Addressing the Unmet Needs of Patients With Moderate to Severe Psoriasis: A Visual Exploration of Disease Pathogenesis and the Clinical Potential of Targeting the TYK2 Pathway as a Novel Nonbiologic Oral Therapeutic Option

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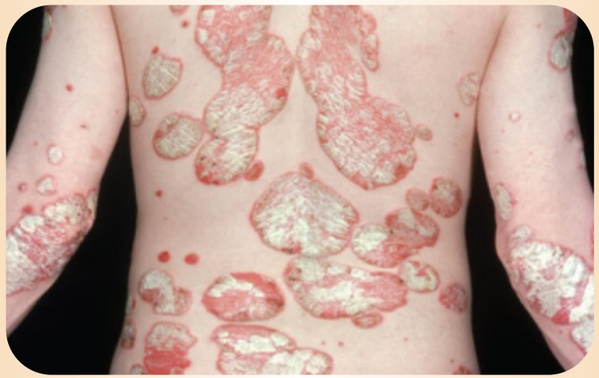
Rationale for Therapeutic Targeting of the JAK-STAT Signaling Pathway in Psoriasis

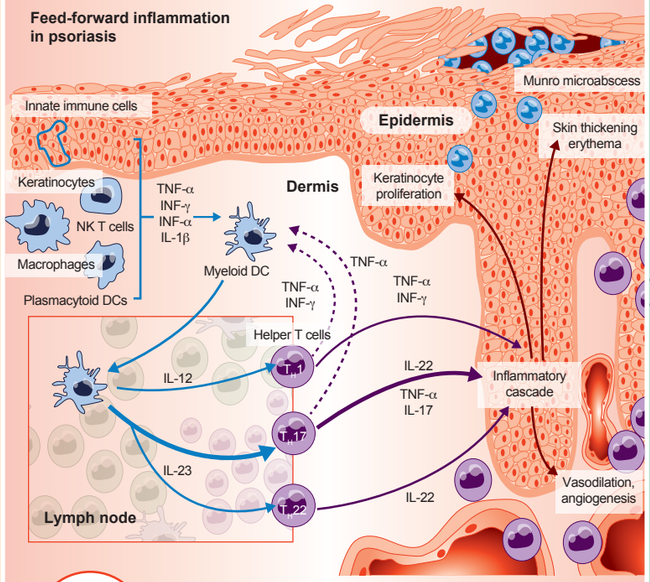
Burden[1-4]

Psoriasis is a chronic inflammatory skin condition that is often associated with systemic manifestations



Commonly used clinical measures to assess psoriasis severity may not adequately convey patient impact

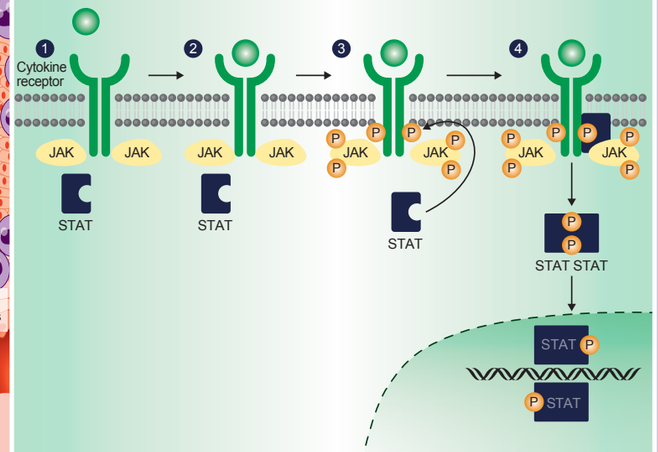
Pathophysiology[5-9]



Dysregulation or alteration of components of the innate and adaptive immune systems, keratinocyte function, and vascular structure contribute to disease manifestations

JAK-STAT Pathway[8,10]

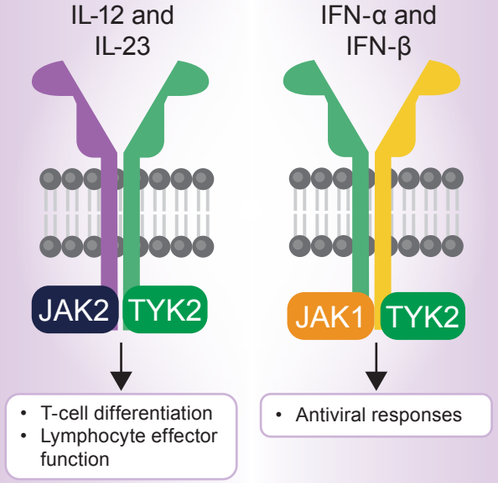
Plays a major role in intracellular cytokine signaling in inflammatory processes involved in psoriasis



Inhibition of the JAK-STAT pathway appears to be effective in psoriasis

TYK2[5,8,11-24]

Mediates signaling and functional responses downstream of the IL-12, IL-23, and type 1 IFN receptors



Selective, allosteric inhibition of TYK2 reduces the potential for toxicities associated with JAK inhibitors

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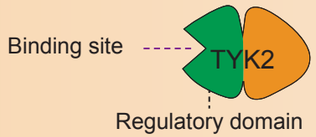
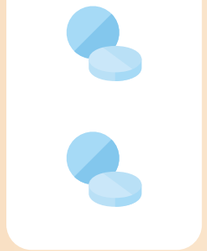
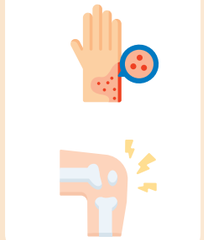
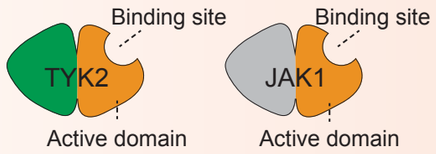
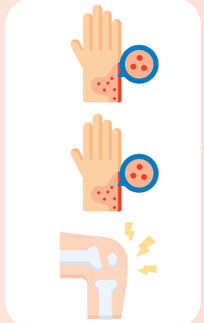
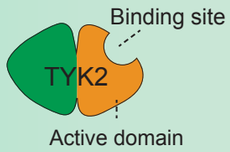
Targeting the TYK2 Pathway for the Treatment of Psoriasis: A Closer Look at the Latest Evidence and Clinical Application

Agent	MOA	Formulation	Disease	Efficacy	Common AEs
Deucravacitinib[25-33]	**TYK2 inhibitor** 			• **Phase 3 POETYK PSO-1 and POETYK PSO-2 trials:** significantly ↑ patients treated with deucravacitinib achieved PASI 75 and sPGA 0/1 compared with patients treated with placebo and apremilast at week 16, with ↑ benefit vs apremilast at week 24 and maintained through week 52 • **Phase 2 trial:** significantly greater ACR 20 responses compared with placebo at 16 weeks, and met all key secondary endpoints in patients with active PsA	Nasopharyngitis and URTI Nasopharyngitis, sinusitis, headache, and rash
Brepocitinib[34]	**Dual TYK2/JAK1 inhibitor** 			• **Phase 2a trial:** statistically significant differences in change from baseline PASI scores at week 12 were observed in five out of seven treatment groups; no future studies are planned for oral brepocitinib in moderate to severe psoriasis N/A; phase 2b trial underway (NCT03850483) N/A; phase 2b trial underway (NCT03963401)	Nasopharyngitis, URTI, and headache
PF-06826647[35]	**TYK2 inhibitor** 			• **Phase 1 trial:** significant improvement in disease activity within 4 weeks of dosing • **Phase 2 trial:** completed (NCT03895372); results N/A	All TEAEs mild in severity, except one moderate TEAE of vomiting reported in the placebo group