Assessing the Growing Evidence in **Alopecia Areata:**

THE ROLE OF JAK INHIBITORS

WEDNESDAY, FEBRUARY 9, 2022

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Assessing the Growing Evidence in Alopecia Areata: THE ROLE OF JAK INHIBITORS

AGENDA

I. Overview of Alopecia Areata

a. Incidence and prevalence
b. Spectrum of disease
c. Risk factors
d. Presentation
e. Pathogenesis of disease
   (1) JAK-STAT signaling pathway

II. Impact of Alopecia Areata

a. Comorbidities
b. Health-related quality of life
c. Qualitative model of psychosocial burden

III. Current Treatment Strategies

a. Intralesional and topical treatments
b. Systemic treatments

IV. Targeting the Pathophysiology of Alopecia Areata

a. Evolving understanding of disease pathogenesis
b. Mechanism of action of JAK inhibitors
c. Efficacy and safety data of JAK inhibitors
d. Treatment algorithm

V. Psychosocial considerations and approaches

a. Patient concerns
b. Importance of communication

VI. Case studies

VII. Q&A

February 2022

Assessing the Growing Evidence in Alopecia Areata: The Role of JAK Inhibitors

FACULTY

Brett King, MD, PhD
Associated Professor of Dermatology
Yale School of Medicine
New Haven, CT

Sergio Vañó Galván, MD, PhD
Dermatologist
Director of the Alopecia Unit
Ramon y Cajal Hospital
Professor
University of Alcala
Madrid, Spain

PROGRAM OVERVIEW

This live virtual activity discusses the underlying autoimmune causes of alopecia areata (AA) and the rationale of targeted treatment approaches. The burden of AA and its associated comorbidities will also be presented, and you will hear strategies to effectively address the psychosocial impacts of this disease with your patients. Features of this program include whiteboard animations, case presentations, and a Q&A session.

TARGET AUDIENCE

This educational activity is intended for dermatology professionals who care for patients with AA.

Learning Objectives

- Explain the pathogenesis of AA and discuss current and emerging treatments for AA
- Determine which patients with AA are and are not candidates for JAK inhibitors
- Create treatment plans for patients with AA that address the comorbidities and psychosocial impacts of the disease

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Purpose: This program would be beneficial for nurses involved in the therapeutic management of patients with AA.
CNE Credits: 1.5 ANCC Contact Hour(s).

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Sergio Vañó Galván, PhD has served on advisory boards and/or is a consultant for Eli Lilly and Company and Pfizer Inc.

CME Content Review

The content of this activity was independently peer-reviewed.
The reviewer of this activity has nothing to disclose.

CNE Content Review

The content of this activity was peer reviewed by a nurse reviewer.

Douglas Cox, MSN, MHA, RN
Ultimate Medical Academy/CCM – Lead Nurse Planner

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A Whiteboard View of the New Era in Alopecia Areata: The Role of JAK Inhibitors

Brett King, MD, PhD
Associate Professor of Dermatology
Yale University School of Medicine
New Haven, CT

Sergio Vaño-Galván, MD, PhD
Dermatologist
Director of the Alopecia Unit
Ramón y Cajal Hospital
Professor
University of Alcalá
Madrid, Spain

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Disclosures

- **Brett King, MD, PhD** has served on advisory boards and/or is a consultant and/or is a clinical trial investigator for Abbvie, Aclaris Therapeutics Inc, AltruBio Inc, Almirall, AnaptysBio, Arena Pharmaceuticals, Bioniz Therapeutics, Bristol-Meyers Squibb, Concert Pharmaceuticals Inc, Dermavant Sciences Inc, Horizon Therapeutics, Eli Lilly and Company, Incyte Corp, LEO Pharma, Otsuka/Visterra Inc, Pfizer Inc, Regeneron, Sanofi Genzyme, TWi Biotechnology Inc, and Viela Bio. He is on speaker bureaus for Pfizer Inc, Regeneron, and Sanofi Genzyme
- **Sergio Vañó Galván, PhD** has served on advisory boards and/or is a consultant for Eli Lilly and Company and Pfizer Inc.
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Educational Objectives

- Explain the pathogenesis of AA and discuss current and emerging treatments for AA
- Determine which patients with AA are and are not candidates for JAK inhibitor therapy
- Create treatment plans for patients with AA that address the comorbidities and psychosocial impacts of the disease

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Overview of Alopecia Areata

Sergio Vaño-Galván, MD, PhD

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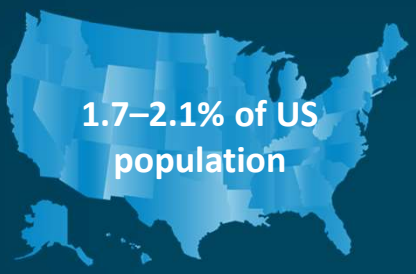
AA Incidence/Prevalence (US and Worldwide)

Alopecia areata affects:



- ☑ Males and females are similarly affected
- ☑ Onset typically in the first 4 decades of life
- ☑ No known racial preference

AA = alopecia areata; US = United states.

Mirzoyev SA, et al. *J Invest Dermatol*. 2014;134:1141-1142. Safavi K. *Arch Dermatol*. 1992;128:702. Muller SA, Winkelmann RK. *Arch Dermatol*. 1963;88:290-297. Liu LY, et al. *J Am Acad Dermatol*. 2017;76:22-28. Fricke ACV, Miteva M. *Clin Cosmet Investig Dermatol*. 2015;8:397-403. Strazzulla LC, et al. *J Am Acad Dermatol*. 2018;78:15-24.

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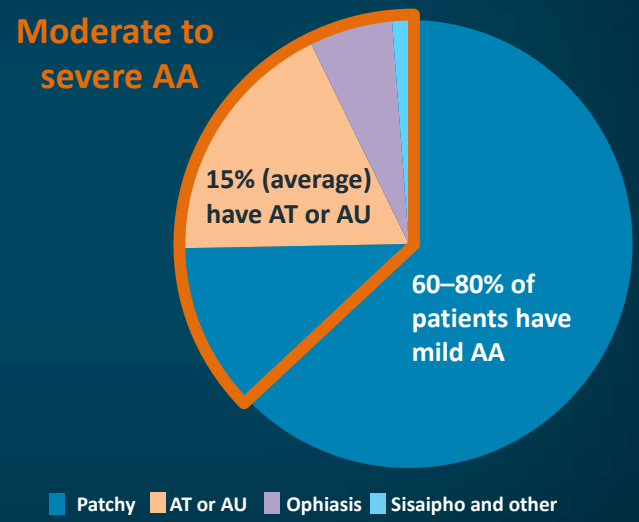
Natural History of AA

- **Most** cases are ***mild* at onset,** and many patients will recover within 6 months to 1 year, although most will experience another episode
  - *AA is a chronic **relapsing and remitting** disease*
- **Progression to *more severe disease* *can* occur *over weeks to years***
- Scalp is involved in the ***vast majority*** of cases, but all hair-bearing sites may be affected



AA = alopecia areata; AT = alopecia totalis; AU = alopecia universalis.

Muller SA, Winkelmann RK. *Arch Dermatol*. 1963;88:290-297. Fricke ACV, Miteva M. *Clin Cosmet Investig Dermatol*. 2015;8:397-403. Safavi K. *Arch Dermatol*. 1992;128:702. Lepe K. *Stat Pearls*. https://www.statpearls.com/articlelibrary/viewarticle/17385/. Accessed 12/11/20. Cranwell WC, et al. *Australas J Dermatol*. 2019:60:163-170. Safavi KH, et al. *Mayo Clin Proc*. 1995;70;:628-633.

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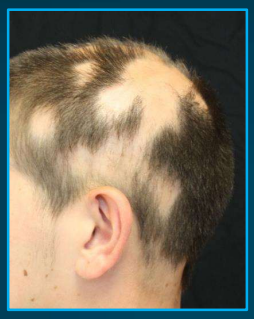
Spectrum of Disease

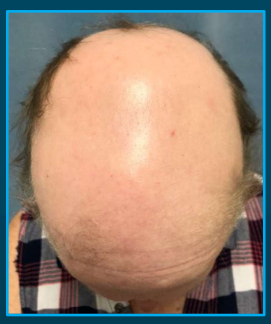
Patchy AA

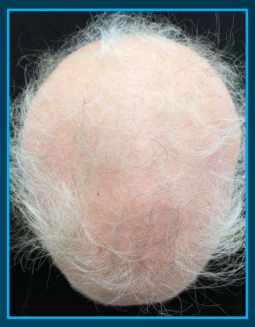
Circular areas of hair loss



Sisaipho AA

Involvement of top of scalp, sparing lateral scalp and occiput



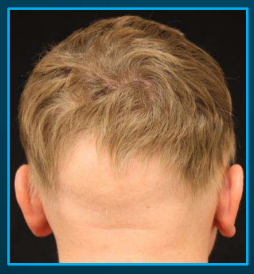


Diffuse AA

Diffuse thinning of scalp hair

Ophiasis AA

Band-like area extending from right to left ear



AT/AU

Total loss of hair over scalp (totalis) or entire body (universalis)

Images courtesy of Dr. Brett King. Messenger AG. *UpToDate.* 2019 (https://www.uptodate.com/contents/alopecia-areata-clinical-manifestations-and-diagnosis?topicRef=7631&source=see_link). Accessed 12/11/20.

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Spectrum of Disease (continued)

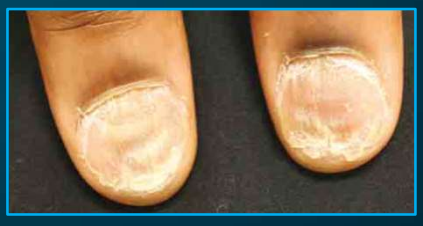
Eyebrows involvement

Eyebrows and eyelashes involvement

Beard involvement

Eyelashes involvement

Nail involvement



Dhayalan A, King BA. *JAMA Dermatol.* 2016;152:492-493. Craiglow BG, King BA. *J Invest Dermatol.* 2014;134:2988-2990. Craiglow BG. *J AAD Case Rep.* 2018; 4:988-989. *Additional images courtesy of Dr. Brett King.*

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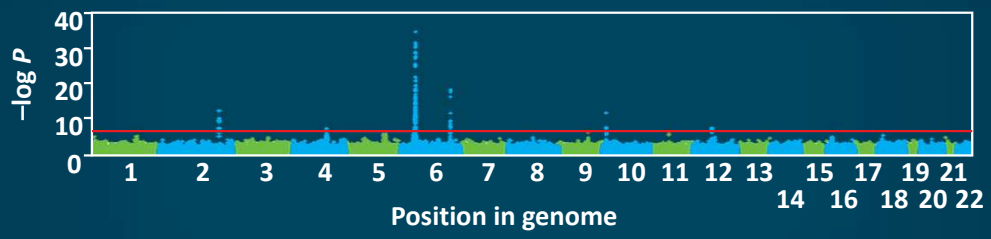
Risk Factors for AA

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

Manhattan plot of joint analysis of discovery GWAS and the replication GWAS



Genetics are ***important***

Triggers/Environmental factors are poorly understood

GWAS = genome-wide association study.

Jackow C, et al. *J Am Acad Dermatol.*1998;38:418-425. Petukhova L, et al. *Nature*. 2010;466:113-117.

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Presentation of Alopecia Areata

General features

- Altered sensation
- Patches appear overnight due to breakage
- Circular bald patches that enlarge circumferentially
- Colliding patches produce polycyclic shapes
  - Associated ↑ hair shedding that can be localized or generalized
  - Exclamation-mark hairs
- Nail pits and trachyonychia

Histology

- Peri-bulbar lymphocytic inflammatory infiltrate
- Multiple catagen hairs
- Multiple vellus-like hairs
- Non-scarring

Gilmore S, Sinclair RD. *Exp Dermatol.* 2010; 19:575. Baldari M, et al. *JEADV.* 2009;23:702-738. University of Michigan. Alopecia Areata. 2019 (https://www.uofmhealth.org/health-library/ug2838spec). Accessed 12/14/20. Whiting D. *JAMA Dermatol.* 2003;139:1555-1559.

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Trichoscopic Signs of AA and Their Relationship With Disease Activity

AD12

Signs of Activity	Inactive Disease	Signs of Hair Repopulation
Black dots Exclamation mark hairs Broken hairs Tapered hairs Pseudo-monilethrix	Yellow dots Vellus hairs Empty follicular orifices	Straight regrowing hairs Pigtail hairs Vellus hairs

EXCLAMATION MARK HAIRS

BLACK DOTS

PIGTAIL HAIRS

Waśkiel A, et al. *J Dermatol*. 2018;45(6):692-700.

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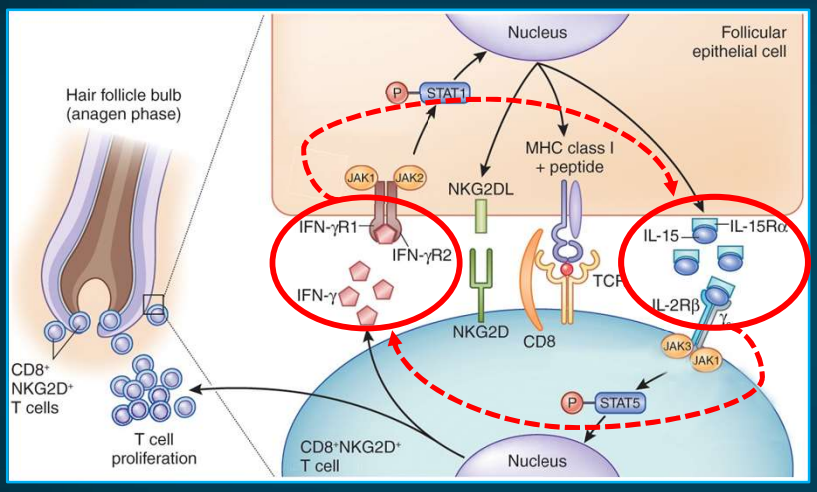
Alopecia Areata Pathogenesis



AA involves cytotoxic T lymphocytes

- **Secretion of IL-15** in follicular epithelial cells recruits and activates cytotoxic T cells
- Cytotoxic T cells **secrete IFN-γ**, which binds its receptor on the follicular epithelial cell, ***leading to further secretion of IL-15***
- This **cyclical action** leads to inflammation and subsequent hair loss

IL = interleukin; IFN = interferon; MHC = major histocompatibility complex; CD = cluster of differentiation

Gilhar A, et al. *J Clin Invest*. 2007;117:2019-2027. Xing L, et al. *Nat Med*. 2014;20:1043-1049. Divito SJ, Kupper TS. *Nat Med*. 2014:20:989-990.

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Impact of Alopecia Areata

Brett King, MD, PhD

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The Impact of Alopecia Areata

HAIR IS A BIG DEAL!

- Comorbid autoimmune and inflammatory diseases are common in patients with AA
- AA can have a significant negative impact on patients *and* their families

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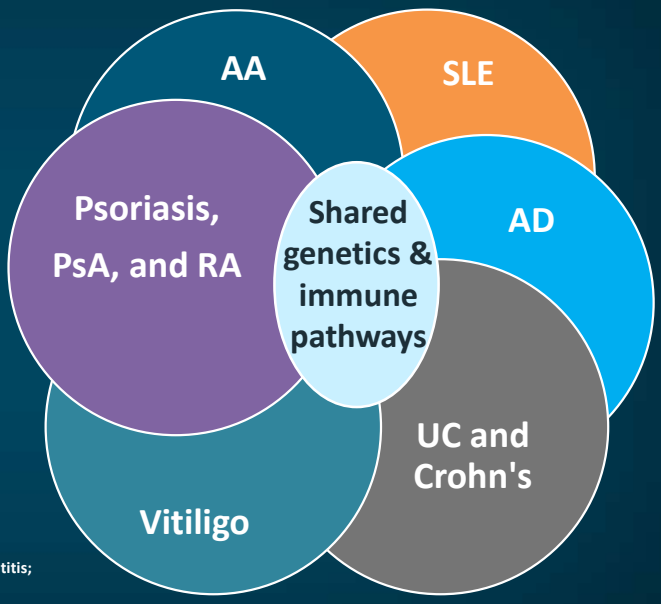
Alopecia Areata: Comorbidities

- Comorbid **autoimmune disease**
  - Thyroid disorders—Hashimoto's thyroiditis (OR = 2.15) and Graves' disease (OR = 2.07)
- Comorbid **atopic disease**
  - Atopic dermatitis (OR = 2.36), asthma (OR = 1.24), and allergic rhinitis (OR = 1.33)
- Comorbid **psychiatric disease**
  - Lifetime prevalence of depression and anxiety up to 39%



OR = odds ratio; AA = alopecia areata; SLE = systemic lupus erythematosus; AD = atopic dermatitis; UC = ulcerative colitis; PsA = psoriatic arthritis ; RA = rheumatoid arthritis

Lee S, et al. *J Am Acad Dermatol*. 2019;80:466-477.e16. Kridin K, et al. *J Allergy Clin Immunol Pract*. 2020;8:1323-1328. Colón EA et al. *Compr Psychiatry*. 1991;32:245-251. Petukhova L, et al. *Nature*. 2010;466:113-117. Gilhar A, et al. *J Allergy Clin Immunol*. 2019;144:1478-1489. Damsky W, King BA. *J Am Acad Dermatol*. 2017;76:736-744.

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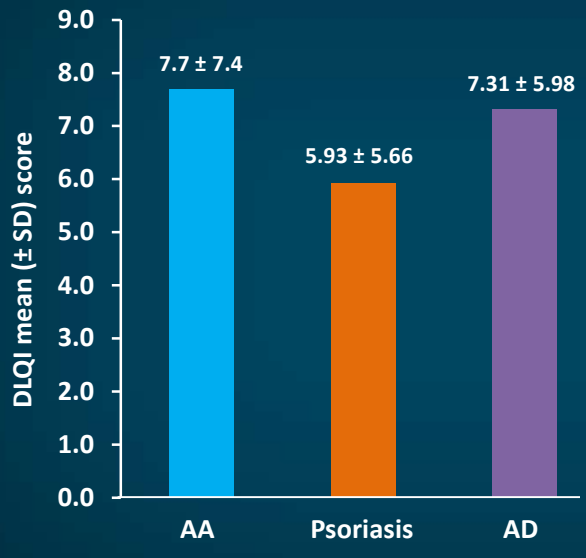
Health-Related Quality of Life in AA, Psoriasis, and AD*



AA has a detrimental effect on HRQoL similar to that of other chronic dermatologic diseases

We do not hesitate to treat patients who have psoriasis and AD with systemic therapies, and so we should not hesitate to treat patients with AA with systemic therapies

*Comparing DLQI from different studies.

DLQI = Dermatology Life Quality Index; SD = standard deviation; AA = alopecia areata; AD = atopic dermatitis; HRQoL = health-related quality of life

Liu LY, et al. *J Am Acad Dermatol*. 2018;79:556-558.e1. Lundberg L, et al. *Acta Derm Venereol*. 2000;80:430-434.

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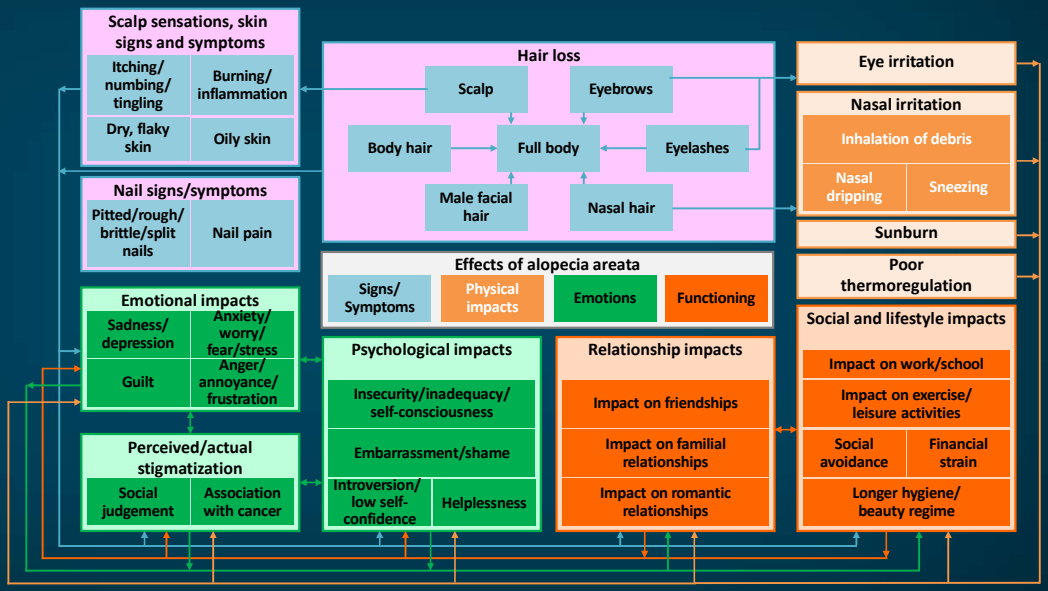
Qualitative Model of Psychosocial Burden of Alopecia Areata

From interviews with 45 patients with AA, 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.

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Current Treatment Strategies

Sergio Vaño-Galván, MD, PhD

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Intralesional and Topical Treatments*

Agent	Cellular Effect	Adverse events
Intralesional triamcinolone	Inhibits T cells	Skin atrophy at injection site, small risk for ↑ IOP, glaucoma, cataracts with injections near eyes
Topical corticosteroids	Inhibits T cells	Mild itching, burning, acneiform eruption, striae, telangiectasia, skin atrophy
Topical immunotherapy (eg, diphenylcyclopropenone, squaric acid)	Alters immune milieu via allergic contact dermatitis	Teratogenic effects, severe eczema, cervical/occipital LAD
Topical minoxidil	Mechanism of action unknown	Scalp itching, dermatitis, vellus hairs on other body parts, tachycardia

IOP = intraocular pressure; LAD = lymphadenopathy.

See prescribing information (PI) for individual agents. PDR. Strazzulla LC, et al. *J Am Acad Dermatol.* 2018;78:15-24. Minoxidil. 2020 (https://www.pdr.net/drug-summary/Minoxidil-minoxidil-774). Accessed 12/11/20.

**Triamcinolone, corticosteroids, minoxidil, and topical immunotherapy are not FDA-approved for treatment of AA.*

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Systemic Treatments

Agent	Description	Cellular Effect	Adverse events
Azathioprine*	Antimetabolite	Inhibits T-cells	Serious infection, nausea, vomiting, diarrhea, hepatotoxicity
Cyclosporine*	Calcineurin inhibitor	Down-regulation of NFAT transcription factor, preventing transcription of T-cell effector cytokines	Serious infection, nephrotoxicity, hepatotoxicity, neurotoxicity
Methotrexate*	Antimetabolite	Interferes with DNA synthesis, repair and cellular replication	Serious infection, renal, GI, hepatic, pulmonary toxicity, hypersensitivity and dermatologic reactions
Prednisone/ Prednisolone/ Dexamethasone*	Corticosteroid	Inhibits T- and B-lymphocyte proliferative responses	Osteopenia/porosis, osteonecrosis, glaucoma, cataracts, steroid myopathy, weight gain, mood change, HTN, DM, Pituitary-adrenal axis suppression
Minoxidil*	Non-specific hair growth stimulator	Mechanism of action in hair cycle unknown	Hypertrichosis, pruritis, xerosis, nausea, vomiting, edema, CV events

NFAT = nuclear factor of activated T cells: DNA = deoxyribonucleic acid; GI = gastrointestinal; HTN = hypertension; DM = diabetes mellitus; CV = cardiovascular; black box = black box warning.

See prescribing information (PI) for individual agents. Cyclosporine A (www.invivogen.com/cyclosporin-a). Accessed 12/7/2020. Chow CW, et al. *Mol Cell Biol.* 1999;19:2300-2307. Lai VWY, Sinclair R. *J Eur Acad Dermatol Venereol.* 2020;Aug 10: Epub ahead of print. Minoxidil. 2020 (https://www.pdr.net/drug-summary/Minoxidil-minoxidil-774). Accessed 12/11/20. Strazzulla LC, et al. *J Am Acad Dermatol.* 2018;78:15-24. Vañó-Galván S, et al. *J Am Acad Dermatol.* 2016;74(5):1005-1007.

**Azathioprine, cyclosporine, methotrexate, prednisolone and minoxidil are not FDA-approved for treatment of AA.*

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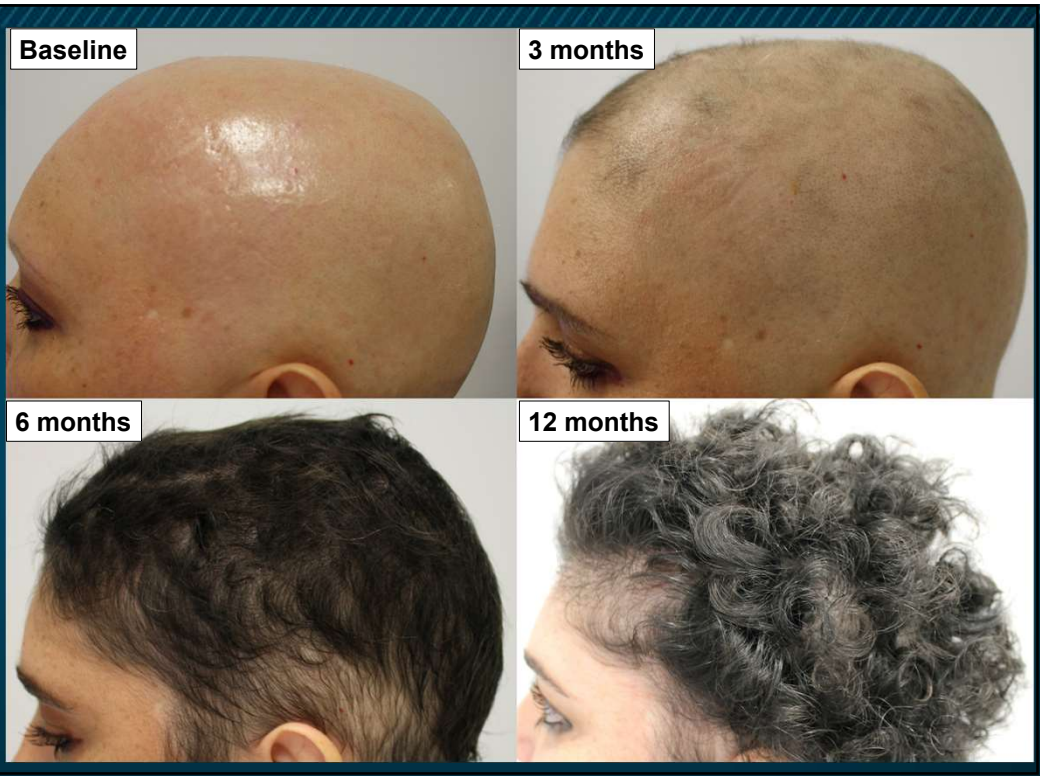
- 35-year-old female with alopecia universalis
- Treatment with oral dexamethasone, 8 mg every Friday and Saturday



Images courtesy of Dr Sergio Vaño-Galván.

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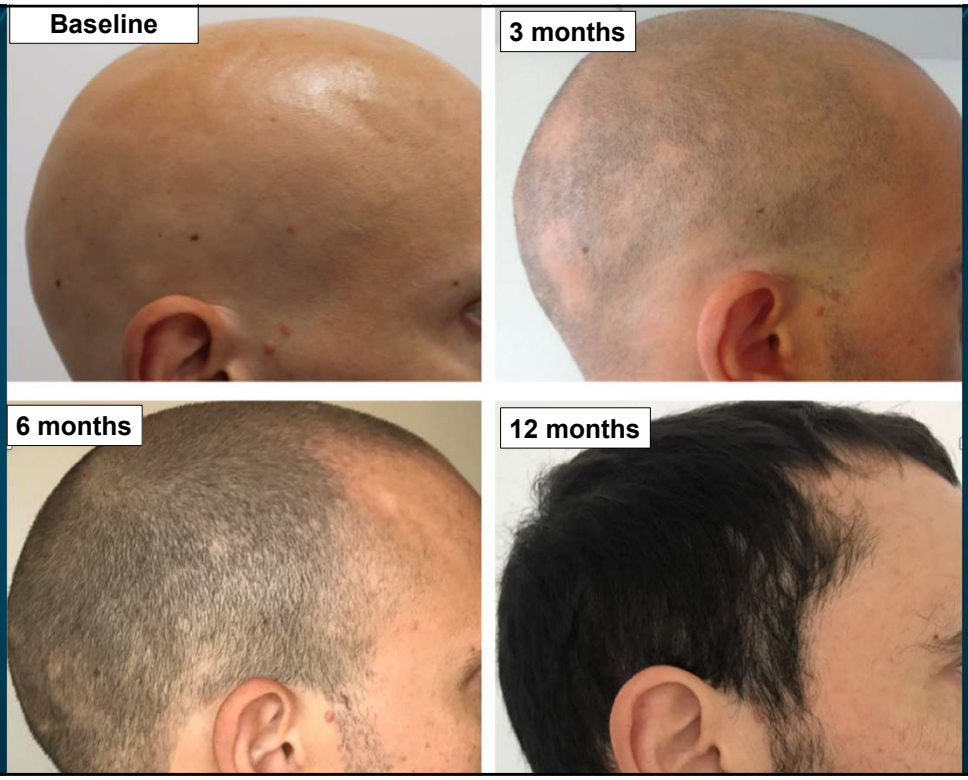
- 37-year-old male with alopecia universalis
- Treatment with oral dexamethasone, 8 mg every Friday and Saturday



Images courtesy of Dr Sergio Vaño-Galván.

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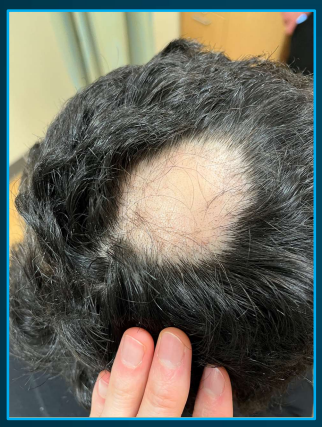
Use Intralesional Corticosteroids for Small Areas



Images courtesy of Dr. Brett King.

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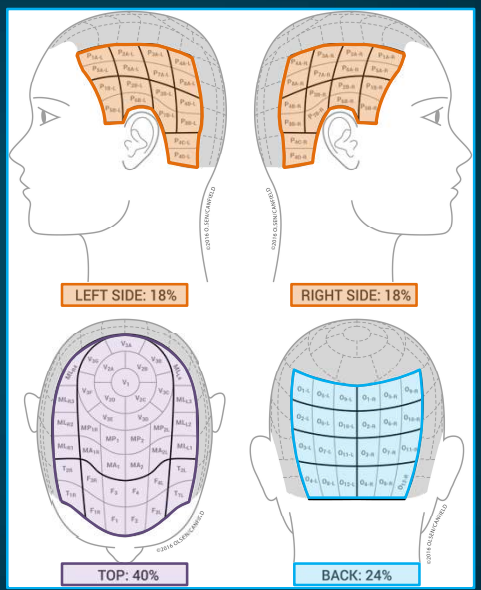
Intralesional Treatment Considerations

- 1% of the SSA is ~7 cm^2
- Intralesional triamcinolone 0.1 ml every 1–2 cm^2
- 10% loss = ~70 cm^2 = average ~35 injections
- 20% loss = ~140 cm^2 = average ~70 injections

AA involving >20% of the SSA may be an indication for systemic therapy



SSA = scalp surface area.

Cranwell WC, et al. *Australas J Dermatol.* 2019:60:163-170. Olsen EA, Canfield D. *J Am Acad Dermatol.* 2016;75:1268-1270. Messenger AG. Alopecia Areata: Management. *UpToDate.* 2019 (https://www.uptodate.com/contents/alopecia-areata-management?topicRef=3320&source=related_link#H2659264073). Accessed 12/11/20.

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AD15

28-year-old female with patchy alopecia areata treated with 2 sessions of intralesional triamcinolone 8 mg/ml

Images courtesy of Dr Sergio Vañó-Galván.

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AD16

31-year-old female with patchy alopecia areata treated with single session of intralesional triamcinolone 12 mg/ml

Images courtesy of Dr Sergio Vañó-Galván.

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25-year-old female with alopecia areata involving eyebrow treated with single session of intralesional triamcinolone 4 mg/ml

Images courtesy of Dr Sergio Vañó-Galván.

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Systemic Therapy Continuation Rates at 12 Months

Agent	Non-Responders n/N (%)	Responders n/N (%)	Responders Using Concurrent Prednisolone n/N (%)	Average daily dose of concurrent prednisolone (mg)
Cyclosporine	17/43 (40%)	26/43 (60%)	15/26 (58%)	8.7
Methotrexate	11/22 (50%)	11/22 (50%)	7/11 (64%)	5.0
Azathioprine	18/73 (25%)	55/73 (75%)	37/55 (67%)	5.6

- **Responders** are defined as patients who have either continued therapy for 12 months or longer or who have stopped therapy due to *complete remission*
- **Non-responders** are defined as patients who *stopped therapy prior to 12 months,* either due to side effects or lack of efficacy (including relapse while on treatment)

Lai VWY, Sinclair R. *J Eur Acad Dermatol Venereol.* 2020;Aug 10: Epub ahead of print.

28

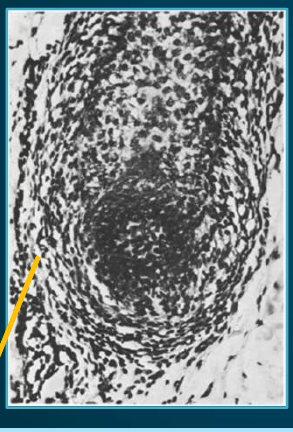
Targeting the Pathophysiology of Alopecia Areata

Brett King, MD, PhD

29

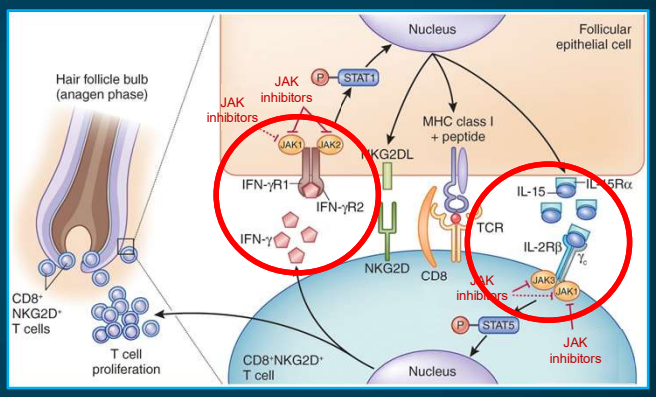
Evolving Understanding of Disease Pathogenesis

1982



Hair bulb surrounded by lymphocytic infiltrate

2014

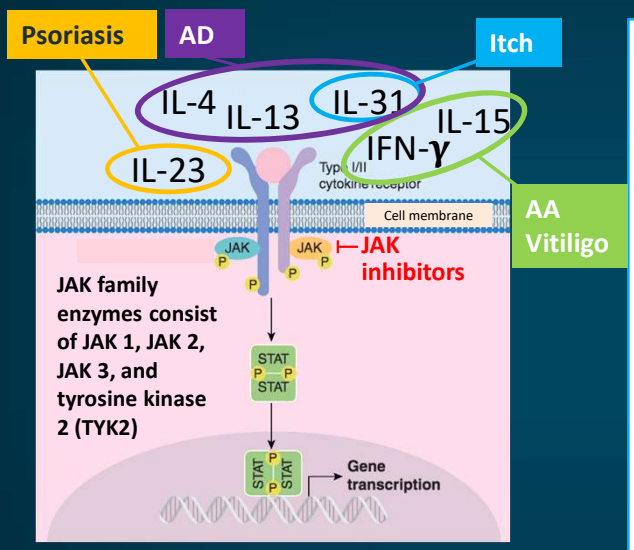


STAT = signal transducer and activator of transcription; TCR = T cell receptor.

Perrett C, et al. *Arch Dermatol Res.* 1982;273:155-158. Petukhova L, et al. *Nature.* 2010;466:113-117. Divito SJ, Kupper TS. *Nat Med.* 2014:20:989-990. Xing L, et al. *Nat Med.* 2014;20:1043-1049.

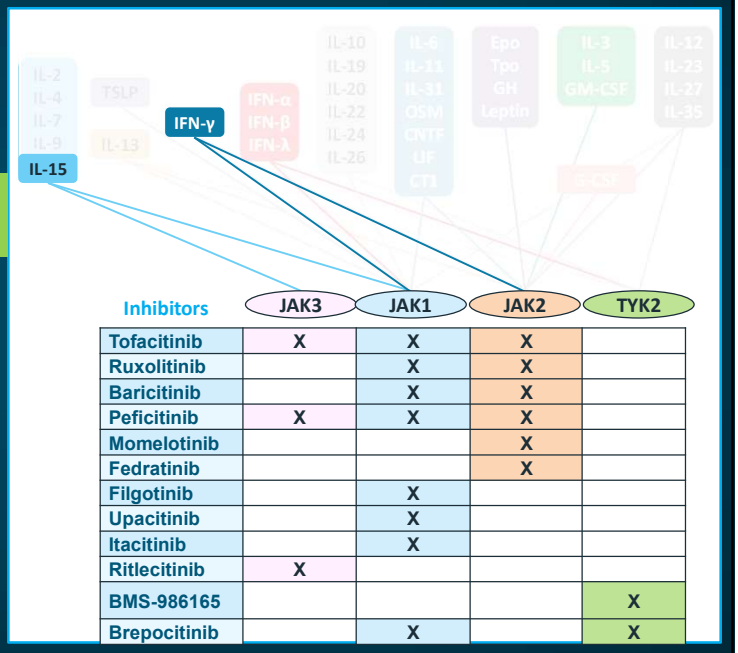
30

JAK Inhibitors Modulate Skin Disease and Cytokine Signaling



IL = interleukin; IFN-γ = interferon gamma; JAK = Janus kinase; TYK2 = tyrosine kinase 2

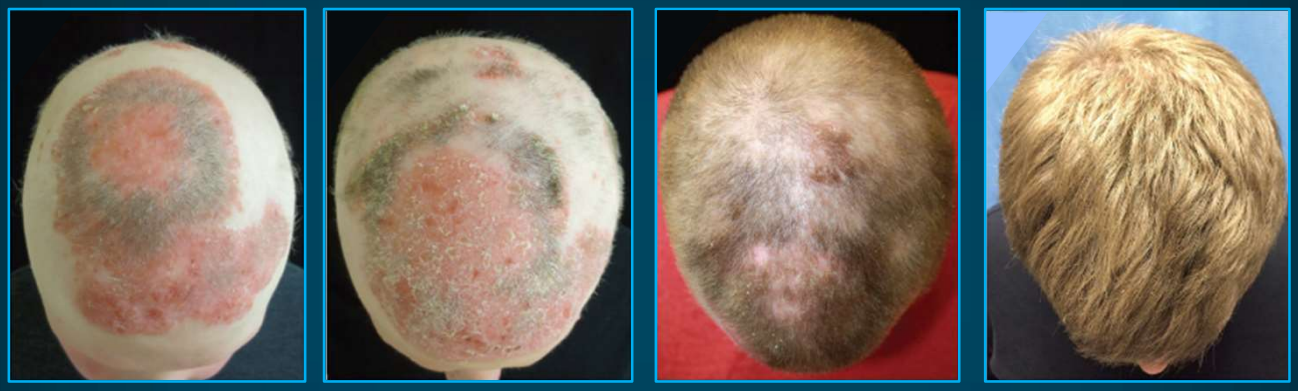
Adapted from Gadina M et al. *J Leukoc Biol.* 2018:104:499-514.



Inhibitors	JAK3	JAK1	JAK2	TYK2
Tofacitinib	X	X	X	
Ruxolitinib		X	X	
Baricitinib		X	X	
Peficitinib	X	X	X	
Momelotinib			X	
Fedratinib			X	
Filgotinib		X		
Upacitinib		X		
Itacitinib		X		
Ritlecitinib	X			
BMS-986165				X
Brepocitinib		X		X

31

Effect of Oral Tofacitinib on AU in Patient with Plaque Psoriasis



Baseline | 2 months Tofa 5 mg BID | 5 months Tofa 10 + 5 mg daily | 8 months Tofa 10 + 5 mg daily

Tofa = tofacitinib; BID = twice daily.

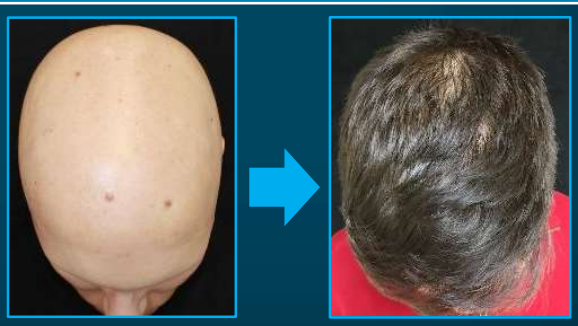
Craiglow BG, King BA. *J Invest Dermatol.* 2014;134:2988-2990.

32

Randomized Controlled Trials of JAK Inhibitors* in AA

- Topical ruxolitinib 1.5% cream
- Ritlecitinib (PF-06651600)
- Deuruxolitinib (CTP-543)
- Baricitinib

The primary outcome measure in AA clinical trials is scalp hair regrowth. The Severity of Alopecia Tool (SALT) score is an assessment of the amount of scalp hair loss in a patient.



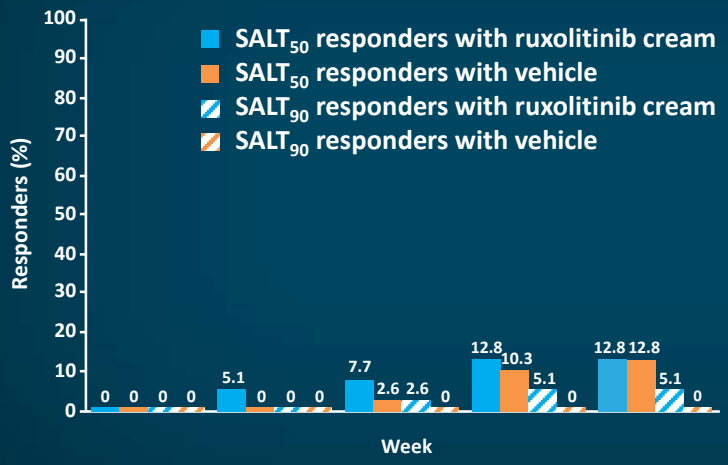
SALT score = 100 SALT score = 0

Olsen EA, et al. *J Am Acad Dermatol.* 2020;82:412-419. Olsen EA, et al. *J Am Acad Dermatol.* 2004; 51:440-447. *Images courtesy of Dr. Brett King.*

*JAK inhibitors are not FDA-approved for treatment of AA.

33

Ruxolitinib* Cream: Phase 2 Results



Ruxolitinib 1.5% cream was ***ineffective*** in the treatment of AA

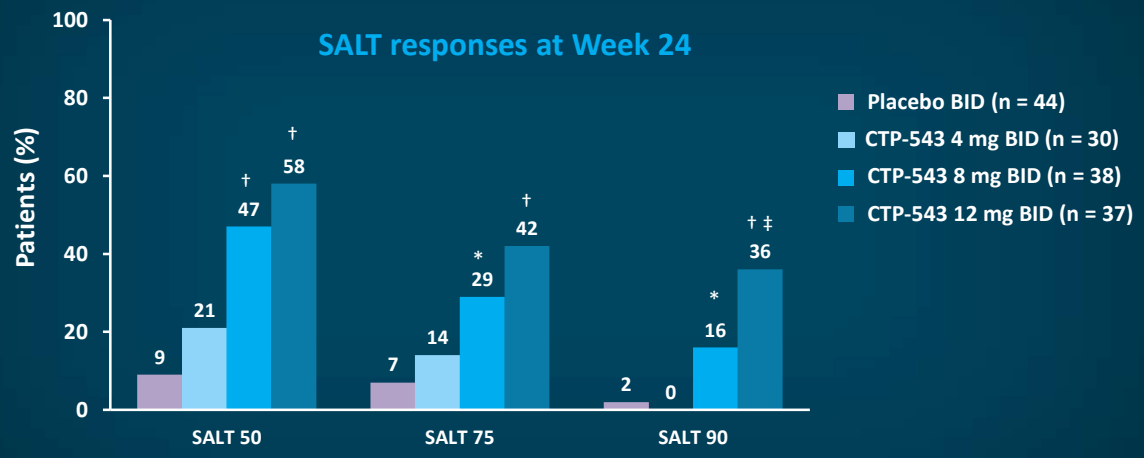
SALT50 = 50% improvement in SALT score; SALT90 = 90% improvement in SALT score.

Olsen EA, et al. *J Am Acad Dermatol.* 2020;82:412-419.

*JAK inhibitors are not FDA-approved for treatment of AA.

34

Deuruxolitinib* (CTP-543): Phase 2 Results



SALT50 = 50% improvement in SALT score; SALT75 = 75% improvement in SALT score ; SALT90 = 90% improvement in SALT score; BID = twice daily.

*P <.05 vs PBO; †P <.001 vs PBO; ‡P <.05 vs CTP-543 8 mg BID.

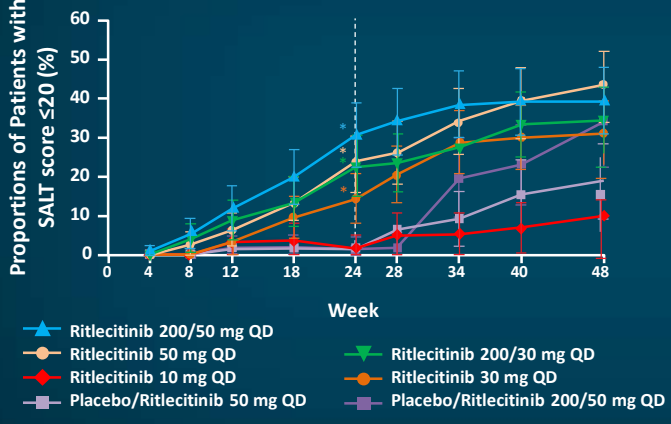
Casella J, et al. Presentation at EADV congress, 2019.

*Deuruxolitinib is not FDA-approved for treating AA.

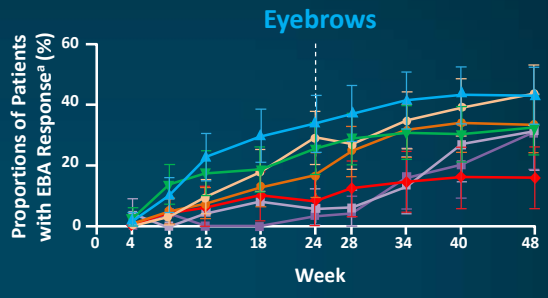
35

Ritlecitinib* (PF-06651600): Phase 3 Results

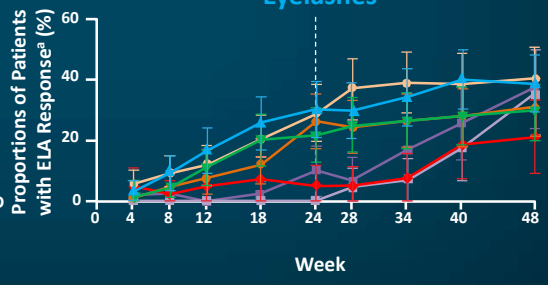
Primary endpoint of SALT score ≤20 at Week 24 met for 200/50 mg, 200/30 mg, 50 mg, and 30 mg ritlecitinib groups



Eyebrows



Eyelashes



[a]Among participants without normal eyebrows/eyelashes at baseline.
EBA = eyebrow assessment scale; ELA = eyelash assessment scale; QD = once daily; SALT = Severity of Alopecia Tool.

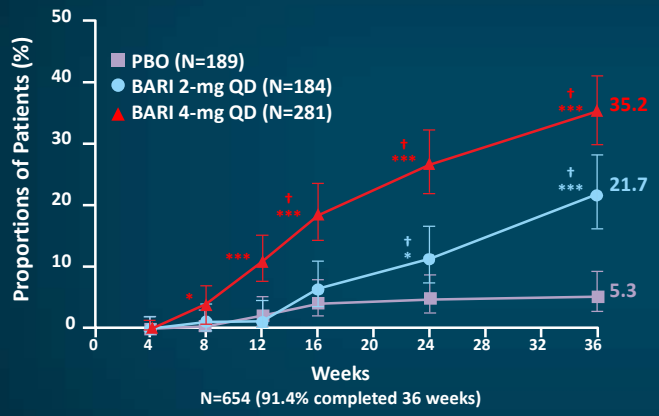
King B, et al. EADV Congress 2021. Presentation.

*Ritlecitinib is not FDA-approved for treating AA.

36

Baricitinib*: Phase 3 Results

Primary endpoint of SALT score ≤20 at Week 36 met for baricitinib 4 mg and 2 mg groups



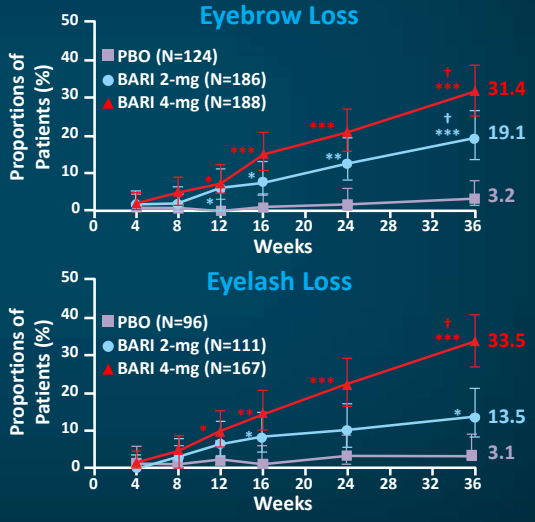
N=654 (91.4% completed 36 weeks)

† Statistically significant vs. PBO after multiplicity adjustment in graphical testing schemes; * p≤0.05, ** p≤0.01, *** p≤0.001 vs. PBO without adjustment for multiple comparisons

BARI = baricitinib; ClinRO = clinician-reported outcome ; QD = once daily; SALT = Severity of Alopecia Tool.

ClinRO measure for eyebrow and eyelash loss (0, 1) through Week 36

(0 = normal, 1 = minimal gaps/even distribution)



King B, et al. EADV Congress 2021. Presentation.

*Baricitinib is not FDA-approved for treating AA.

37

JAK Inhibitors* for Which There Are Reports of Efficacy or Clinical Trials Showing Efficacy in AA

The mechanism of action of JAK inhibitors includes blocking signaling of JAK-STAT dependent cytokines, including IL-15 and IFN-γ

JAK Inhibitors Showing Efficacy in AA		
Agent	**JAK Specificity**	**Adverse Events**
Baricitinib	JAK 1/2 inhibitor	Infection, URI, nausea, herpes simplex and herpes zoster [redacted]
Tofacitinib	JAK 1/3 inhibitor	Infection, thrombosis, URI, nasopharyngitis, diarrhea, headache, ↑ serum CPK, rash, herpes zoster [redacted]
Ruxolitinib	JAK 1/2 inhibitor	Infection, thrombocytopenia, anemia, neutropenia [redacted]
Ritlecitinib (investigational)	JAK 3/TEC inhibitor	Infection, arthralgia, pruritis, hepatoxicity *(phase 2 findings)*
CTP-543 (investigational) *Deuterium-modified ruxolitinib*	JAK 1/2 inhibitor	Nasopharyngitis, acne, headache, ↑ serum CPK, URI, ↑ weight, ↑ lipase *(phase 2 findings)*

CPK = creatinine phosphokinase; black box = black box warning.

See individual PIs for information on agents with an indication. Robinson MF, et al. *Arthritis Rheumatol*. 2020;72:1621-1631. Concert Pharmaceuticals press release (https://ir.concertpharma.com/node/11551/pdf). Accessed 12/7/2020. Bechman K, et al. *Pharmacol Res*. 2019;147:104392. Robinson MF, et al. *Arthritis Rheumatol*. 2020;72:1621-1631. Cassella J, et al. EADV 2020. Gadina M et al. *J Leukoc Biol*. 2018:104:499-514.

*JAK inhibitors are not FDA-approved for treatment of AA.

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Can Treatment Be Achieved With Other Therapeutics?

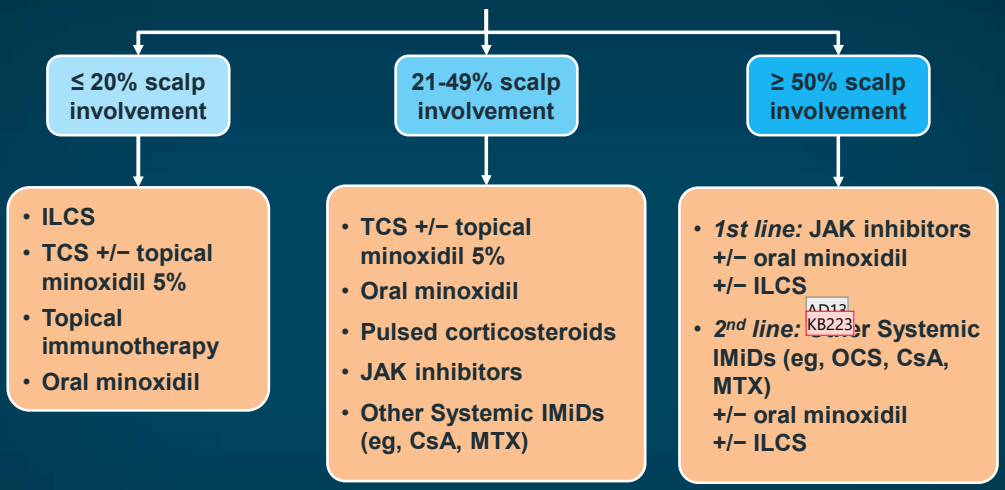
Agent	Description	Mechanism of Action	Does it work?
Apremilast	Small molecule	PDE4 inhibitors	No
Secukinumab	Monoclonal antibody	Binds IL-17	No
Ustekinumab	Monoclonal antibody	Binds subunit, blocking IL12/23	No
Dupilumab	Monoclonal antibody	Binds IL4R-alpha receptor, blocking IL4/13 signaling	Case reports of new-onset AA after starting dupilumab **as well as** hair regrowth with dupilumab
IL-2	Cytokine	Regulatory T cell homeostasis	No
Abatacept	Fusion protein (CTLA-4 linked to modified Fc)	Selective T-cell costimulation modulator, blocking CD28 interaction	No

PDE4 = phosphodiesterase-4.

Keren A, et al. *J Dermatol Sci.* 2015;77:74-76. Mikhaylov D, et al. *Arch Dermatol Res*. 2019; 311:29-36. Liu LY, King BA. *J Am Acad Dermatol*. 2017;77:773-774. Guttman-Yassky E, et al. *Arch Dermatol Res*. 2018;310:607-614. Guttman-Yassky E, et al. *J Allergy Clin Immunol*. 2016;137:301-304. Slowińska M, et al. *J Dermatol Case Rep*. 2010;4:15-17. Verros C, et al. *Dermatol Online J*. 2012;18:14. Aleisa A, et al. *Pediatr Dermatol*. 2019;36:e44-e45. Ortolan LS, et al. *J Allergy Clin Immunol*. 2019;144:1731-1734.e1. Mitchell K, Levitt J. *JAAD Case Rep*. 2018;4:143-144. Darrigade AS, et al. *Br J Dermatol*. 2018;179:534-536. Penzi LR, et al. *JAMA Dermatol*. 2018;154:1358-1360. Flanagan K, et al. *JAAD Case Rep*. 2018;5:54-56. Mackay-Wiggan J, et al. *J Am Acad Dermatol*. 2020;Oct 9: Epub ahead of print. Castela E, et al. *JAMA Dermatol*. 2014;150:748-751.

39

Developing a Treatment Algorithm for AA



ILCS = intralesional corticosteroids; MTX = methotrexate; CsA = cyclosporin; IMiD = immune modulating drugs; OCS = oral corticosteroids.
Algorithm courtesy of Dr. Brett King with adaptation from Strazzulla LC, et al. *J Am Acad Dermatol.* 2018;78:15–24.

**None of the therapies listed above are FDA-approved for treatment of AA.*

40

Psychosocial Considerations and Approaches

Sergio Vaño-Galván, MD, PhD

41

Patients With AA Often Feel HCPs Are Dismissive of Them and Their Disease

- There is history of AA being said to be caused by patients' stress/depression/anxiety

AA is an autoimmune disease with genetic predisposition that has a profound negative impact on HRQoL

- Support groups may provide some benefit from patients knowing they are not alone
- As with ANY disease or event that causes distress, therapy/counseling may provide some benefit to those suffering distress from AA

Counseling and/or medical management of patients' stress/depression/anxiety *must never be confused with treatment of their AA*

What we want for patients with AA is what patients with AA want and that is *effective treatment of their AA…*

HCP = healthcare provider.

Liu L et al. *J Am Acad Dermatol.* 2018;79:556-558. Shapiro J. *J Invest Derm Symp Proceed.* 2013;16:S42-S44. Cipriani R, et al. *Int J Dermatol.* 2001;40:600-601. Liu LY, et al. *J Am Acad Dermatol.* 2018;78:597-599.e2.

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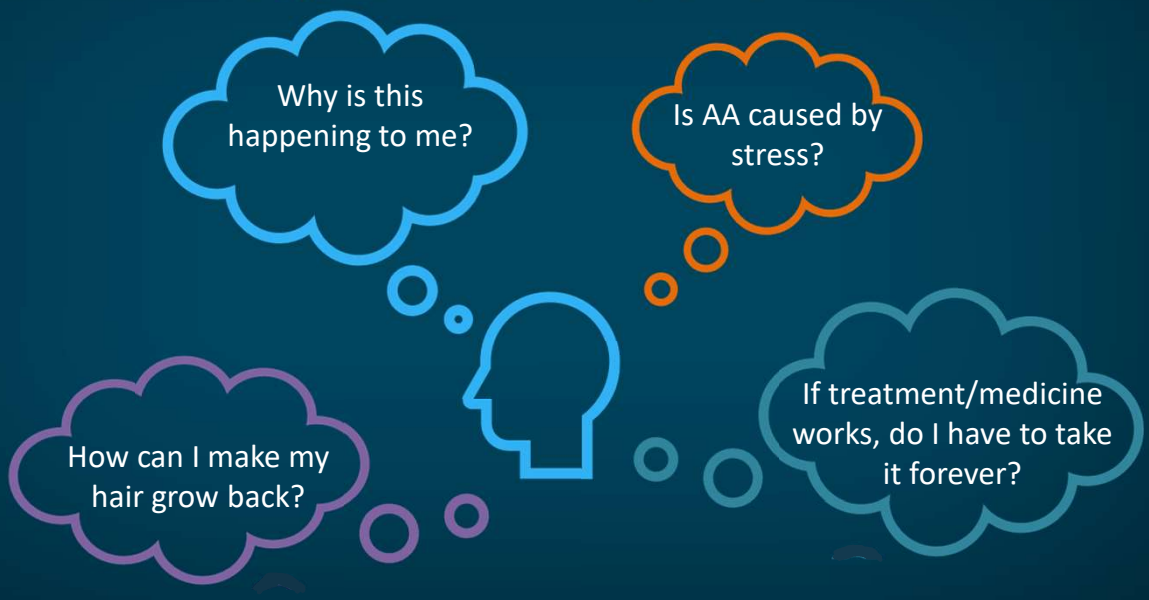
Patient Concerns

Every patient with AA wants to know…



43

The Importance of Communication

Ask Patients About…

- **Psychosocial impact of AA**
  - On a scale of 0 to 10, how bothered are you by your hair loss?
  - Does your hair loss keep you from participating in activities? If so, what activities? Why?
  - Has your hair loss affected your personal or professional relationships? In what way(s)?
  - **How many times each day do you think about your hair?**

Ask kids specifically about:

- Days missed at school
- Participation in extracurricular and social activities

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The Importance of Communication

Acknowledge the patient…

"You are not alone. Many people with AA experience severe distress. It's a really natural response."

"We know a lot about what causes AA, and it's not because of anything you did or didn't do or ate or didn't eat…AA is an autoimmune disease."

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Conclusions

- AA is a complex polygenic autoimmune disease
- There is a long history of attributing AA to stress. But, with recent advancements in our understanding of AA, **we can move beyond stress and instead describe the genetics and autoimmune pathogenesis**, including **IL-15 and IFN-γ as important mediators of AA**; this has led to therapeutic advances
- **Intralesional corticosteroids** are the mainstay of therapy for adults with ≤**20% scalp hair loss**
- **Moderate to severe AA** may be defined as >**20% scalp hair loss**

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Conclusions (continued)

- Patients with moderate to severe disease (>20% scalp hair loss), chronic AA, or severe emotional distress may be candidates for systemic therapy
- In the absence of evidence-based guidelines, use **expert consensus opinion to guide therapy in AA**
- **JAK inhibitors are an emerging therapy for AA, showing promise in phase 2 and phase 3 clinical trials**

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Case 1: Sudden Onset Alopecia Areata

Sergio Vaño-Galván, MD, PhD

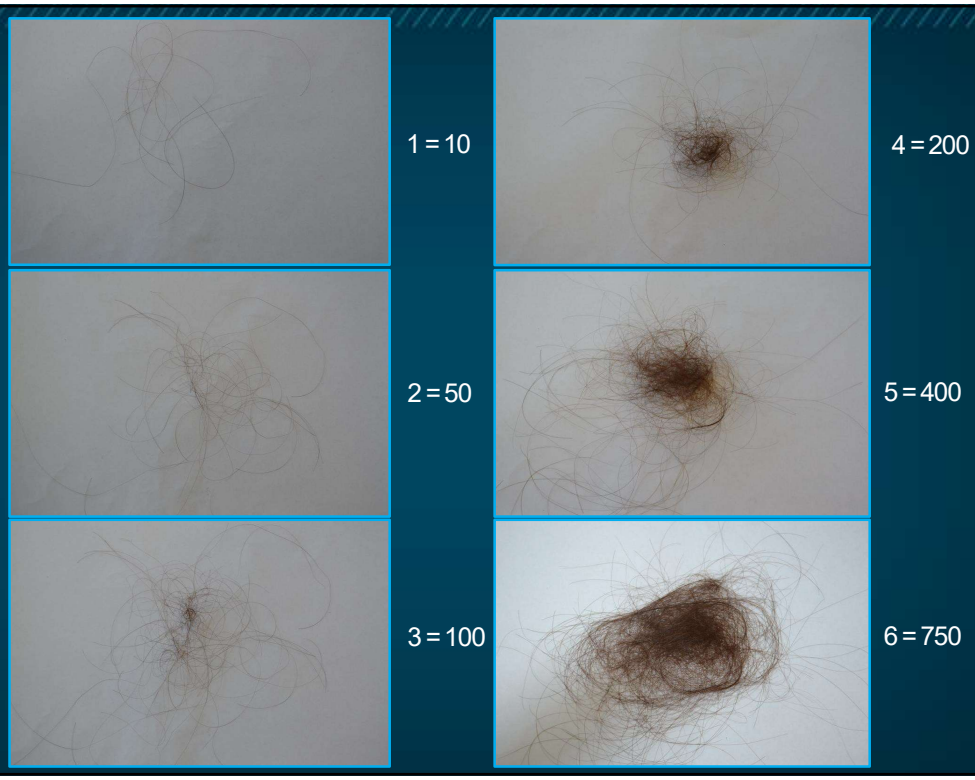
48

A 16-Year-Old Girl Urgently Referred by Another Dermatologist in September 2016…

- Previously healthy high school junior with a 3-week history of sudden onset of increased hair shedding
- Stage 6 shedding 4–5 times per day; normally, stage 3 and 4 shedding after twice-weekly washing.
- Seen by dermatologist 7 days ago and started on prednisolone 25 mg orally daily in the morning and mometasone furoate lotion topically
- Blood tests all normal, except high thyroid autoantibodies
- Entire family distress +++. Patient, parents, and grandparent distraught and crying. Family already ordered a $6000 wig for her.
- Patient agitated and unable to sleep

49

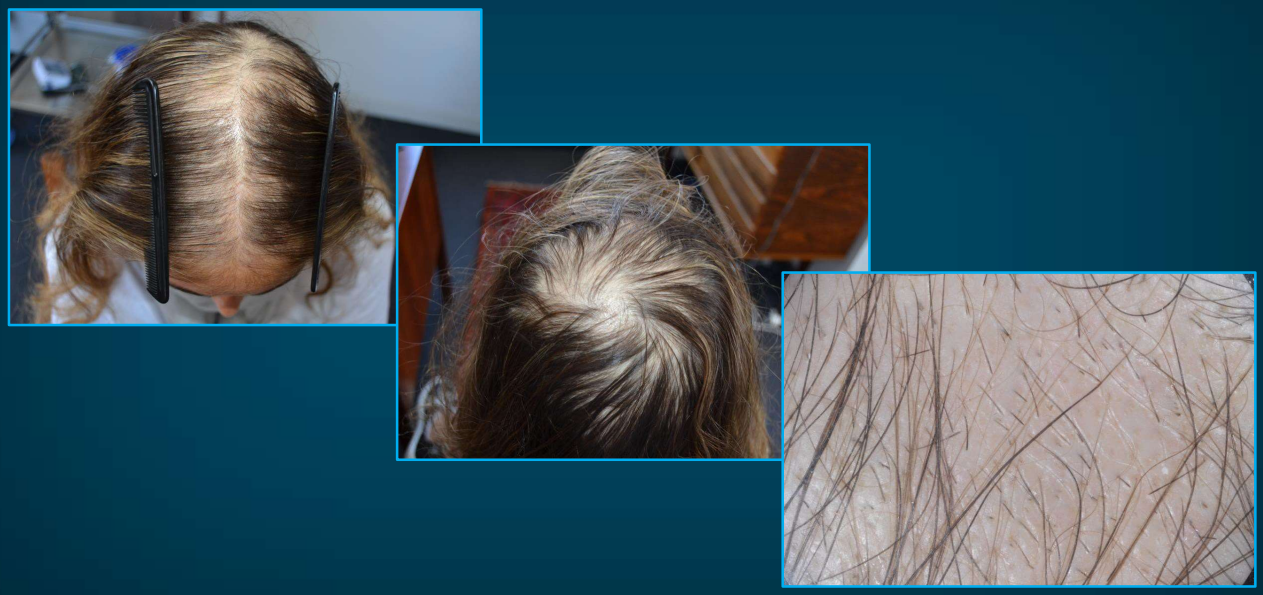
Stages of Hair Shedding



Images courtesy of Dr. Rodney Sinclair.

50

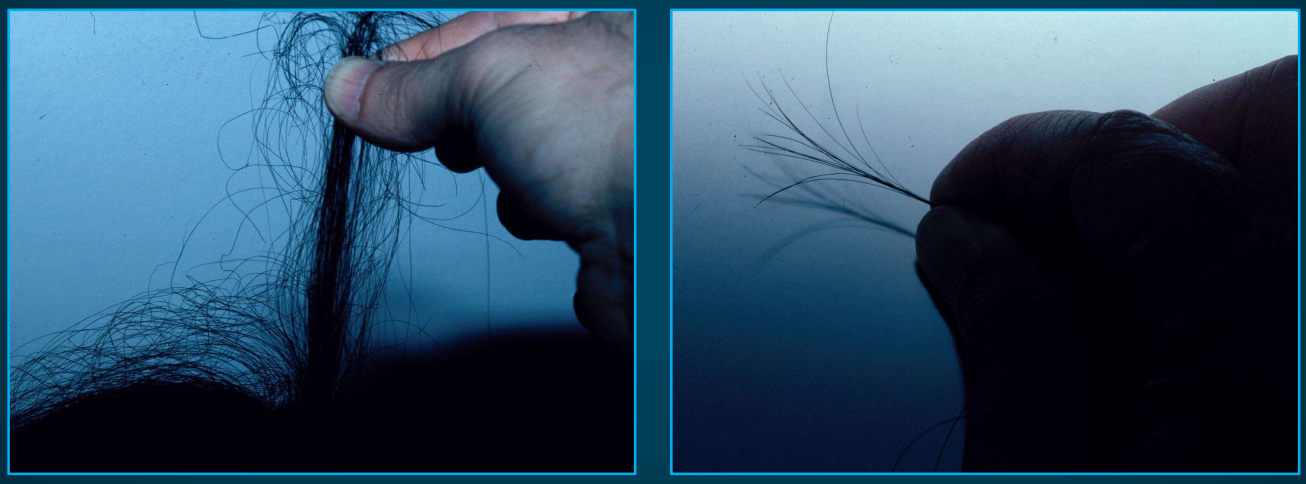
Patient With Sudden Onset AA



Images courtesy of Dr. Rodney Sinclair.

51

Patient With Sudden Onset AA: Pull Test



Images courtesy of Dr. Rodney Sinclair.

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Intervention and Follow-up

- Decision was made to taper prednisolone to 12.5 mg daily in morning in view of mood disturbance; she was started on cyclosporine 3 mg /kg and reviewed in 3 weeks.
- Patient returned 3 weeks later
  - No side-effects
  - No weight gain
  - Sleeping normally
  - BP = 130/75
- Shedding reduced to stage 5
- **BUT…**hair loss was worse!

BP = blood pressure.

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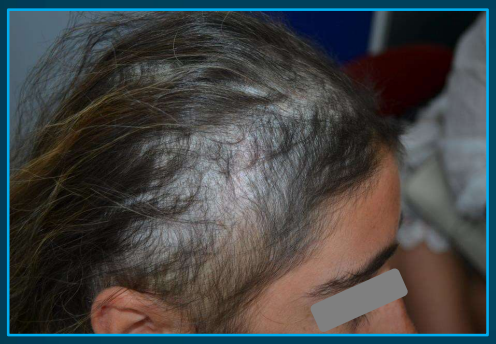
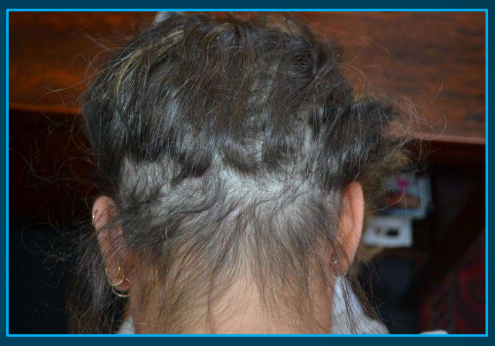
Sudden Onset AA: First Follow-Up





Images courtesy of Dr. Rodney Sinclair.

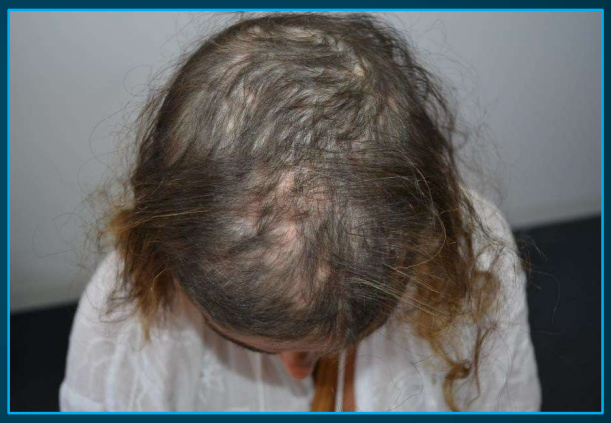
54

Sudden Onset AA: 2nd Intervention and Follow-up

- Decision made to taper prednisolone further to 6.25 mg daily in the morning, increase cyclosporine to 5 mg/kg, and review in 3 weeks
- Patient returned 3 weeks later, on Christmas Eve
  - No side-effects
  - No weight gain
  - Sleeping normally
  - BP = 130/85
- Shedding reduced to stage 3
- **AND…**hair starting to regrow

55

Sudden Onset AA: Second Follow-Up



Images courtesy of Dr. Rodney Sinclair.

56

Sudden Onset AA: Third Intervention and Follow-up

- Decision was made to taper prednisolone further to 5 mg daily in the morning, continue cyclosporine at 5 mg/kg, and review in 6 weeks
- Patient returned 6 weeks later, when school had just restarted
  - No side-effects
  - No weight gain
  - Sleeping normally
  - BP = 130/85
- Shedding reduced to stage 5
- **AND…**hair had been regrowing beautifully until 7 days ago when it started coming out again

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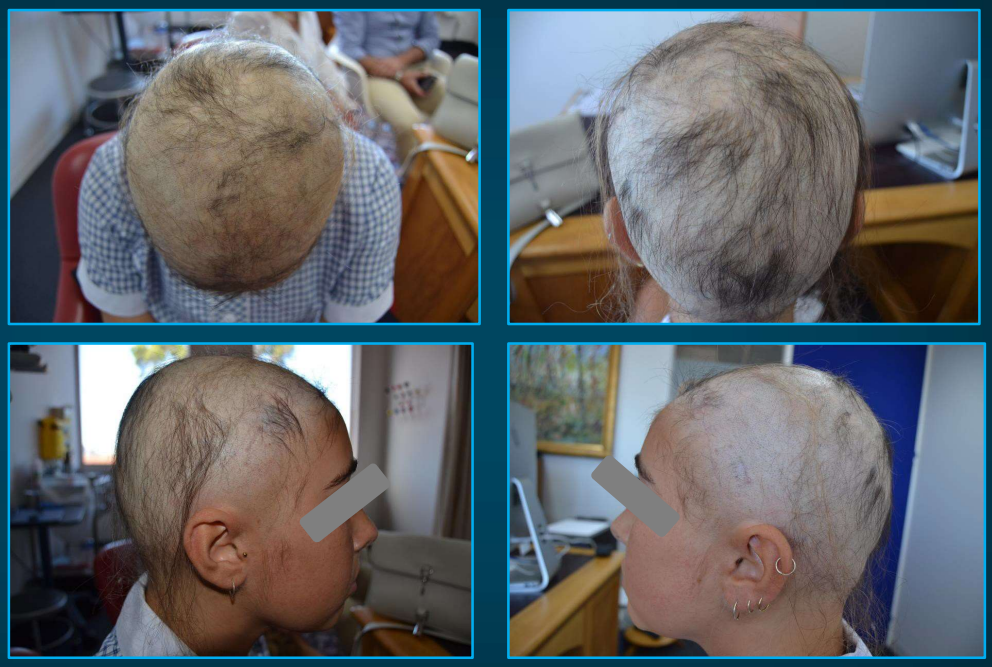
Sudden Onset AA: Third Follow-Up



Images courtesy of Dr. Rodney Sinclair.

58

Sudden Onset AA: Fourth Intervention and Follow-up

- Decision made to reintroduce prednisolone 25 mg daily in the morning, continue cyclosporine at 5 mg/kg, and review in 2 weeks to watch for mood and sleep disturbance
- Patient returned 2 weeks later, reporting no side effects
  - Sleeping normally
  - BP = 135/90
- Still shedding at stage 6
- **AND…**hair loss is worse!!!

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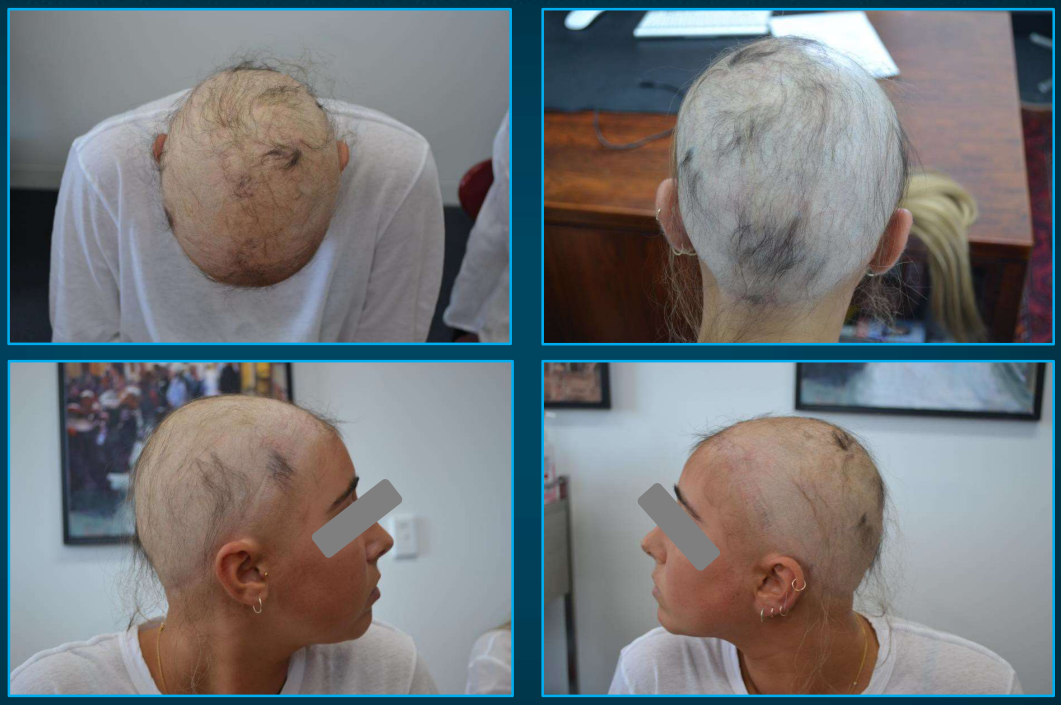
Sudden Onset AA: Fourth Follow-Up



Images courtesy of Dr. Rodney Sinclair.

60

Sudden Onset AA: Fifth Follow-Up

AND Hair Loss Is Worse Again !!!

Images courtesy of Dr. Rodney Sinclair.

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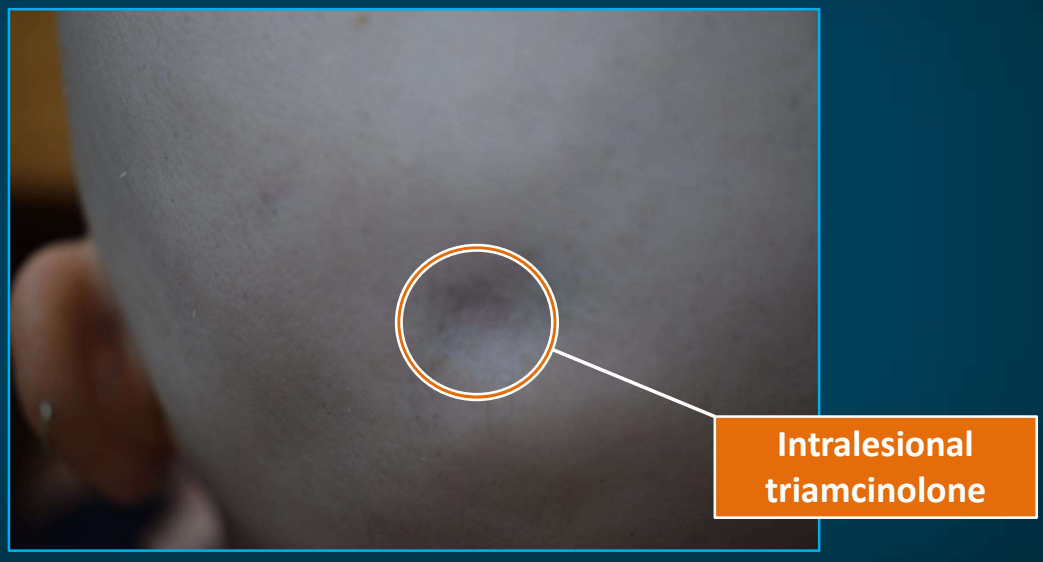
Sudden Onset AA: What Caused the Dimple?



Images courtesy of Dr. Rodney Sinclair.

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Sudden Onset AA: Fifth Intervention and Follow-up

- Decision made to start JAK inhibitor, stop cyclosporine, and taper prednisolone
- Patient returned after 4, 8, 12, 16, and 20 weeks with no hair regrowth
- At 24 weeks, fine downy fuzz was visible on scalp
- At weeks 28, 32, 36, and 40, hair grew longer, and most areas on scalp filled in; however, hair density was low
- Oral minoxidil was added December 2017, and hair density and length increased progressively over the next 12 months
- Patient remained in complete remission for over 2 years, with occasional new spots treated with intralesional triamcinolone

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Sudden Onset AA: Outcomes Trend After Fifth Intervention

Images courtesy of Dr. Rodney Sinclair.

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Case 2: Severe AA in Setting of Long-Standing AA

Brett King, MD, PhD

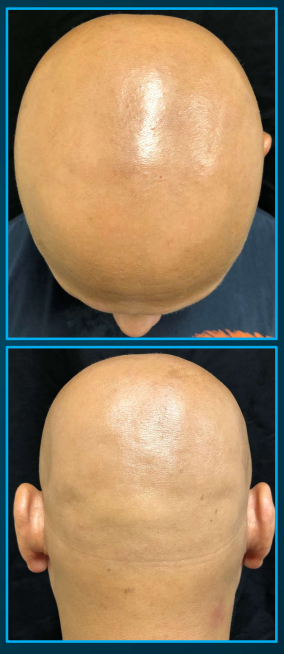
65

38-Year-Old Man Presents with 8-Year History of Severe AA…

- Has a 30-year history of alopecia areata

HPI:

- At age 8, he developed a quarter-sized round spot of alopecia that was attributed to a ”bad haircut.” The spot spontaneously resolved over several months.
- At age 13, he developed two quarter-sized spots of alopecia for which he saw a dermatologist. He was treated with combination clobetasol solution and topical minoxidil 5% liquid BID for 6 months with hair regrowth
- At age 30, he developed a quarter-sized spot of alopecia that progressed over 8 months to complete scalp hair loss as well as involvement of eyebrows, eyelashes, and facial and body hair



HPI = history of present illness.

Images courtesy of Dr. Brett King.

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Severe AA in Long-Standing AA: Interval History

- He has seen 4 dermatologists in the past 8 years for AA
- Treatment in the past 8 years includes:
  - Clobetasol solution and cream BID for months
  - Topical minoxidil 5% solution BID for months
  - Pimecrolimus cream BID for 3 months
  - ILK every 4–8 weeks for multiple for 1 year
  - Prednisone taper (3 different times)
  - Methotrexate for months
  - Excimer laser for few months
  - PRP (3 times)

ILK = intralesional triamcinolone acetonide; PRP = platelet-rich plasma.

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Severe AA in Long-Standing AA: Interval History (continued)

- Past Medical History
  - Atopic dermatitis
  - Hashimoto thyroiditis (taking levothyroxine)
- Family History
  - Father with androgenetic alopecia
  - Mother with thyroid disease (also takes levothyroxine)

PMH = past medical history; FH = family history.

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Severe AA in Long-Standing AA: Patient Concerns

What questions does the patient have?

"Why does this keep happening?"

"It's an autoimmune disease. We know a lot about the genetics, and we know a lot about the immune reaction happening around the hair follicles."

"I have been under a lot of stress in the past 8 years because… Is this problem caused by stress?"

"Remember, this is an autoimmune disease, and we know a lot about the genetics underlying the disease. You did NOT cause your genetics. You did NOT make AA happen."

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Severe AA in Long-Standing AA: Patient Concerns (continued)

"How can I make my hair grow back?"

"There is a very good chance we can make your hair grow back. Indeed, there are several promising treatments in development."

"If treatment/medicine works, do I have to take it forever?"

"I don't know. It is likely that you will need treatment for a long time, and maybe forever. But, just as your disease once remitted for a very long time, it may be that after we treat you successfully for a while you will be able to stop treatment."

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Severe AA in Long-Standing AA: Communication Approaches

Ask patients about:

- Psychosocial impact of AA
  - How bothered are you by your hair loss?
  - Does your hair loss keep you from participating in activities? If so, what activities? Why?
  - Has your hair loss affected your personal or professional relationships? How so?
  - **How many times each day do you think about your hair?**
- Their understanding of AA
  - What do you know about AA? What have you read about it?

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Severe AA in Long-Standing AA: Communication Approaches (continued)

Explain their disease to them

- You *did not* give yourself AA – you *did not* make this happen
- AA is an autoimmune disease
- People with AA have a genetic predisposition
- There are emerging therapies for the treatment of AA that are *often* (but not always) effective

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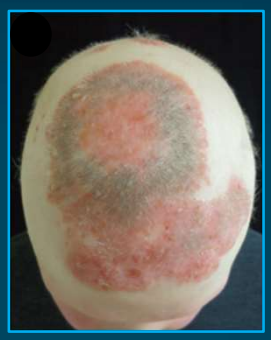
Severe AA in Long-Standing AA: Why a JAK Inhibitor?

Why JAK inhibitor treatment?

- AA mechanism of disease involves IL-15 and IFN-γ
- Both IL-15 and IFN-γ signal via JAK-STAT pathway
- Case reports and case series support JAK inhibitor treatment of AA
- Randomized placebo-controlled trials of investigational JAK inhibitors seem to show efficacy for the treatment of AA



Craiglow BG, King BA. *J Invest Dermatol.* 2014;134:2988-2990.

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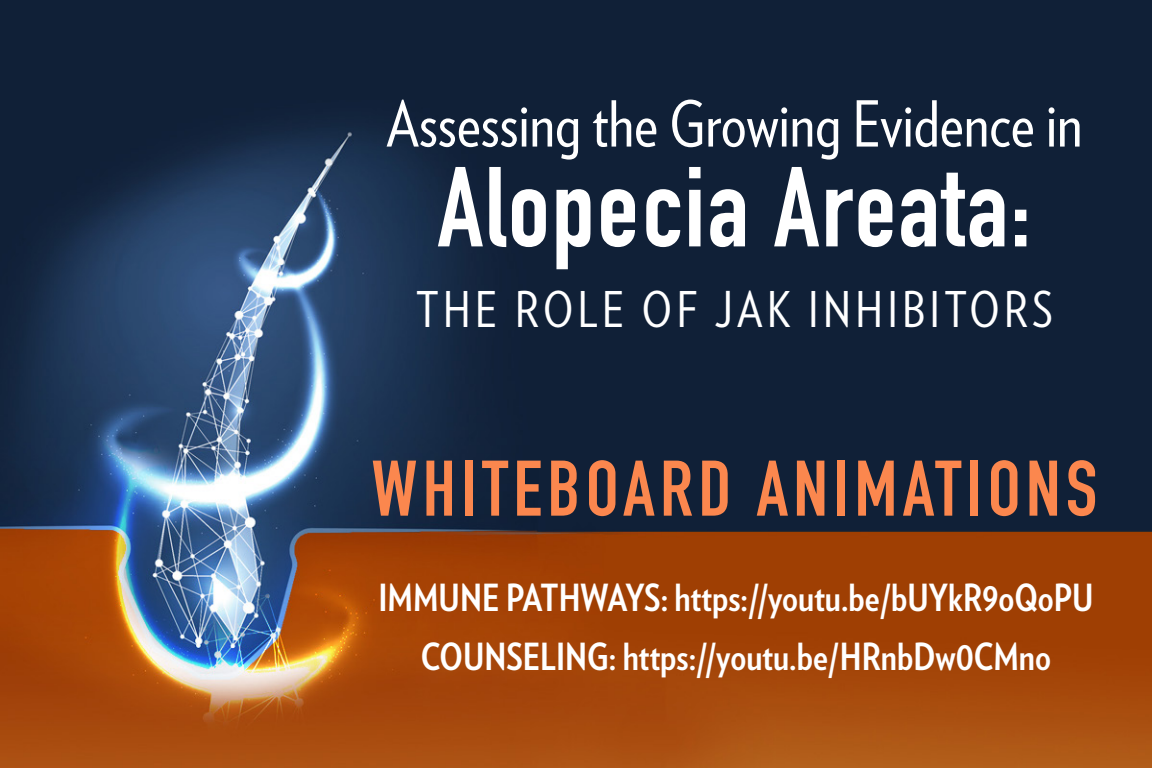
Assessing the Growing Evidence in
Alopecia Areata:
THE ROLE OF JAK INHIBITORS
WHITEBOARD ANIMATIONS
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Assessing the Growing Evidence in Alopecia Areata:

THE ROLE OF JAK INHIBITORS

Alopecia Areata Overview

Resource	Address
Aita VM, Christiano AM. The genetics of alopecia areata. *Dermatol Ther*. 2001;14(4):329-339.	https://onlinelibrary.wiley.com/doi/abs/10.1046/j.1529-8019.2001.01041.x
Colón EA, Popkin MK, Callies AL, Dessert NJ, Hordinsky MK. Lifetime prevalence of psychiatric disorders in patients with alopecia areata. *Compr Psychiatry*. 1991;32(3):245-251.	https://pubmed.ncbi.nlm.nih.gov/1884604/
Craiglow BG. Topical tofacitinib solution for the treatment of alopecia areata affecting eyelashes. *JAAD Case Rep*. 2018;4(10):988-989.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6218694/
Craiglow BG, King BA. Killing two birds with one stone: Oral tofacitinib reverses alopecia universalis in a patient with plaque psoriasis. *J Invest Dermatol*. 2014;134(12):2988-2990.	https://pubmed.ncbi.nlm.nih.gov/24940651/
Cranwell WC, Lai VWY, Photiou L, et al. Treatment of alopecia areata: An Australian expert consensus statement. *Australas J Dermatol. 2019*;60:163-170.	https://onlinelibrary.wiley.com/doi/epdf/10.1111/ajd.12941
Damsky W, King BA. JAK inhibitors in dermatology: The promise of a new drug class. *J Am Acad Dermatol*. 2017;76(4):736-744.	https://pubmed.ncbi.nlm.nih.gov/28139263/
Fricke ACV, Miteva M. Epidemiology and burden of alopecia areata: A systematic review. *Clin Cosmet Investig Dermatol*. 2015;8:397-403.	https://pubmed.ncbi.nlm.nih.gov/26244028/
Gilhar A, Laufer-Britva R, Keren A, Paus R. Frontiers in alopecia areata pathobiology research. *J Allergy Clin Immunol*. 2019;144(6):1478-1489.	https://pubmed.ncbi.nlm.nih.gov/31606262/
Jackow C, Puffer N, Hordinsky M, Nelson J, Tarrand J, Duvic M. Alopecia areata and cytomegalovirus infection in twins: Genes versus environment? *J Am Acad Dermatol*. 1998;38(3):418-425.	https://pubmed.ncbi.nlm.nih.gov/9520023/
Lee S, Lee H, Lee CH, Lee WS. Comorbidities in alopecia areata: A systematic review and	https://pubmed.ncbi.nlm.nih.gov/30031145/

meta-analysis. *J Am Acad Dermatol*. 2019;80(2):466-477.e16.	
Lepe K. Stat Pearls: Alopecia areata. Updated November 15 2021.	https://www.statpearls.com/articlelibrary/viewarticle/17385/
Liu LY, Craiglow BG, Dai F, King BA. Tofacitinib for the treatment of severe alopecia areata and variants: A study of 90 patients. *J Am Acad Dermatol*. 2017;76(1):22-28.	https://pubmed.ncbi.nlm.nih.gov/27816293/
Mirzoyev SA, Schrum AG, Davis MDP, Torgerson RR. Lifetime incidence risk of alopecia areata estimated at 2.1 percent by Rochester Epidemiology Project, 1990-2009. *J Invest Dermatol.* 2014;134(4):1141-1142.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3961558/pdf/nihms536907.pdf
Muller SA, Winkelmann RK. Alopecia areata: An evaluation of 736 patients. *Arch Dermatol.* 1963;88(3):290-297.	https://jamanetwork.com/journals/jamadermatology/article-abstract/528193
Olsen EA, Hordinsky MK, Price VH, et al. Alopecia areata investigational assessment guidelines—Part II. National Alopecia Areata Foundation. *J Am Acad Dermatol*. 2004;51(3):440-447.	https://pubmed.ncbi.nlm.nih.gov/15337988/
Petukhova L, Duvic M, Hordinsky M, et al. Genome-wide association study in alopecia areata implicates both innate and adaptive immunity. *Nature.* 2010;466(7302):113-117.	https://pubmed.ncbi.nlm.nih.gov/20596022/
Safavi K. Prevalence of alopecia areata in the First National Health and Nutrition Examination Survey. *Arch Dermatol.* 1992;128(5):702.	https://jamanetwork.com/journals/jamadermatology/article-abstract/554138
Strazzulla LC, Wang EHC, Avila L, et al. Alopecia areata: Disease characteristics, clinical evaluation, and new perspectives on pathogenesis. *J Am Acad Dermatol.* 2018;78(1):1-12.	https://www.sciencedirect.com/science/article/abs/pii/S019096221731873X
Tosti A, Morelli R, Bardazzi F, Peluso AM. Prevalence of nail abnormalities in children with alopecia areata. *Pediatr Dermatol*. 1994;11(2):112-115.	https://pubmed.ncbi.nlm.nih.gov/8041648/
Whiting DA. Histopathologic features of alopecia areata: A new look. *Arch Dermatol*. 2003;139(12):1555-1559.	https://pubmed.ncbi.nlm.nih.gov/14676070/

Pathophysiology of Alopecia Areata

Resource	Address
Divito SJ, Kupper TS. Inhibiting Janus kinases to treat alopecia areata. *Nat Med.* 2014;20:989-990.	https://www.nature.com/articles/nm.3685
Gilhar A, Paus R, Kalish RS. Lymphocytes, neuropeptides, and genes involved in alopecia areata. *J Clin Invest.* 2007;117(8):2019-2027.	https://www.jci.org/articles/view/31942/pdf
Perret C, Bröcker EB, Wiesner-Menzel L, Happle R. In situ demonstration of T cells in alopecia areata. *Arch Dermatol Res.* 1982;273:155-158.	https://link.springer.com/article/10.1007%2FBF00509041
Petukhova L, Duvic M, Hordinsky M, et al. Genome-wide association study in alopecia areata implicates both innate and adaptive immunity. *Nature*. 2010;466(7302):113-117.	https://pubmed.ncbi.nlm.nih.gov/20596022/
Xing L, Dai Z, Jabbari A, et al. Alopecia areata is driven by cytotoxic T lymphocytes and is reversed by JAK inhibition. *Nat Med.* 2014;20(9):1043-1049.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4362521/pdf/nihms643218.pdf

Diagnosis of Alopecia Areata

Resource	Address
Baldari M, Montinari M, Guarrera M, Rebora A. Trichodynia is a distinguishing symptom of telogen effluvium. *J Eur Acad Dermatol Venereol. 2009*;23(6):733-734.	https://onlinelibrary.wiley.com/doi/epdf/10.1111/j.1468-3083.2009.03201.x
Gilmore S, Sinclair R. Spreading hair loss in alopecia areata: The domino effect immunobiology, alopecia areata. *Exp Dermatol.* 2010;19(6):575.	https://www.researchgate.net/publication/231513618_Spreading_hair_loss_in_alopecia_areata_the_domino_effect_Immunobiology_Alopecia_Areata
Majid I, Keen A. Management of alopecia areata: An update. *BJMP*. 2012;5(3):a530.	https://www.bjmp.org/content/management-alopecia-areata-update
Olsen EA, Canfield D. SALT II: A new take on the Severity of Alopecia Tool (SALT) for determining percentage scalp hair loss. *J Am Acad Dermatol*. 2016;75(6):1268-1270.	https://pubmed.ncbi.nlm.nih.gov/27846957/
Olsen EA, Hordinsky MK, Price VH, et al. Alopecia areata investigational assessment guidelines—Part II. National Alopecia Areata	https://pubmed.ncbi.nlm.nih.gov/15337988/

Foundation. *J Am Acad Dermatol*. 2004;51(3):440-447.	
Whiting DA. Histopathologic features of alopecia areata: A new look. *Arch Dermatol.* 2003;139(12):1555-1559.	https://jamanetwork.com/journals/jamadermatology/fullarticle/479618

Current Treatments

Resource	Address
Chow CW, Rincón M, Davis RJ. Requirement for transcription factor NFAT in interleukin-2 expression. *Mol Cell Biol.* 1999;19(3):2300-2307.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC84022/pdf/mb002300.pdf
Cranwell WC, Lai VW, Photiou L, et al. Treatment of alopecia areata: An Australian expert consensus statement. *Australas J Dermatol*. 2019;60(2):163-170.	https://pubmed.ncbi.nlm.nih.gov/30411329/
Lai VWY, Sinclair R. Utility of azathioprine, methotrexate and cyclosporine as steroid-sparing agents in chronic alopecia areata: A retrospective study of continuation rates in 138 patients. *J Eur Acad Dermatol Venereol.* 2020;34(11):2606-2612.	https://onlinelibrary.wiley.com/doi/abs/10.1111/jdv.16858
Olsen EA, Canfield D. SALT II: A new take on the Severity of Alopecia Tool (SALT) for determining percentage scalp hair loss. *J Am Acad Dermatol*. 2016;75:1268-1270.	https://pubmed.ncbi.nlm.nih.gov/27846957/
Strazzulla LC, Wang EHC, Avila L, et al. Alopecia areata: An appraisal of new treatment approaches and overview of current therapies. *J Am Acad Dermatol*. 2018;78(1):15-24.	https://pubmed.ncbi.nlm.nih.gov/29241773/

Emerging Treatments

Resource	Address
Bechman K, Yates M, Galloway JB. The new entries in the therapeutic armamentarium: The small molecule JAK inhibitors. *Pharmacol Res.* 2019;147:104392.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6876279/
Craiglow BG, Liu LY, King BA. Tofacitinib for the treatment of alopecia areata and	https://www.jaad.org/action/showPdf?pii=S0190-9622%2816%2930762-9

variants in adolescents. *J Am Acad Dermatol.* 2017;76(1):29-32.	
Craiglow BG, King BA. Killing two birds with one stone: Oral tofacitinib reverses alopecia universalis in a patient with plaque psoriasis. *J Invest Dermatol.* 2014;134:2988-2990.	https://www.jidonline.org/action/showPdf?pii=S0022-202X%2815%2936586-6
Gadina M, Johnson C, Schwartz D, et al. Translational and clinical advances in JAK-STAT biology: The present and future of jakinibs. *J Leukoc Biol*. 2018;104(3):499-514.	https://pubmed.ncbi.nlm.nih.gov/29999544/
Gilhar A, Keren A, Paus R. JAK inhibitors and alopecia areata. *Lancet*. 2019;393:318-319.	https://www.thelancet.com/action/showPdf?pii=S0140-6736%2818%2932987-8
Kennedy Crispin M, Ko JM, Craiglow BG, et al. Safety and efficacy of the JAK inhibitor tofacitinib citrate in patients with alopecia areata. *JCI Insight.* 2016;1(15):e89776.	https://insight.jci.org/articles/view/89776/pdf
King B, Guttman-Yassky E, Peeva E, et al. A phase 2a randomized, placebo-controlled study to evaluate the efficacy and safety of the oral Janus kinas inhibitors ritlecitinib and brepocitinib in alopecia areata: 24-week results. *J Am Acad Dermatol*. 2021;85(2):379-387.	https://pubmed.ncbi.nlm.nih.gov/33757798/
King B, Ko J, Forman S, et al. Efficacy and safety of the oral Janus kinase inhibitor baricitinib in the treatment of adults with alopecia areata: Phase 2 results from a randomized controlled study. *J Am Acad Dermatol*. 2021;85(4):847-853.	https://pubmed.ncbi.nlm.nih.gov/34090959/
Liu LY, King BA. Lack of efficacy of apremilast in 9 patients with severe alopecia areata. *J Am Acad Dermatol.* 2017;77(4):773-774.	https://www.jaad.org/action/showPdf?pii=S0190-9622%2817%2931782-6
Liu LY, King BA. Tofacitinib for the treatment of severe alopecia areata in adults and adolescents. *J Investig Dermatol Symp Proc*. 2018;19(1):S18-S20.	https://pubmed.ncbi.nlm.nih.gov/29273099/
Olsen EA, Hordinsky MK, Price VH, et al. Alopecia areata investigational assessment guidelines -- Part II. National Alopecia Areata Foundation. *J Am Acad Dermatol*. 2004;51(3):440-447.	https://pubmed.ncbi.nlm.nih.gov/15337988/

Olsen EA, Kornacki D, Sun K, Hordinsky MK. Ruxolitinib cream for the treatment of patients with alopecia areata: A 2-part, double-blind, randomized, vehicle-controlled phase 2 study. *J Am Acad Dermatol*. 2020;82(2):412-419.	https://pubmed.ncbi.nlm.nih.gov/31622643/
Robinson MF, Damjanov N, Stamenkovic B, et al. Efficacy and safety of PF-06651600 (ritlecitinib), a novel JAK3/TEC Inhibitor, in patients with moderate-to-severe rheumatoid arthritis and an inadequate response to methotrexate. *Arthritis Rheumatol*. 2020;72(10):1621-1631.	https://onlinelibrary.wiley.com/doi/epdf/10.1002/art.41316
Pfizer presents positive phase 2 data in alopecia areata during late-breaker session at the 27th European Academy of Dermatology and Venereology (EADV) congress. [press release]. September 14, 2018.	https://www.pfizer.com/news/press-release/press-release-detail/pfizer_presents_positive_phase_2_data_in_alopecia_areata_during_late_breaker_session_at_the_27th_european_academy_of_dermatology_and_venereology_eadv_congress

Psychosocial Interventions

Resource	Address
Aldhouse NVJ, Kitchen H, Knight S, et al. "'You lose your hair, what's the big deal?' I was so embarrassed, I was so self-conscious, I was so depressed:" A qualitative interview study to understand the psychosocial burden of alopecia areata. *J Patient Rep Outcomes.* 2020;4:76.	https://jpro.springeropen.com/articles/10.1186/s41687-020-00240-7
Cipriani R, Perini GI, Rampinelli S. Paroxetine in alopecia areata. *Int J Dermatol.* 2001;40(9):600-601.	https://onlinelibrary.wiley.com/doi/abs/10.1046/j.1365-4362.2001.01261-3.x
Lee S, Lee H, Lee CH, Lee WS. Comorbidities in alopecia areata: A systematic review and meta-analysis. *J Am Acad Dermatol*. 2019;80(2):466-477.e16.	https://pubmed.ncbi.nlm.nih.gov/30031145/
Liu LY, Craiglow BG, King BA. Successful treatment of moderate-to-severe alopecia areata improves health-related quality of	https://pubmed.ncbi.nlm.nih.gov/29128459/

life. *J Am Acad Dermatol*. 2018;78(3):597-599.e2.	
Liu LY, King BA, Craiglow BG. Alopecia areata is associated with impaired health-related quality of life: A survey of affected adults and children and their families. *J Am Acad Dermatol*. 2018;79(3):556-558.e1.	https://pubmed.ncbi.nlm.nih.gov/29425723/
Shapiro J. Current treatment of alopecia areata. *J Investig Dermatol Symp Proc.* 2013;16(1):S42-S44.	https://www.jidsponline.org/article/S1087-0024(15)30530-X/fulltext