involvement of patient and caregiver voice from start to finish, focus on equity, diversity and inclusiveness, clear translation of evidence to clinically actionable and contextual recommendations and novel approaches to facilitate knowledge translation
- emphasize in addition to standards of trustworthiness, the third principle of evidence-based medicine: that evidence alone is never enough; that patient values and preferences must be carefully considered when determining optimal treatments for patients and populations
  - Supplement provides 1-2 page patient-friendly handouts to facilitate education, discussion, and shared decision-making

Ann Allergy Asthma Immunol 2024;132:274

Guidelines of care for the management of atopic dermatitis in adults with topical therapies

Robert Sidbury, MD, MPH, Co-Chair,[a] Ali Alikhan, MD,[b] Lionel Bercovitch, MD,[c] David E. Cohen, MD, MPH,[d] Jennifer M. Darr, LCSW,[e] Aaron M. Drucker, MD, ScM,[f,g] Lawrence F. Eichenfield, MD,[h] Lindsy Frazer-Green, PhD,[i] Amy S. Paller, MD,[j] Kathryn Schwarzenberger, MD,[k] Jonathan I. Silverberg, MD, PhD, MPH,[l] Anne Marie Singh, MD,[m] Peggy A. Wu, MD, MPH,[n] and Dawn M. R. Davis, MD, Co-Chair[o]

J Am Acad Dermatol 2023;89:e1-20

ARTICLE IN PRESS

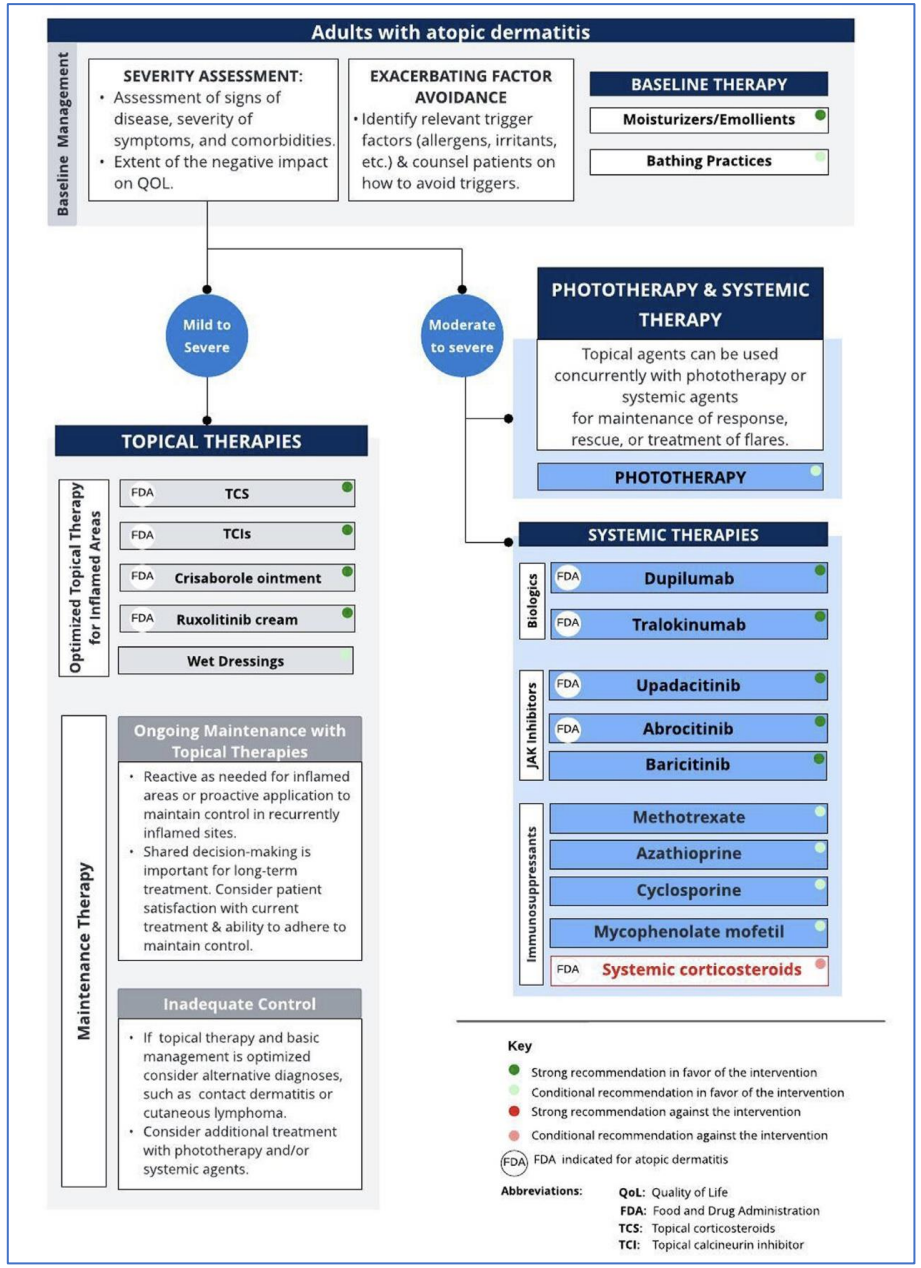
FROM THE ACADEMY

Guidelines of care for the management of atopic dermatitis in adults with phototherapy and systemic therapies

Dawn M. R. Davis, MD (Co-Chair), [a] Aaron M. Drucker, MD, ScM,[b,c] Ali Alikhan, MD,[d] Lionel Bercovitch, MD,[e] David E. Cohen, MD, MPH,[f] Jennifer M. Darr, LCSW,[g] Lawrence F. Eichenfield, MD,[h] Lindsy Frazer-Green, PhD,[i] Amy S. Paller, MD,[j] Kathryn Schwarzenberger, MD,[k] Jonathan I. Silverberg, MD, PhD, MPH,[l] Anne Marie Singh, MD,[m] Peggy A. Wu, MD, MPH,[n] and Robert Sidbury, MD, MPH (Co-Chair)[o]

J Am Acad Dermatol 2024; 90:e43-56

AAD treatment algorithm for adults with atopic dermatitis



J Am Acad Dermatol 2024; 90:e43-56

Atopic Dermatitis Yardstick Update

- AD Yardstick published in 2018
- Update addresses:
  - Biologics: dupilumab, tralokinumab
  - JAK inhibitors: ruxolitinib, abrocitinib, upadacitinib
- **Incorporates Expert Commentary from group of allergist-immunologists and dermatologists**

Boguniewicz M, Fonacier L, et al. Ann Allergy Asthma Immunol 2023; 130:811

Conjunctivitis in dupilumab clinical trials

- Evaluation of randomized placebo-controlled trials of dupilumab in AD (n = 2629), asthma (n = 2876), CRSwNP (n = 60) and EoE (n = 47)
- Conjunctivitis more frequent with dupilumab treatment in most AD trials
- In dupilumab trials in other type 2 diseases, incidence of conjunctivitis overall very low and similar for dupilumab and placebo
- In AD, incidence of conjunctivitis associated with AD severity and prior history of conjunctivitis
- Etiology and treatment of conjunctivitis in dupilumab-treated patients require further study

Br J Dermatol 2019;181:459

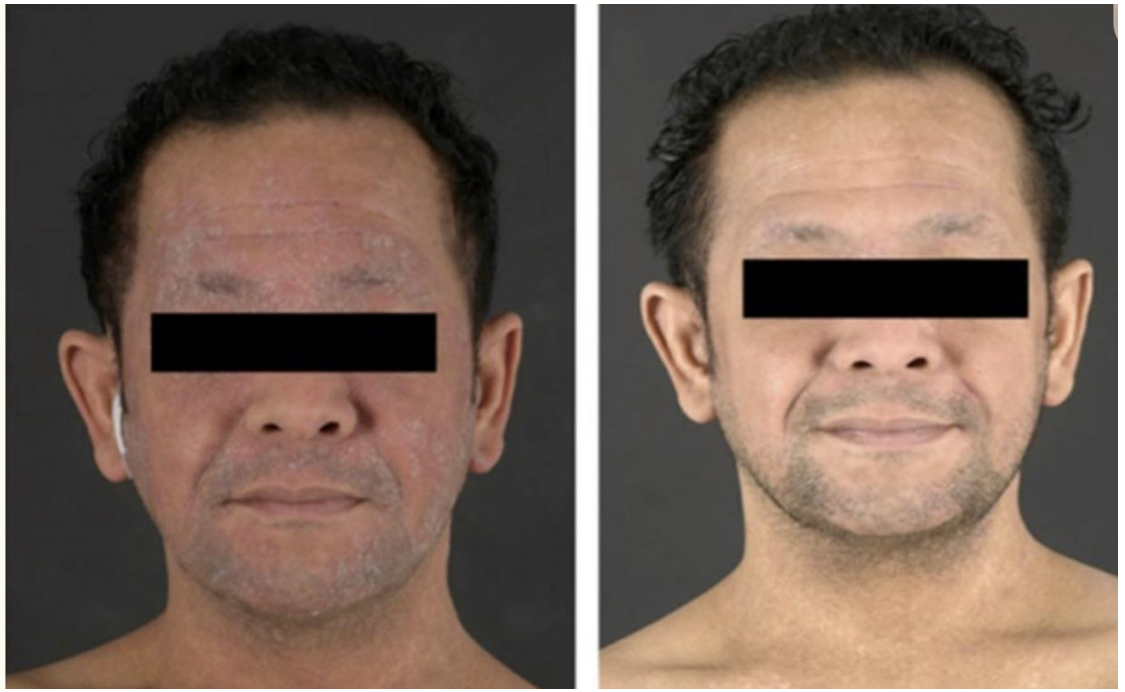
Atopic Dermatitis Yardstick Update: Expert Commentary

- AD patients starting treatment with dupilumab with a history of any preceding ocular signs or symptoms should be educated on recognizing early signs of ocular surface disease which may include sensation of dryness or grittiness
- This can often be adequately treated with lubricating tears while continuing on dupilumab
- In some patients, reducing the frequency of injections has allowed for maintaining control of the skin disease while minimizing ocular surface disease symptoms

Boguniewicz M, Fonacier L, et al. Ann Allergy Asthma Immunol 2023; 130:811

Dupilumab facial redness: Positive effect of itraconazole

- Case reports describe ACD, *Malassezia* hypersensitivity, rosacea and psoriasis



Adult with DFR & elevated serum *Malassezia*-specific IgE, responsive to itraconazole while continuing on dupilumab

JAAD Case Rep 2019;5: 888

Atopic Dermatitis Yardstick Update: Expert Commentary

- Case reports of psoriasiform eruptions in patients treated with dupilumab have led to questions related to blocking type 2 immune responses with shift to a type 1 response.
- …it is important for clinicians to establish a diagnosis of AD, as patients with other inflammatory diseases including psoriasis have been erroneously treated with dupilumab.
- …the Asian AD phenotype … combines features of atopic dermatitis and psoriasis with increased T_H17 polarization.
- Consider patch testing, trial on a TCI...

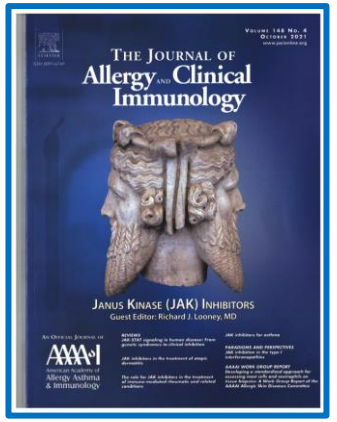
Boguniewicz M, Fonacier L, et al. Ann Allergy Asthma Immunol 2023; 130:811

Atopic Dermatitis Yardstick Update: Expert Commentary

- A current clinical challenge is to identify patients who would maintain disease control with less frequent dosing
- This may be especially relevant given indication for dupilumab in a younger AD population
- It may be reasonable (though off-label) to taper dupilumab to an every 3 or 4 week dosing regimen in a patient who has been clear/almost clear for at least 6-12 months, while monitoring for relapse
  - OLE 5 year experience forthcoming - If clear/almost clear (IGA 0/1) at 2 successive 3 month f/u visits, dupilumab held and re-started if needed

Boguniewicz M, Fonacier L, et al. Ann Allergy Asthma Immunol 2023; 130:811

Topical and oral JAK inhibitors



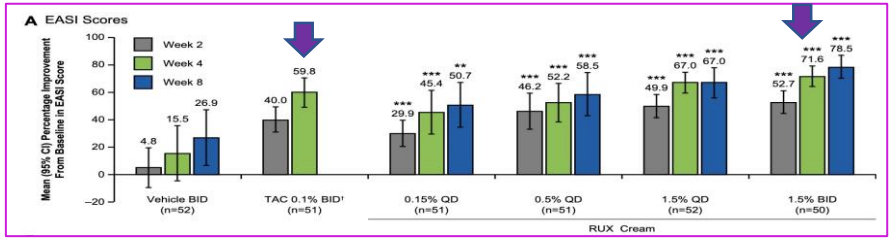
- Ruxolitinib (topical JAK1/2 inhibitor) approved in 09/2021
  - For short term and non-continuous chronic treatment of mild to moderate AD in non-immunocompromised patients 12 years and older whose disease is not adequately controlled with topical prescription therapies or when those therapies not advisable
  - Twice daily up to 20% BSA involved areas, no more than 60g/week
  - Lab monitoring optional

- Abrocitinib (oral JAK 1 inhibitor) approved 01/2022
  - For adults and pediatric patients 12 years and older with moderate-to-severe AD whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies is inadvisable
  - Recommended dose 100 mg QD and 200 mg QD if inadequate response ~~after 12W~~ [**updated 12/23: If an adequate response is not achieved with CIBINQO 100 mg once daily, consider increasing the dosage to 200 mg once daily]
  - 50 mg dose approved to treat moderate-to-severe AD specifically in pts with moderate renal impairment, certain patients receiving treatment with inhibitors of cytochrome P450 (CYP) 2C19 or poor metabolizers of CYP2C19
- Upadacitinib (oral JAK 1 inhibitor) approved 01/2022
  - Indicated for treatment of moderate to severe AD in adults and children 12 yrs and older whose disease did not respond to previous treatment and is not well controlled with other pills or injections, including biologic medicines, or when use of other pills or injections is not recommended
  - 15 mg once daily can be initiated in adults and children 12 yrs of age and older weighing at least 40 kg
  - In children and adults < 65 yrs of age who do not achieve an adequate response, dose may be increased to 30 mg once daily

Boguniewicz M, et al. Ann Allergy Asthma Immunol 2023; 130:811

Atopic Dermatitis Yardstick Update: Expert Commentary

- ...few direct comparative studies between topical JAK inhibitors vs currently available topical ... such as TCS and TCI
  - In a P2 trial, both ruxolitinib 1.5% cream and triamcinolone 0.1% cream attained nearly equal efficacy in EASI improvement at week 12 (84.9% vs 86.8%); anti-itch effect was 3x greater for ruxolitinib 1.5% cream and 2x greater for triamcinolone 0.1% cream vs placebo, suggesting that ruxolitinib 1.5% cream may have a slight advantage in patients with significant pruritus
- ... clinicians may need to treat with this medication off-label in more severe patients with greater BSA involvement
  - open-label study ... 41 adolescents and adults with mild to severe AD applied ruxolitinib 1.5% cream BID for 28 days to all AD lesions. At 28 days, if there was no safety concern, subjects continued the medication for another 28 days
  - mean BSA of cohort was 31.2% (range: 25 - 90%) and mean EASI score was 20.8
  - 6 subjects had TEAEs: 1 subject had neutropenia, 3 subjects had elevated transaminase levels, 1 had dyspnea and 1 had hemoglobin decrease



Boguniewicz M, Fonacier L, et al. Ann Allergy Asthma Immunol 2023; 130:811

Atopic Dermatitis Yardstick Update: Expert Commentary

- …there is a benefit to their (JAK inhibitors) use in patients that do not want an injectable therapy, and want an oral medication that allows flexibility of dosing, as well as in patients that failed or could not sustain response on dupilumab or other biologics, including those patients that have side effects on dupilumab (e.g. conjunctivitis, occurrence or exacerbation of facial rashes, or arthralgias)
- … patients with more moderate disease that do not want to be on a systemic medication continuously may be able to take an oral JAK inhibitor intermittently, rather than stop and restart a biologic, which could be problematic (e.g. development of ADA)
- …JAK inhibitors may likely …control majority of AD subtypes that show skewing of more than just Th2 pathway. However, careful monitoring needs to be instituted and particular caution should be exercised in patients over 65 years of age

Boguniewicz M, Fonacier L, et al. Ann Allergy Asthma Immunol 2023; 130:811

JAK inhibitor Boxed Warnings

- **Serious infections. ...** including TB and infections caused by bacteria, fungi, or viruses that can spread throughout the body. HCP should test you for TB before starting [JAK inhibitor] and check you closely for signs and symptoms of TB during treatment.... You may be at higher risk of developing shingles (herpes zoster).
- **Increased risk of death in people ≥ 50 years who have at least 1 cardiovascular risk factor**
- **Cancer and immune system problems.** Follow HCP's advice about having your skin checked for skin cancer during treatment with [JAK inhibitor] . Limit the amount of time you spend in sunlight. Wear protective clothing when you are in the sun and use sunscreen.
- **Increased risk of major cardiovascular (CV) events, such as heart attack, stroke, or death, in people ≥ 50 years who have at least 1 CV risk factor, especially if a current or past smoker.**
- **Blood clots. ...** more often in people who are ≥ 50 years and older and with at least 1 CV risk factor.
- **Allergic reactions. ...**seen in people taking [JAK inhibitor].
- **Tears in the stomach or intestines and changes in certain laboratory tests.** Your HCP should do blood tests before you start taking [JAK inhibitor] and while you take it.

JAK inhibitor checklist for the Atopic Dermatitis Yardstick Update

- **ASK:**
  - CV risks factors, smoking, blood clots
  - skin cancer
  - TB
  - vaccine status (H zoster*, Varicella)
  - pregnancy

* Per CDC, recommended for ≥ 19 yrs with weakened immune systems because of disease or therapy

- **SCREEN:**
  - for TB before starting JAK inhibitor and check for signs and symptoms of TB during treatment
  - monitor for shingles (H zoster)
  - skin checks for skin cancer during treatment & limit amount of time in sunlight (protective clothing and sunscreen)
- **TEST:**
  - CBC w/diff before starting & after ~ 4W on treatment & after increasing dose; LFTs & baseline hepatitis B & C serology; lipid profile after ~ 4 (12)W treatment

Boguniewicz M, Fonacier L, et al. Ann Allergy Asthma Immunol 2023; 130:811