SKIN

RESEARCH LETTER

Emerging Therapies in Hidradenitis Suppurativa: An Update for Practicing Dermatologists

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ABSTRACT

Hidradenitis suppurativa (HS) is a chronic, treatment-resistant inflammatory skin disease marked by painful nodules, abscesses, and sinus tracts. Recent FDA approvals of IL-17 inhibitors, such as bimekizumab and secukinumab, represent major therapeutic advances. This review highlights emerging therapies and key clinical trials that may further transform HS management. A systematic review was conducted per PRISMA guidelines using ClinicalTrials.gov, PubMed, and Embase. Inclusion criteria consisted of active, recruiting, or pending Phase 2/3 trials and publications within the last five years evaluating investigational HS treatments. Studies involving FDA-approved drugs, procedural interventions, or lacking efficacy data were excluded. Fifty-six studies were included: 22 publications and 38 trial records. Therapeutic targets have broadened to include IL-1, IL-36, JAK1/2, TYK2, and other inflammatory pathways. Spesolimab, an IL-36R inhibitor, recently completed a Phase 2/3 trial and may benefit patients with tunnel-predominant HS. Povorcitinib, a JAK1 inhibitor, showed significant HiSCR improvement in Phase 2 and is now in Phase 3. Sonelokimab, an IL-17A/F inhibitor, and lutikizumab, an IL-1α/β inhibitor, have both advanced to Phase 3 trials with promising early results. These investigational agents demonstrate diverse mechanisms aligned with HS pathophysiology and offer hope for patients unresponsive to existing therapies. Dermatologists should remain informed on trial progress and anticipate data that may inform future clinical decision-making.

INTRODUCTION

Hidradenitis suppurativa (HS) is a chronic inflammatory disease with painful nodules, abscesses, and sinus tracts, often treatment resistant. Recent FDA approvals of the IL-17A/F inhibitor bimekizumab and IL-17A inhibitor secukinumab mark major progress. This letter reviews key clinical trials and highlights emerging therapies dermatologists should be following.

METHODS

A systematic review was conducted per PRISMA guidelines using ClinicalTrials.gov, PubMed, and Embase. Search terms included combinations of ‘hidradenitis

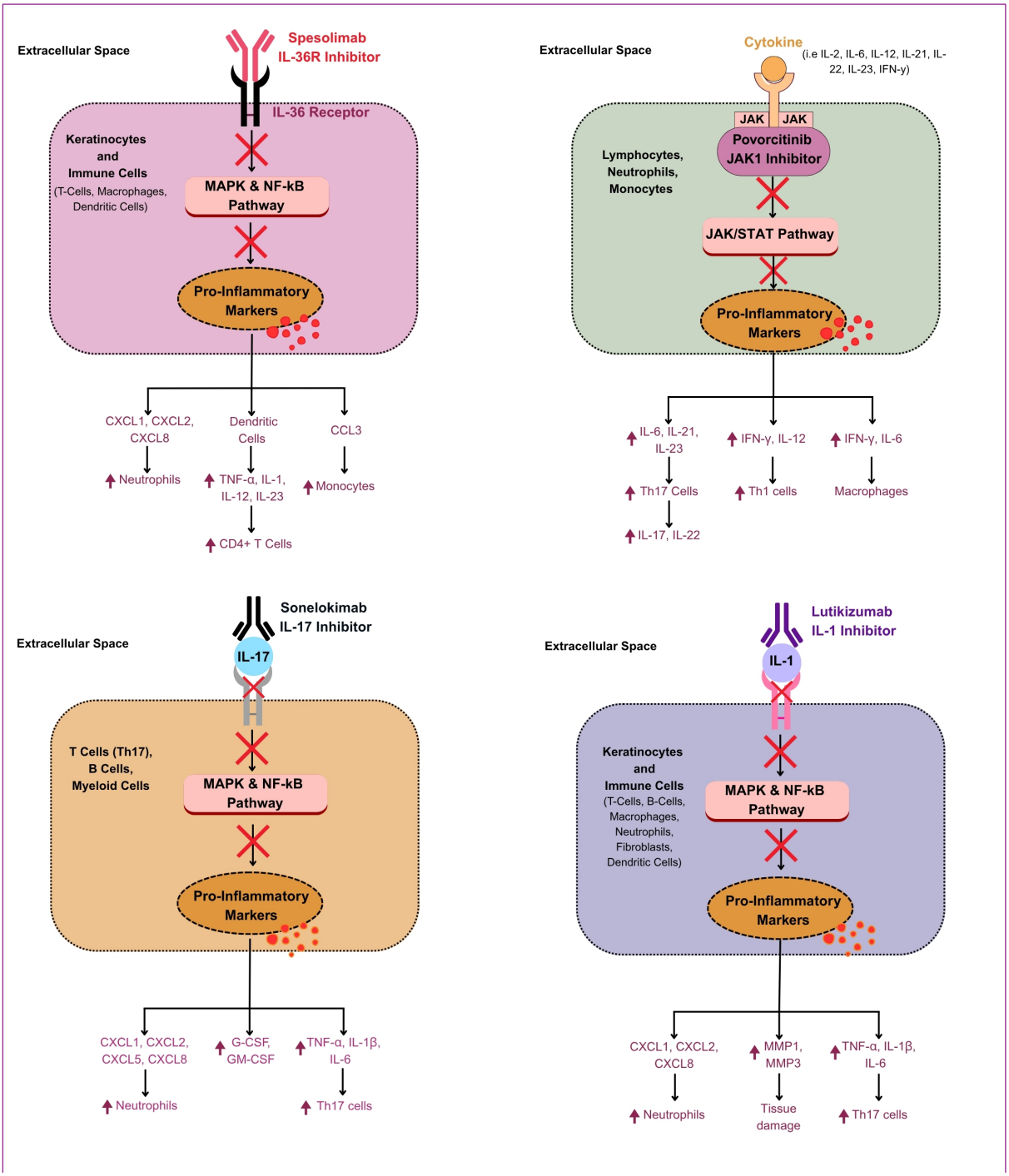

Figure 1. Drug mechanisms

suppurativa' with trial-related and therapeutic keywords (**Supplementary Table 1**). Inclusion criteria included active, recruiting, or pending Phase 2/3 trials and relevant literature on therapies in progress or with significant results in the past five years. Exclusion criteria included FDA-approved drugs, non-HS studies, lack of efficacy data, outdated or procedural trials, and other minor criteria (**Supplementary Table 2**). A total of 56 studies were included: 22 publications and 38 trial records (**Supplementary Figure 1**).

Table 1. Summary of Emerging Therapies in HS in Current Phase 2 or 3 Clinical Trials with Previous Published Efficacy Outcomes

Agent	Mechanism	Published Efficacy Outcomes	Current Status and Phase	Study Design
Spesolimab	IL-36R inhibitor	*Proof of Concept Study (2024)* **IHS4 mean change: -13.9** (95% CI –25.6 to –2.3) **dT tunnel count change: 96.6%** (95% CI –154.5 to –38.8) **% with dT count of 0: 18.3%** (95% CI –7.9 to 37.5)	NCT04876391 Phase 2 Completed, Results Submitted and Under Review	Open-label, Long-term extension Single group assignment
			NCT05322473 Phase 2 Completed, Results Pending	Randomized, Parallel-group, Double-blind, Placebo-controlled
			NCT05819398 Phase 2/3 Completed, Results Pending	Randomized, Double-blind, Placebo-Controlled
Povorcitinib	JAK1 inhibitor	*Phase 2 Efficacy and Safety (2024)* **AN count** at Week 16: 15 mg: **–5.2** (P = .0277) 45 mg: **–6.9** (P = .0006) 75 mg: **–6.3** (P = .0021) **HiSCR rates** placebo: **28.8%** 15 mg: **48.1%** (P = .0445) 45 mg: **44.2%** (P = .0998) 75 mg: **45.3%** (P = .0829)	NCT05620823 Phase 3 Active	Randomized, Double-Blind, Placebo-Controlled
			NCT06212999 Phase 3 Recruiting	Randomized, Double-Blind
			NCT06855498 Phase 3 Recruiting	Open-label, Multicenter, Rollover

Sonelokimab	IL-17 A/F inhibitor	*Phase 2 MIRA trial (2024)* **HiSCR75** at week 24 120 mg: **56.9%** (vs. 43.3% at Week 12) 240 mg: **37.9%** (vs. 34.8% at Week 12)	NCT06411379 Phase 3 Recruiting	Randomized, Double-blind, Placebo-controlled, Multicenter
			NCT06768671 Phase 3 Recruiting (Adolescents)	Open-label, Single-arm Study
Lutikizumab	IL-1α/β inhibitor	*Phase 2 Efficacy and Safety (NCT05139602) (2024)* **HiSCR50** at Week 16 placebo: **35.0%** 300 mg EOW: **59.5%** 300 mg EW: **48.7%**	NCT05139602 Phase 2 Active	Randomized, Double-Blind, Placebo-Controlled, Multicenter
			NCT06524635 Phase 2 Recruiting	Multicenter Open-Label
			NCT06468228 Phase 3 Recruiting	Randomized, Double-Blind, Placebo-Controlled, Multicenter

HS, hidradenitis suppurativa; IL, interleukin; JAK, Janus kinase; IFN, interferon; TNF, tumor necrosis factor; IHS4, International Hidradenitis Suppurativa Severity Score System; dT, draining tunnels; AN, abscess and inflammatory nodule; HiSCR, Hidradenitis Suppurativa Clinical Response; EOW, every other week; EW, every week; CI, confidence interval; NRS30, 30% reduction in numeric rating scale pain score.

RESULTS

Therapeutic targets have expanded to additional cytokine and kinase pathways such as IL-1α/β, IL-36, TNF, JAK1/2, TYK2, and others in 22 active trials (**Supplementary Table 2**). Many of these genes may be upregulated in HS such as IL-1A, TNF, and members of the IFN, IL-17, and TYK family.[1] Several investigational therapies showing early efficacy are expected to complete trials within the next 12-18 months. Spesolimab, an IL-36R inhibitor, recently completed a Phase 2/3 trial in April 2025, with results pending. In HS, keratinocytes may have an exaggerated response to follicular bacteria, promoting IL-36 dysregulation and inflammation.[2] Earlier data showed a 96.6% reduction in draining tunnels with a far lesser effect on abscesses and nodules, supporting its potential in tunnel-predominant HS.[3] Povorcitinib, a JAK1 inhibitor, is in an active and recruiting phase 3 trial with estimated completion in January 2026. In a Phase 2 study, it significantly reduced abscess and inflammatory nodule (AN) counts at all doses, with the 15 mg dose achieving a HS clinical response (HiSCR) rate of 48.1% vs 28.8% with placebo (p= .0445).[4] It also downregulated JAK/STAT-regulated genes, lowering the expression of HS-related inflammatory markers.[1] Similar to bimekizumab, sonelokimab inhibits IL-17A/F, a cytokine increased in HS that drives

chemokine production and keratinocyte proliferation.[2] It's Phase 2 trial demonstrated HiSCR75 rates of 56.9% at 120 mg versus 43.4% and is now in two Phase 3 recruiting studies (adults and adolescent) with expected completion in 2026.[5] Lutikizumab neutralizes IL-1α/1β to suppress the upregulated IL-1 pathway in HS which promotes inflammasome-mediated inflammation.[2] It demonstrated promising Phase 2 results among anti-TNF resistant patients, achieving HiSCR50 rates up to 59.5% versus 35.0% in placebo and meaningful pain reduction in NRS30 (34.5% vs 12.9%).[5] It is now in an active phase 3 trial and two other recruiting phase 3 trials with completion expected in 2026. Results and drug mechanisms are summarized in **Figure 1** and **Table 1**.

DISCUSSION

Immunomodulators have ushered in a new era in HS therapy. Dermatologists should remain aware of ongoing trials to guide patients towards recruiting trials and anticipate therapies that may soon impact clinical practice. Upcoming data may reshape HS treatment algorithms and enhance long-term disease control in this challenging condition.

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References:

1. Liu H, Kircik LH, Kimball AB, et al. Modulation of disease-associated pathways in hidradenitis suppurativa by the Janus kinase 1 inhibitor povorcitinib: transcriptomic and proteomic analyses of two phase 2 studies. *Int J Mol Sci*. 2023;24(8):7185. http://doi.org/10.3390/ijms24087185
2. Witte-Händel E, Wolk K, Tsaousi A, et al. The IL-1 pathway is hyperactive in hidradenitis suppurativa and contributes to skin infiltration and destruction. *J Invest Dermatol*. 2019;139(6):1294–1305. http://doi.org/10.1016/j.jid.2018.11.018
3. Alavi A, Prens EP, Kimball AB, et al. Proof-of-concept study exploring the effect of spesolimab in patients with moderate-to-severe hidradenitis suppurativa: a randomized double-blind placebo-controlled clinical trial. *Br J Dermatol*. 2024;191(4):508–518. http://doi.org/10.1093/bjd/ljae144
4. Kirby JS, Okun MM, Alavi A, et al. Efficacy and safety of the oral Janus kinase 1 inhibitor povorcitinib (INCB054707) in patients with hidradenitis suppurativa in a phase 2, randomized, double-blind, dose-ranging, placebo-controlled study. *J Am Acad Dermatol*. 2024;90(3):521–529. http://doi.org/10.1016/j.jaad.2023.10.034
5. Fraser KA. American Academy of Dermatology Annual Meeting: San Diego, CA, USA, 8–12 March 2024. *Am J Clin Dermatol*. 2024;25:509–512. Available from: http://doi.org/10.1007/s40257-024-00860-5

Supplementary Table 1. Keyword Search Strategy

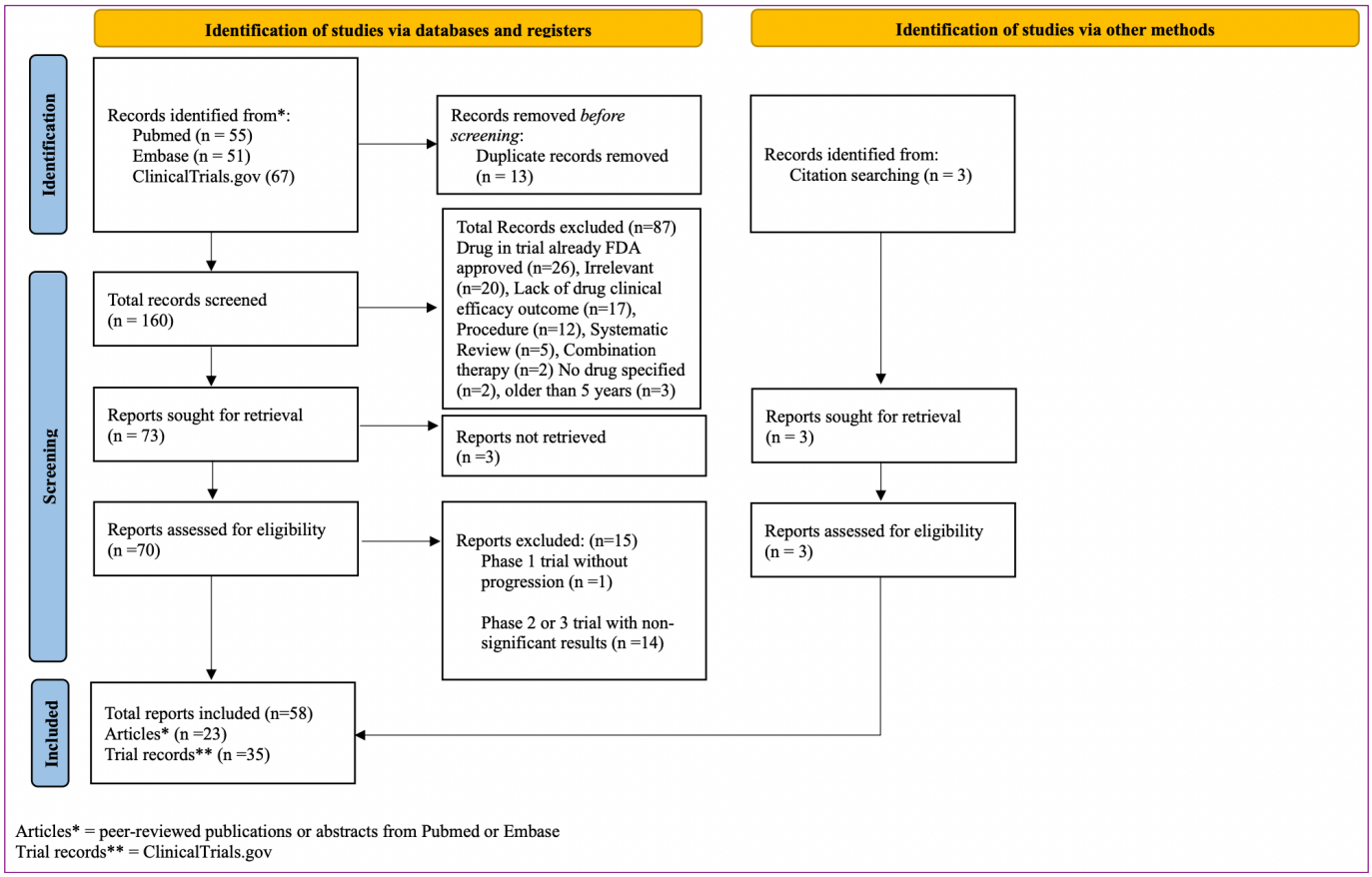
Database	Keywords (obtained from relevant trials on ClinicalTrials.gov)
PubMed	(("remibrutinib"[Title/Abstract] OR "sonelokimab"[Title/Abstract] OR "eltrekibart"[Title/Abstract] OR "upadacitinib"[Title/Abstract] OR "brensocatib"[Title/Abstract] OR "deucravacitinib"[Title/Abstract] OR "ruxolitinib"[Title/Abstract] OR "LY3041658"[Title/Abstract] OR "lutikizumab"[Title/Abstract] OR "anifrolumab"[Title/Abstract] OR "amlitelimab"[Title/Abstract] OR "AVTX-006"[Title/Abstract] OR "HB0043"[Title/Abstract] OR "gentian violet"[Title/Abstract] OR "kt-

	474"[Title/Abstract] OR "lt-002-158"[Title/Abstract] OR "povorcitinib"[Title/Abstract]) AND ((y_5[Filter]) AND (clinicaltrial[Filter] OR randomizedcontrolledtrial[Filter] OR "clinical trial"[Title/Abstract] OR "clinical trials"[Title/Abstract]))) AND (hidradenitis) OR (hidradenitis suppurativa)
Embase	('remibrutinib':ab,ti OR 'sonelokimab':ab,ti OR 'eltrekibart':ab,ti OR 'upadacitinib':ab,ti OR 'brensocatib':ab,ti OR 'deucravacitinib':ab,ti OR 'ruxolitinib':ab,ti OR lutikizumab:ab,ti OR 'anifrolumab':ab,ti OR 'amlitelimab':ab,ti OR 'avtx-009':ab,ti OR 'hb0043':ab,ti OR 'gentian violet':ab,ti OR 'kt-474':ab,ti OR 'lt-002-158':ab,ti OR 'povorcitinib':ab,ti OR 'clinical trial':ab,ti OR ('clinical trial':ab,ti AND topic:ab,ti)) AND ('hidradenitis':ab,ti OR 'suppurative hidradenitis':ab,ti) AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim) AND [2020-2025]/py
Exclusion criteria: FDA-approved drugs, studies unrelated to HS, lack of clinical efficacy outcomes, procedural interventions, review articles, combination therapies, non-specific drug interventions, and trials with results older than five years	

Supplementary Table 2. Summary of Active, Recruiting, and Not Yet Recruiting Clinical Trials for HS

Clinical Trial No.	Phase	Trial Status	Agent	Target/Mechanism	Expected Completion
NCT06555328	2	Recruiting	INF904	C5aR inhibitor	12/2025
NCT06932003	1/2	Recruiting	LT-002-158	IRAK4 degrader	12/2025
NCT05139602	2	Active	Lutikizumab	IL-1α/IL-1β inhibitor	01/2026
NCT05620823	3	Active	Povorcitinib	JAK1 inhibitor	01/2026
NCT06768671	3	Recruiting	Sonelokimab	IL-17A/IL-17F inhibitor	03/2026
NCT06895499	1/2	Recruiting	HB0043	IL-17A/IL-36 inhibitor	03/2026
NCT06411379	3	Recruiting	Sonelokimab	IL-17A/IL-17F inhibitor	06/2026
NCT06603077	2	Recruiting	AVTX-009	IL-1β inhibitor	07/2026
NCT06046729	2	Recruiting	Eltrekibart	CXCR1/CXCR2 inhibitor	07/2026
NCT06028230	2	Recruiting	KT-474	IRAK4 degrader	07/2026
NCT06468228	3	Recruiting	Lutikizumab	IL-1α/IL-1β inhibitor	12/2026
NCT03827798	2	Active	CFZ533 (Iscalimab) LYS006 MAS825 LOU064 VAY736	CD40 inhibitor Leukotriene A4 hydrolase inhibitor IL-1β/IL-18 inhibitor BTK inhibitor B-cell targeting inhibitor	12/2026
NCT05997277	2	Recruiting	Deucravacitinib	TYK2 inhibitor	12/2026
NCT06374212	2	Recruiting	Anifrolumab	IFN receptor 1 inhibitor	12/2026
NCT06212999	3	Recruiting	Povorcitinib	JAK1 inhibitor	12/2026

NCT06685835	2	Recruiting	Brensocatib	Dipeptidyl peptidase 1 inhibitor	01/2027
NCT06118099	2	Active	Amlitelimab	OX-40 ligand inhibitor	01/2027
NCT06524635	2	Recruiting	Lutikizumab	IL-1α/IL-1β inhibitor	02/2027
NCT05889182	3	Recruiting	Upadacitinib	JAK1 inhibitor	08/2027
NCT04414514	2	Recruiting	Ruxolitinib	JAK1/JAK2 inhibitor	01/2028
NCT06855498	3	Recruiting	Povorcitinib	JAK1 inhibitor	02/2028
NCT06840392	3	Recruiting	Remibrutinib (LOU064)	BTK inhibitor	10/2028



Supplementary Figure 1. Search strategy