



## Epidemiology of AA



AA is a common, chronic, tissue-specific, autoimmune disease affecting up to 2% of the global population<sup>1,6</sup>



Clinically manifests as non-scarring patches of alopecia<sup>1,3</sup>



CD4+ and CD8+ cytotoxic T lymphocytes are thought to mediate HF damage due to antigenic recognition<sup>3</sup>

## Current Treatment Options

- AA therapies are now more specific, due to improved pathophysiology understanding<sup>3</sup>
- Ideal intervention: targeted small molecule therapy<sup>3</sup>
- Various ISA for AA treatment act by modulating the immune response
- Until recently, none of the approved drugs targeted the JAK pathway<sup>3</sup>



**Baricitinib**, an oral JAK1 and JAK2 inhibitor, gained FDA approval for the treatment of adults with severe AA<sup>3</sup>

## Spotlighting JAK Inhibitors

- JAKi target chronic inflammatory skin conditions, like atopic dermatitis, AA, vitiligo, psoriasis, and lichen planus<sup>3</sup>
- Baricitinib approved following clinical trials showing:<sup>4</sup>



Hair regrowth in ~1/3 of patients with severe AA



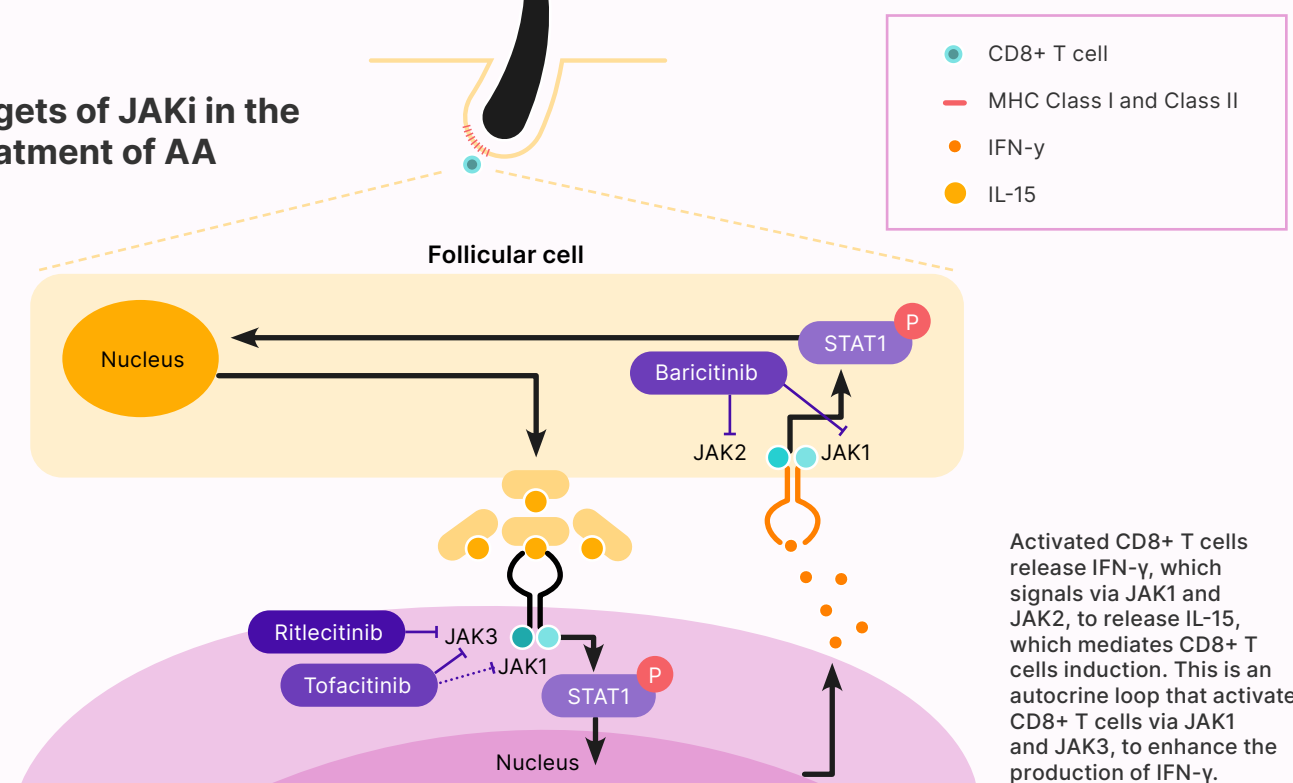
~80% scalp coverage in these patients



Eyebrow and eyelash regrowth

- JAKi interfere with inflammatory signals<sup>4</sup>

## Targets of JAKi in the Treatment of AA



- There are several studies endorsing the efficacy of novel JAKi in AA (ritlecitinib, tofacitinib, and brepocitinib)
- A meta-analysis of 7 RCTs of JAKi identified 30–90% improvement in SALT scores from baseline compared with placebo<sup>2</sup>
- Although there are case reports of topical JAKi for AA, they have not demonstrated efficacy in clinical trials<sup>5</sup>

### Key:

AA: alopecia areata; FDA: U.S. Food and Drug Administration; HF: hair follicle; IFN: interferon; ISA: immunosuppressive agents; JAK: Janus kinase inhibitor; MHC: major histocompatibility complex RCT: randomized controlled trial; SALT: severity of alopecia tool.

### References:

1. Pratt CH et al. Alopecia areata. Nat Rev Dis Primers. 2017;3:17011.
2. Liu M et al. Janus kinase inhibitors for alopecia areata: a systematic review and meta-analysis. JAMA Network Open. 2023;6(6):e2320351.
3. Sardana K et al. Which is the ideal JAK inhibitor for alopecia areata - baricitinib, tofacitinib, ritlecitinib or rfidancitinib - revisiting the immunomechanisms of the JAK pathway. Indian Dermatol Online J. 2023;14(4):465-74.
4. American Academy of Dermatology Association (AAD). JAK inhibitors: what your dermatologist wants you to know. 2023. Available at <https://www.aad.org/public/diseases/a-z/jak-inhibitors>. Last accessed: 28 February 2024.
5. King BA, Craiglow BG. Janus kinase inhibitors for alopecia areata. J Am Acad Dermatol. 2023;89(2S):S29-32.
6. Zhou C et al. Alopecia areata: an update on etiopathogenesis, diagnosis, and management. Clin Rev Allergy Immunol. 2021;61(3):403-23.

## Future Directions



- This class of drugs can help replace the widespread use of steroids with its myriad regimens and doses, which lead to side effects<sup>3</sup>
- Ideal JAKi for AA remains unclear, despite acceptable safety and tolerability<sup>3</sup>
- Longer RCTs, larger samples, and head-to-head comparisons in AA needed<sup>3</sup>
- Further assessment of long-term recurrence required<sup>2</sup>