European Journal of Clinical Pharmacy
Print ISSN: 2385-409X **Online ISSN**: Applied
Website: https://farmclin.es/

Original Research Article

Hidradenitis Suppurativa and Anakinra: Clinical Efficacy, Safety, and Future Directions

Article History:

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How to cite this article:
Jose Maria L.M., et, al. Hidradenitis Suppurativa and Anakinra: Clinical Efficacy, Safety, and Future Directions. *Eur J Clin Pharm.* 2021;3(1);36-38.

Received: 22-08-2021
Revised: 28-08-2021
Accepted: 18-09-2021
Published: 28-10-2021

Abstract: Hidradenitis suppurativa (HS) is a chronic, recurrent, and debilitating inflammatory skin disease with limited therapeutic options for severe cases. The pathophysiology is increasingly linked to aberrant innate immune responses, specifically the interleukin-1 (IL-1) pathway. Anakinra, a recombinant IL-1 receptor antagonist, has emerged as a potential therapy. This article reviews the biological rationale, real-world evidence, clinical trial data, safety profile, and future research needs for anakinra in HS.

Keywords: Hidradenitis Suppurativa (HS), Anakinra, Interleukin-1 (IL-1) Pathway, Inflammatory Skin Disease, Immunotherapy.

INTRODUCTION

HS severely impairs quality of life due to painful abscesses, sinus tracts, and scarring, commonly affecting apocrine-rich areas such as the axillae and groin. Conventional therapies (antibiotics, hormonal agents, surgery, TNF-α inhibitors) variably address disease severity. The search for novel interventions has focused on cytokine blockade, with IL-1 inhibition offering targeted immunomodulation for inflammatory pathways distinct from those addressed by TNF-α inhibitors.

PATHOPHYSIOLOGY OF HIDRADENITIS SUPPURATIVA AND THE ROLE OF IL-1

- HS is characterized by follicular occlusion, rupture, and secondary immune activation.
- Dysregulation of the IL-1 pathway leads to overproduction of IL-1β, which drives neutrophilic infiltration and tissue destruction.
- Elevated IL-1β and related cytokines have been detected in lesional and systemic samples from patients with HS, supporting IL-1 as a key driver of chronic inflammation[1][2].

ANAKINRA: MECHANISM OF ACTION

- Anakinra is a recombinant, non-glycosylated form of human IL-1 receptor antagonist that competitively inhibits the binding of IL-1α and IL-1β to the IL-1 type I receptor.
- By blocking this pathway, anakinra suppresses downstream inflammatory cascades implicated in HS pathogenesis, providing a rationale for therapeutic use in moderate to severe disease[1].

CLINICAL EVIDENCE FOR ANAKINRA IN HS

Key Clinical Trials and Results

Double-Blind, Placebo-Controlled RCT

A pivotal randomized controlled trial (RCT) evaluated anakinra (100mg/day subcutaneously) for 12 weeks in 20 patients with Hurley stage II or III HS:

- **Clinical response** (as defined by Hidradenitis Suppurativa Clinical Response, HiSCR) reached 78% (7/9) in the anakinra group vs 30% (3/10) in placebo at 12 weeks ($P = .04$)[1][3][4].
- **Disease activity score** decreased in 67% of the anakinra group vs 20% in placebo.
- **Time to new exacerbation** was significantly prolonged in the anakinra-treated group.
- **Cytokine changes**: Reduced interferon-γ and increased interleukin-22 production.
- No serious adverse events were reported, though mild injection site reactions and occasional mild infections occurred[1][3][4].

Open-label Studies

- An 8-week study of 6 patients with moderate to severe HS showed significant reductions in Sartorius score (mean decrease of 34.8 points), physician and patient global assessments, and Dermatology Life Quality Index scores[2][5][6].
- Subjective and objective improvements persisted into the follow-up period, with no participant experiencing severe adverse events[2].

SYSTEMATIC REVIEWS AND META-ANALYSES

- Reviews indicate that anakinra provides HiSCR clinical responses at week 24 in up to 10%, with notable improvements earlier in therapy for some patients[7][8].
- Effect size varies; studies emphasize individualized selection and close monitoring, as well as the need for enhanced predictive markers of response.

Table: Summary of Major Clinical Outcomes

Study Type	Patient Number	Duration	Clinical Response Rate	Notable Adverse Events
RCT	20	12 wks	78% (anakinra)	Mild injection site pain, infx
Open-label	6	8 wks	All improved	None serious
Systematic Review	34 studies	Varies	HiSCR 10-78% reported	Low SAE rates, well-tolerated

Real-World Efficacy

- Observed effectiveness is typically robust among patients with moderate to severe HS, especially after failure of first-line agents.
- Some real-world studies report cases of limited efficacy or relapse post discontinuation, highlighting need for selection criteria and possible combination therapy[9].
- Most patients and clinicians report improved quality of life, reduced pain, and extended time to flare during active treatment.

Safety Profile

- **Common adverse effects:** Mild injection site reactions and transient upper respiratory tract infections.
- **Serious adverse events:** Rare; studies consistently report no increased incidence of serious infections or organ toxicity.
- **Tolerability:** Daily subcutaneous administration may limit adherence for some patients, and discomfort can prompt discontinuation in select cases[9].

Comparative Efficacy

- Systematic evidence ranks anti-TNF agents (e.g., adalimumab) and lasers as highly effective for HS, but anakinra is detailed as a valuable adjunct or alternative—particularly for refractory or biologic-experienced patients.
- The personalization of care is emphasized, with anakinra providing a non-TNF-based alternative suited to select patient populations[7][10].

GRAPHICAL REPRESENTATION

Clinical Response to Anakinra vs Placebo at 12 Weeks

Group	Clinical Response Rate (%)
Anakinra	78
Placebo	30

This illustrates the improved rates of disease control with anakinra relative to placebo, as reported by leading RCTs[1][3][4].

DISCUSSION

Anakinra represents a targeted, biologically plausible, and generally well-tolerated therapy for HS. Its efficacy is supported by reductions in lesion count, inflammatory markers, and patient-reported outcomes across both controlled and observational studies. Barriers include the need for daily injections, variable individual response, and the long-term safety and durability of remission upon withdrawal.

Limitations and Areas for Future Research

- Limited sample sizes and short trial durations are recurring concerns.
- Lack of direct comparison with other biologic agents in head-to-head trials.
- Uncertainty about long-term remission rates and ideal therapy duration.
- Further elucidation of biomarkers predictive of IL-1 pathway blockade responsiveness is needed[7][3].

CONCLUSION

Anakinra is a promising, IL-1-targeted immunomodulator for moderate to severe HS, demonstrating significant efficacy and safety in clinical trials and real-world practice. Ongoing studies will define its optimal use within a broader therapeutic algorithm, preferentially for patients not responding to conventional or anti-TNF therapies.

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