Evolving Management Options for Alopecia Areata: Clinical Burden, Cost-Effective Care, and Emerging Treatments

AMCP Nexus 2022 Conference
Tuesday, October 11, 2022
6:00 PM – 7:30 PM EDT

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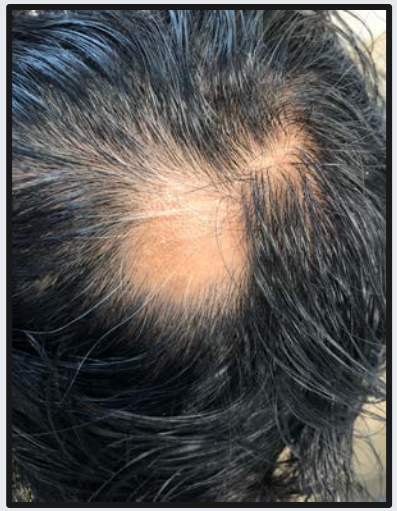
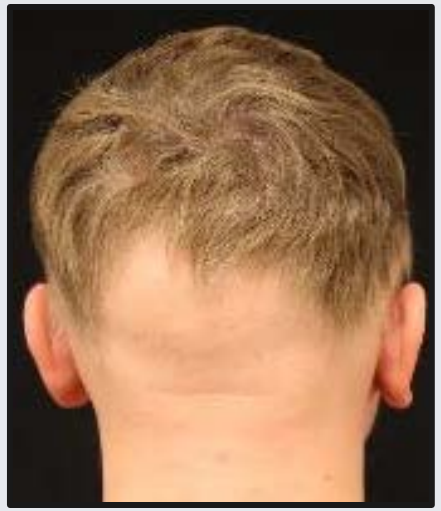
The Clinical Spectrum of AA

Patchy AA (limited)

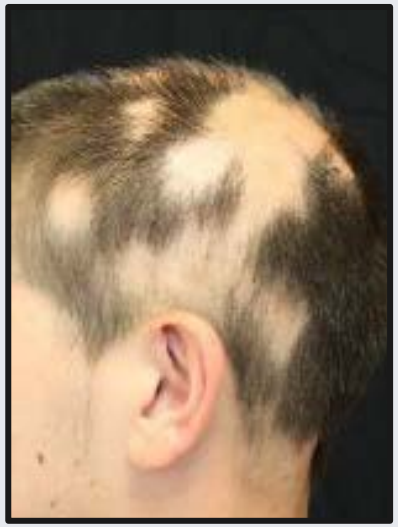


Ophiasis AA

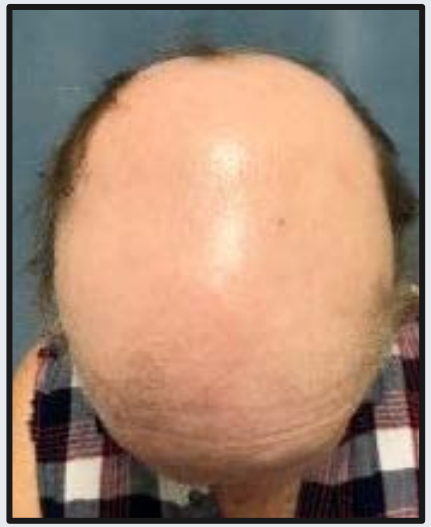


Diffuse AA

Patchy AA (mod/sev)



Sisaipho AA



AT/AU

AT, alopecia totalis; AU, alopecia universalis.

Images courtesy of Dr. Brett King.

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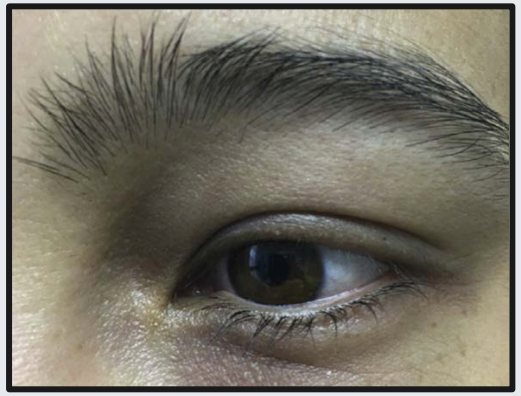
Clinical Spectrum of AA (Continued)

Eyebrow Involvement

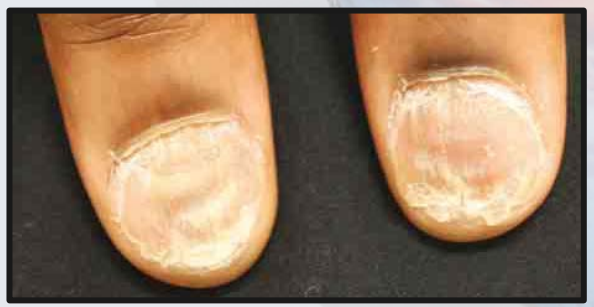
Eyebrow and Eyelash Involvement

Beard Involvement

Eyelash Involvement



Nail Involvement



Images courtesy of Dr. Brett King.

Dhayalan A, et al. *JAMA Dermatol*. 2016;152(4):492-493; Craiglow BG, et al. *J Invest Dermatol*. 2014;134(12):2988-2990; Craiglow BG. *JAAD Case Rep*. 2018;4(10):988-989.

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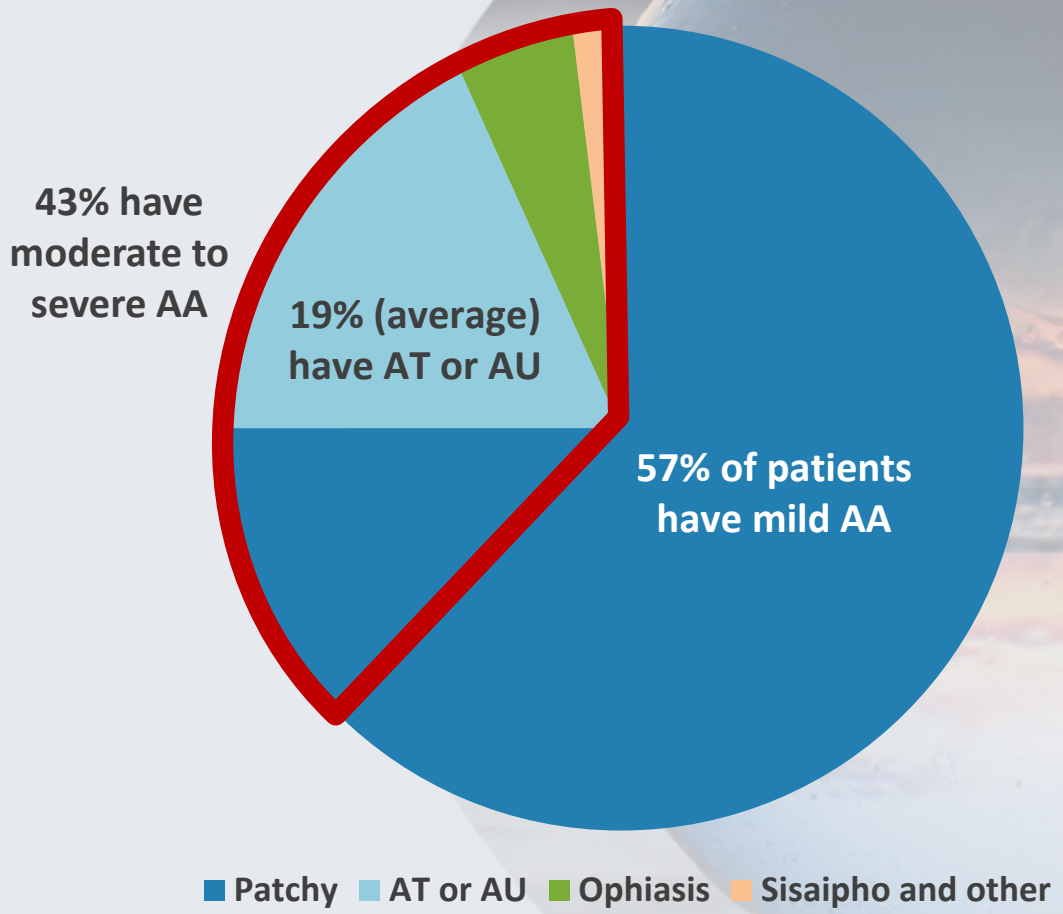
AA Epidemiology

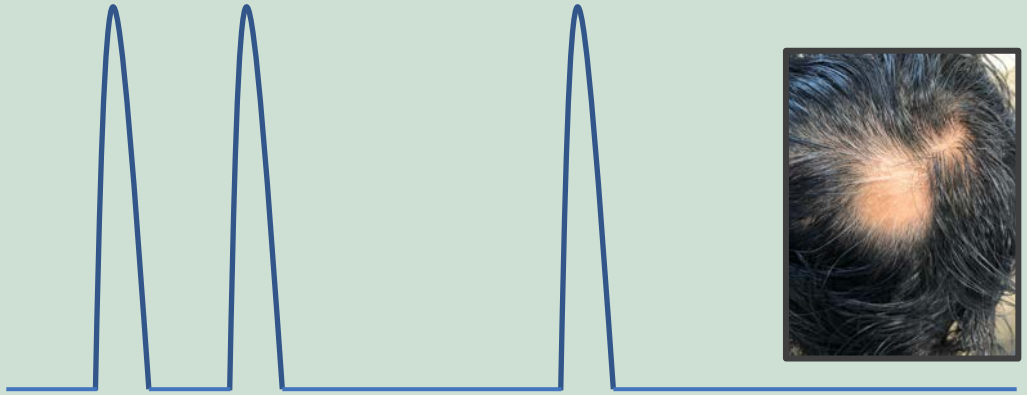
- Lifetime prevalence ~2%
- Males and females similarly affected
- Onset typically in first 40 years of life
- No known racial predominance



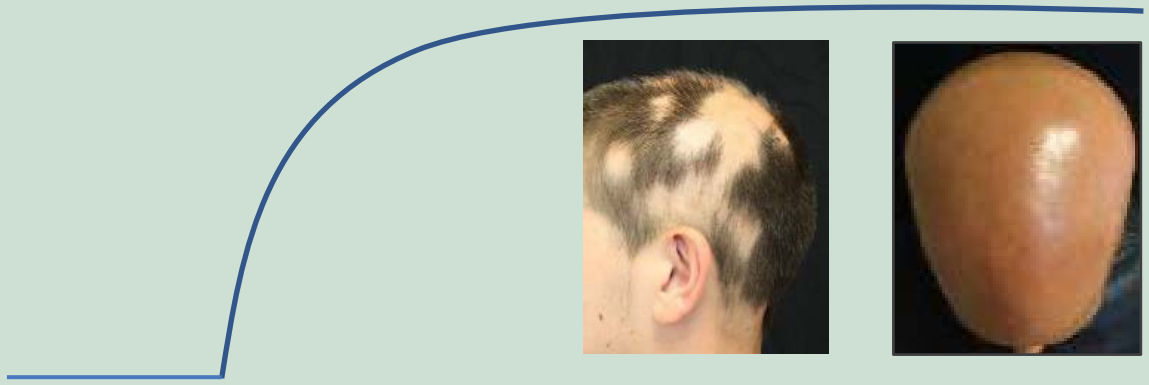
Safavi K. *Arch Dermatol.* 1992;128(5):702; Safavi KH, et al. *Mayo Clin Proc*. 1995;70:628-633; Benigno M, et al. *Clin Cosmet Investig Dermatol.* 2020;13:259-266; Strazzulla LC, et al. *J Am Acad Dermatol*. 2018;78(1):1-12; Benigno M, et al. *Clin Cosmet Investig Dermatol.* 2020;13:259-266.

The Natural History of AA

In cases of *limited hair loss*, spontaneous remission is not uncommon, though many patients will have unpredictable, relapsing and remitting disease



In cases of *severe hair loss*, hair loss is **chronic** and **spontaneous remission is *uncommon***

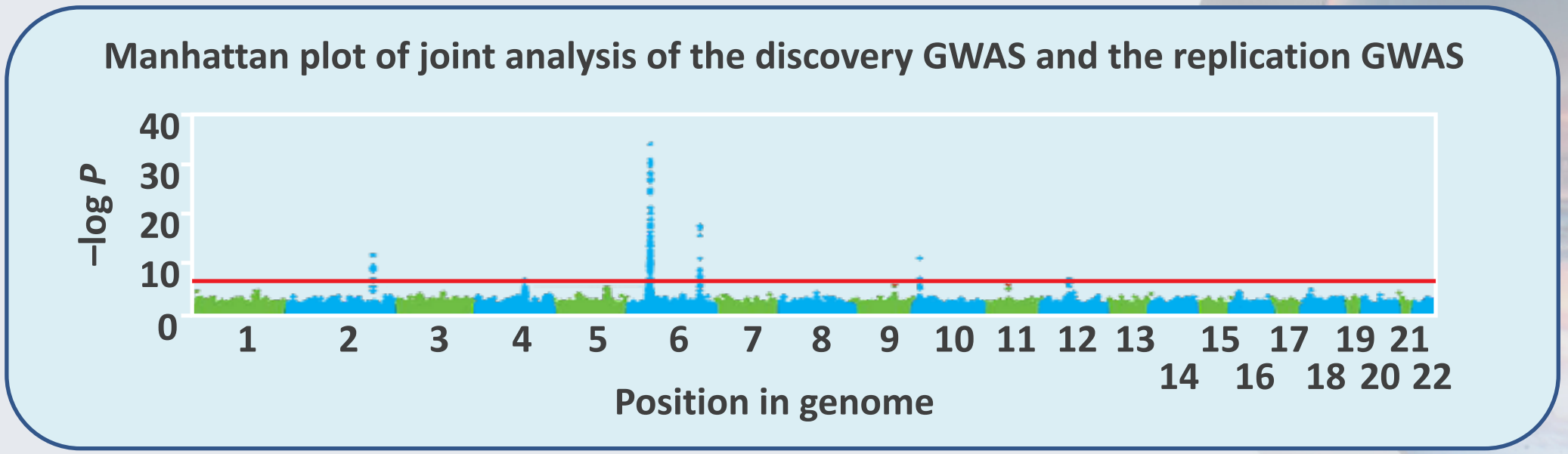


Images courtesy of Dr. Brett King.

Strazzulla LC, et al. *J Am Acad Dermatol.* 2018;78:1-12; Tosti A, et al. *J Am Acad Dermatol*. 2006;55:438-441.

Risk Factors for AA

- **~20%** of patients with AA ***can identify a family member who also has AA***
- Concordance among monozygotic twins is 55%

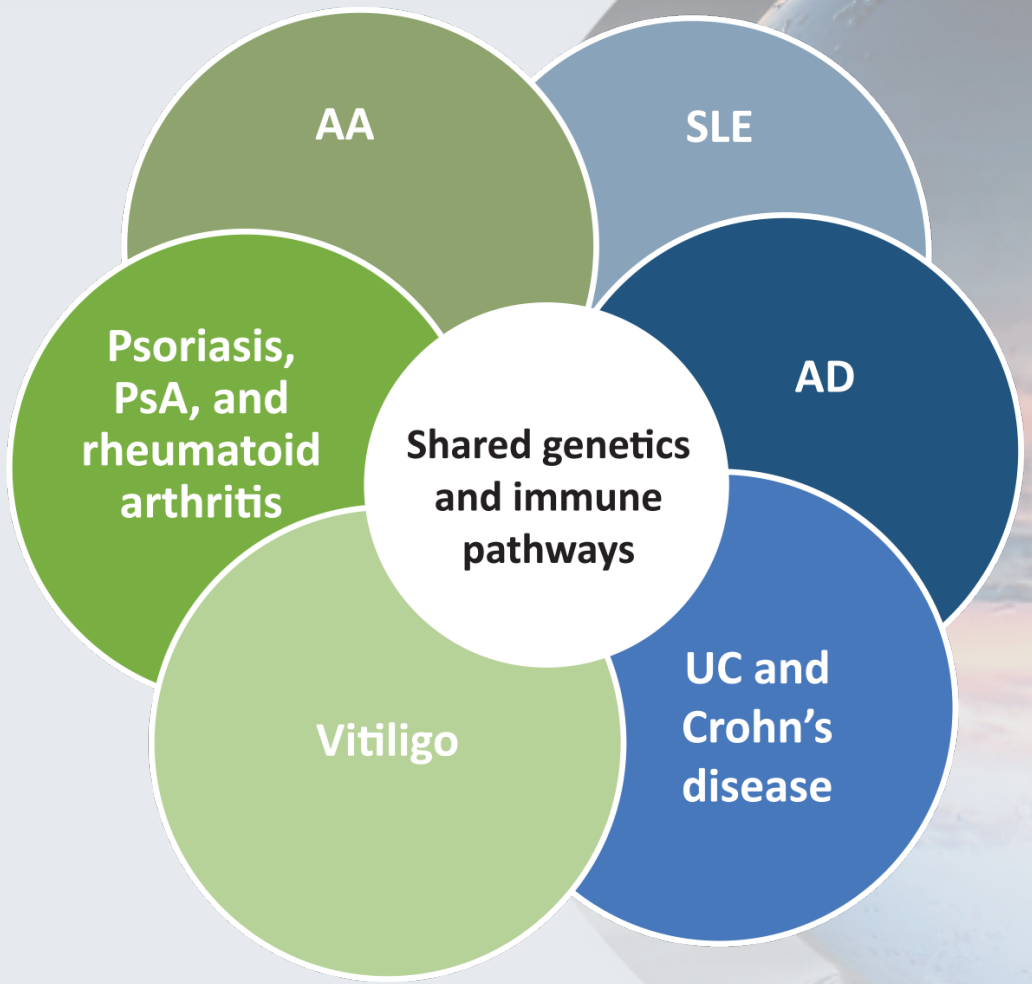


GWAS, genome-wide association study.

Jackow C, et al. *J Am Acad Dermatol*. 1998;38(3):418-425; Petukhova L, et al. *Nature*. 2010;466(7302):113-117; Whiting DA. *Arch Dermatol*. 2003;139(12):1555-1559.

Comorbidities: Associated Autoimmune and Inflammatory Disease

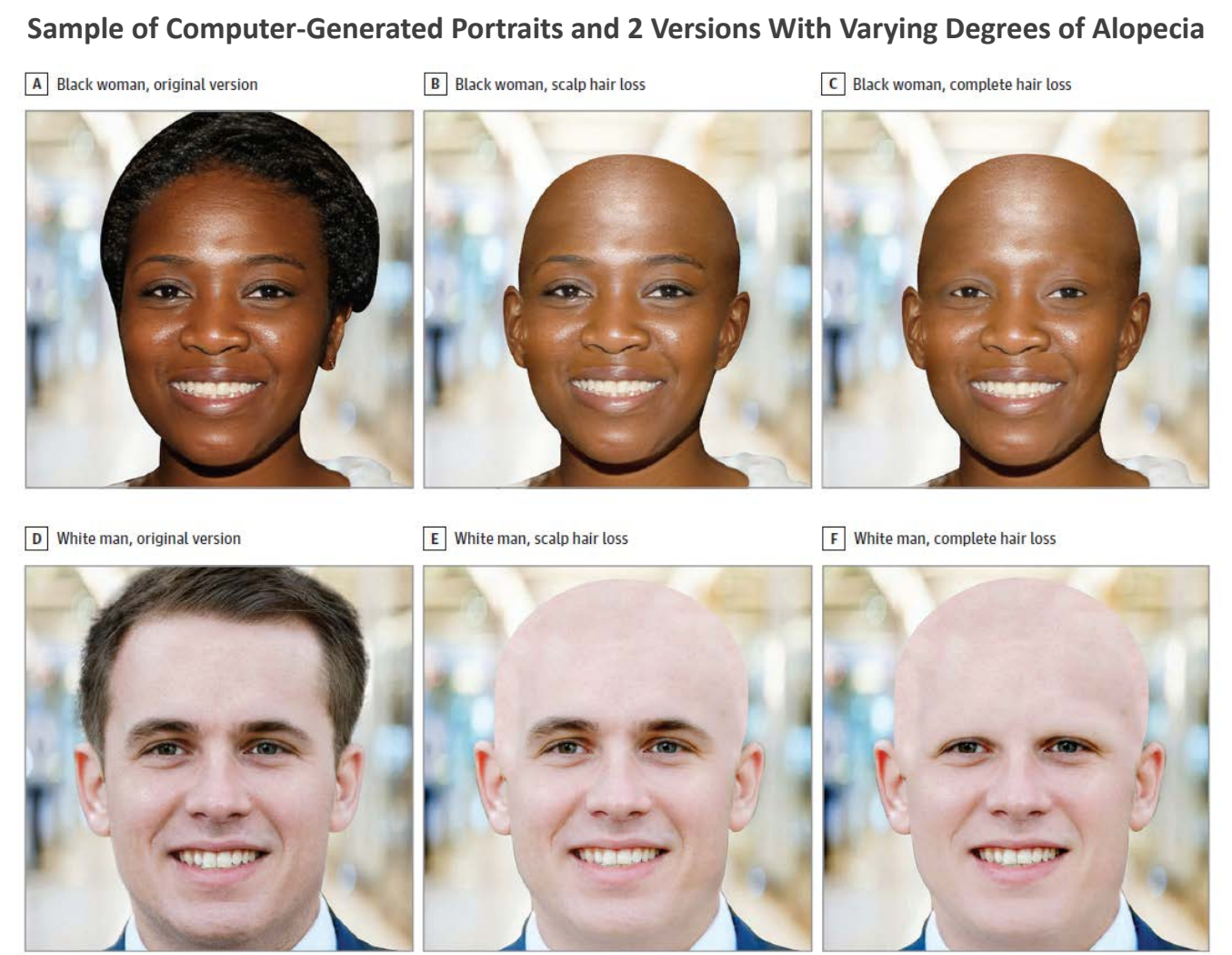
- **Comorbid autoimmune disease**
  - Including psoriasis, PsA, rheumatoid arthritis, and thyroid disorders (Hashimoto's thyroiditis [OR=2.15] and Graves' disease [OR=2.07])
- **Comorbid atopic disease**
  - Including atopic dermatitis (OR=2.36), allergic asthma (OR=1.24), and allergic rhinitis (OR=1.33)



PsA, psoriatic arthritis; OR, odds ratio; SLE, systemic lupus erythematosus; UC, ulcerative colitis.

Lee S, et al. *J Am Acad Dermatol*. 2019;80(2):466-477.e16; Colón EA, et al. *Compr Psychiatry*. 1991;32(3):245-251; Petukhova L, et al. *Nature*. 2010;466(7302):113-117; Gilhar A, et al. *J Allergy Clin Immunol*. 2019;144(6):1478-1489; Damsky W, et al. *J Am Acad Dermatol*. 2017;76(4):736-744; Peterson D, King BA. Submitted for publication.

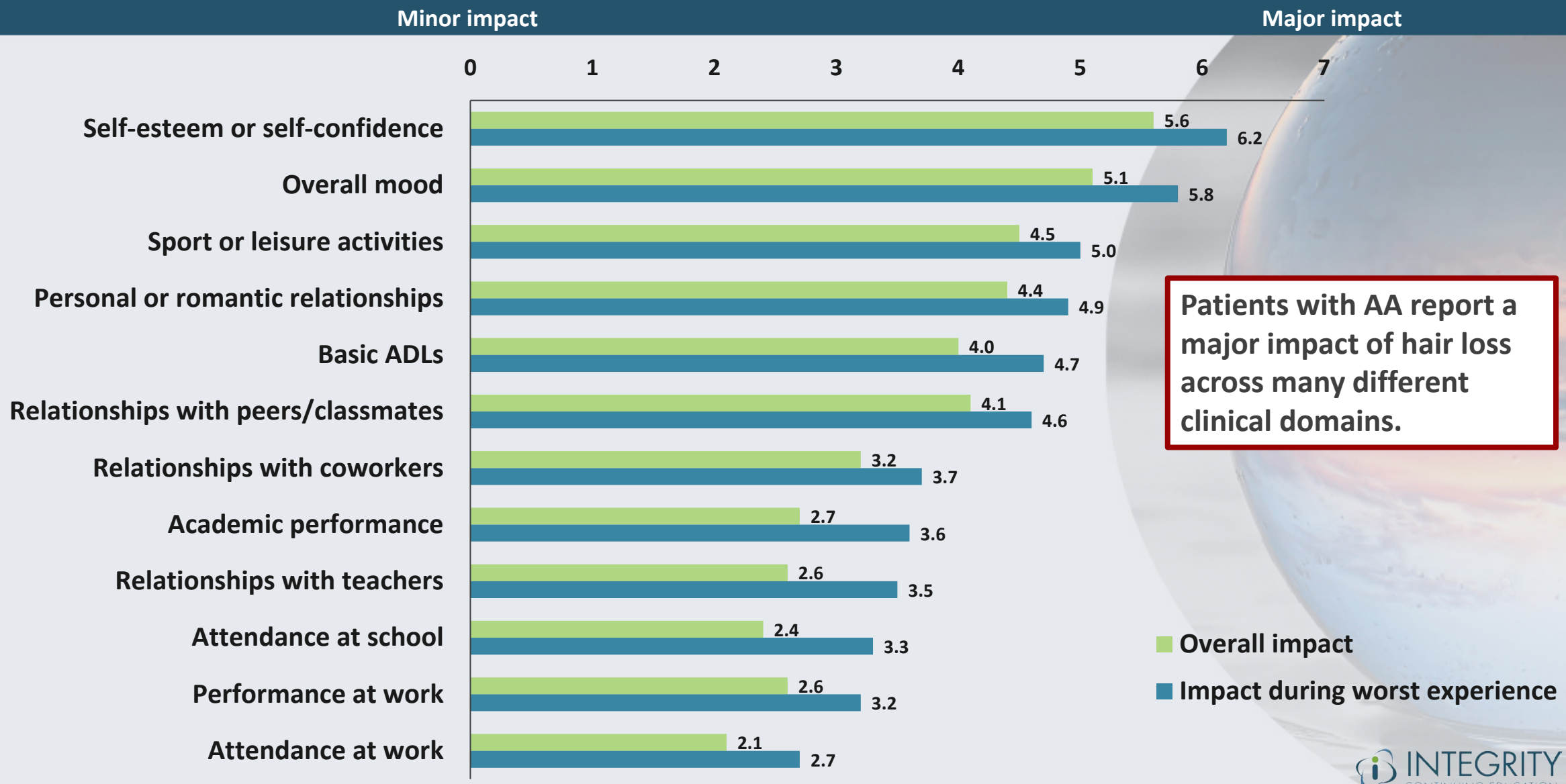
The Stigma of Hair Loss



- 2,015 laypersons shown 3 images of the same individual with different degrees of hair loss
- Patients with the most severe hair loss were perceived as being the following:
  - **Sick (29.8%)**
  - **Not attractive (27.2%)**
  - **Contagious (9.9%)**

Creadore A, et al. *JAMA Dermatol*. 2021;157:392-398.

Patient-Reported Clinical Burden of Hair Loss



Patients with AA report a major impact of hair loss across many different clinical domains.

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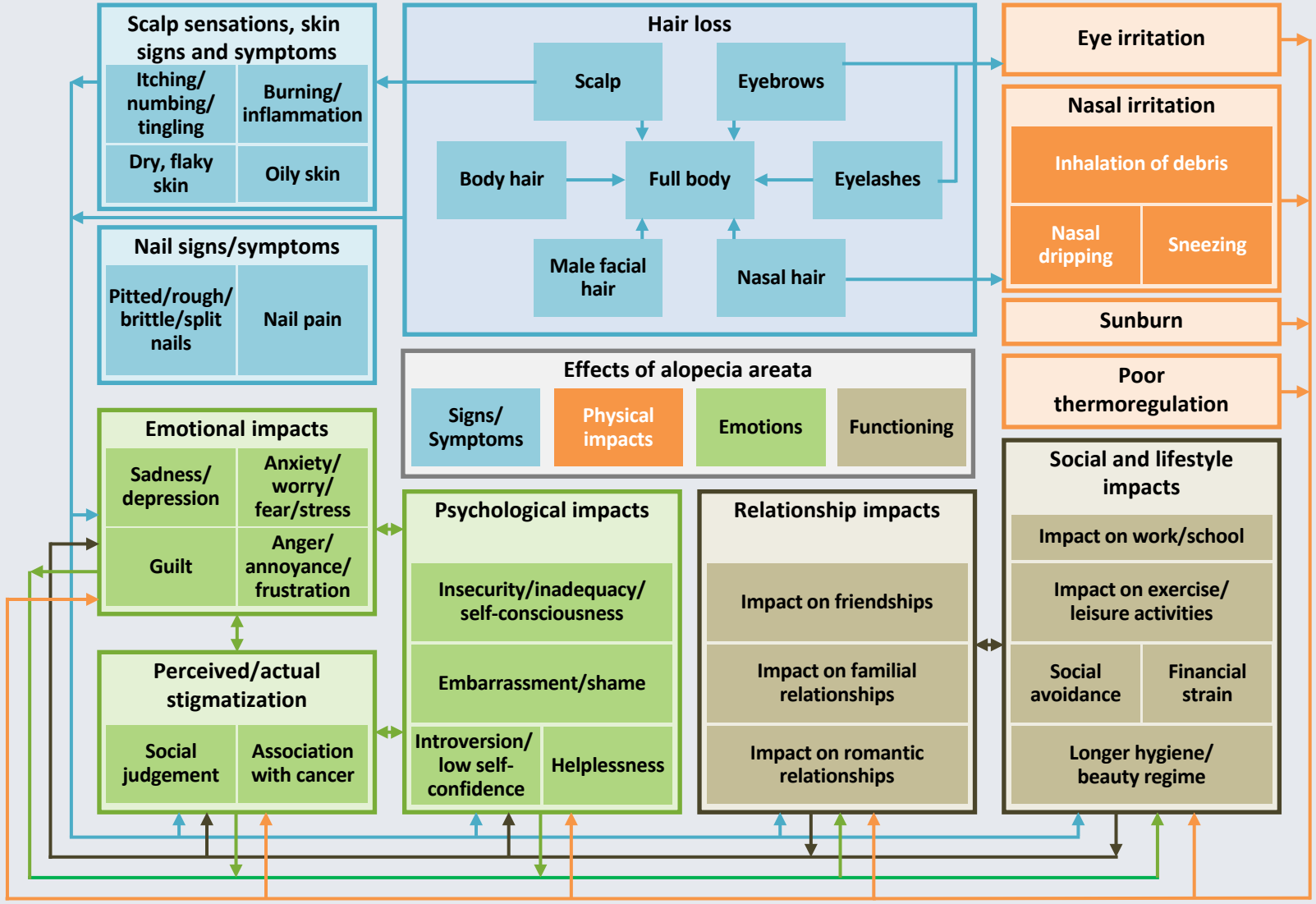
Mesinkovska N, et al. *J Investig Dermatol Symp Proc.* 2020;20:S62-S68.

Qualitative Model of Psychosocial Burden of AA

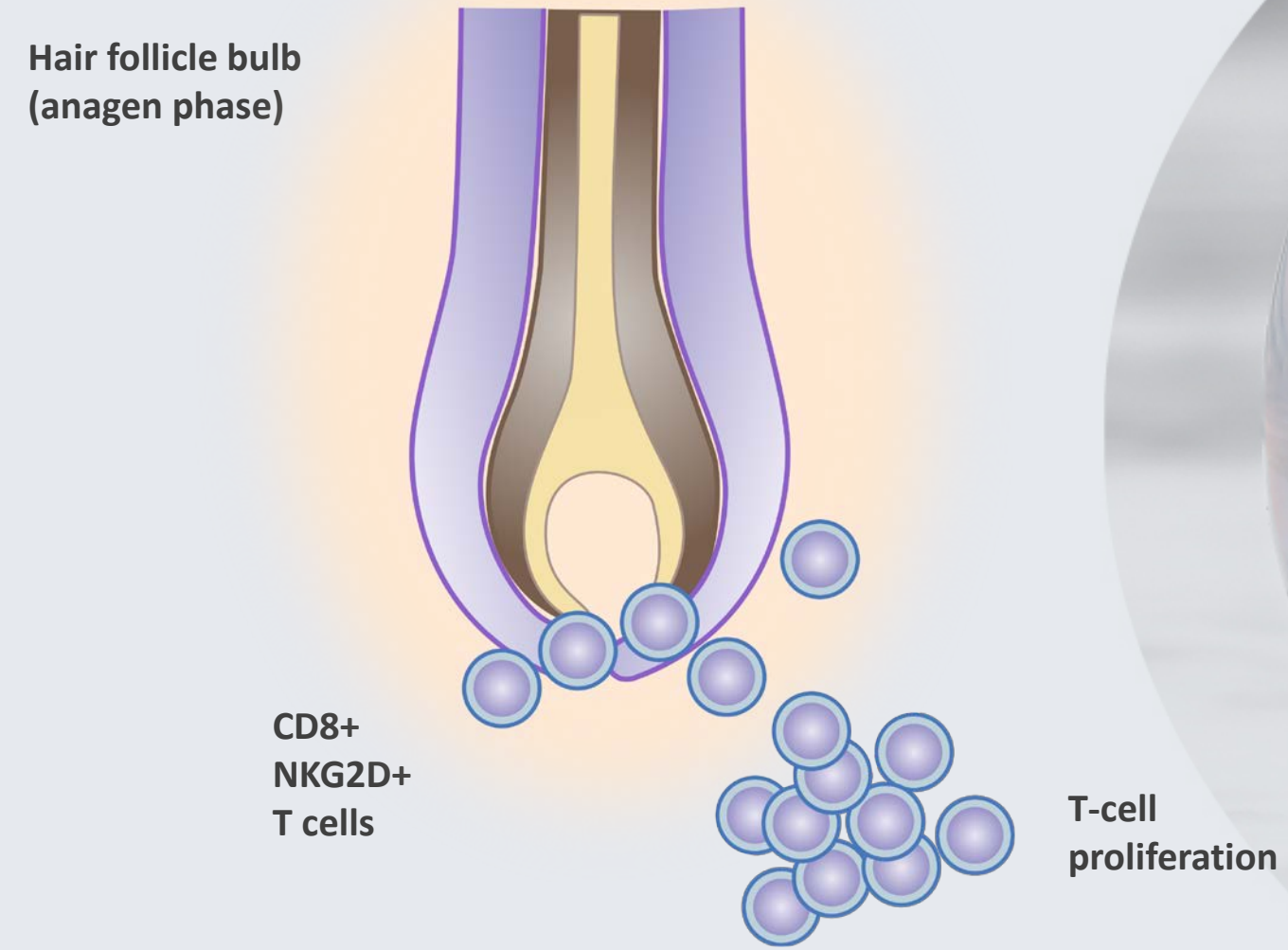


From 45 AA patient interviews, concepts were elicited and grouped into either physical or psychosocial domains and further separated into subdomains

Adapted from Aldhouse NVJ, et al. *J Patient Rep Outcomes.* 2020;4:76.

JAK Inhibitor Therapies for the Treatment of AA

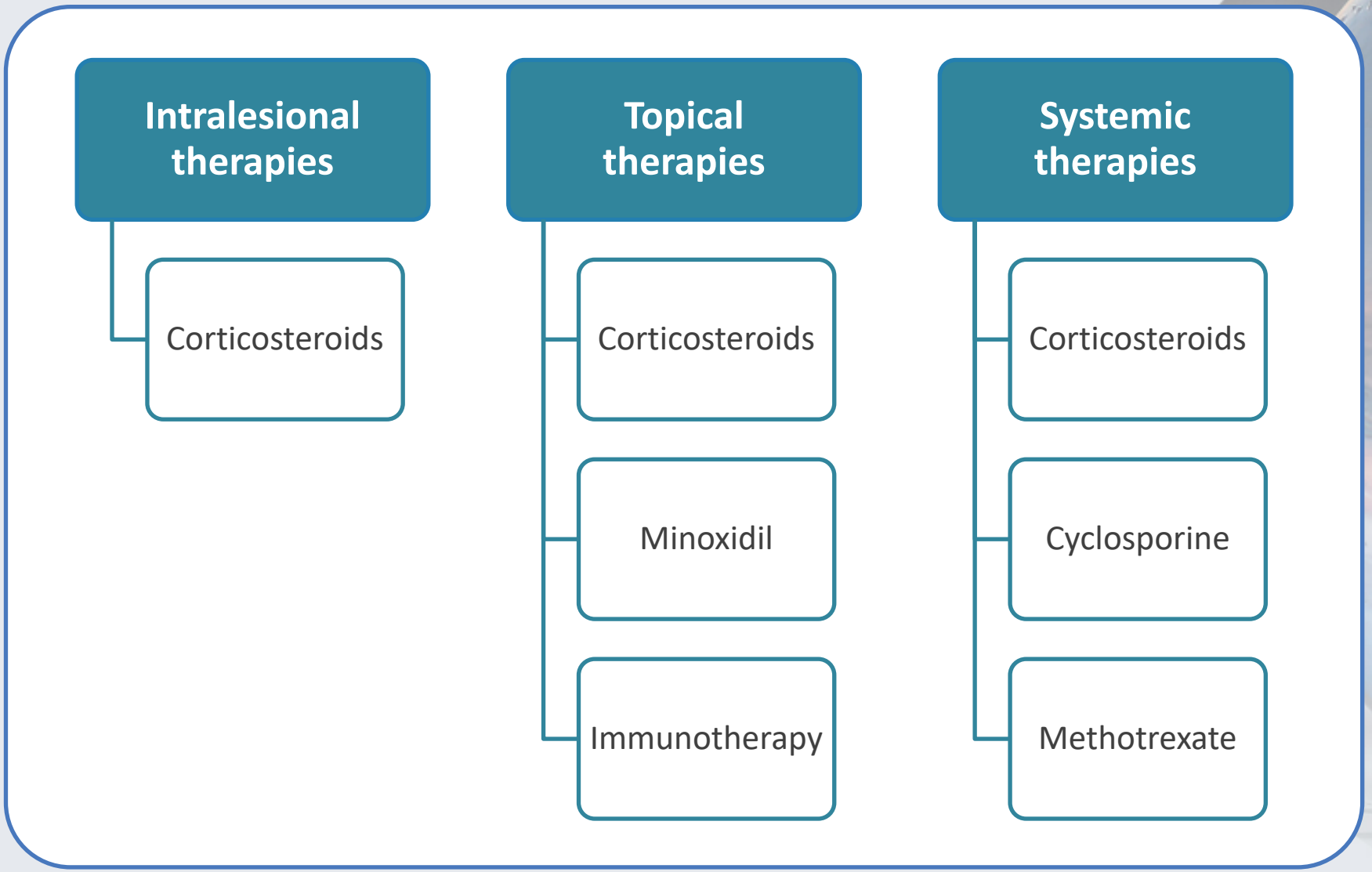
Alopecia Areata Pathogenesis: Past Understanding



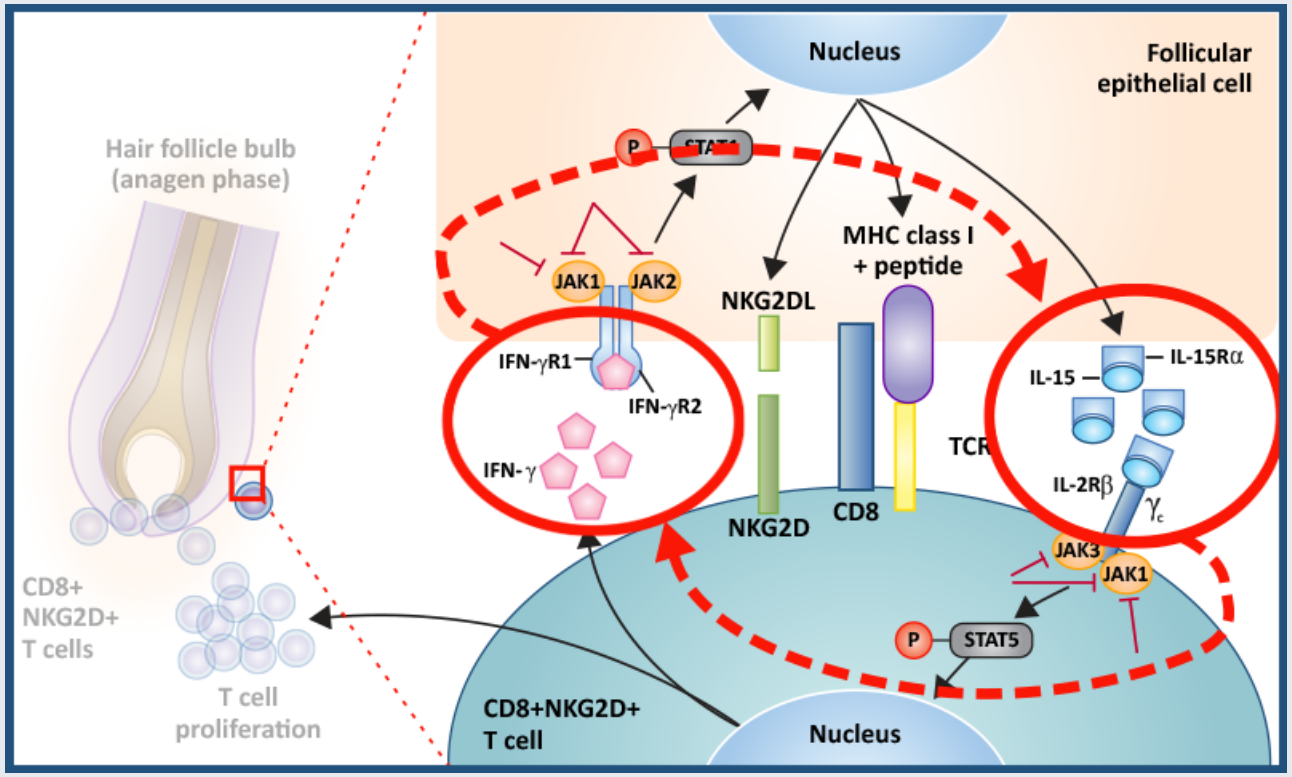
CD; cluster of differentiation.

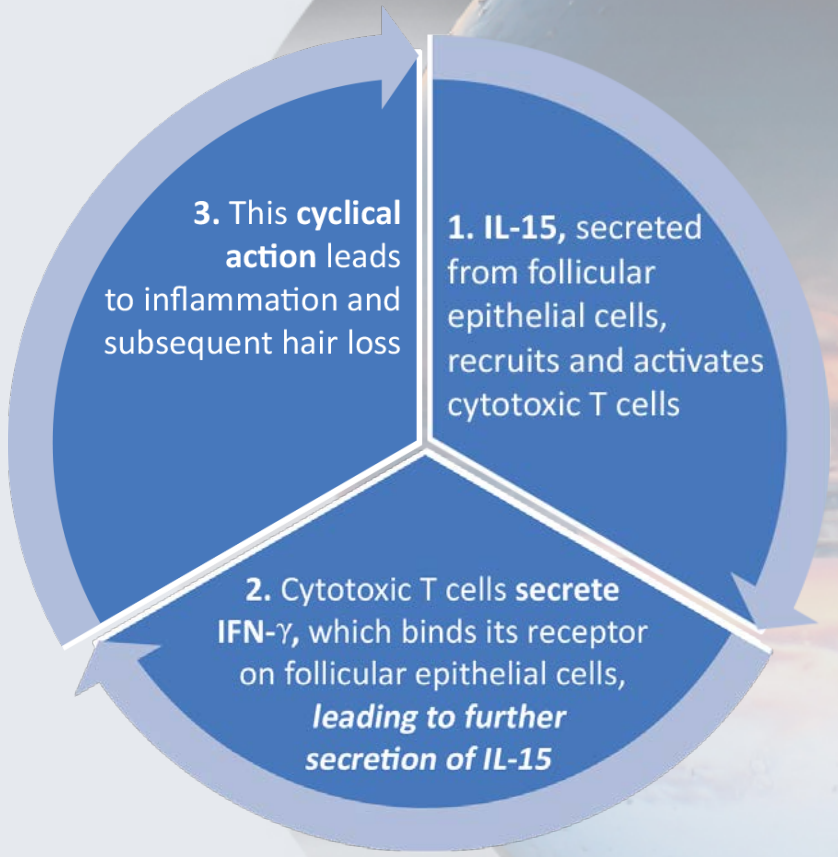
Divito SJ, et al. *Nat Med*. 2014;20(9):989-990; Xing L, et al. *Nat Med*. 2014;20(9):1043-1049.

Traditional Treatment of AA



Alopecia Areata Pathogenesis





IFN, interferon; IL, interleukin; JAK, Janus kinase; MHC, major histocompatibility complex; STAT5, signal transducer and activator of transcription 5; TCR, T-cell receptor; Th1, T helper type 1 (cells).

Divito SJ, et al. *Nat Med*. 2014;20(9):989-990; Xing L, et al. *Nat Med*. 2014;20(9):1043-1049.

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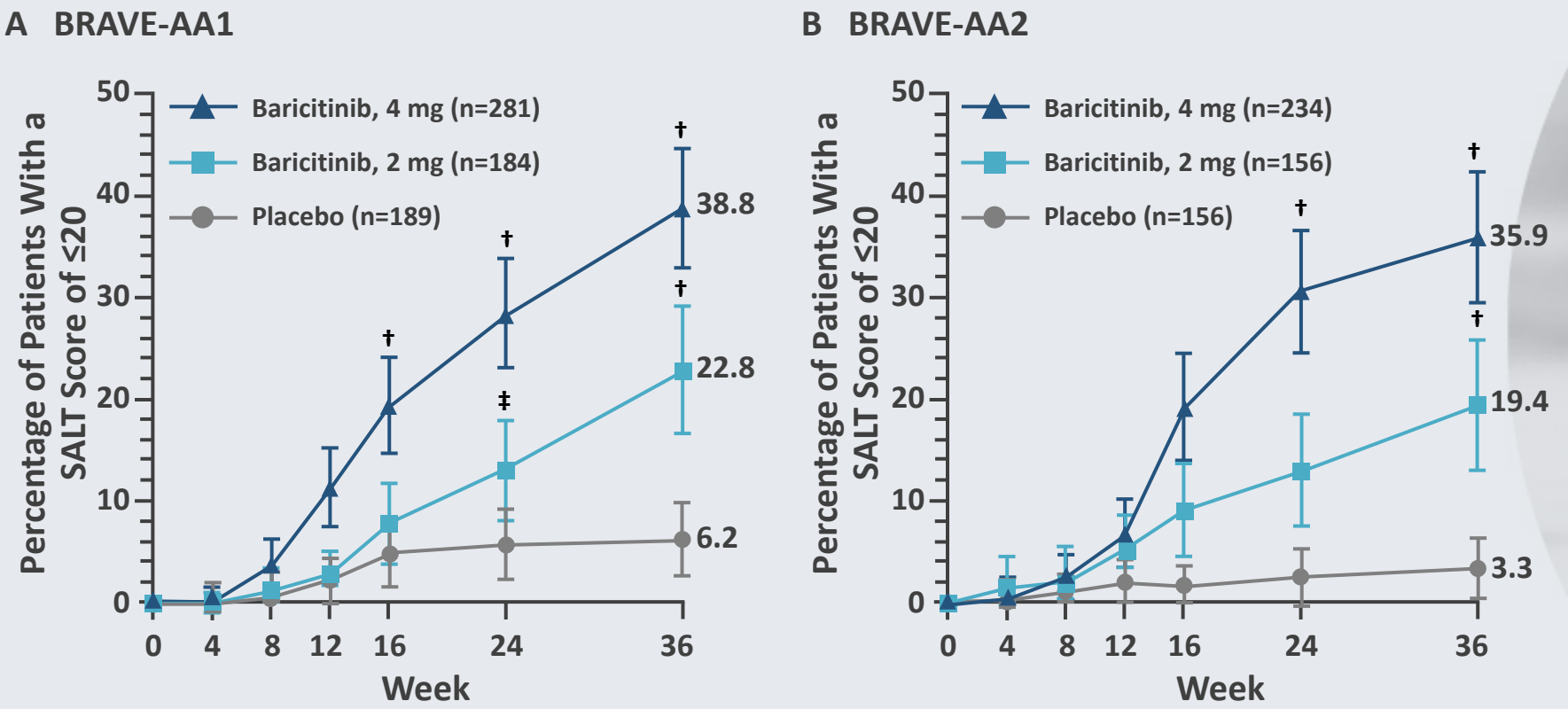
BRAVE-AA1 and AA2: Efficacy and Safety of Baricitinib Treatment in Patients With AA

Primary endpoint: Achievement of SALT Score ≤20 (20% or less scalp hair loss)



Most common (≥5%) AEs:

BRAVE-AA1

- **URI**: 4.9% & 7.5% (baricitinib 2- and 4-mg) vs 5.3% (PBO)
- **Headache**: 4.4% & 5.0% (baricitinib 2- and 4-mg) vs 4.8% (PBO)
- **Nasopharyngitis**: 6.6% & 7.5% (baricitinib 2- and 4-mg) vs 6.3% (PBO)

BRAVE-AA2

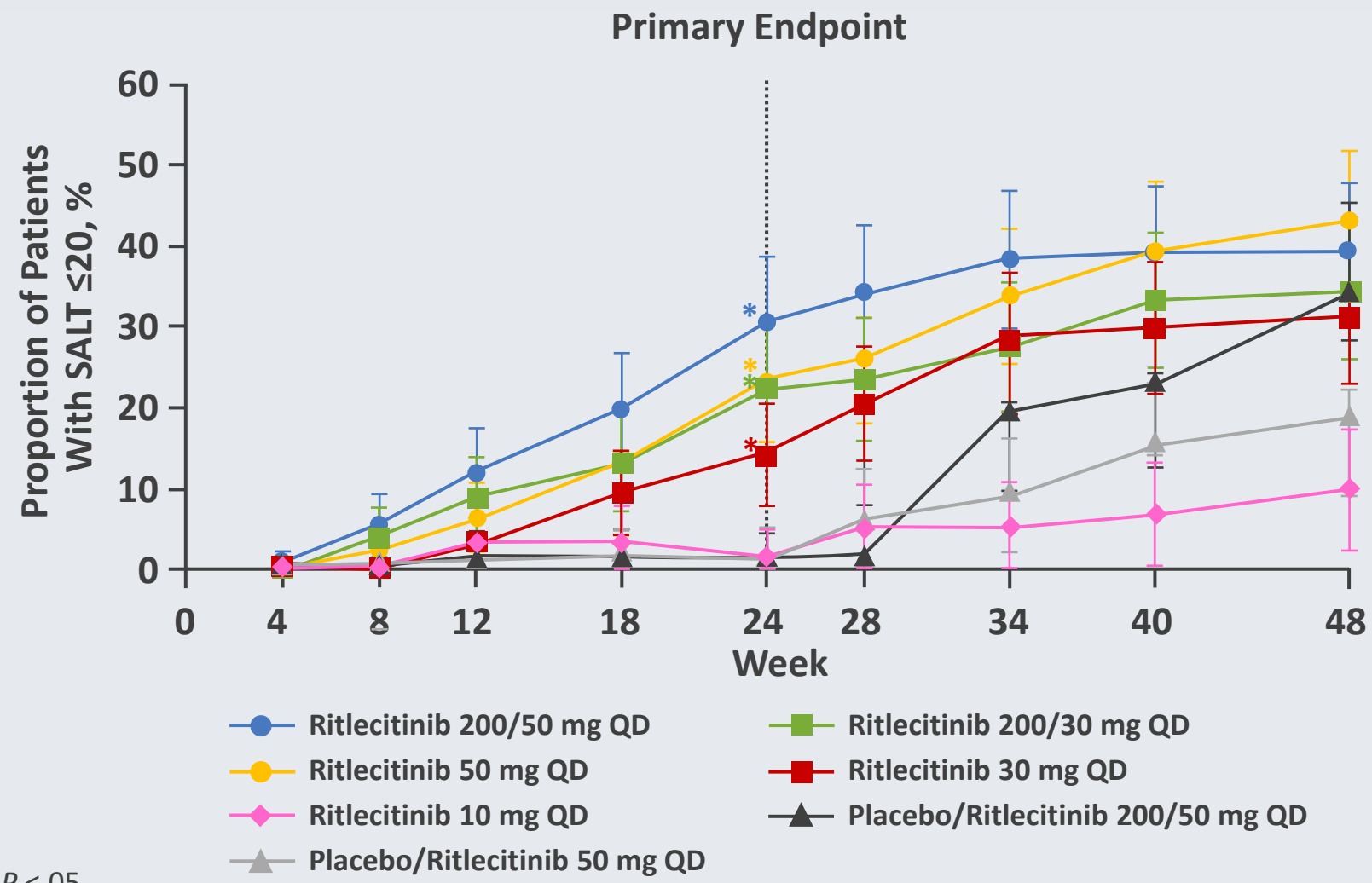
- **URI**: 7.7% & 6.4% (baricitinib 2- and 4-mg) vs 7.1% (PBO),
- **Headache**: 7.7% & 9.0% (baricitinib 2- and 4-mg) vs 6.5% (PBO)
- **Nasopharyngitis**: 1.3% & 6.4% (baricitinib 2- and 4-mg) vs 4.5% (PBO)

†*P* <.001; ‡*P* <.01.

AE, adverse event; PBO, placebo; SALT, Severity of Alopecia Tool; URI, upper respiratory infection

King B, et al. *New Engl J Med*. 2022;386:1687-1699.

ALLEGRO: Efficacy and Safety of Ritlecitinib in Patients With AA



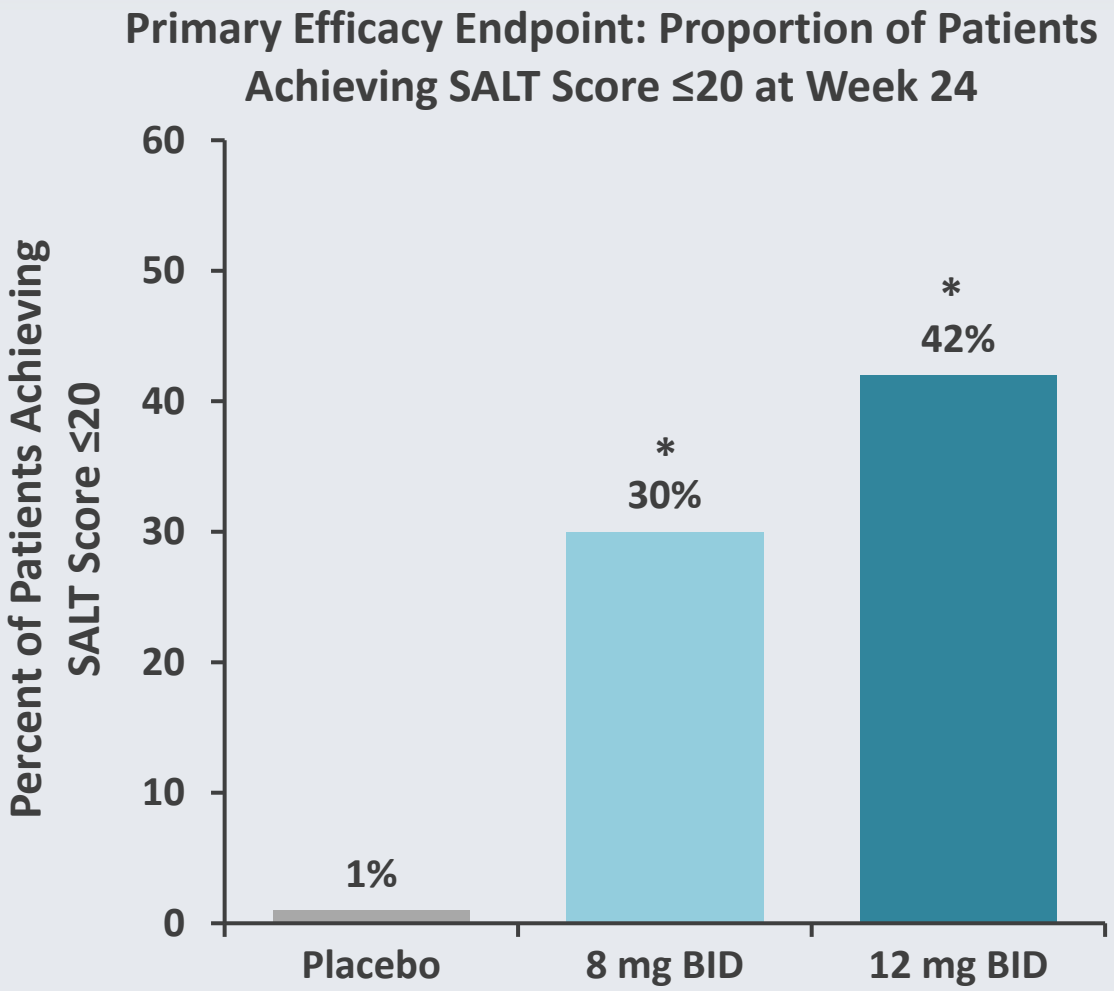
*P <.05
QD, once daily

Most common (≥5%) AEs:

- **Headache**: 10.9% to 19.4% (baricitinib groups) vs 12.1% to 12.3% (PBO groups)
- **Nasopharyngitis**: 11.3% to 16.3% (baricitinib groups) vs 6.1 to 10.8% (PBO groups)
- **URI**: 3.2 to 13.7% (baricitinib groups) vs 9.1 to 10.8% (PBO groups)

King B. Presented at the *30th Congress of the EADV.* 2021.

THRIVE-AA1: Efficacy of Deuruxolitinib



Treatment Emergent Adverse Events (TEAE) ≥5%	Placebo (n=140)	8 mg BID (n=350)	12 mg BID (n=215)
COVID-19	8 (5.7)	19 (5.4)	15 (7.0)
Nasopharyngitis	5 (3.6)	18 (5.1)	8 (3.7)
Upper respiratory tract infection	9 (6.4)	9 (2.6)	8 (3.7)
Blood creatine phosphokinase (increase)	2 (1.4)	21 (6.0)	11 (5.1)
Headache	8 (5.7)	41 (11.7)	24 (11.2)
Acne	7 (5.0)	31 (8.9)	26 (12.1)

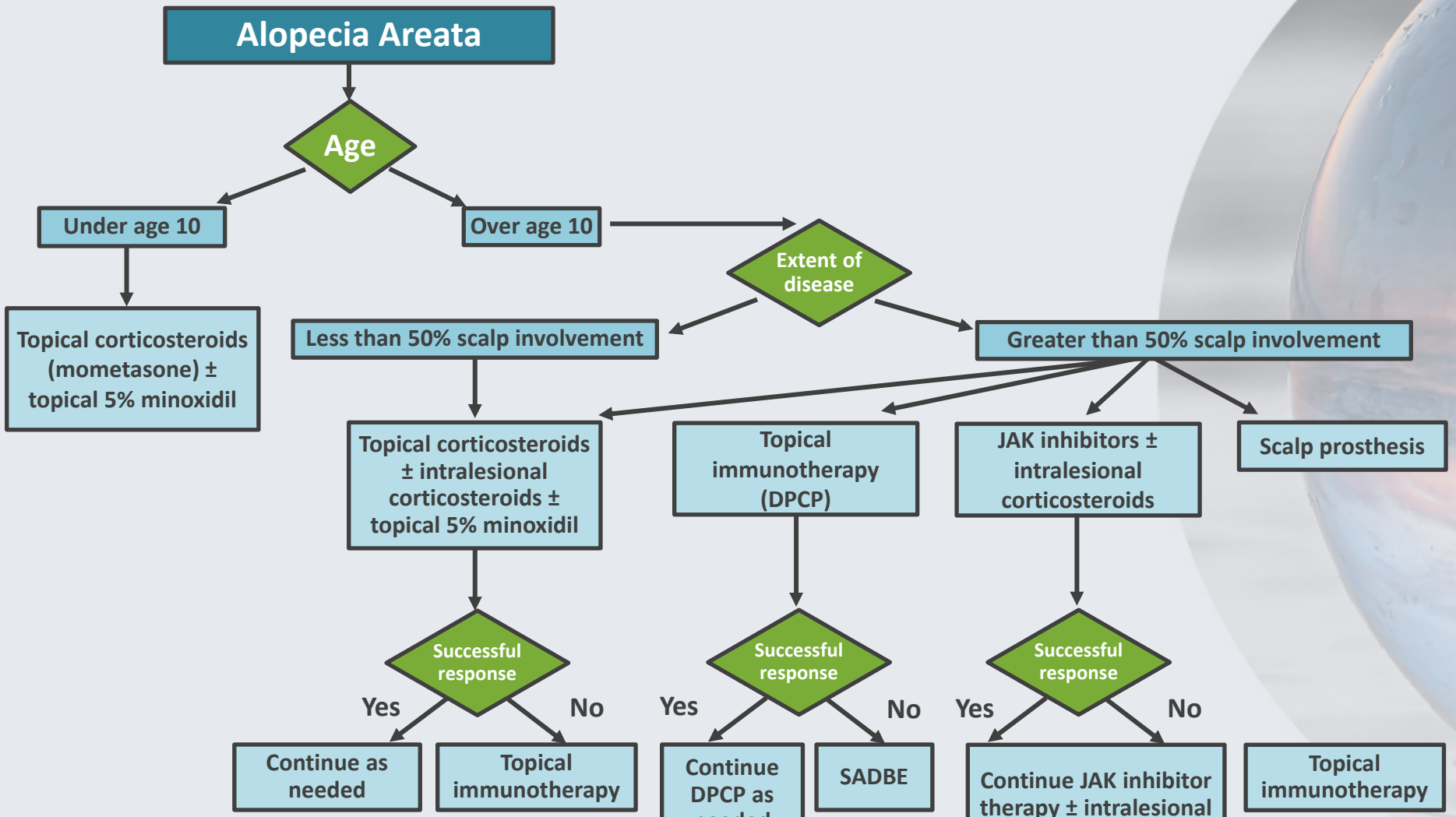
BID, twice a day.

King, B. Presented at the *31th Congress of the EADV*. 2022.

Case Patient Introduction

- 35-year-old man
- 12-year history of moderate-to-severe AA (SALT score=70)
- Duration of current hair loss: 4 years
- Previous medications include topical and oral corticosteroids

Recommendations for AA Management



DPCP, diphenylcyclopropenone; SADBE, squaric acid dibutyl ester.

Strazzulla LC, et al. *JAAD.* 2018;78:15-24.

Understanding the Pharmacoeconomics of AA Treatment

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Healthcare Utilization for AA

Healthcare Resource Utilization Within 365 Days Post-Index

Variable	AA Cases (N=14,340)	Matched Controls (N=42,998)	*P* Value
Inpatient visits, number			
Mean (SD)	0.05 (0.28)	0.05 (0.29)	.50
Median (IQR)	0 (0–0)	0 (0–0)	
ED visits, number			
Mean (SD)	0.23 (0.66)	0.18 (0.73)	<.0001
Median (IQR)	0 (0–0)	0 (0–0)	
Ambulatory visits, number			
Mean (SD)	13.7 (13.2)	7.6 (10.2)	<.0001
Median (IQR)	10 (5–17)	4 (2–10)	
Other visits,* number			
Mean (SD)	1.02 (4.33)	0.65 (3.50)	<.0001
Median (IQR)	0 (0–1)	0 (0–0)	<.0001
Pharmacy prescriptions filled, number			
Mean (SD)	16.9 (21.6)	14.6 (21.3)	<.0001
Median (IQR)	10 (3–23)	6 (1–20)	

*Includes durable medical equipment, home healthcare, and additional miscellaneous categories.

ED, emergency department; IQR, interquartile range; SD, standard deviation.

Mostaghimi A, et al. *Dermatol Ther.* 2022;12:1027-1040.

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Costs Associated With AA Management

Healthcare Resource Utilization Costs Within 365 Days Post-Index

Cost by Variable	AA (N=14,340)	Matched Controls (N=42,998)	*P* Value	Difference	% of Total Difference
Inpatient visits, $	1173 (9620)	1157 (11,456)	<.0001	16	0.5
ED visits, $	491 (2067)	327 (1592)	<.0001	164	4.9
Ambulatory visits, $	3640 (7625)	2062 (6257)	<.0001	1578	46.9
Other visits*, $	561 (2960)	396 (4303)		165	4.9
Filled pharmacy prescriptions, $	3287 (15,727)	1843 (12,306)	<.0001	1444	42.9
Total, $ **Mean (SD)** **Median (IQR)**	 9154 (23,963) 2986 (1266–7500)	 5788 (21,511) 1310 (347–4144)	<.0001	3367	100
Adjusted total all-cause, mean, $ (95% CI)	8557 (7679–9535)	6314 (4455–8947)	<.0001	–	–

*Includes durable medical equipment, home healthcare, and additional miscellaneous categories.
CI, confidence interval.

Mostaghimi A, et al. *Dermatol Ther.* 2022;12:1027-1040.

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Economic Burden of AA on the Individual Patient

Out-of-Pocket Costs Reported by 675 Patients With Alopecia Areata in the Past Year

Category	Costs, $		Patients, Number (%)
	Total	Median (IQR)	
Transportation/parking to doctor visits in the past year	77,100	10 (0–50)	370 (54.8)
Copays/out-of-pocket deductibles for doctor visits in the past year	211,940	50 (0–300)	387 (57.3)
Medications (over the counter and prescription) for hair loss in the past year	138,152	15 (0–200)	348 (51.6)
Vitamins, supplements, or other treatments in the past year	112,736	50 (0–200)	457 (67.7)
Complementary and alternative therapies[a] in the past year	123,825	0 (0–100)	210 (31.1)
Headwear or cosmetic options[b] in the past year	907,856	450 (50–1500)	552 (81.8)
Hair appointments[c]	195,607	50 (0–300)	378 (56.0)
Total out-of-pocket spending	1,767,225	1354 (537–3300)	NA
Approximate lost income/wages/earnings for patients who missed work[d]	279,412	500 (200–2500)	NA

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Li SJ, et al. *JAMA Dermatology*. 2019;155:493-494.

Case Patient: Navigating the Cost Challenges

- The patient is identified as a good candidate for JAK inhibitor therapy
- He and his doctor discuss the pros and cons of initiating treatment
- The patient asks what his options are if his insurance will not cover the treatment

Additional Considerations for Improving AA Management

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Improving Outcomes Through Multi-Stakeholder Collaboration

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Considerations for Formulary Development

Medication Attributes

- Indications for use
- Contraindications
- Route of delivery
- Delivery channel
- Safety and tolerability

Patient Factors

- Extent/location disease
- Patient reported outcomes
- Treatment history and responses
- Comorbidities

Clinical Criteria Factors

- Evidence-based guidelines/association recommendations
- Costs
- Ability to define disease severity
- Availability of real-world evidence

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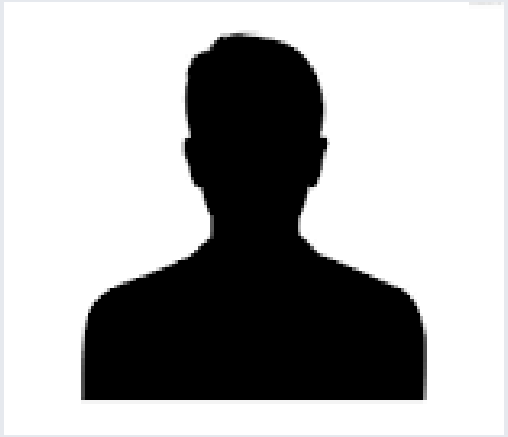
Case Patient: Managing the Side Effects of AA Therapy



- 1-year follow-up visit
- Significant improvement in AA
  - SALT=20
- Patient reports a substantial positive impact on QOL
- Side effects
  - Occasional headache and GI symptoms
  - One episode of pneumonia

GI, gastrointestinal; QOL, quality of life.

Safety Profile of JAK Inhibitors

AEs Commonly Reported

- Upper respiratory tract infection
- Headache
- Nasopharyngitis
- Nausea
- Acne

Black Box Warning

- Serious infection
- Major adverse cardiovascular events
- Thromboembolic events
- Malignancy

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Best Practices for Pharmacist-Conducted Patient Education and Counseling

Establish caring relationships with patients

- Introduce yourself
- Explain purpose of counseling
- Obtain participation agreement
- Determine primary spoken language

Assess patient knowledge

- Health problems
- Medications
- Ability to use medications
- Attitudes & expectations about health & medications

For patients seeking refills:

- Use of medications
- Problems, concerns, or uncertainties with medications

Fill patient gaps in knowledge & understanding

- Provide information orally
- Use visual aids or demonstrations
- If required, adjust pharmacotherapeutic regimens according to protocols & notify prescribers

Verify patient knowledge & understanding of medication use

Ask patients:

- To demonstrate medication use
- To identify medication effects

Assess:

- Medication-use accuracy
- Adherence attitudes
- Monitoring plans

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Am J Health-System Pharmacy. 1997;54:431-434.

Key Points

- AA is an autoimmune condition characterized by T-cell mediated hair loss that imposes a significant disease burden and has profound emotional and psychosocial effects on patients
- Factors contributing to AA severity include scalp hair loss as well as eyebrow/eyelash involvement, treatment refractoriness, rapid progression, and psychosocial impact
- Traditional treatments (glucocorticoids, other immunosuppressive agents, and topical immunotherapy) have variable efficacy for severe AA and are not approved for this indication
- Based on increased understanding of AA pathogenesis, JAK inhibitors (which block T-cell mediated inflammation) have been investigated for AA treatment and have demonstrated good efficacy and safety in phase 3 clinical trials
- In June of this year, the JAK 1/2 inhibitor baricitinib became the first systemic treatment to be approved for AA