

Understanding alopecia areata: Current perspectives and emerging therapies for a complex disease



Practice aid for alopecia areata

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Understanding and assessing severity of AA^{1,2}

Factors contributing to severity of AA

Hair loss

- Extent
- Location
- Duration
- Pattern

Other

- Nails
 - Pitting
 - Trachyonychia

Assessment tools to measure impact of AA

• SALT score (clinical trial measure) – extent of hair loss

- SALT II – extent of smaller patches of AA

• Trichoscopy/hair pull test – disease activity

• Skindex-16 – symptoms, emotions and functioning

• AA Symptom Impact Scale – symptoms of AA and impact on daily functioning

• HADS – symptoms of psychological impact

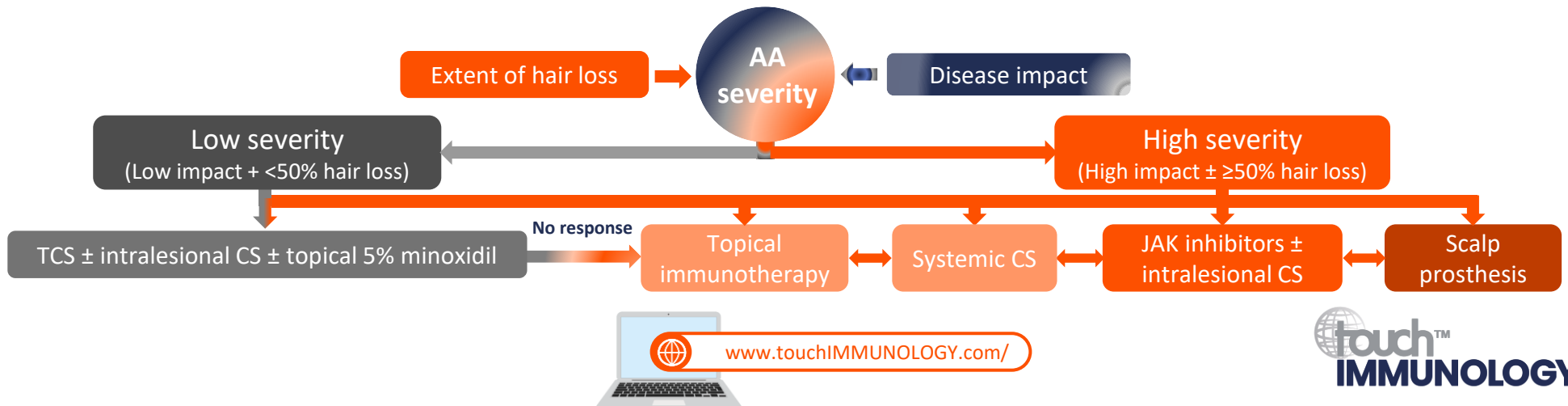
- ### Physical impacts
- Eye irritation
 - Nasal irritation
 - Sunburn risk
 - Thermoregulation

- ### Other
- Autoimmune comorbidities
 - Treatment burden

- ### Psychosocial impacts
- Perceived/actual stigmatization
 - Relationships
 - Emotional state
 - Psychological state
 - Lifestyle and social functioning

There is no consensus on tools for assessing AA-related HRQoL

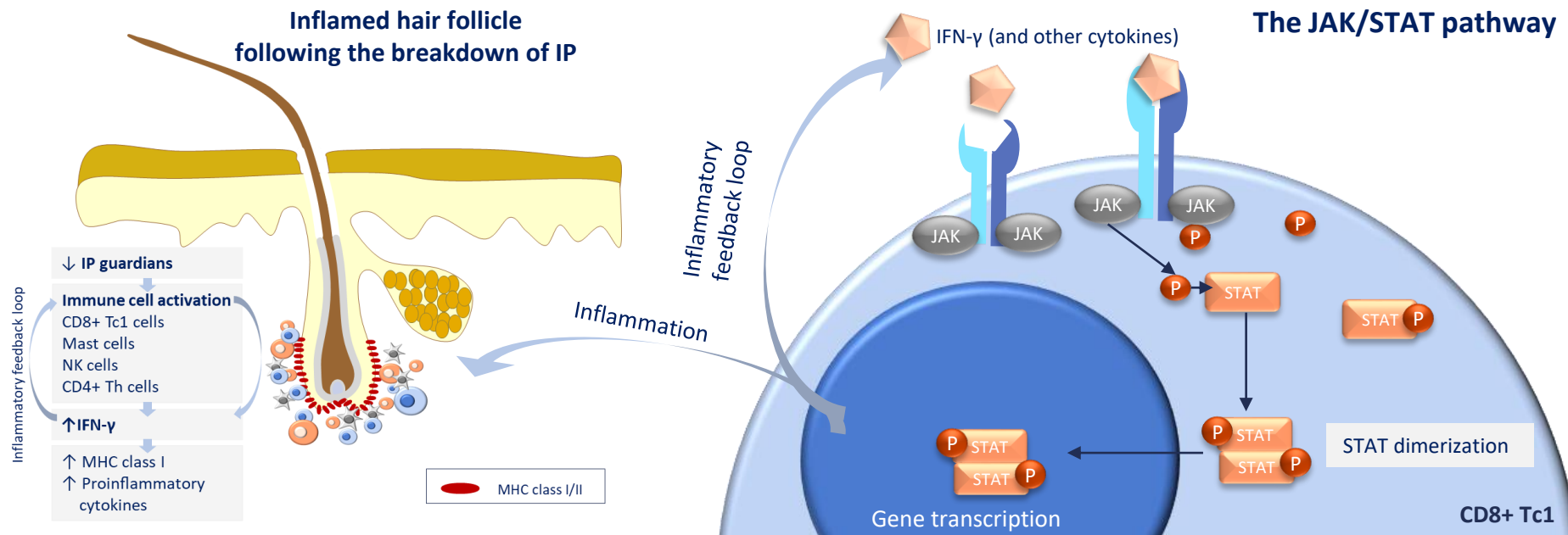
Factoring disease impact into the treatment decision-making algorithm in patients ≥10 years of age³⁻⁵



Immune privilege and the pathophysiology of AA^{6,7}



- Immune privilege (IP) is a term that is applied to certain organs (including the hair follicle) that are able to tolerate the introduction of antigens without eliciting an inflammatory response and being attacked by the immune system^{5,8}
- IP is attributed to a range of mechanisms, including:⁶
 - Low expression of MHC molecules
 - Local production of immunosuppressive cytokines such as TGF- β



- AA is hypothesized to initiate with a failure in immune privilege in the hair follicle; the reasons are unknown
 - Factors such as genetic susceptibility, hair follicle trauma, viral infection, or emotional/physical stress may be involved
- The inflammatory perifollicular infiltrate, consisting of CD8+ T cells, CD4+ T cells, mast cells, NK cells and dendritic cells, attacks the bulb region in the form of a 'swarm of bees'; the hair follicle stem cell compartment is spared

- IFN- γ , released by activated CD8+ Tc1 cells, promotes the production of IL-15, which binds to receptors on CD8+ T cells, inducing JAK1/JAK3-mediated IFN- γ production, to promote the inflammatory feedback loop
- JAK activation results in phosphorylation and release of substance P.
- Substance P attracts and activates STAT proteins. They dimerize, translocate to the cell nucleus to modulate gene expression and ultimately promote the production of proinflammatory cytokines
- JAK inhibitors block the JAK/STAT pathway, disrupting the inflammatory feedback loop and hence damping down inflammation in the hair follicle



Safety considerations



JAK inhibitors (clinical trial data*)

Baricitinib⁹

- Acne, elevated CK, increased LDL and HDL cholesterol

Ruxolitinib¹⁰

- Headache, acne, URTI, elevated CK, nasopharyngitis

Ritlecitinib^{11,12}

- Acne, URTIs, nasopharyngitis, headache, diarrhoea, nausea

*As of September 2022, only baricitinib has received FDA approval for treatment of AA



Corticosteroids⁵

Topical (Long-term use)

- Skin thinning, skin reddening

Intralesional

- Skin thinning, injection discomfort

Systemic

(Short-term use)

- Heartburn, susceptibility to infection

(Long-term use)

- Diabetes, high blood pressure, bone thinning



Topical immunotherapy^{4,5}

DPCP/SADBE

- Dryness/redness of the skin
- Pompholyx (itchy blisters on feet/hands)
- Vitiligo
- Enlarged lymph glands (neck and armpits)

(Practitioner should wear gloves and other PPE during application)

Abbreviations

AA, alopecia areata; CD, cluster of differentiation; CK, creatine kinase; CS, corticosteroid; DPCP, diphenylcyclopropenone; HADS, Hospital Anxiety Depression Scale; HDL, high-density lipoprotein; HRQoL, health-related quality of life; IFN- γ , interferon-gamma; IL, interleukin; IP, immune privilege; JAK, Janus kinase; LDL, low-density lipoprotein; MHC, major histocompatibility complex; NK, natural killer; P, phosphorylate; PPE, personal protective equipment; SADBE, squaric acid dibutylester; SALT, Severity of Alopecia Tool; STAT, signal transducer and activator of transcription; Tc1, cytotoxic T cell type 1; TCS, topical corticosteroid; TGF- β , transforming growth factor-beta; Th, T helper; URTI, upper respiratory tract infection.

References

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