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

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Alopecia areata: Clinical features, risk factors and disease burden

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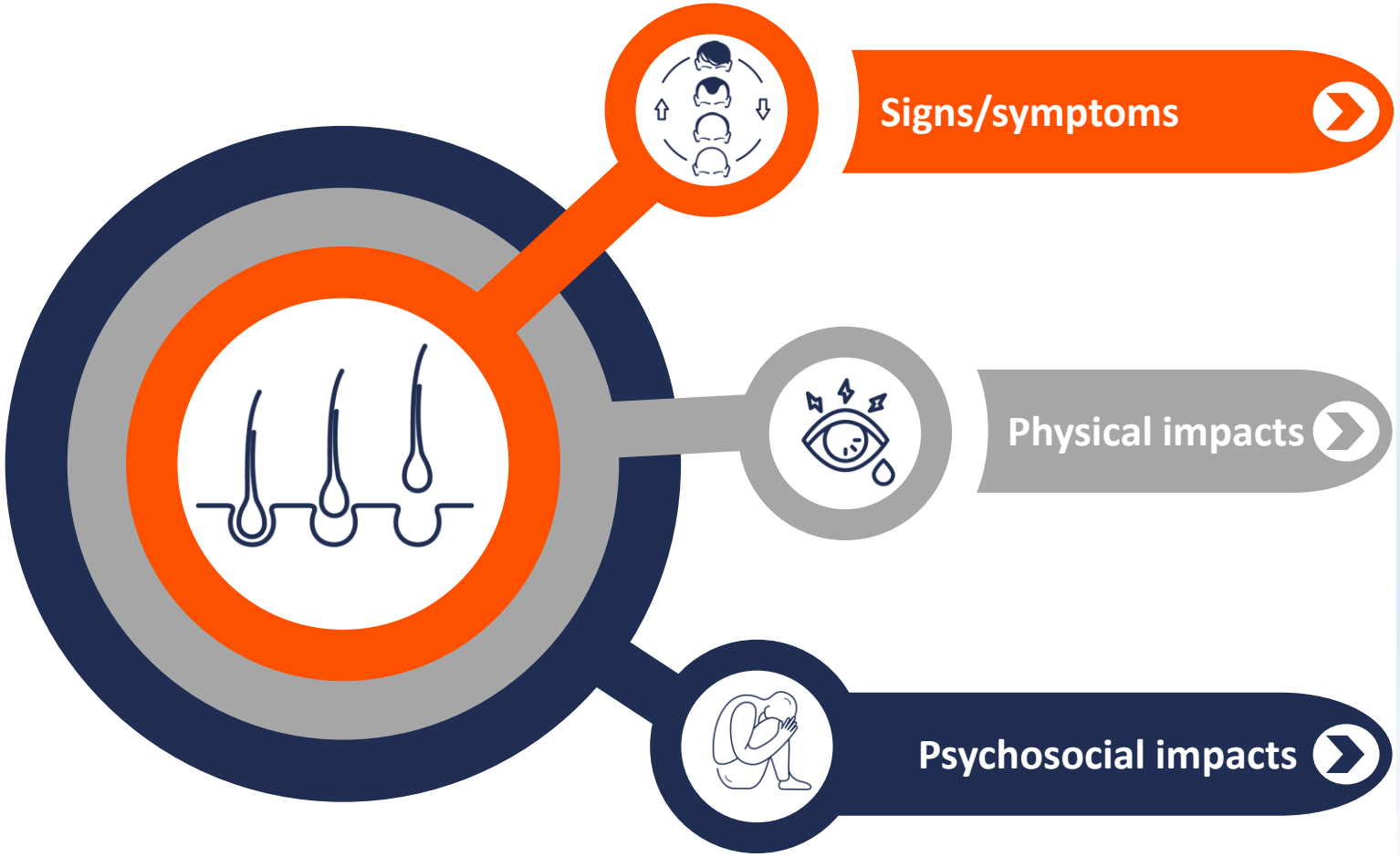
Alopecia areata severity: A multidimensional construct[1,2]



Hair loss
- Extent
- Location
- Duration
- Pattern

Other
- Nails
  - Pitting
  - Trachyonychia

- Eye irritation
- Nasal irritation
- Sunburn risk
- Thermoregulation
- Autoimmune comorbidities
- Treatment burden

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

A patient's perception of their alopecia areata and additional impacts such as eye irritation or eyebrow loss are consistently predictive of QoL[3]

QoL, quality of life.

1. King BA, et al. *Dermatol Ther (Heidelb).* 2022;12:825–34; 2. Aldhouse, NVJ, et al. *J Patient Rep Outcomes*. 2020;4:76; 3. Senna M, et al. *J Invest Dermatol*. 2022:doi.org/10.1016/j.jid.2022.02.019.

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Exploring the pathophysiology of alopecia areata: The role of the immune system and Janus kinase signalling pathways

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Immune privilege[1–3]

Immune privileged organs include: the eye, the central nervous system, the testes and the hair follicle

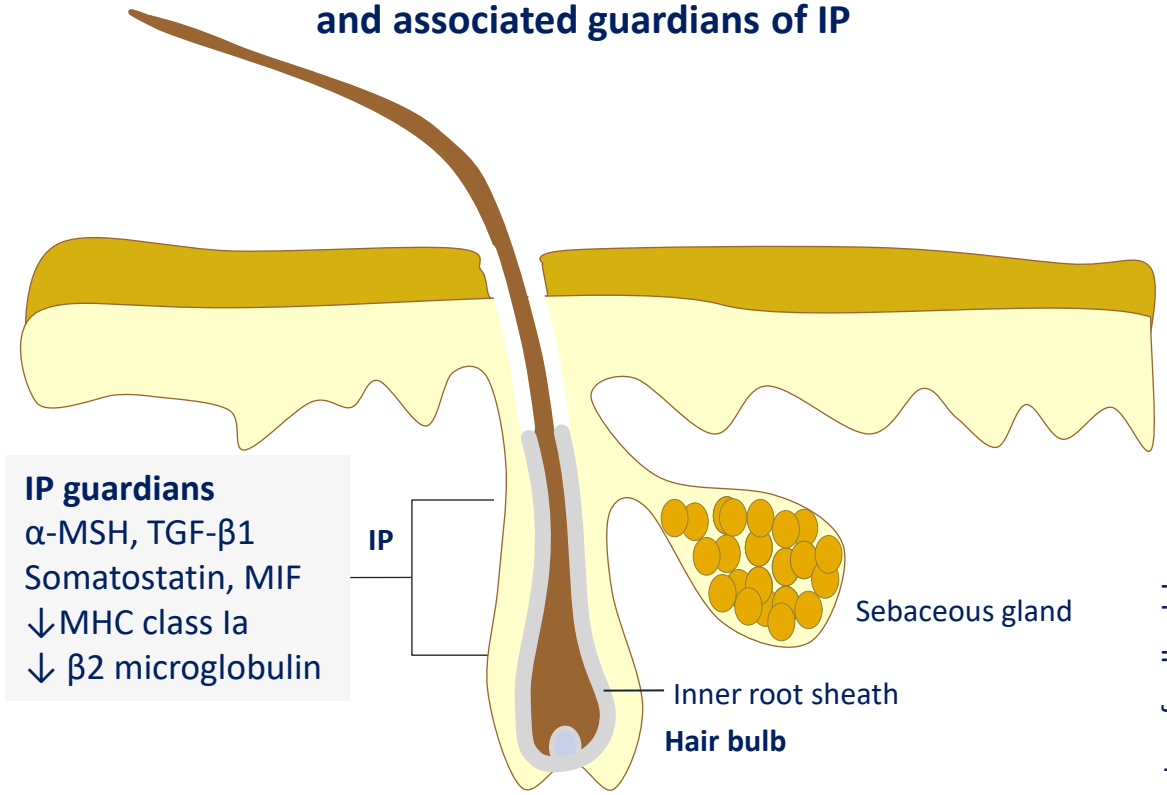
- Immune privilege is a term that is applied to certain organs that are able to tolerate the introduction of antigens without eliciting an inflammatory response and being attacked by the immune system
- Immune privilege is attributed to a range of mechanisms including:
  - Low expression of MHC molecules
  - Local production of immunosuppressive cytokines such as TGF-β1

MHC, major histocompatibility complex; TGF-β1, transforming growth factor-beta 1.

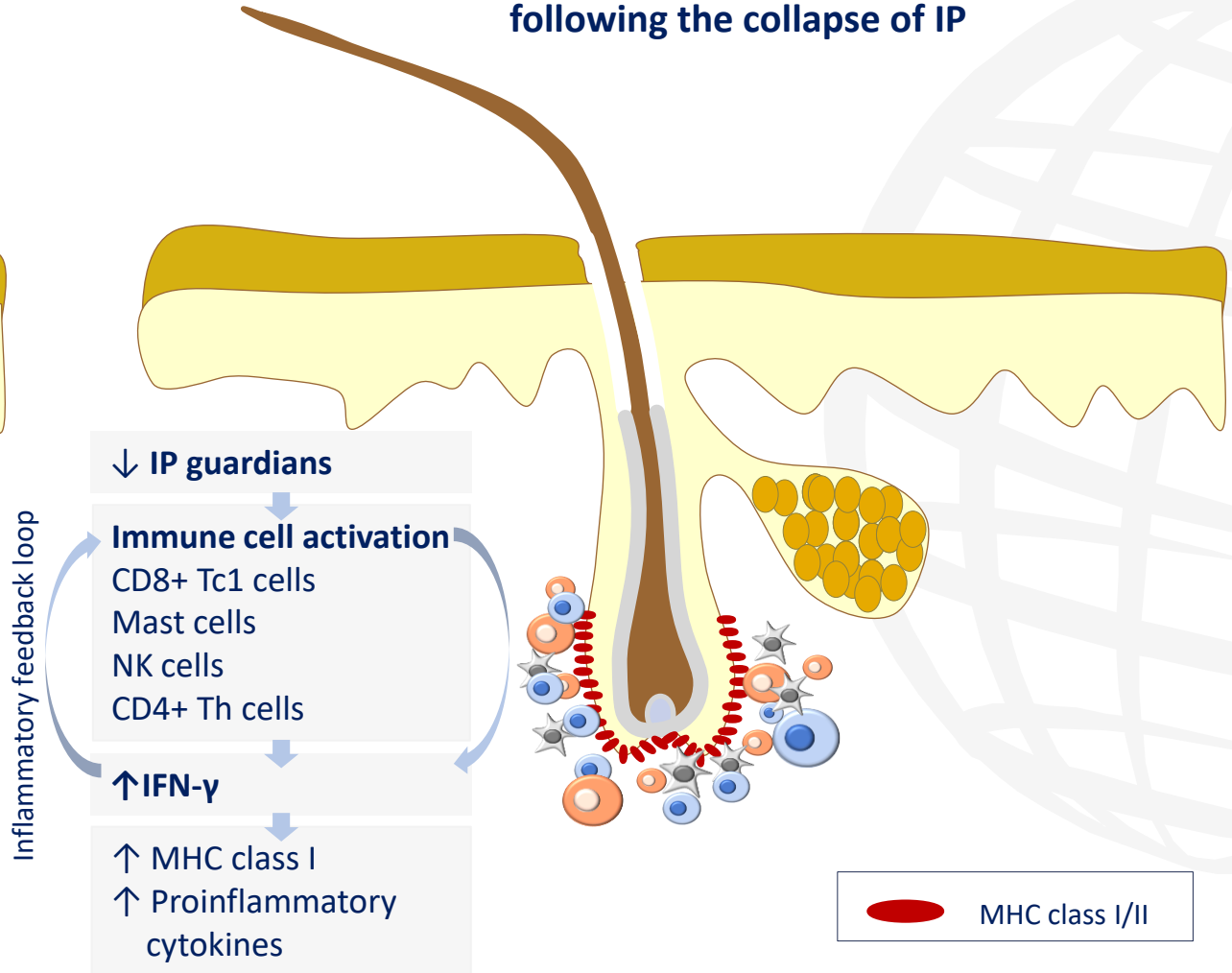
1. Barker CF, Billingham RE. *Adv Immunol*. 1977;25:1–54. 2. Hong S, van Kaer L. *J Exp Med*. 1999;190:1197–200; 3. Lintzeri DA, et al. *J Dtsch Dermatol Ges*. 2022;20:59–90.

Comparison of a healthy versus an inflamed hair follicle[1,2]

Healthy hair follicle and associated guardians of IP



Inflamed hair follicle following the collapse of IP



CD, cluster of differentiation; IFN-γ, interferon-gamma; IP, immune privilege; MHC, major histocompatibility complex; MIF, macrophage migration inhibitory factor; α-MSH, alpha melanocyte-stimulating hormone; NK, natural killer; Tc1, cytotoxic T cell type 1; TGF-β1, transforming growth factor-beta 1; Th, T helper.

1. Lintzeri DA, et al. *J Dtsch Dermatol Ges*. 2022;20:59–90; 2. Pratt CH, et al. *Nat Rev Dis Primers*. 2017:3;17011.

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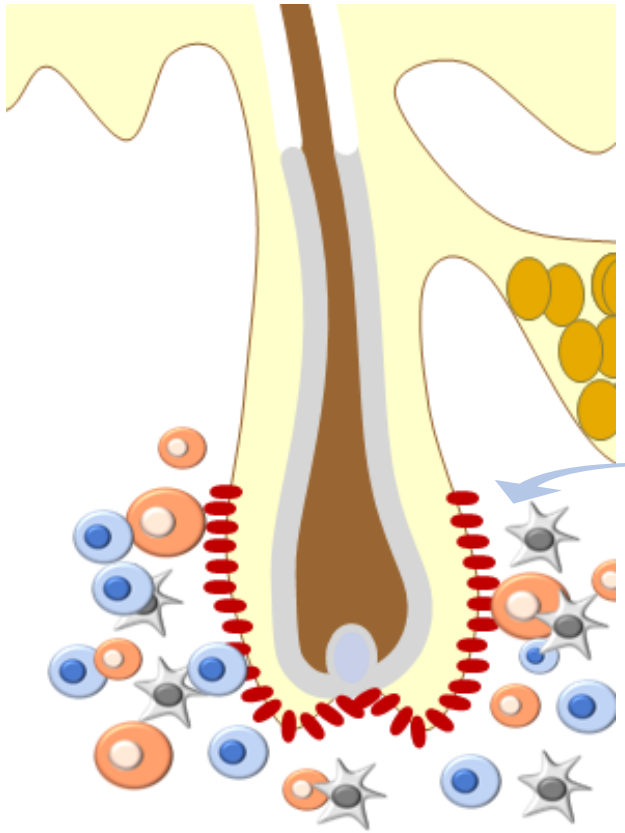
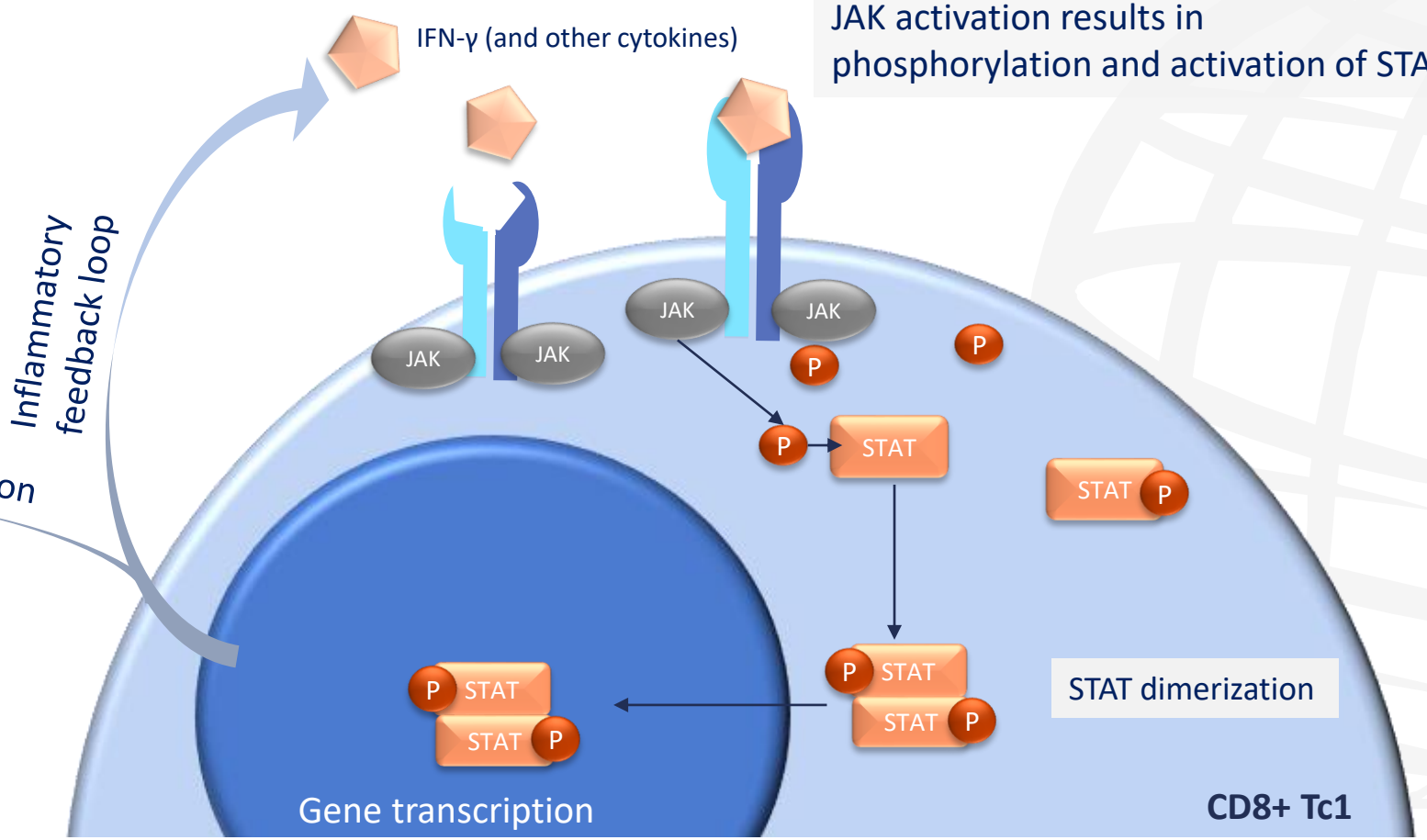
JAK/STAT pathway and inflammatory feedback loop[1,2]





CD, cluster of differentiation; IFN-γ, interferon-gamma; JAK, Janus kinase; P, phosphorylate; STAT, signal transducer and activator of transcription; Tc1, cytotoxic T cell type 1.

1. Lintzeri DA, et al. *J Dtsch Dermatol Ges.* 2022;20:59–90; 2. Pratt CH, et al. *Nat Rev Dis Primers*. 2017:3;17011.

Current treatment landscape and emerging therapies for alopecia areata: Focus on JAK inhibitors

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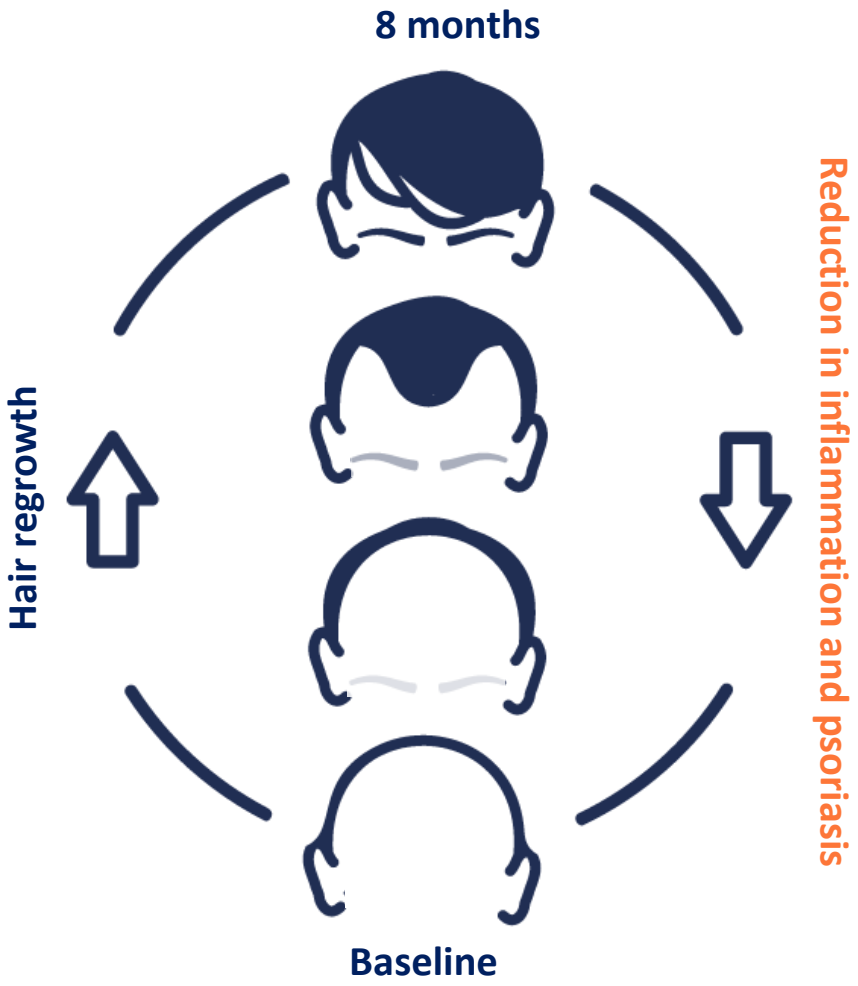
Early evidence for efficacy of JAK inhibitors in alopecia areata



Overview of an early case study that provided the first evidence that a pathogenesis-based therapy could be used to manage alopecia areata

Patient: 25-year-old male with alopecia universalis and plaque psoriasis
Treatment: Tofacitinib, 5 mg twice daily increasing to 15 mg daily
(10 mg in the morning, 5 mg in the evening)
Results: Reduction of psoriasis and full hair regrowth

JAK, Janus kinase.
Craiglow BG, King BA. *J Invest Dermatol*. 2014;134:2988–90.

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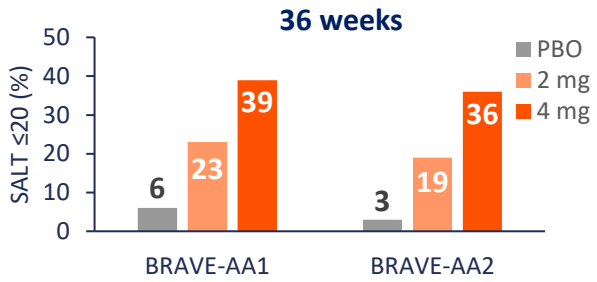
Phase III clinical trials of oral JAK inhibitors to treat alopecia areata

Baricitinib[1]
Target: JAK1, JAK2

Adults with severe alopecia areata
SALT score ≥50, mean (BL) ≈85;
mean disease duration ≥3.5 years

BRAVE-AA1 (N=654) **BRAVE-AA2 (N=546)**



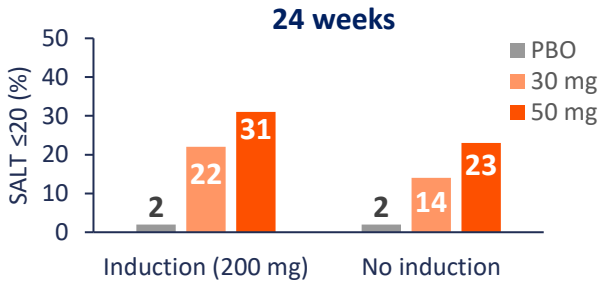
Both dose groups vs PBO, p<0.001

Serious AEs: <4% all treatment groups
Common AEs in any dose group include:
Acne, elevated CK, increased LDL and HDL cholesterol

Ritlecitinib (PF-06651600)[2,3]
Target: JAK3 and TEC family of kinases

Adults with moderate to severe alopecia areata
SALT score ≥50

ALLEGRO-2b/3 (N=718)



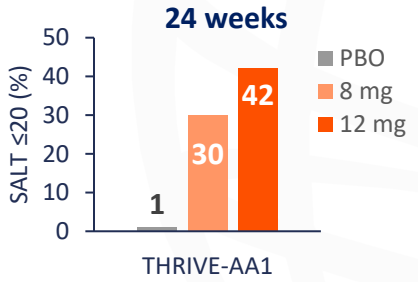
Both dose groups vs PBO, p<0.001

Serious AEs: <5% all treatment groups
Common AEs in any dose group include:
Acne, URTIs, nasopharyngitis, headache, diarrhoea, nausea

Deuruxolitinib (CTP 543)[4]
Target: JAK1, JAK2

Adults with moderate to severe alopecia areata
SALT score ≥50

THRIVE-AA1 (N=706)



Both dose groups vs PBO, p<0.0001

Serious AEs: 9/706 (<2%) patients
Common AEs in any dose group include:
Headache, nasopharyngitis, URTI, elevated CK, COVID-19 and acne

AE, adverse event; BL, baseline; CK, creatine kinase; HDL, high-density lipoprotein; JAK, Janus kinase; LDL, low-density lipoprotein; PBO, placebo; SALT, Severity of Alopecia Tool; URTI, upper respiratory tract infection.

1. King B, et al. *N Engl J Med*. 2022;386:1687–99; 2. ClinicalTrials.gov. NCT03732807. Available at: clinicaltrials.gov/ct2/show/results/NCT03732807 (accessed 7 September 2022); 3. Ramírez-Marín HA, et al. *Drug Des Devel Ther*. 2022;16:363–74; 4. King B, et al. Presented at the 31st EADV Congress, Milan 7–10 September 2022. Abstr. No. 3473.

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