JAK Inhibitors in Hidradenitis Suppurativa: A Systematic Review

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Background

Hidradenitis suppurativa (HS) is a chronic, recurrent inflammatory skin disorder that causes a tremendous impact on patient quality of life. It is characterized by painful nodules, abscesses, draining sinus tracts, and disfiguring scarring in areas such as the axillae, groin, and inframammary folds. Despite a growing catalogue of therapies ranging from topical and systemic antibiotics to biologics and surgery, many patients continue to experience flares, pain, and functional disability.

Emerging evidence implicates dysregulation of the immune system, particularly overactive cytokine signaling pathways, in the pathogenesis of HS. The Janus kinase (JAK)-signal transducer and activator of transcription (STAT) pathway plays a key role in this inflammatory cascade. JAK inhibitors offer a novel, targeted approach to HS management. This systematic review assesses the efficacy, safety, and clinical relevance of JAK inhibitors such as tofacitinib, upadacitinib, povorcitinib, baricitinib, and abrocitinib, in the management of HS.

Literature Search

A PRISMA-guided systematic review was registered with PROSPERO (CRD42024556540) and conducted. Comprehensive searches were performed across PubMed, Ovid, Cochrane Library, and Google Scholar from inception through May 2024.

Studies were eligible if they evaluated the use of JAK inhibitors in human HS cases and reported clinical outcomes. Ten studies met inclusion criteria: 4 case reports, 2 case series, 2 clinical trials, 2 proof-of-concept studies, and 1 retrospective cohort. In total, data from 344 patients were reviewed.

Aggregate Clinical Outcomes

Among the 344 HS patients treated with JAK inhibitors, symptom alleviation was reported in 48% (165/344). Treatment-emergent adverse events (AEs) were documented in 43% (150/344), while serious AEs were rare, occurring in just 2.6% (9/344).

Reported AEs included fatigue, headache, upper respiratory infections, and laboratory abnormalities such as elevated creatine kinase and transaminitis. HiSCR (Hidradenitis Suppurativa Clinical Response) was used in most studies as the primary clinical endpoint. This metric requires at least a 50% reduction in abscess and nodule count with no increase in abscesses or draining fistulas. Overall, results suggest that JAK inhibitors may provide meaningful clinical benefit with manageable safety concerns.

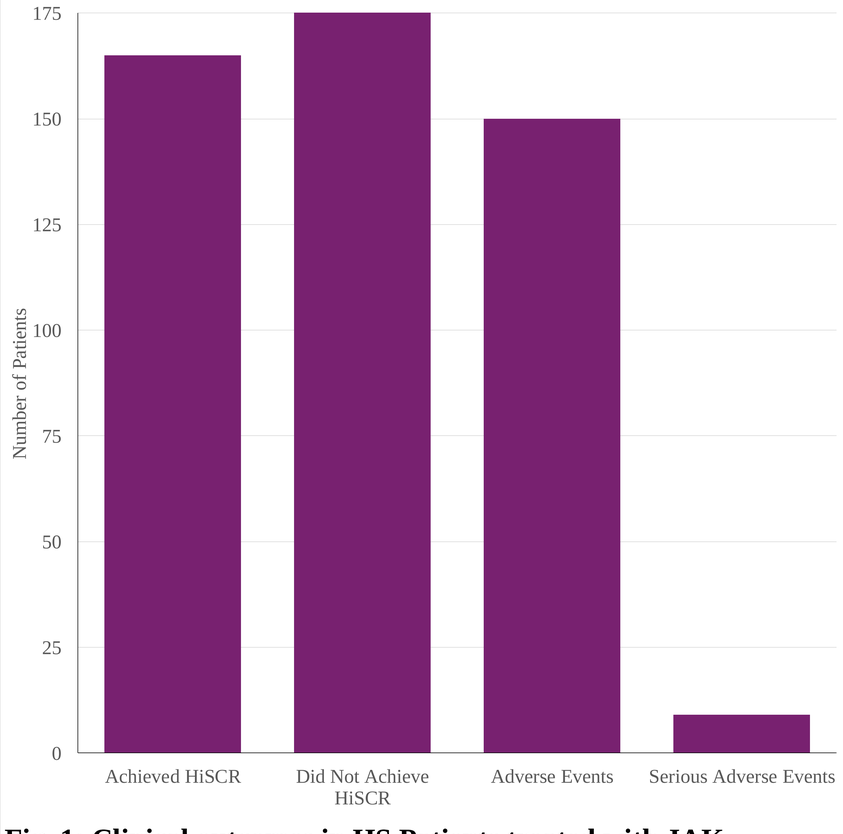

Fig. 1: Clinical outcomes in HS Patients treated with JAK Inhibitors (n=344)

Agent-Specific Highlights

Upadacitinib:

- In a retrospective cohort (n=20), 100% of patients achieved HiSCR by week 12.
- In a phase 2 randomized control trial (n=21), 38.3% of patients achieved HiSCR (vs. 25.0% placebo) by week 12.
- One reported case of VZV reactivation and HLH in an immunosuppressed patient.

Povorcitinib:

- In a phase 2 randomized control trial (n=209), 45.9% of patients achieved HiSCR (vs. 28.8% placebo) by week 16.
- No relationship between dosages administered and treatment-emergent adverse effects.

Tofacitinib:

- Several case reports demonstrating resolution or improvement of HS symptoms, with relapse upon discontinuation of therapy.
- One report of paradoxical HS, a phenomenon observed also seen with use of biologics.

Baricitinib:

- Single report showing complete remission in an HS patient with a STAT1 gain-of-function mutation and subsequent recurrence upon drug discontinuation.

Abrocitinib:

- Reported use in one pediatric case which resulted in near-complete resolution of HS lesions by week 6.

Conclusions

The evolving body of evidence suggests that JAK inhibition may become an important pillar in HS treatment; especially in patients unresponsive to conventional therapies. Nearly half of patients demonstrated improvement, with most adverse effects being mild and manageable. Though severe adverse events were rare, prescribing clinicians should monitor their patients closely. Further randomized controlled trials with longer durations and broader populations are essential to establish long-term safety, efficacy, and optimal use of these agents.