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Beyond Current Biologics: Exploring Novel Strategies in Hidradenitis Suppurativa

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Learning Objectives

- Recognize the clinical presentations, high-risk features, and consequences of delayed diagnosis in HS to support timely, evidence-based intervention and prevent disease progression
- Explain the role of the JAK/STAT signaling pathway in HS pathogenesis and describe the mechanisms by which oral JAK1 inhibitors may modulate disease activity
- Evaluate the efficacy and safety data for biologic therapies and oral JAK inhibitors in HS to inform individualized treatment selection
- Apply evidence-based treatment strategies for patients with moderate-to-severe HS, incorporating patient preferences, comorbidities, prior treatment response, and practical considerations into shared decision-making

Enhancing HS Outcomes: Early Detection and the Power of Multidisciplinary Care

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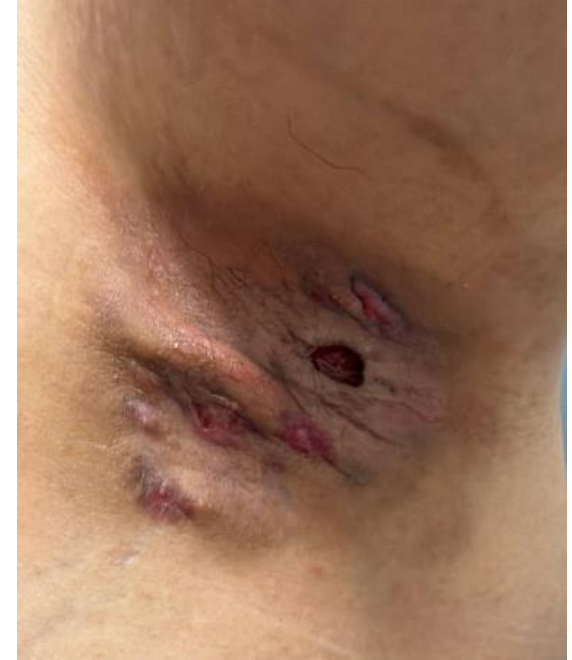
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The Importance of Early Detection and Multidisciplinary Management



Baseline



12 months later

- Comorbid conditions: Type 2 diabetes, obesity, irregular menses, depression, anxiety, metabolic syndrome, atherosclerotic cardiovascular disease

Clinical Signs and Symptoms

- **Lesion types:** Inflammatory nodules, abscesses, tunnels, and hypertrophic scars
- **Affected areas:** Axillae, inframammary, inguinal, perianal, buttocks
- Progressive disease leads to irreversible tissue destruction and scarring



Ulcerative Lesions Are a Less Common Presentation



Improvement after 3.5 months of IL-17A/F inhibition (bimekizumab)

IL = interleukin.

The Problem of Diagnostic Delay

Journey to diagnosis

- Average 10 years from symptom onset to diagnosis
- Patients consult >3 different specialties on average
- Receive >3 misdiagnoses before accurate diagnosis
 - Acne, folliculitis, staph infection

Consequences

- Greater disease severity at diagnosis
- Higher number of comorbidities
- Irreversible tissue damage
- Reduced quality of life
- More recalcitrant to treatment

Ultrasound for Hidradenitis Suppurativa

Ultrasound Frequently Reveals More Extensive Disease Than Clinical Examination

Clinical examination

Surface morphology
Palpable nodules/abscesses
Visible drainage openings

Ultrasound adds

Depth, occult collections
Subclinical tunnels
Connectivity, vascular activity

Potential consequence

Higher severity classification
Systemic therapy escalation
Procedure/surgery modification

- In an Italian multicenter study, 28.7% of patients were classified as more severe by SOS-HS than by Hurley staging
- In a Spanish multicenter cohort, ultrasound shifted the distribution toward higher Hurley-equivalent stages ($P<0.01$)
- Subclinical tunnels are especially important because they may represent persistent structural disease despite apparent surface improvement

SOS = sonographic scoring system.

Mendes-Bastos P, et al. *Br J Dermatol*. 2023;188(5):591-600.

Ultrasound Can Guide Procedures and Surgical Planning

Map tunnels

Define length, depth, branches, and communication

Target procedures

Guide drainage, intralesional therapy, or deroofing

Define margins

Identify occult extension before excision

Postoperative follow-up

Assess residual or recurrent disease

The 2026 international consensus includes ultrasound support for image-guided procedures and surgical planning among the recommended applications

HS Imposes Multidimensional Disease Burden with Great Impact on Quality of Life

Physical

Pain, drainage, malodor, pruritus
Scarring, restricted movement

Psychological

Embarrassment, stigma, anxiety
Depression, body-image distress

Social / intimate

Sexual dysfunction
Clothing adaptations
Social withdrawal, relationship strain

Sleep / daily activity

Sleep disturbance, fatigue
Exercise and self-care limitations

Work / education

Absenteeism, presenteeism
Reduced productivity

Healthcare burden

Repeated visits
Antibiotics, procedures
Surgery, biologic therapy

Quality-of-Life Tools in HS: What Each Instrument Adds

Tool	Length / Format	Type	Strength	Caveat
DLQI	10 items	Dermatology-specific	Very widely used; interpretable bands/MCID	May miss HS-specific emotional/adaptive burden
HiSQOL	17 items; 7-day recall	HS-specific	Symptoms + psychosocial/emotional + activities/adaptations	Validated for trials and real-world use
HIDRAdisk	10 domains; visual disk	HS-specific burden	Rapid visual discussion of multidimensional burden	Validated; intuitive for clinic
HSIA	HS impact PROM	HS-specific	Impact of HS on daily life	Validated; used in development programs
HSQOL-24 / QOL-HS	HS-specific	HS-specific QOL	Short recall; practical options	Less universally used than DLQI/HiSQOL
EQ-5D / SF-36	Generic health status	Generic	Cross-disease comparisons / health economics	Less sensitive to HS-specific issues

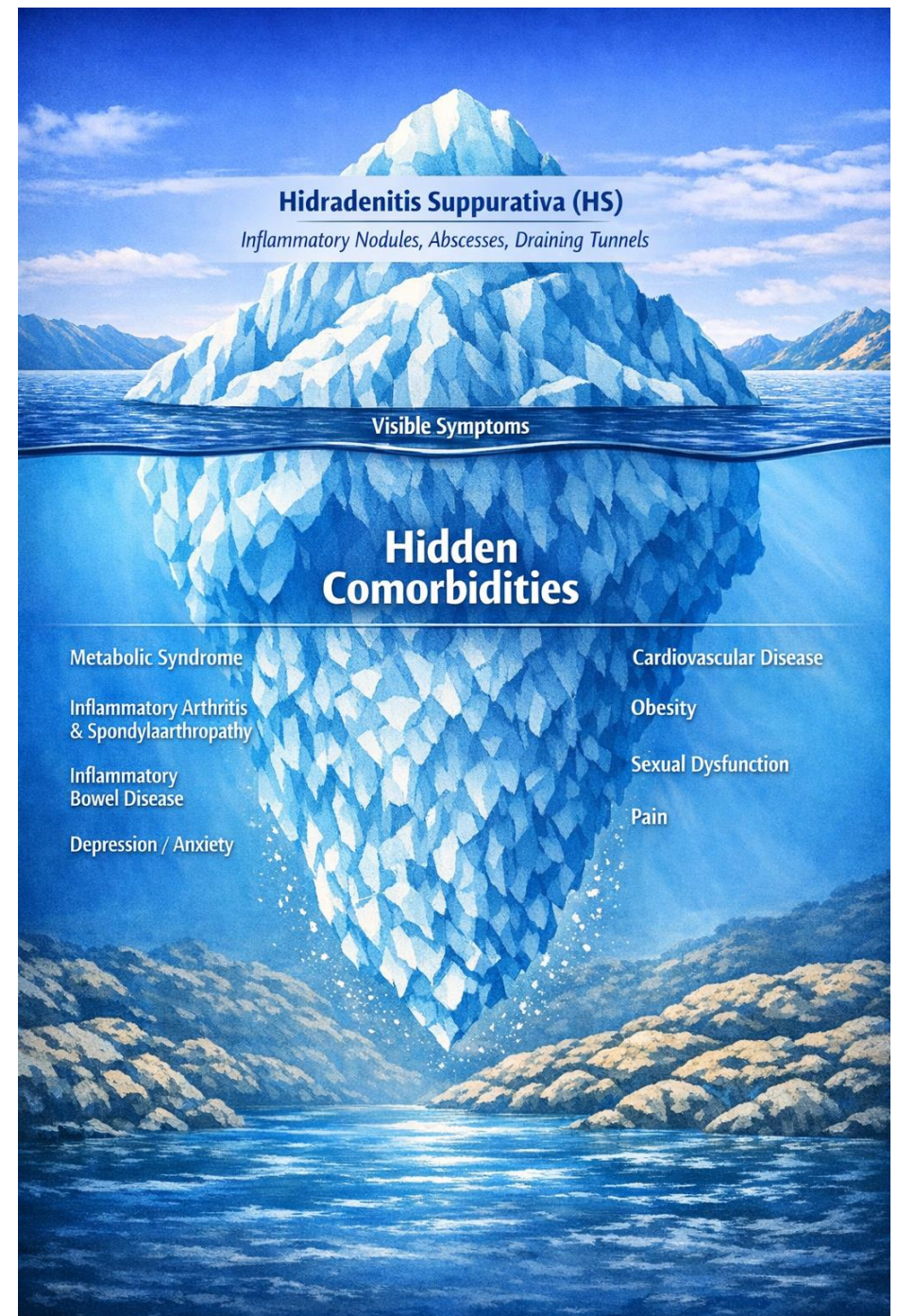
DLQI = Dermatology Life Quality Index; HiSQoL = HS Quality of Life; HIDRAdisk = HS-specific disk-format QOL questionnaire; HSIA = HS Impact Assessment; EQ-5D = EuroQOL 5-Dimension; SF-36 = Short-Form 36 Health Survey; MCID = minimal clinically important difference. Chernyshov PV, et al. *Int J Dermatol*. 2026;65(10):2008-2017. Kimball AB, et al. *Dermatol Ther* (Heidelb). 2024;14(1):83-98.

How Do We Shorten the Journey to Diagnosis?

- Educating providers
 - Recognition of HS
 - Reducing misdiagnoses
- Patient advocacy
- Improving access to dermatologists
- Optimizing referral pathways

Practical Tips for Screening

- Space it out over multiple visits!
- Collaborate with the patient's existing care team
- Combine screening labs with other lab testing
 - Eg, check Hgb A1c with other routine biologic labs



Multidisciplinary Care Is NOT Optional

- **Dermatology:** Diagnosis, medical management, and procedures
- **Surgery:** Procedural interventions
- **Primary care:** Comorbidity management
- **Mental health:** Depression, anxiety, social support
- **Pain management:** Chronic pain control
- **Other specialists as needed:** Gastroenterology (IBD), gynecology (PCOS), endocrinology, rheumatology (SpA), cardiology
- **Referral to clinical trials** (if available)

Hidradenitis Suppurativa: Present and Future Management

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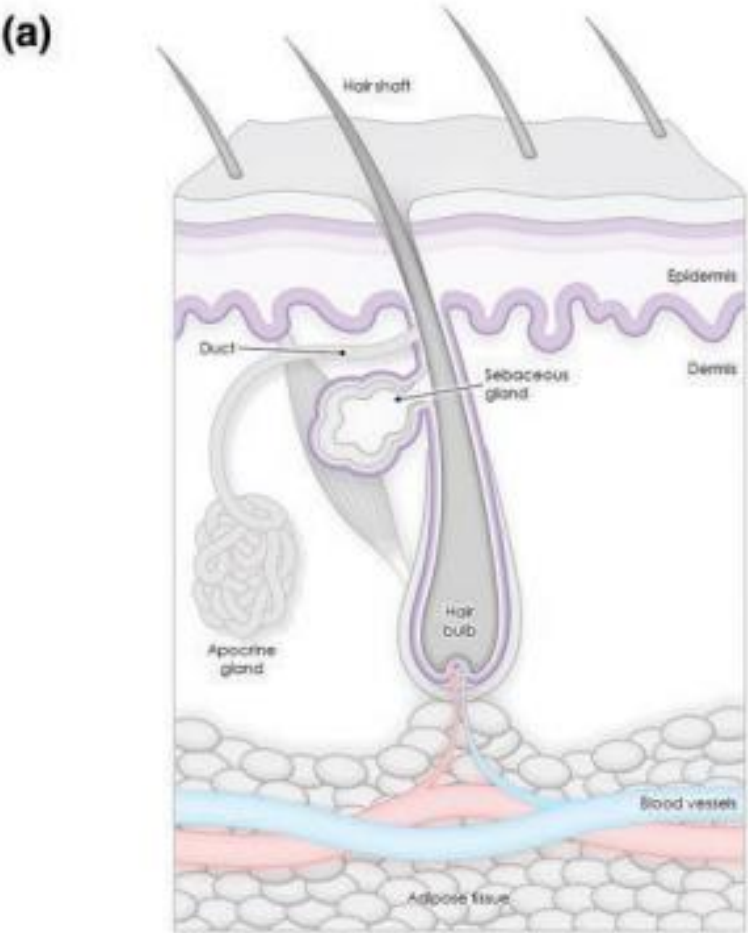
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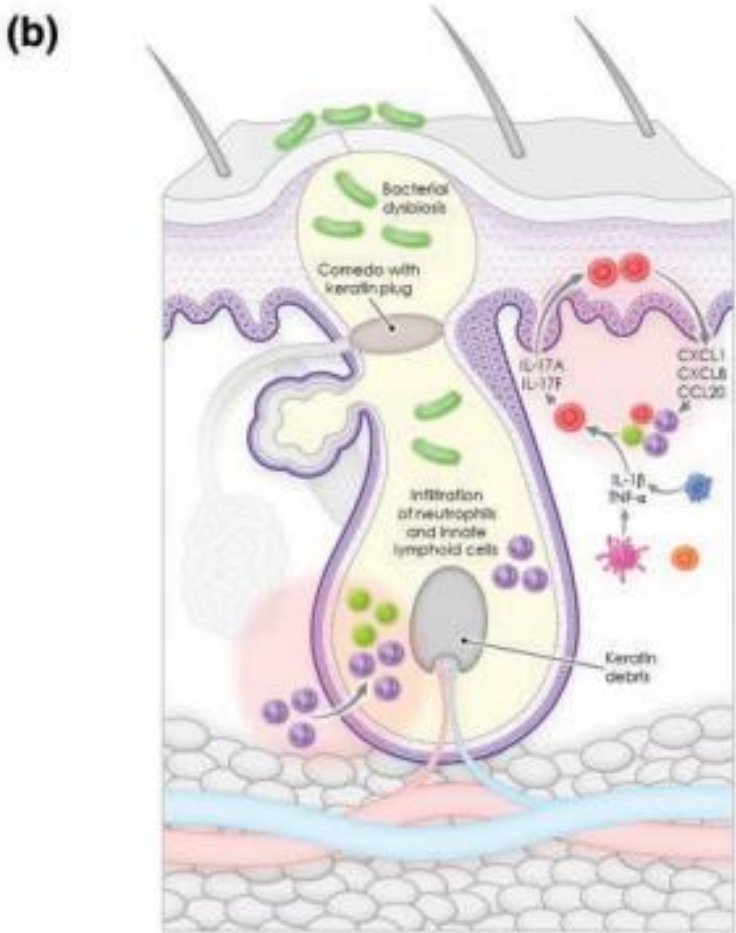
Agenda

- Pathogenesis
- Current biologics
- Antibiotics
- Hormonal treatments
- Procedures
- Emerging drugs

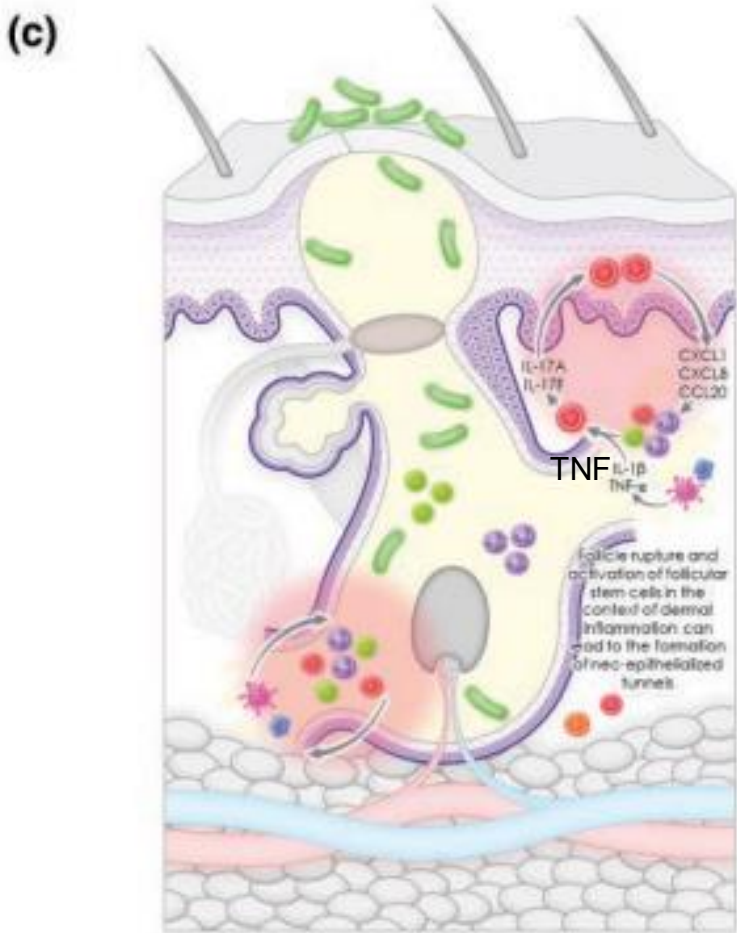
Pathogenesis



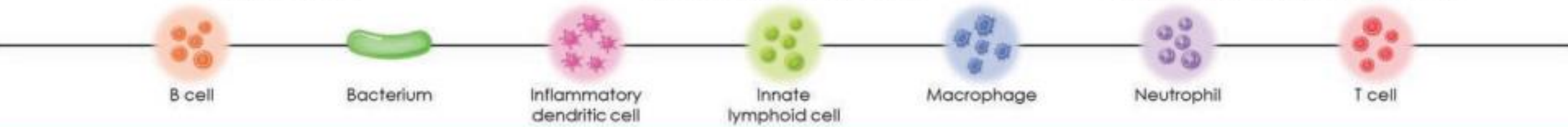
Normal skin and hair follicle



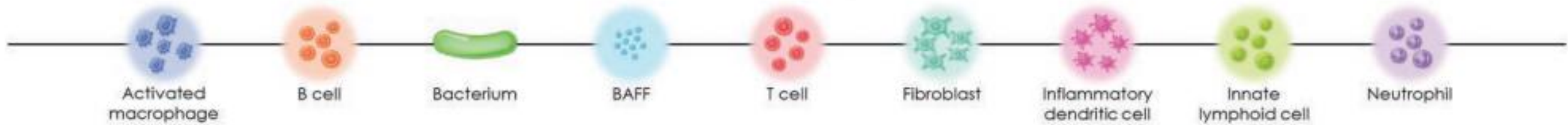
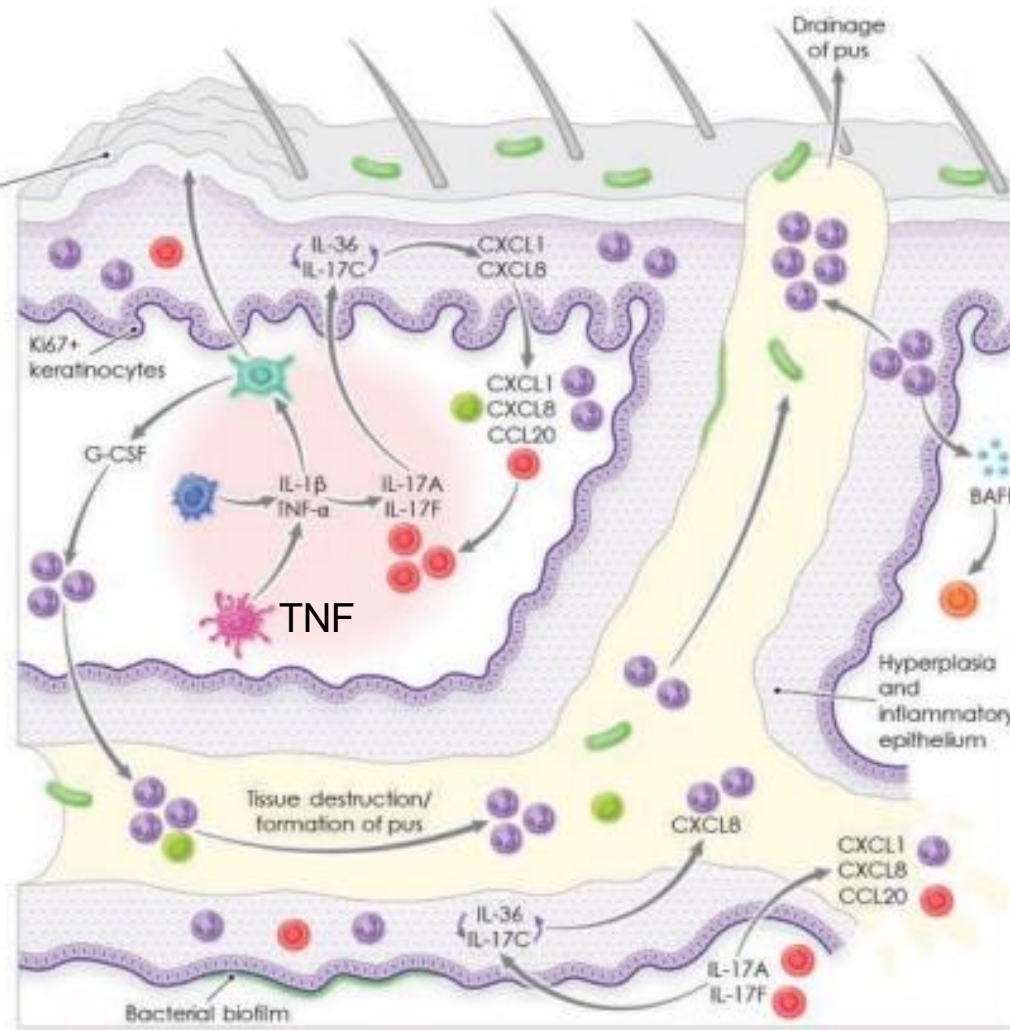
Early HS with acneiform lesions and folliculitis



Advanced HS with formation of nodules and abscesses



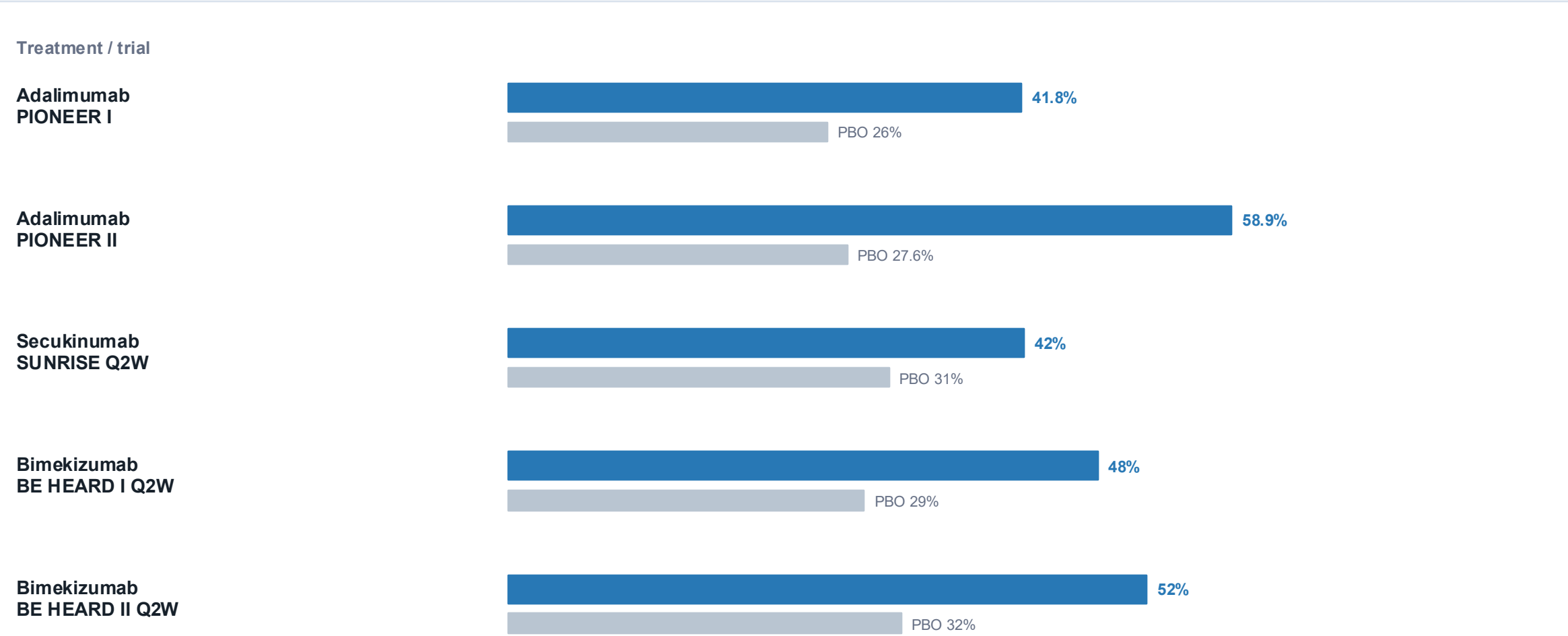
In 'end stage' disease, considerable scarring may be present, which can disrupt the cellular organization of late-stage tunnels and associated inflammation, and restrict motility of affected skin regions



Current Biologics for HS

FDA-Approved Biologics: Pivotal Efficacy

HiSCR50 at primary endpoint; values shown by pivotal trial



Key: blue = active; gray = placebo (PBO). Secukinumab value shown from SUNRISE; SUNSHINE Q2W did not meet its prespecified primary comparison. Infliximab, IV golimumab used off-label. Evidence summarized through Aug 2026; cross-trial comparisons are indirect. Full prescribing information should be consulted for contraindications, boxed warnings, monitoring, pregnancy, vaccination, and drug interactions. Kimball AB, et al. *N Engl J Med.* 2016;375(5):422-434. Kimball AB, et al. *Lancet.* 2023;401(10378):747-761. Kimball AB, et al. *Lancet.* 2024;403(10443):2504-2519.

Comparative Efficacy of Systemic Therapies for Hidradenitis Suppurativa: Living Systematic Review and Network Meta-Analysis

Study design

- Living systematic review + network meta-analysis of Phase 2 and 3 RCTs in moderate-to-severe HS
- Included 25 RCTs, 5767 patients, 39 unique therapies
- Primary outcome: HiSCR-50 at 12-16 weeks

Clinical interpretation

- Multiple cytokine inhibitors demonstrated significantly higher HiSCR-50 vs placebo
- Most differences vs adalimumab were not statistically significant — no definitive superior agent
- Safety/tolerability generally similar across active therapies and placebo

Non-Biologic Treatments

Antibiotics: Useful Anti-Inflammatory Therapy, but Relapse Is Common

Topical clindamycin	RCT evidence for pustules; limited effect on deep nodules/abscesses	Resistance; local irritation
Tetracyclines	Guideline-supported 12-week course for mild-moderate HS; modest evidence	GI upset, photosensitivity; esophagitis; pregnancy restrictions
Clindamycin + rifampin	Observational response often substantial; commonly used 8-12 weeks	Diarrhea/C. difficile; drug interactions; hepatotoxicity; rifampin discoloration
Moxifloxacin + metronidazole + rifampin	Second/third-line; retrospective benefit, less reliable in Hurley III	Neuropathy, QT/tendon risks, interactions, GI toxicity
IV ertapenem	Rapid rescue/bridge in severe disease; improvement often temporary without consolidation	IV-line complications, resistance, GI effects

Evidence for antibiotic regimens is less standardized than pivotal biologic RCT evidence; antimicrobial stewardship is essential.
GI = gastrointestinal.
Full prescribing information should be consulted for contraindications, boxed warnings, monitoring, pregnancy, vaccination, and drug interactions.
Alikhan A, et al. *J Am Acad Dermatol.* 2019;81(1):76-101.

Hormonal and Metabolic Therapy

Best suited to selected patients—especially women with cyclic flares, PCOS features, or metabolic comorbidity

Spironolactone

- Efficacy: Retrospective series suggest improvement in inflammatory lesion burden; no large phase 3 HS RCT
- AEs: Diuresis, dizziness, hyperkalemia, menstrual irregularity, breast tenderness; avoid in pregnancy; monitor potassium selectively

Metformin

- Efficacy: Uncontrolled/observational data suggest benefit in some patients, particularly those with insulin resistance/PCOS phenotype
- AEs: GI intolerance, B12 deficiency with long-term use; rare lactic acidosis in high-risk settings

Combined OCP / finasteride

- Efficacy: Limited studies/case series; may help hormonally driven disease
- AEs: OCP—VTE risk and estrogen contraindications; finasteride—teratogenic risk to male fetus, sexual/endocrine effects
- Progestin-only regimens may worsen HS in some patients

Evidence summarized through Aug 2026; cross-trial comparisons are indirect.
AEs = adverse events; OCP = oral contraceptive pill; VTE = venous thromboembolism.
Full prescribing information should be consulted for contraindications, boxed warnings, monitoring, pregnancy, vaccination, and drug interactions.
Alikhan A, et al. *J Am Acad Dermatol*. 2019;81(1):76-101.

Procedural Treatment: Critical for Tunnels and Irreversible Anatomy

Intralesional corticosteroid

- Rapid reduction in pain/inflammation for individual nodules; short-term lesion-directed benefit
- AEs: Atrophy, hypopigmentation, telangiectasia

Nd:YAG / follicular laser

- RCT + series support reduced inflammatory activity, particularly Hurley II–III
- AEs: Pain, burns, pigment change; multiple sessions

Deroofing

- High local control for persistent tunnels/nodules with tissue preservation
- AEs: Bleeding, infection, delayed healing, scarring; local recurrence possible

CO₂ laser / local excision

- Effective for fibrotic sinus tracts and localized chronic disease; recurrence depends on technique and disease field; healing by secondary intention is common
- AEs: Wound care burden, pain, scarring, contracture/pigment change

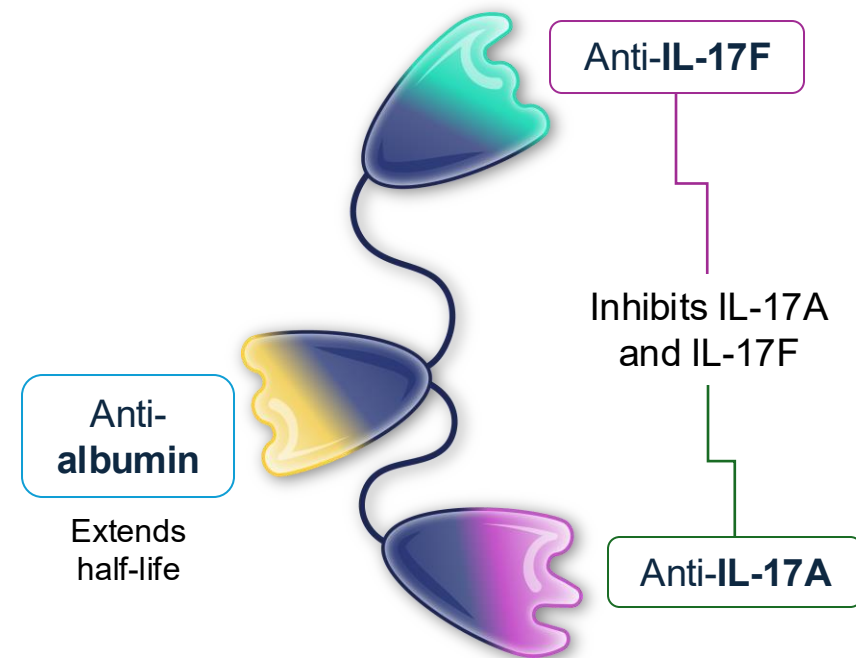
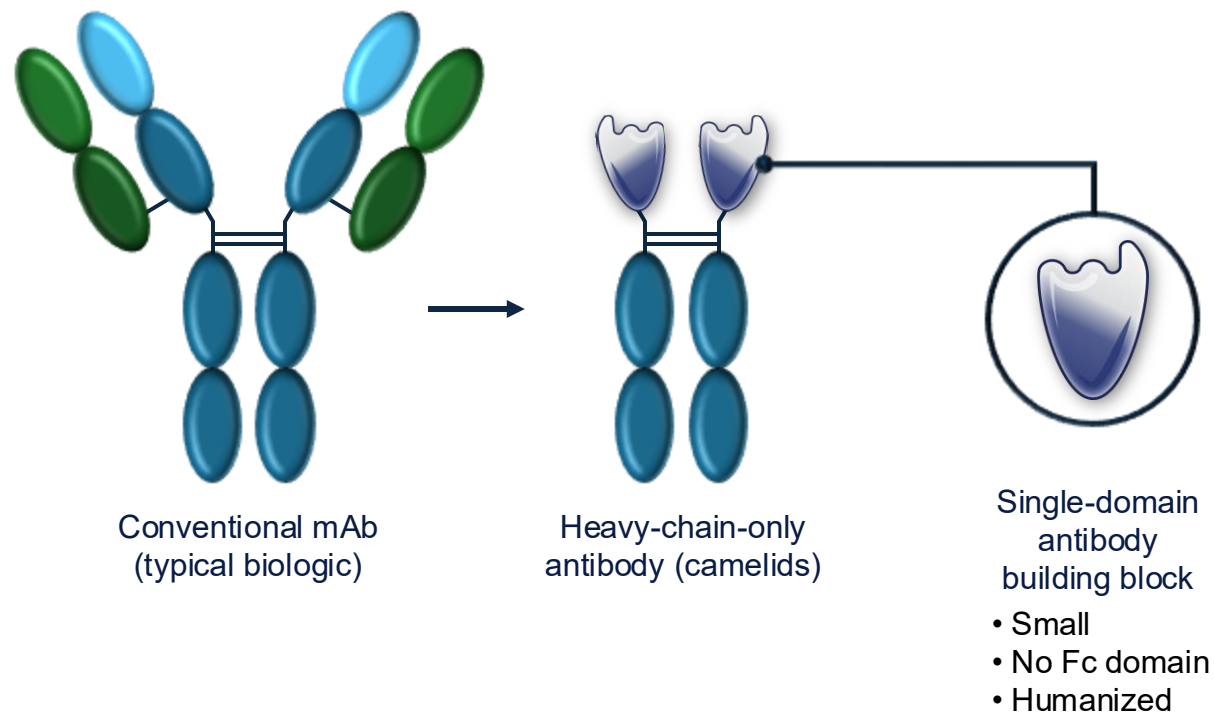
Wide excision

- Most definitive local option for extensive irreversible disease; can produce durable clearance in excised field
- AEs: Major wound burden, graft/flap complications, infection, functional limitation; HS can develop outside excised field

Evidence summarized through Aug 2026; cross-trial comparisons are indirect.
Full prescribing information should be consulted for contraindications, boxed warnings, monitoring, pregnancy, vaccination, and drug interactions.
Alikhan A, et al. *J Am Acad Dermatol*. 2019;81(1):76-101.

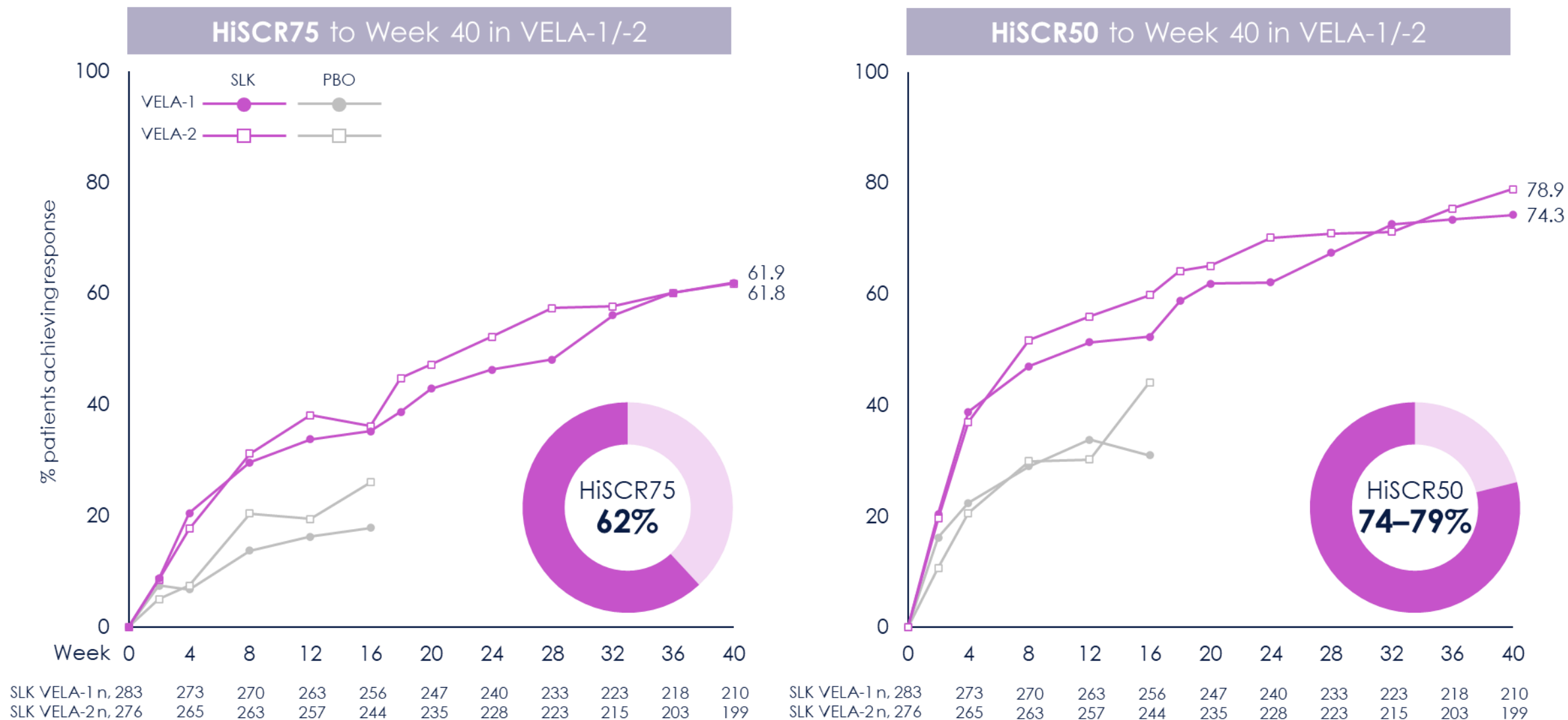
Drugs in Development (Phases 2 and 3)

Sonelokimab: Single-Domain Antibody Targeting Anti-IL-17 A, F



Sonelokimab is a novel IL-17A- and IL-17F-inhibiting single-domain antibody.

34/17.5
34/24.9



HiSCR75/50 outcomes continue to improve through Week 40.

Kimball AB, et al. Presented at: American Academy of Dermatology (AAD) Annual Meeting; March 27-31, 2026; Denver, CO. S034.

JAK Inhibitors

JAK1 Signaling Mediates Multiple Inflammatory Pathways Involved in HS

Early HS

Acneiform lesions and folliculitis

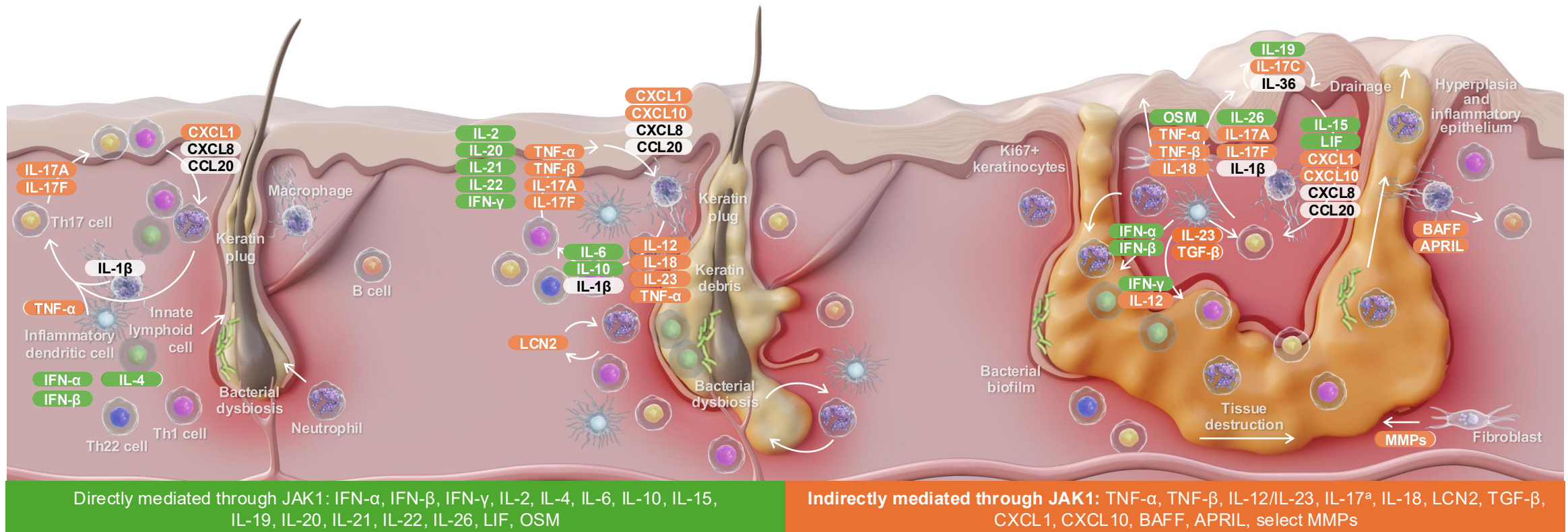


Advanced HS

Formation of nodules and abscesses



Deep dermal tunnels



^aThe role of JAK1 in relation to IL-17 in HS remains to be fully elucidated.

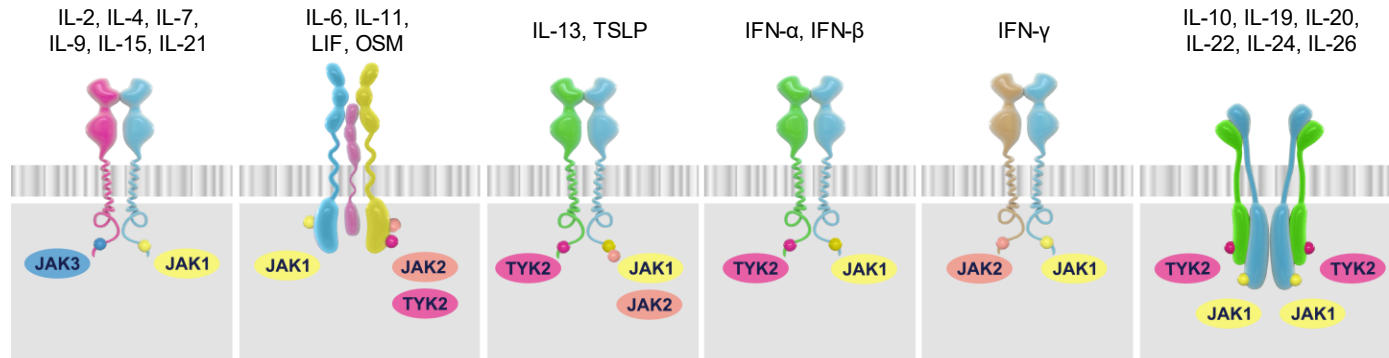
APRIL = a proliferation-inducing ligand; BAFF = B-cell activating factor; CCL = C-C motif chemokine ligand; CXCL = C-X-C motif chemokine ligand; IFN = interferon; LCN2 = lipocalin-2; LIF = leukemia inhibitory factor; MMP = matrix metalloproteinase; OSM = oncostatin M; TGF- β = transforming growth factor beta; TNF = tumor necrosis factor.

Krueger JG, et al. *Br J Dermatol.* 2024;190:149-162. Maronese CA, et al. *Expert Rev Clin Immunol.* 2024;20:525-545. van Straalen KR, et al. *J Allergy Clin Immunol.* 2022;149:1150-1161. Vossen ARJV, et al. *Front Immunol.* 2018;9:2965. Wolk K, et al. *Br J Dermatol.* 2020;183:999-1010. Del Duca E, et al. *Int J Mol Sci.* 2020;21:8436. Sabat R, et al. *Nat Rev Dis Primers.* 2020;6:18. Freudenberg JM, et al. *PLoS ONE.* 2023;18:e0284047. Carmona-Rivera C, et al. *J Invest Dermatol.* 2022;142:924-935. Cao Y, et al. *J Invest Dermatol.* 2021;141:2730-2740. Byrd AZ, et al. *Sci Transl Med.* 2019;11:eaav5908. van Straalen KR, et al. *J Clin Invest.* 2024;134:e169225. Kashyap MP, et al. *Proc Natl Acad Sci USA.* 2024;121:e2409274121. Luo H, et al. *J Dermatol.* 2025;52:481-492. Gadina M, et al. *J Leukocyte Biol.* 2018;104:499-514. Morris R, et al. *Protein Science.* 2018;27:1984-2009. Hu X, et al. *Signal Transduct Target Ther.* 2021;6:402. Virtanen A, et al. *Nat Rev Rheumatol.* 2024;20:649-665. Rumberger BE, et al. *Inflamm Res.* 2020;69:967-973. Tanaka Y, et al. *Nat Rev Rheumatol.* 2022;18:133-145.

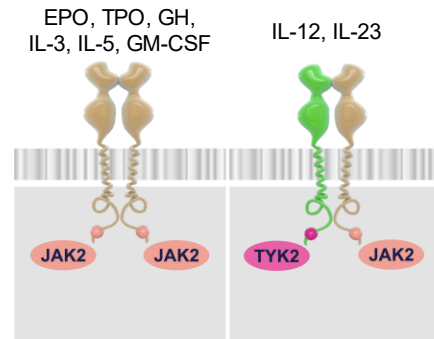
Povorcitinib

Povorocitinib Is a Highly Selective JAK1 Inhibitor Intentionally Designed for Inflammatory Conditions Like HS

JAK1 directly modulates multiple cytokines involved in inflammatory skin conditions



JAK2 modulates certain pathways implicated in hematologic AEs



Povorocitinib demonstrated 52x greater selectivity for **JAK1** over **JAK2** in vitro



Selectivity compared with other JAK inhibitors

Selective inhibition of **JAK1** aims to reduce the risk of **JAK2**-associated hematological adverse events, while preserving clinical utility

EPO = erythropoietin; GH = growth hormone; GM-CSF = granulocyte-macrophage colony-stimulating factor; TPO = thrombopoietin; TSLP = thymic stromal lymphopoietin; TYK = tyrosine kinase.
Virtanen A, et al. *Nat Rev Rheumatol*. 2024;20(10):649-665. Maronese CA, et al. *Expert Rev Clin Immunol*. 2024;20(5):525-545. Sabat R, et al. *Lancet*. 2025;405(10476):420-438. Fay B, et al. *Ann Rheum Dis*. 2019;78(Suppl 2):OP0280. Castelo-Soccio L, et al. *Nat Rev Immunol*. 2023;23(12):787-806.

Povorcitinib Was Associated with Early and Sustained HiSCR50 Improvement

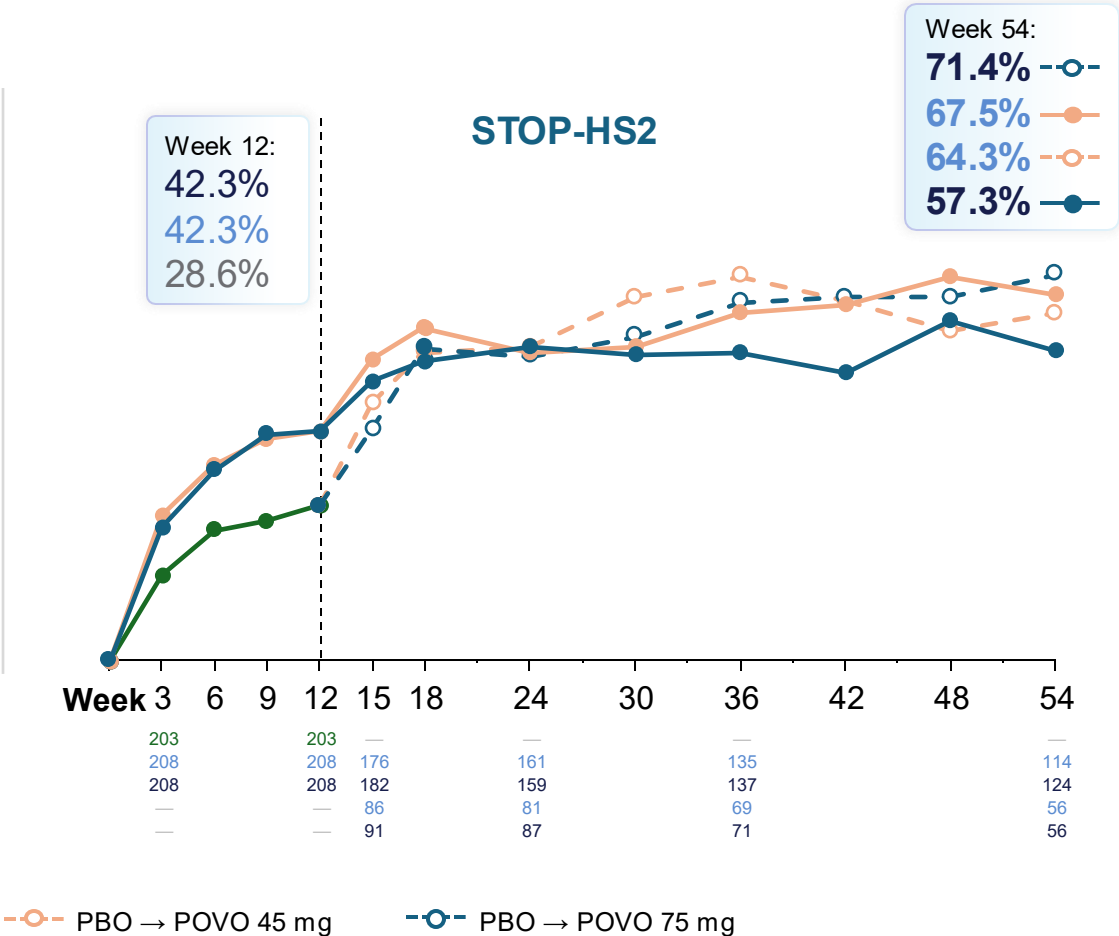
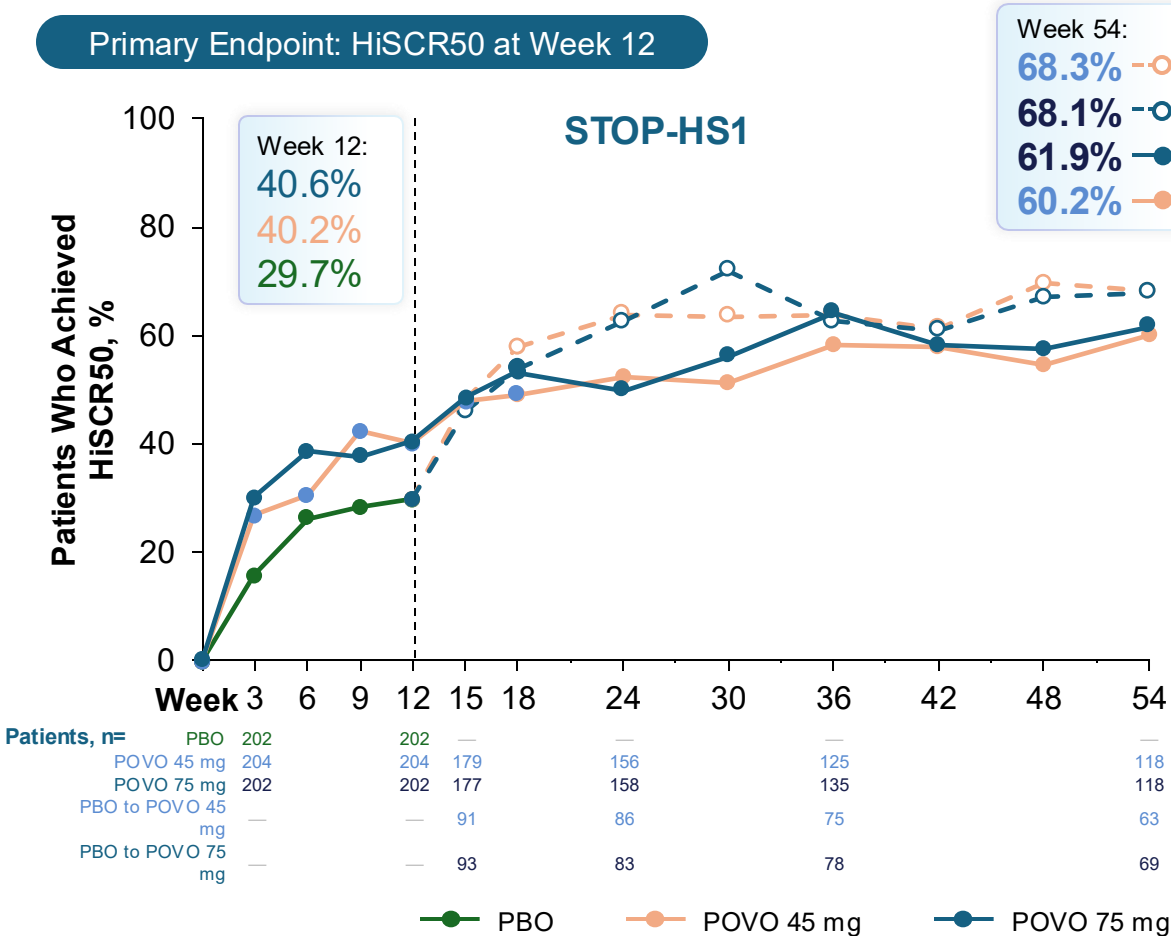
With povorcitinib treatment:

Statistically significant HiSCR50 responses at week 12

Responses observed as early as week 3

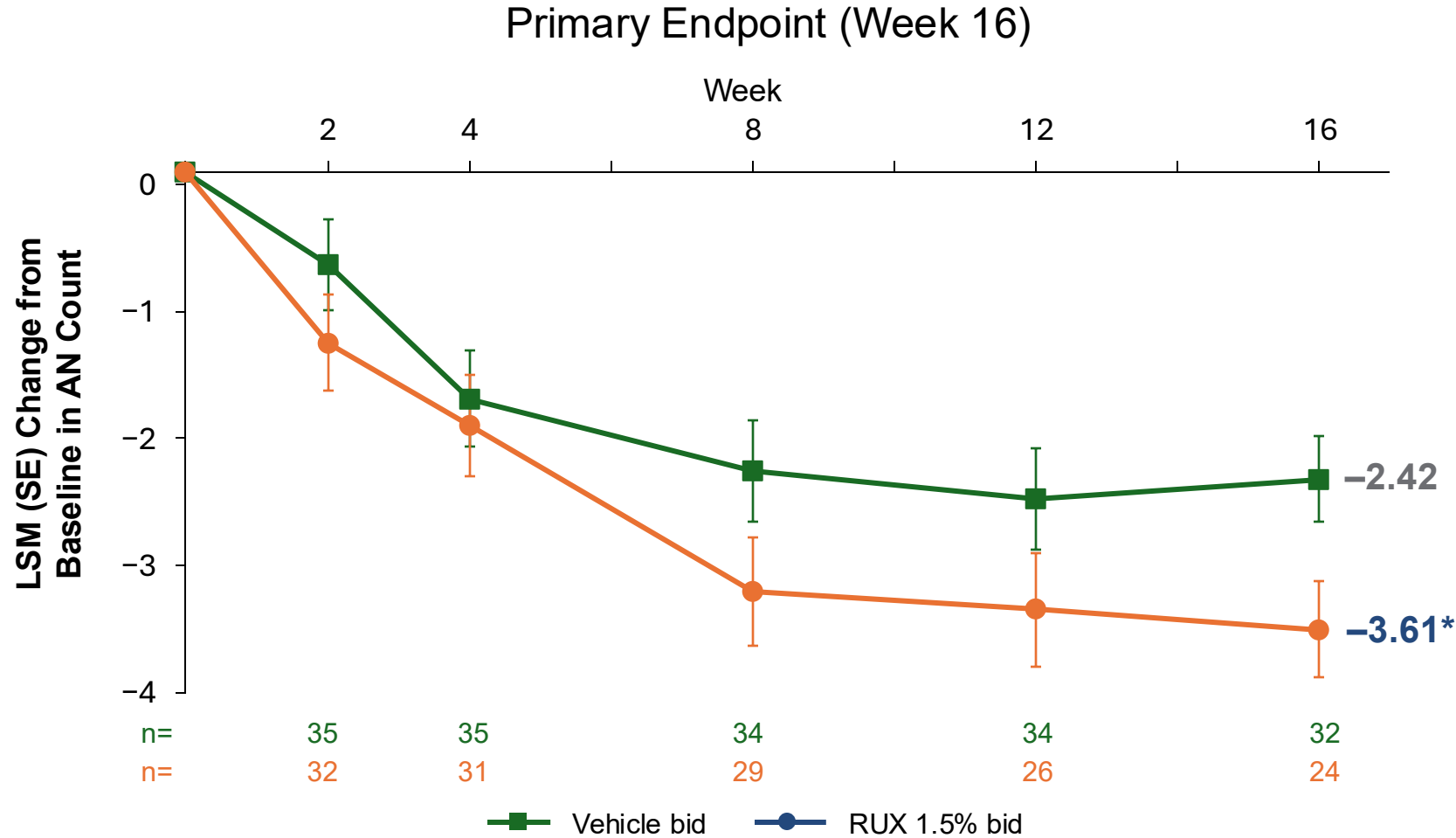
Continued improvement over time

Primary Endpoint: HiSCR50 at Week 12



Ruxolitinib Cream

Least Squares Mean Change from Baseline in AN Count



At week 16, patients who applied RUX 1.5% bid had significantly greater decreases from baseline in AN counts vs patients who applied vehicle bid (P=0.0215)

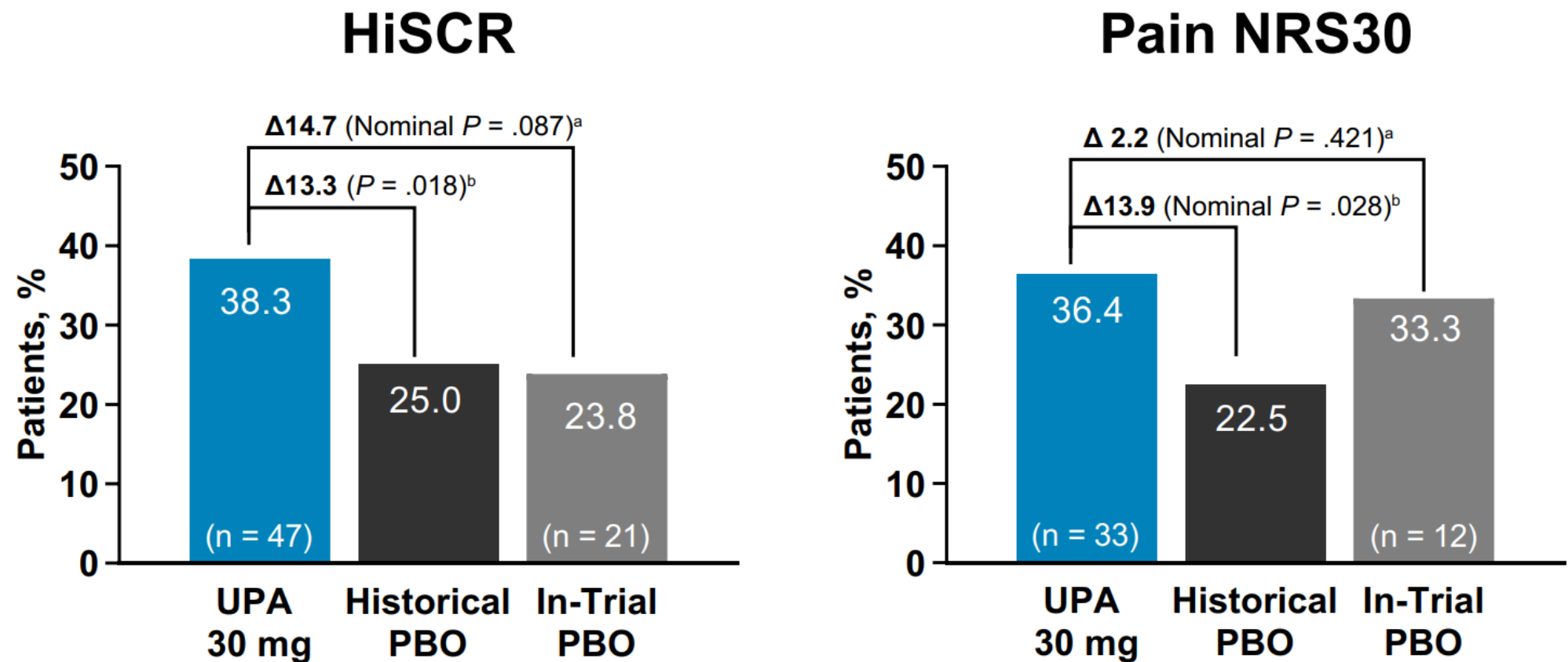
*P=0.0215 vs vehicle; calculated from mixed model for repeated measures with fixed effect of treatment group, stratification factor, visit, and visit by treatment interaction.

AN = abscess and inflammatory nodule; LSM = least squares mean; RUX = ruxolitinib cream.

Porter ML, et al. *J Am Acad Dermatol*. 2026;94(3):879-887. Porter ML, et al. Presented at: AAD Annual Meeting; March 8-12, 2024; San Diego, CA. LB2.

Upadacitinib

Figure 3. Proportion of Patients Achieving the Primary (HiSCR) and Secondary (Pain NRS30) Endpoints at Week 12 (NRI-C)



HiSCR, $\geq 50\%$ reduction from baseline in the total abscess and inflammatory nodule count with no increase in abscess or draining fistula count relative to baseline; NRI-C, nonresponder imputation incorporating multiple imputation for missing data due to COVID-19; NRS30, achievement of $\geq 30\%$ reduction and at least 1 unit reduction from baseline in Patient's Global Assessment of Skin Pain; PBO, placebo; TNFi, tumor necrosis factor inhibitor; UPA, upadacitinib.

^a P values based on the Cochran-Mantel-Haenszel test adjusted for strata (baseline Hurley stage and prior TNFi use).

^b $P \leq .05$ using 1-sample Chi-square analysis based on 1-sided P value.

Targeting IL-1

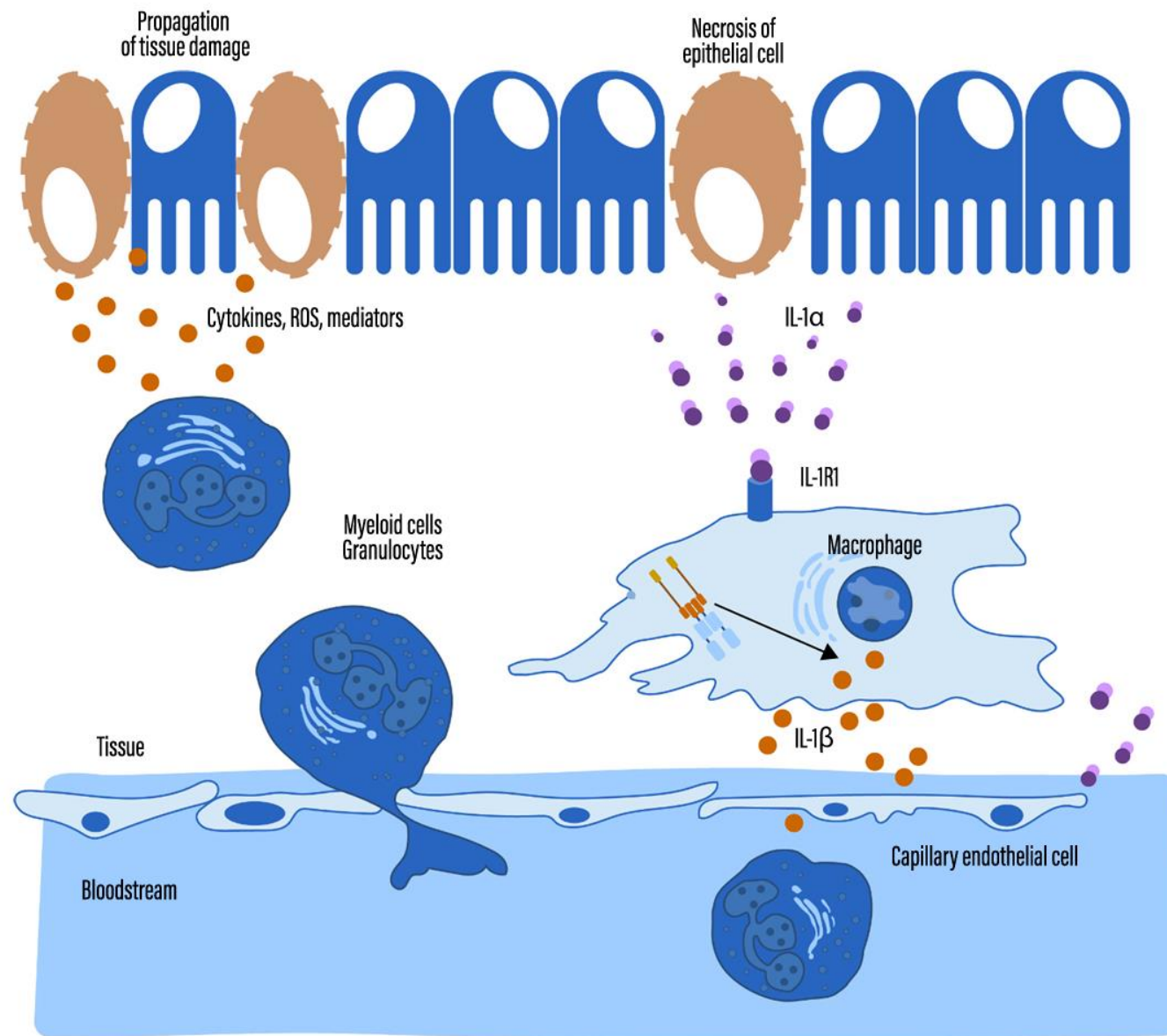
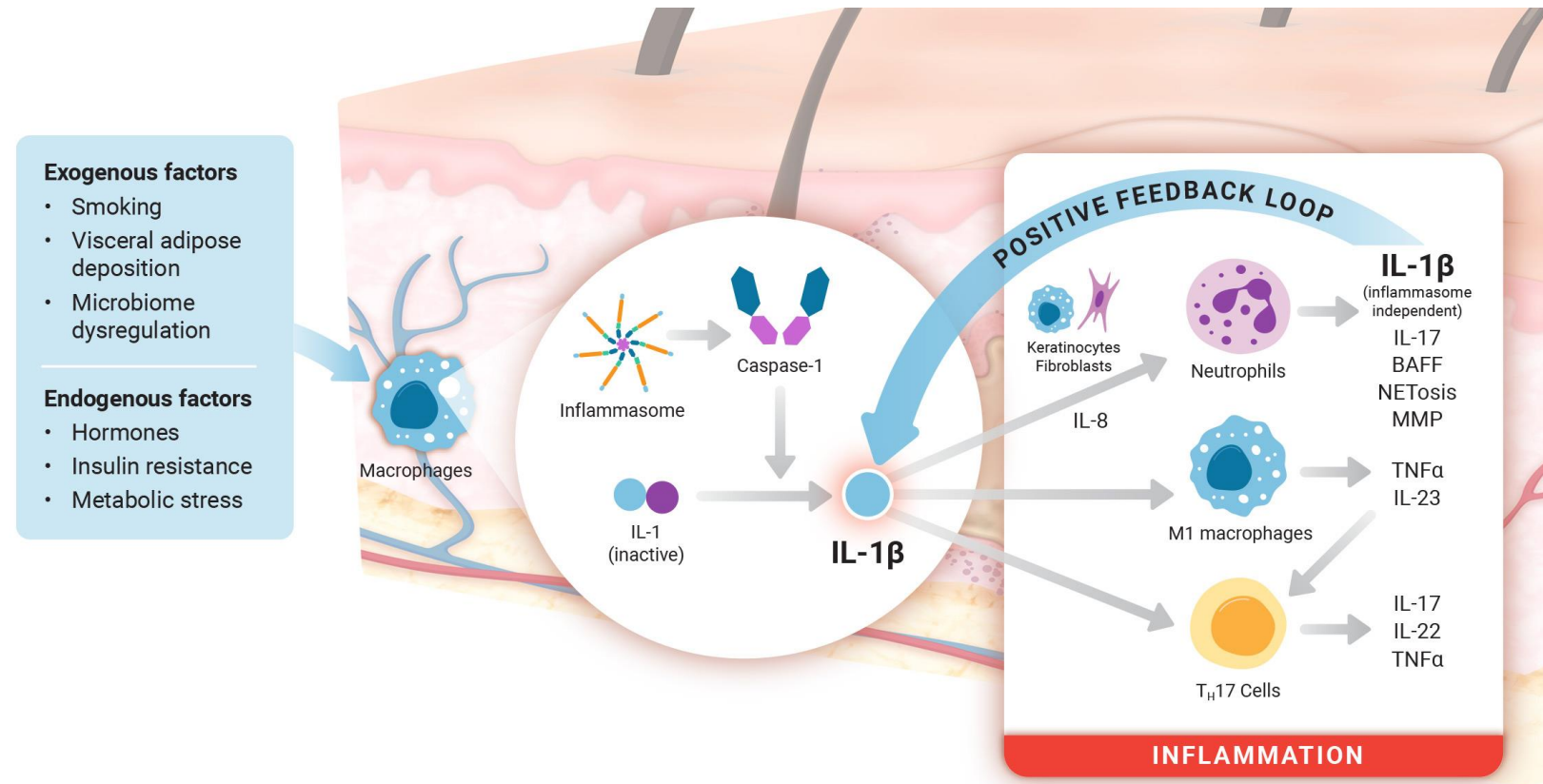


Fig. 1. The IL-1-driven inflammatory loop. Tissue damage triggers release of intracellular IL-1 α from dying cells. This generates an IL-1 α -containing milieu, which is sensed by infiltrating myeloid cells (i.e. monocytes, macrophages) expressing the IL-1R1. These cells in turn activate inflammasome-dependent production of IL-1 β , which initiates a cascade leading to the recruitment of inflammatory myeloid cells (i.e. granulocytes) to the site of tissue damage. Influx of inflammatory cells producing cytokines, reactive oxygen species, and effector mediators propagates tissue damage.

IL-1 β Plays a Central Role in the Pathophysiology of HS

- IL-1 β is a key driver of the inflammatory cascade that leads to the destruction of the pilosebaceous unit
- IL-1 β gene expression is up to 100x increased in HS lesions compared to skin in healthy controls
- IL-1 β is upstream of IL-17 and TNF α , both major effectors of inflammation
- Clinical benefit in HS has been observed with anti-IL-1 drugs



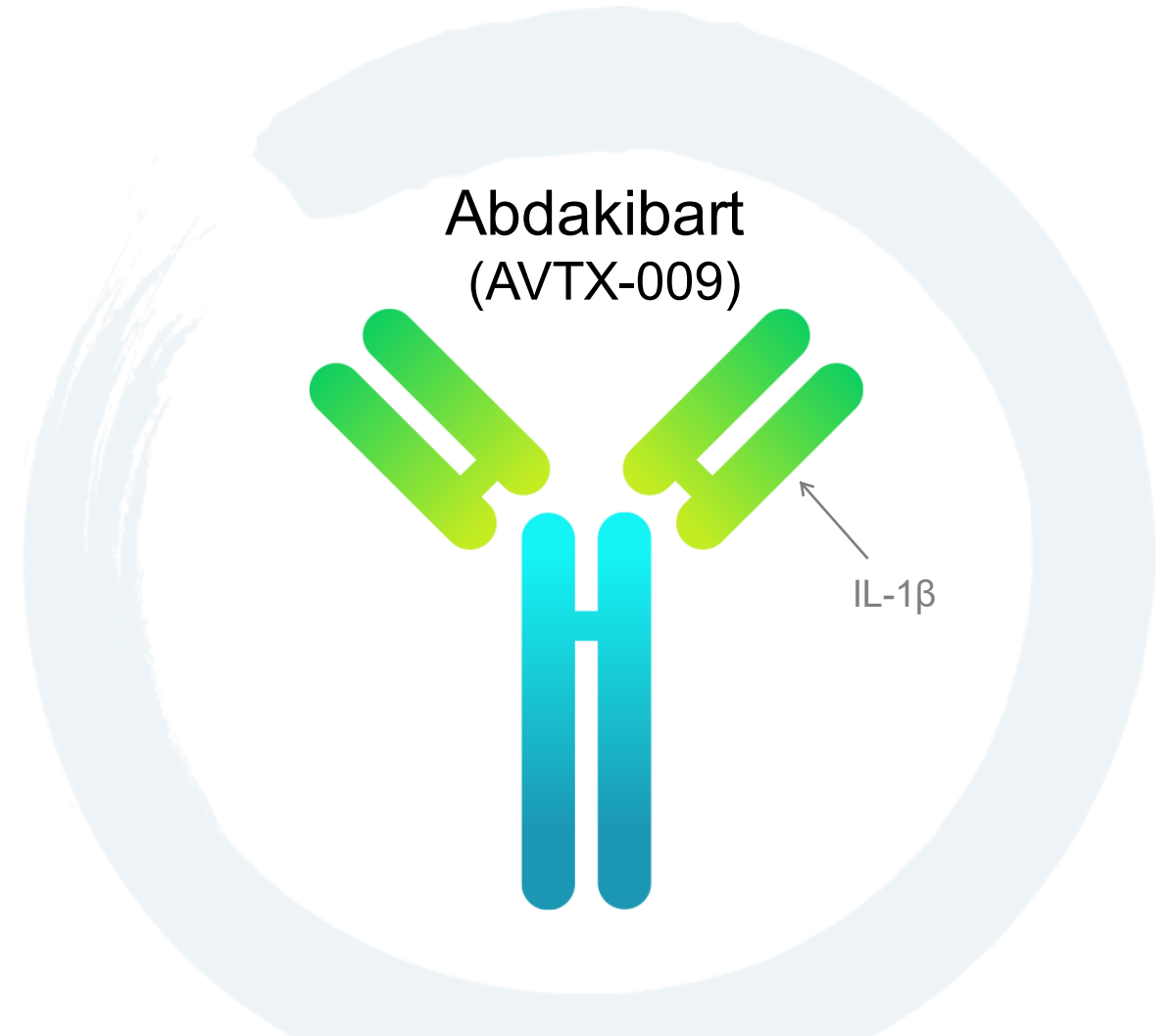
DAMP = damage-associated molecular pattern molecule; **DC** = dendritic cell; **R**, receptor; **PAMP** = pathogen-associated molecular pattern molecule.

Figure adapted from Agnese ER, et al. *Cureus*. 2023;15(11):e49390. Creative Commons license, CC-BY 4.0. Vossen ARJV, et al. *J Invest Dermatol*. 2020;140(7):1463-1466.e2. Kelly G, et al. *Br J Dermatol*. 2015;173(6):1431-1439. Kimball AB, et al. Presented at: AAD Annual Meeting; March 8-12, 2024; San Diego, CA.

Abdakibart (AVTX-009): Selective IL-1 β Inhibition in HS

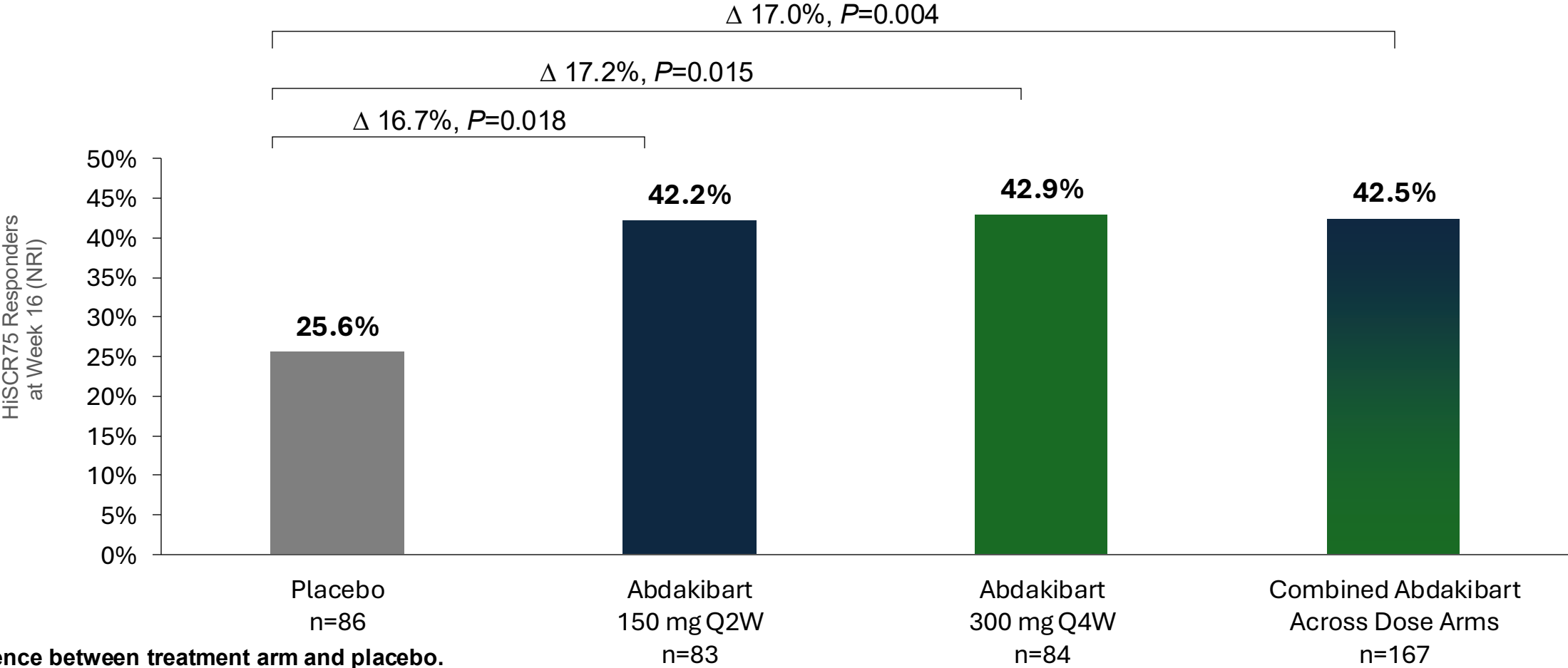
Abdakibart (AVTX-009) Is A Highly Potent, Specific Inhibitor of IL-1 β

- Clinical experience
 - ~245 patients studied in phase 1 and phase 2 trials
 - Significant and rapid lowering of inflammatory biomarkers after a single dose of 0.6 mg
 - Well-tolerated and favorable safety profile at all doses up to 180 mg SC weekly
- Stable 150 mg/mL SC dosage formulation
- Potency and half-life expected to support up to Q4W dosing in hidradenitis suppurativa and potentially a longer dosing interval in other indications



Bihorel S, et al. *AAPS J.* 2014;16(5):1009-1017. Sloan-Lancaster J, et al. *Diabetes Care.* 2013;36(8):2239-2246. GlobeNewswire. May 5, 2026. Accessed September 16, 2026. <https://www.globenewswire.com/news-release/2026/05/05/3288197/0/en/avalon-therapeutics-achieves-positive-topline-results-in-phase-2-lotus-trial-of-abdakibart-avtx-009-in-moderate-to-severe-hidradenitis-suppurativa.html>. ClinicalTrials.gov. Accessed September 16, 2026. <https://clinicaltrials.gov/study/NCT04983732>; <https://clinicaltrials.gov/study/NCT00942188>; <https://clinicaltrials.gov/study/NCT00380744>.

LOTUS Trial: Primary Endpoint of HiSCR75 at Week 16 Was Met for Each Active Dose Group and Both Groups Combined



ΔDifference between treatment arm and placebo.
NRI = non-response imputation.
Subjects who experience an intercurrent event using the composite strategy (eg, use of rescue antibiotics or steroids before Week 16, discontinuation of study treatment due to an adverse event or lack of efficacy) are treated as non-responders following the intercurrent event. Subjects with missing data are imputed as non-responders.
Difference in responder rate and *P*-value are obtained using a Mantel-Haenszel (MH) test stratified by the randomization stratification factors.
GlobeNewswire. May 5, 2026. Accessed September 16, 2026. <https://www.globenewswire.com/news-release/2026/05/05/3288197/0/en/avalo-therapeutics-achieves-positive-topline-results-in-phase-2-lotus-trial-of-abdakibart-avtx-009-in-moderate-to-severe-hidradenitis-suppurativa.html>.

LOTUS Trial: Rates of TEAEs, Including SAEs, Were Similar to Placebo

# of Subjects (%)	Placebo	Abdakibart	
	N=86	150 mg Q2W N=83	300 mg Q4W N=83
Any TEAE*	46 (53.5)	43 (51.8)	46 (55.4)
Any TESAЕ	2 (2.3)	2 (2.4)	1 (1.2)
Non-cardiac chest pain	0	0	1 (1.2)
Major depressive disorder	0	1 (1.2)	0
Hidradenitis	2 (2.3)	1 (1.2)	0
Any TEAE leading to study drug discontinuation	2 (2.3)	2 (2.4)	1 (1.2)
Deaths	0	0	0

*The most common TEAEs reported in both abdakibart arms were headache and nausea. One subject randomized to abdakibart 300 mg Q4W did not receive study drug and therefore is not included in safety population.

TEAE = treatment-emergent AE; TESAЕ = treatment-emergent serious AE.

US SEC. June 2026. Accessed September 16, 2026. <https://www.sec.gov/Archives/edgar/data/1534120/000153412026000042/ex-992avalocorporatepres.htm>.

LOTUS Trial: Few Adverse Events of Special Interest

	Placebo	Abdakibart	
		150 mg Q2W	300 mg Q4W
# of Subjects (%)	N=86	N=83	N=83
Hypersensitivity reaction	0	0	0
Injection site reaction	4 (4.7)	3 (3.6)	5 (6.0)
Leukopenia	0	0	0
Neutropenia	0	0	0
Serious infections	0	0	0
MACE	0	0	0
Malignancy	0	0	0
Opportunistic infections	0	0	0
Tuberculosis	0	0	0

One subject randomized to abdakibart 300 mg Q4W did not receive study drug and therefore is not included in safety population.
MACE = major adverse cardiovascular event.
US SEC. June 2026. Accessed September 16, 2026. <https://www.sec.gov/Archives/edgar/data/1534120/000153412026000042/ex-992avalocorporatepres.htm>.

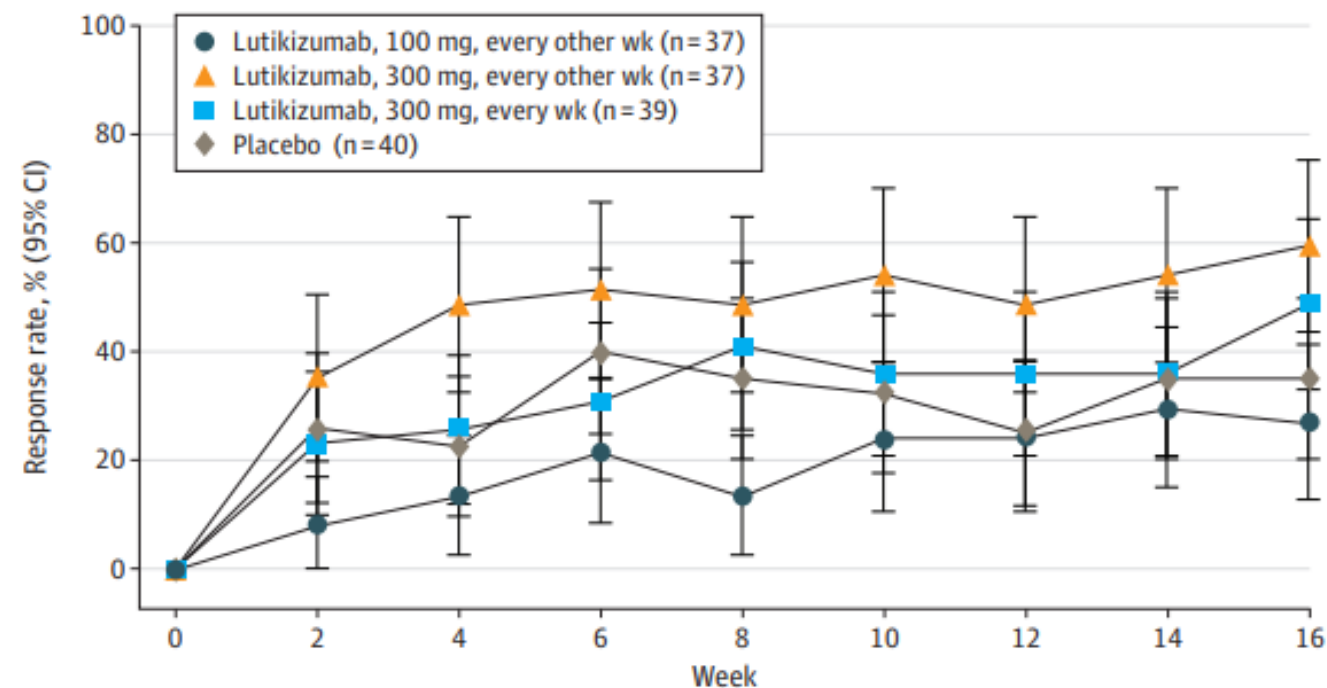
Lutikizumab: Anti-IL-1 $\alpha\beta$

Lutikizumab (ABT-981) in Hidradenitis Suppurativa

Investigational IL-1 α /IL-1 β antagonist — phase 2 efficacy and safety

- Lutikizumab is a dual-variable-domain antagonist of IL-1 α and IL-1 β
- Rationale: IL-1 pathway activation is implicated in HS lesions and provides a mechanistically distinct target from TNF, IL-17, and JAK inhibition
- Phase 2 randomized trial evaluated adults with moderate-to-severe HS after anti-TNF treatment failure; development has advanced into Phase 3

Figure 1. Line Graph of Achievement of Primary End Point



No. (%) at risk

Lutikizumab, 100 mg, every other wk	0 (0)	2 (5.4)	4 (10.8)	6 (16.2)	7 (18.9)	9 (24.3)	8 (21.6)	9 (24.3)
Lutikizumab, 300 mg, every other wk	1 (2.7)	4 (10.8)	3 (8.1)	5 (13.5)	5 (13.5)	5 (13.5)	5 (13.5)	5 (13.5)
Lutikizumab, 300 mg, every wk	0 (0)	1 (2.6)	1 (2.6)	2 (5.1)	3 (7.7)	3 (7.7)	5 (12.8)	4 (10.3)
Placebo	2 (5.0)	2 (5.0)	3 (7.5)	3 (7.5)	6 (15.0)	6 (15.0)	6 (15.0)	7 (17.5)

Response, %	Response (%); adjusted treatment difference vs placebo (%) by Cochran-Mantel-Haenszel test		
Placebo	Lutikizumab, 100 mg/every other wk	Lutikizumab, 300 mg/every other wk	Lutikizumab, 300 mg/every wk
35.0	27.0 Δ -9.7 95% CI (-29.7 to 10.4) nominal P = .35	59.5 Δ 24.1 95% CI (-2.7 to 45.4) nominal P = .03	48.7 Δ 13.8 95% CI (-7.2 to 34.7) nominal P = .20

Lutikizumab Phase 2 in Hidradenitis Suppurativa: Safety Summary

NCT05139602 • 153 adults with moderate-severe HS after anti-TNF failure • 16-week randomized, placebo-controlled trial

Safety outcome	300 mg weekly n=39	300 mg Q2W n=37	100 mg Q2W n=37	Placebo n=40
Any TEAE	69.2%	78.4%	64.9%	75.0%
Drug-related TEAE	33.3%	35.1%	27.0%	17.5%
Serious TEAE	5.1%	5.4%	5.4%	2.5%
Grade ≥3 TEAE	5.1%	10.8%	8.1%	2.5%
Discontinued for TEAE	2.6%	2.7%	8.1%	2.5%
Injection-site reaction	2.6%	8.1%	2.7%	5.0%

Most frequent TEAEs

Only events >10% in any lutikizumab arm:
HS worsening • diarrhea • headache • pruritus

Notable events

1 serious infection (infected stoma; 300 mg Q2W)
1 T-cell lymphoma (300 mg weekly; sponsor judged unrelated)
1 nonserious hepatic event (hepatosplenomegaly; 300 mg Q2W)

Overall Safety Signal

TEAE rates were broadly similar to placebo and most events were mild-moderate
No deaths, neutropenia, serious hypersensitivity, MACE, opportunistic infection, herpes zoster, or tuberculosis; no clear dose-dependent safety trend

Interpretation: Phase 2 sample size and 16-week exposure limit detection of uncommon or long-latency adverse events.
Kimball AB, et al. *JAMA Dermatol.* 2026;162(5):469-477.

Remibrutinib: An Oral BTK Inhibitor for HS

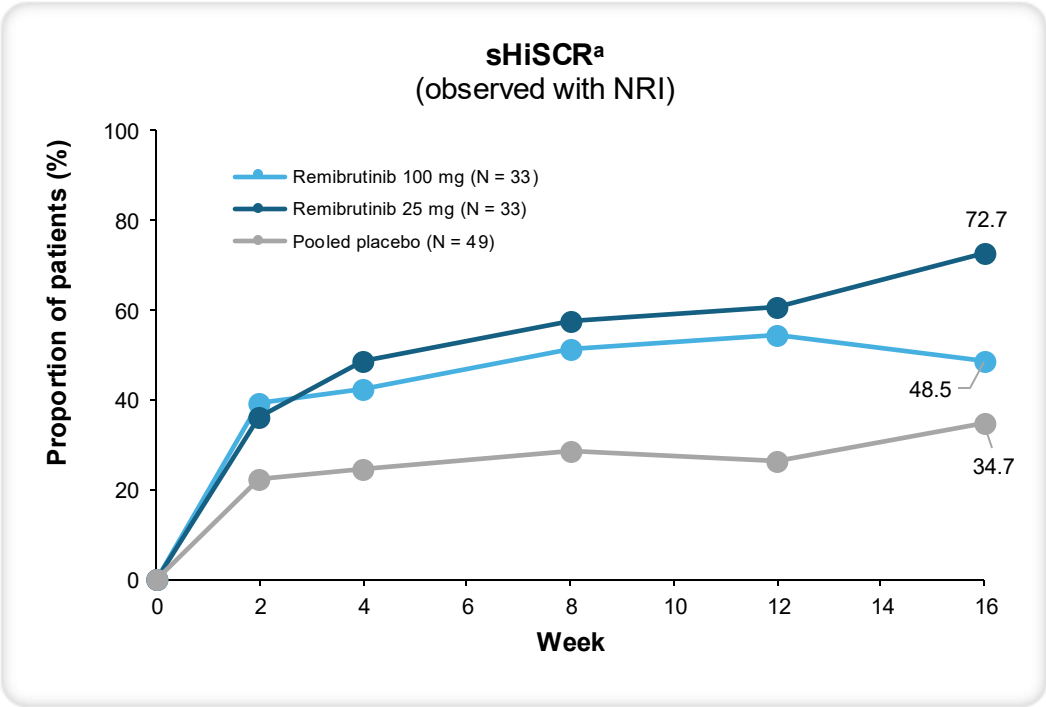
BTK Inhibition for HS

- Remibrutinib is a Bruton's tyrosine kinase (BTK) inhibitor
- BTK (an intracellular messenger) activation is important in the maintenance and production of B cells and plasma cells, which are increased in HS lesions
- BTK inhibition may be a new MOA for the treatment of HS, but the efficacy and safety need to be better understood

Simplified HiSCR (Primary End Point) at Week 16

- The primary end point of this study was met for both doses of remibrutinib; patients treated with remibrutinib reported a greater rate of simplified Hidradenitis Suppurativa Clinical Response (sHiSCR) at week 16 compared with placebo

	Cohort D		Cohorts A-D
	Remibrutinib 25 mg (N = 33)	Remibrutinib 100 mg (N = 33)	Pooled placebo (N = 49)
Proportion of patients with sHiSCR ^a :			
Observed with NRI (%)	72.7	48.5	34.7
Difference ^b (%) (95% CI)	38.0 (21.1-55.0)	13.8 (-4.4, 32.0)	
Bayesian estimated (%)	72.3	48.5	34.9
Difference ^b (%) (95% CI)	37.2 (19.7-53.0)	13.9 (-4.2, 31.9)	
Probability of difference ^c	99.9	89.6	



Permission granted by Kimball AB, et al.

^asHiSCR is defined as a $\geq 50\%$ reduction in the abscess and inflammatory nodule count and no increase in draining tunnels compared with baseline; ^bDifference refers to the difference between remibrutinib (either dose) and pooled placebo at week 16; ^cBayesian posterior probability of remibrutinib (either dose) being better than pooled placebo.
Kimball AB, et al. Presented at: AAD Annual Meeting; March 8-12, 2024; San Diego, CA. S026.

Overview of Safety (2/2)

	Cohort D		Cohorts A-D
	Remibrutinib 25 mg (N = 33)	Remibrutinib 100 mg (N = 33)	Pooled placebo ^a (N = 50)
Most frequent (≥10%) AE by PT, n (%)			
Nasopharyngitis	7 (21.2)	2 (6.1)	1 (2.0)
Headache	4 (12.1)	0 (0.0)	5 (10.0)
Diarrhea	2 (6.1)	3 (9.1)	5 (10.0)
Infections and infestations (SOC)	22 (66.7)	10 (30.3)	15 (30.0)
AEs suggestive of increased tendency to bruise^b	1 (3.0)	2 (6.1)	1 (2.0)
Newly occurring liver transaminase elevations >5× ULN ^c	1 (3.0)	0 (0.0)	1 (2.0)

Permission granted by Kimball AB, et al.

^a1 patient in the pooled placebo group was lost to follow-up and was therefore not included in efficacy analyses but was still included in safety analyses; ^bIncluded the PTs of increased tendency to bruise, hemorrhage subcutaneous, and injection site hematoma; ^cAll elevations were asymptomatic, transient/reversible elevations of ALT/AST with normal bilirubin levels.

AE grading relates to the Common Terminology Criteria for Adverse Events scale of grading (grade 1, mild; grade 2, moderate; grade 3, severe; grade 4, life-threatening).

ALT = alanine aminotransferase; AST = aspartate aminotransferase; PT = preferred term; SOC = system organ class; ULN = upper limit of normal. Kimball AB, et al. Presented at: AAD Annual Meeting; March 8-12, 2024; San Diego, CA. S026.

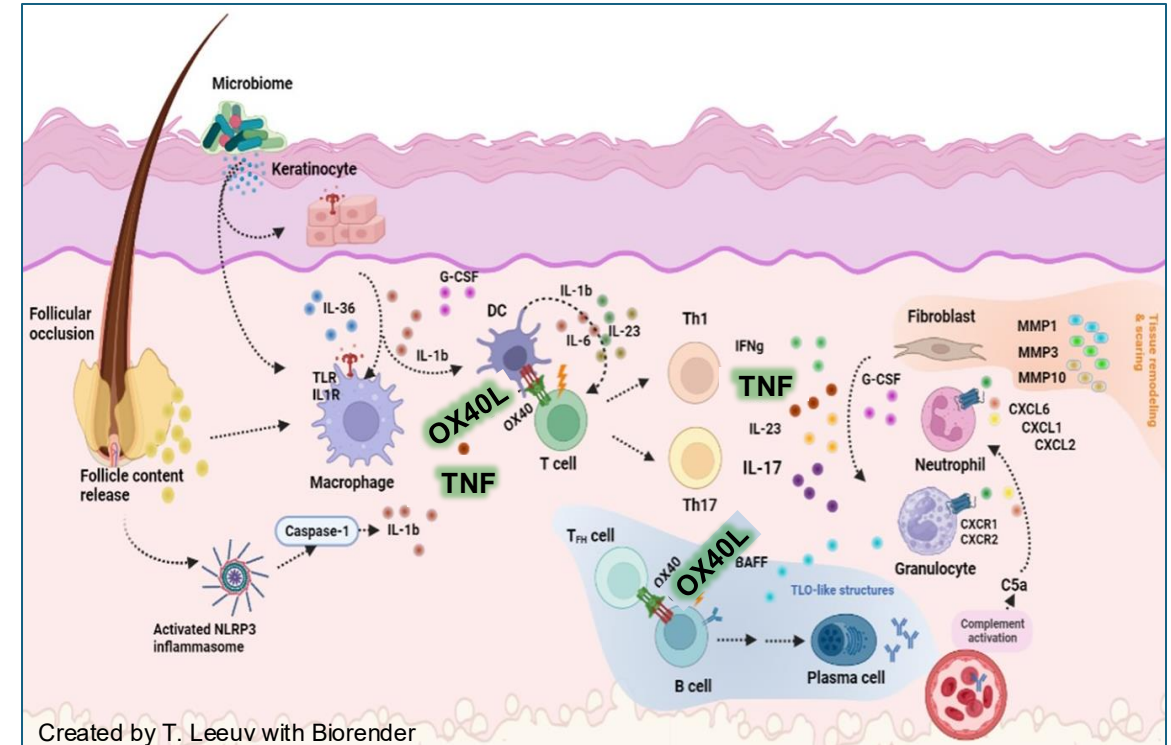
Brivekimig (SAR442970) Is a Novel Dual-Target
Anti-TNF and Anti-OX40L Single-Domain Antibody
Being Investigated as a Therapy for HS

Innate and Adaptive Immune Pathways Contribute to Hidradenitis Suppurativa

Pathways implicated in the pathogenesis of HS include

- **TNF** drives inflammatory cascades and is secreted by macrophages and T cells
- **OX40 ligand (OX40L)** is present on antigen-presenting cells
- Binds to OX40 expressed on T cells, promoting T-cell proliferation, survival, and cytokine release
- Contributes to B-cell differentiation and plasma-cell formation

Role of OX40L and TNF in HS



Currently approved therapies for HS are monoclonal antibodies, each targeting only one cytokine family

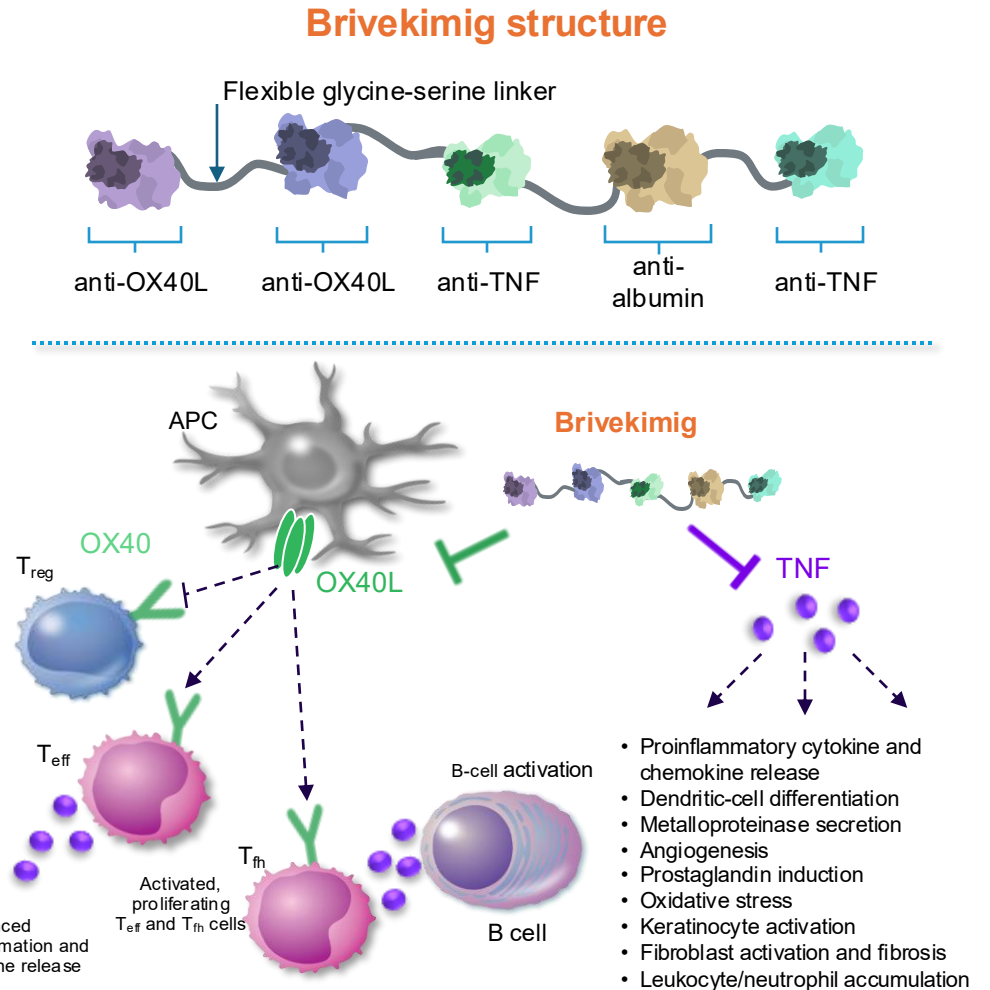
Brivekimig (SAR442970) Is a Novel Dual-Target Anti-TNF and Anti-OX40L Single-Domain Antibody Being Investigated as a Therapy for HS

Brivekimig is a *bispecific*, pentavalent single-domain antibody molecule

- Two units bind to TNF
- Two units bind to OX40L
- One unit binds to serum albumin to extend half-life

Single-domain antibody molecules represent the next generation of antibody-derived biologics

- Multivalent linking enables custom targeting
- One-tenth the size of traditional antibodies
- Stable and fully functional
- Camelid-derived

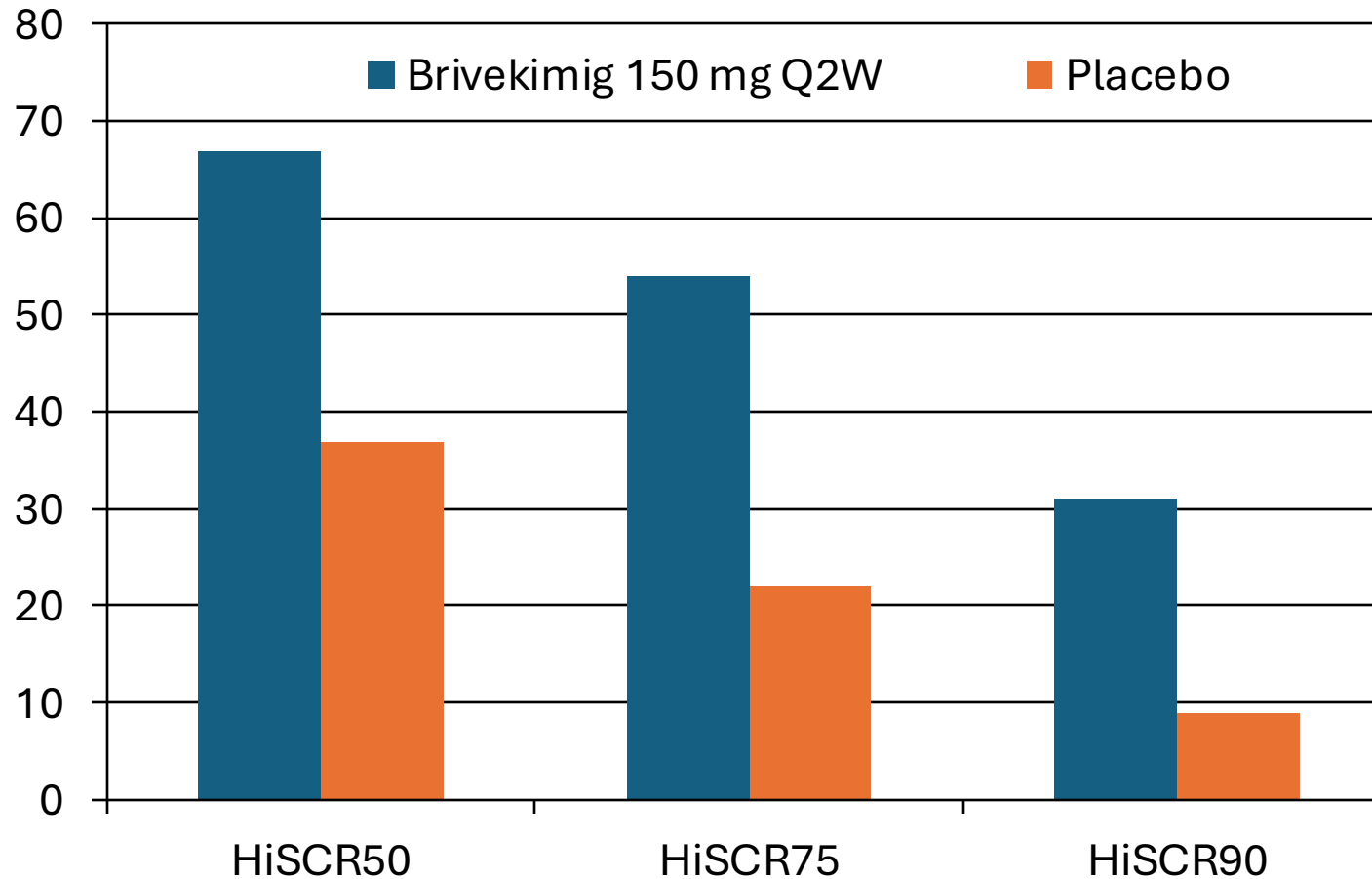


Leeuw T, et al. *J Allergy Clin Immunol Glob*. 2025;4(3):100483. Steeland S, et al. *Drug Discov Today*. 2016;21(7):1076-1113.

Wolfson W. *Chem Biol*. 2006;13(12):1243-1244.

HS-OBTAIN: Week 16 Efficacy

Biologic-naïve population



- HiSCR50: 67% vs 37%; Bayesian estimated difference 29%, 90% credible interval 10%–47%; probability of superiority 99.28%
- HiSCR75: 54% vs 22%; estimated difference 29%, 90% CI 11%–48%; nominal $P=0.0171$
- HiSCR90: 31% vs 9%; estimated difference 20%, 90% CI 5%–34%; nominal $P=0.0576$
- Mean percent change in draining-tunnel count: –56.0% with brivekimig vs +10.9% with placebo (nominal $P=0.005$)

Brivekimig 150 mg SC Q2W Was Generally Well-Tolerated

Safety population^a

Week 16 TEAE Overview Number of Participants (%)	Placebo (n=28)	Brivekimig 150 mg SC Q2W (n=58)
Any TEAE	15 (54)	45 (78)
Any severe TEAE	0	2 (3)
Any serious TEAE	0	0
Any TEAE related to treatment assessed by investigator	6 (21)	15 (26)
Any TEAE leading to permanent study intervention discontinuation ^b	0	2 (3)
Any TEAE leading to death	0	0
Most frequent TEAEs (≥10% of participants; more common with brivekimig 150 mg SC Q2W than placebo)		
Nasopharyngitis	3 (11)	11 (19)
Headache	3 (11)	8 (14)

Two severe TEAEs were observed with brivekimig treatment

- Aspartate aminotransferase increased (deemed related to treatment by investigator)
- Skin pain associated with HS (deemed not related to treatment by investigator)

No serious TEAEs were observed with brivekimig

Nasopharyngitis and headache were the most frequent TEAEs

Of interest, there were two cases of oral candidiasis with brivekimig^c

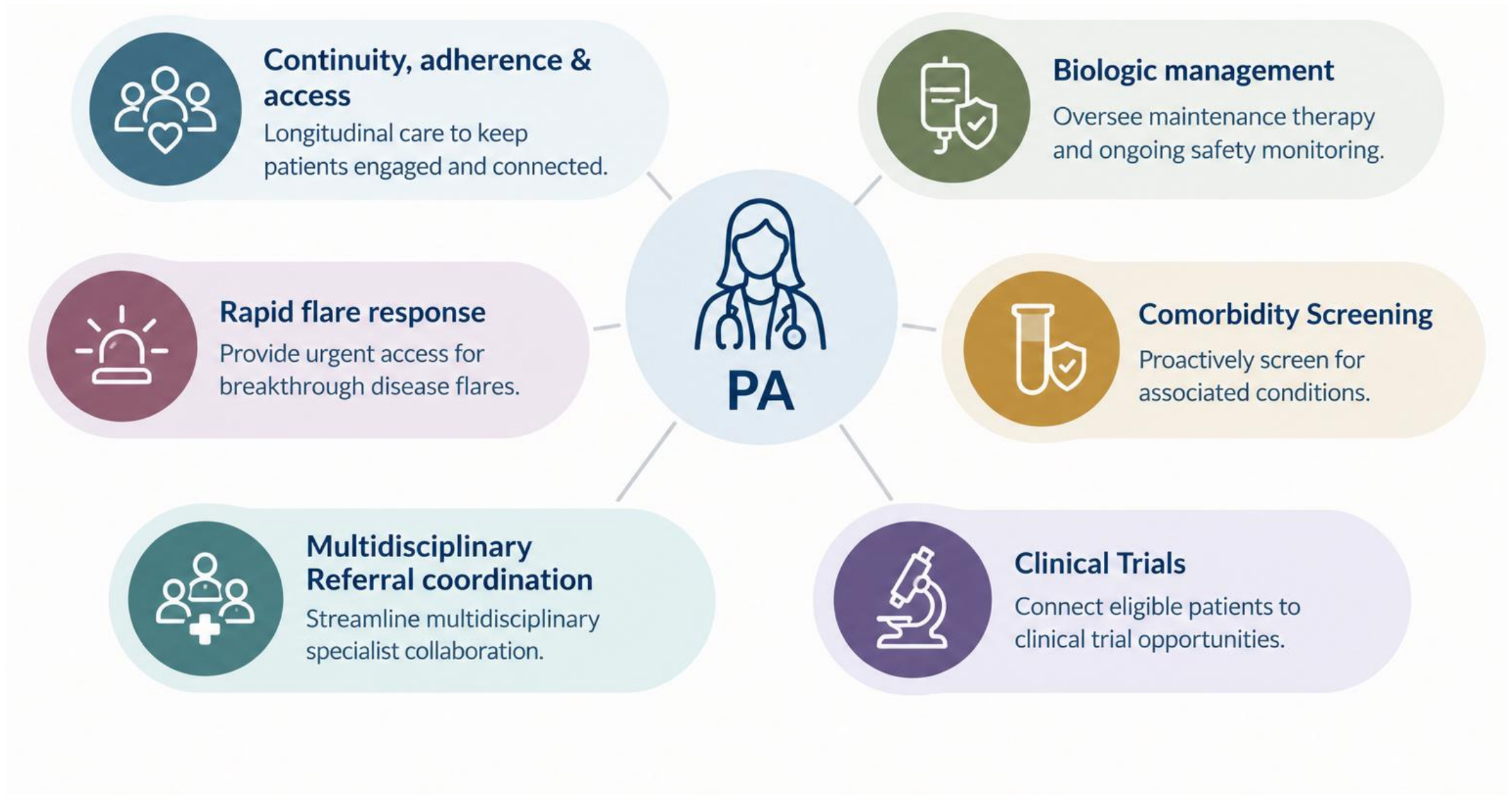
^aAll randomized participants, including exploratory anti-TNF-experienced population (n=15), who took at least one dose of study intervention, regardless of the amount of intervention administered. Participants were analysed according to the intervention they actually received; ^bPermanent discontinuations were due to one case of pregnancy and one case of HS flare; ^cOne mild and one moderate case; both determined to be related to treatment by investigators, and both participants recovered after corrective treatment without the need for study intervention discontinuation.

GlobeNewswire. September 17, 2025. Accessed September 17, 2026. <https://www.globenewswire.com/news-release/2025/09/17/3151353/0/en/Press-Release-EADV-Sanofi-s-brivekimig-achieved-positive-results-in-hidradenitis-suppurativa-in-phase-2a-study.html>.

Role of the PA in the Multidisciplinary Approach to HS

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PA Role in the UTSW Multidisciplinary Program



Patient-Centered Care in HS Management

- Disease understanding — complex combination of genetics and auto-inflammatory processes; not infectious, contagious, or the patient's fault
- Perceptions of treatment risk — proactively address fears (antibiotic resistance, biologic immunosuppression/infection risk, surgical recovery)
- Treatment fatigue — offer fast-acting bridge/symptomatic therapy; set realistic expectations (response typically 3–6 months)
- Address quality-of-life impact — even in clinically mild disease, 39% of Hurley stage I patients report very severe QOL impairment

Psychosocial Burden

- Psychosocial burden is high and severity-independent — pooled prevalence of depression 21–27% and anxiety 12–18% in HS, roughly 2–4x higher than in people without HS
- Burden begins in childhood and adolescence — among pediatric/adolescent patients, ~15.7% (3x control) had a psychiatric comorbidity before age 18, rising to 23.5% (2.7x control) by age 23
- Suicidality is a potentially fatal risk — significantly increased risk of completed suicide in the cohort of patients with HS, which remained increased even after adjustment for confounding factors

Impact on Intimacy and Relationships

- HS ranks among the dermatologic diseases with the greatest impairment of sexual health in large European cohorts

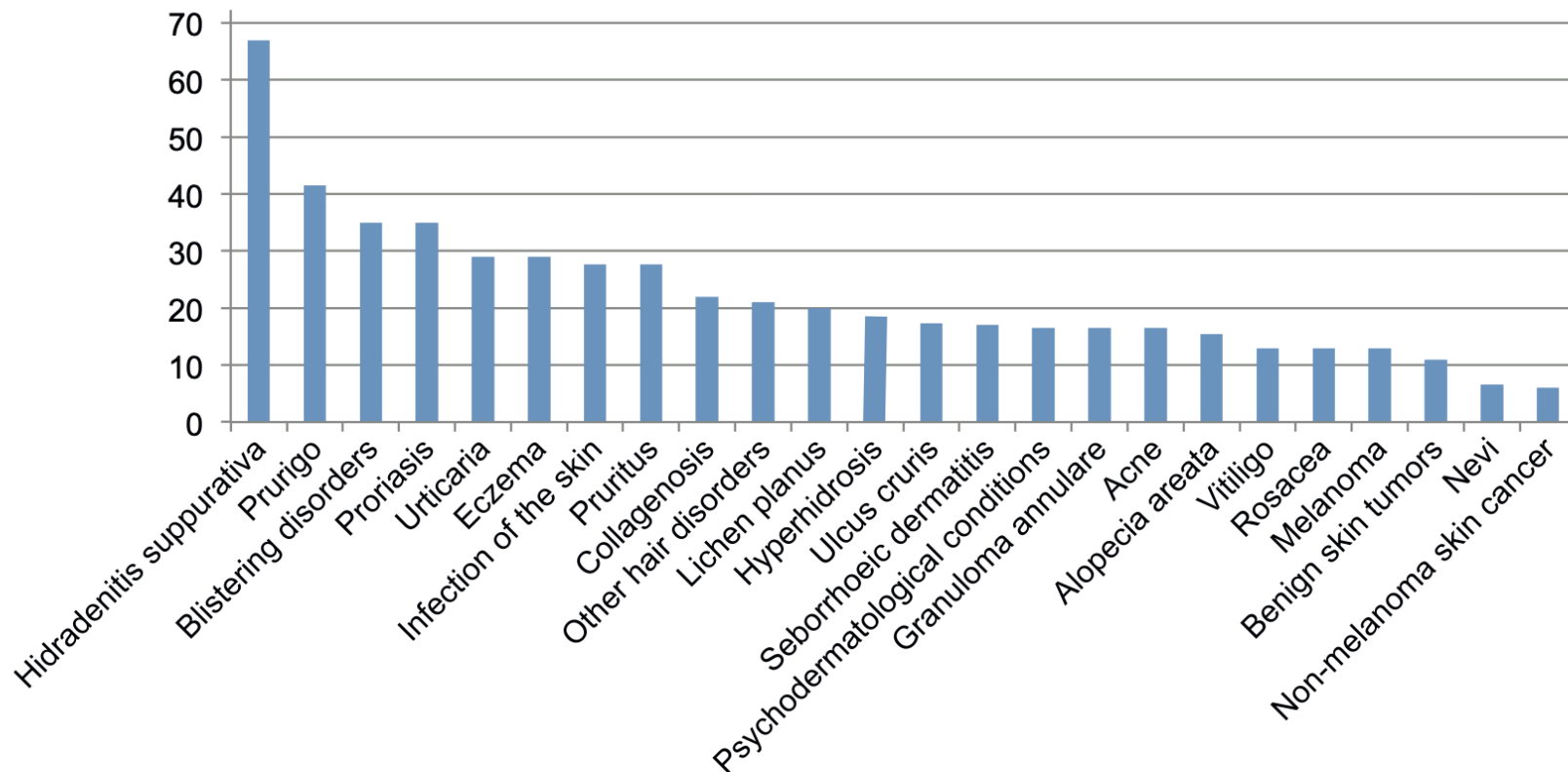
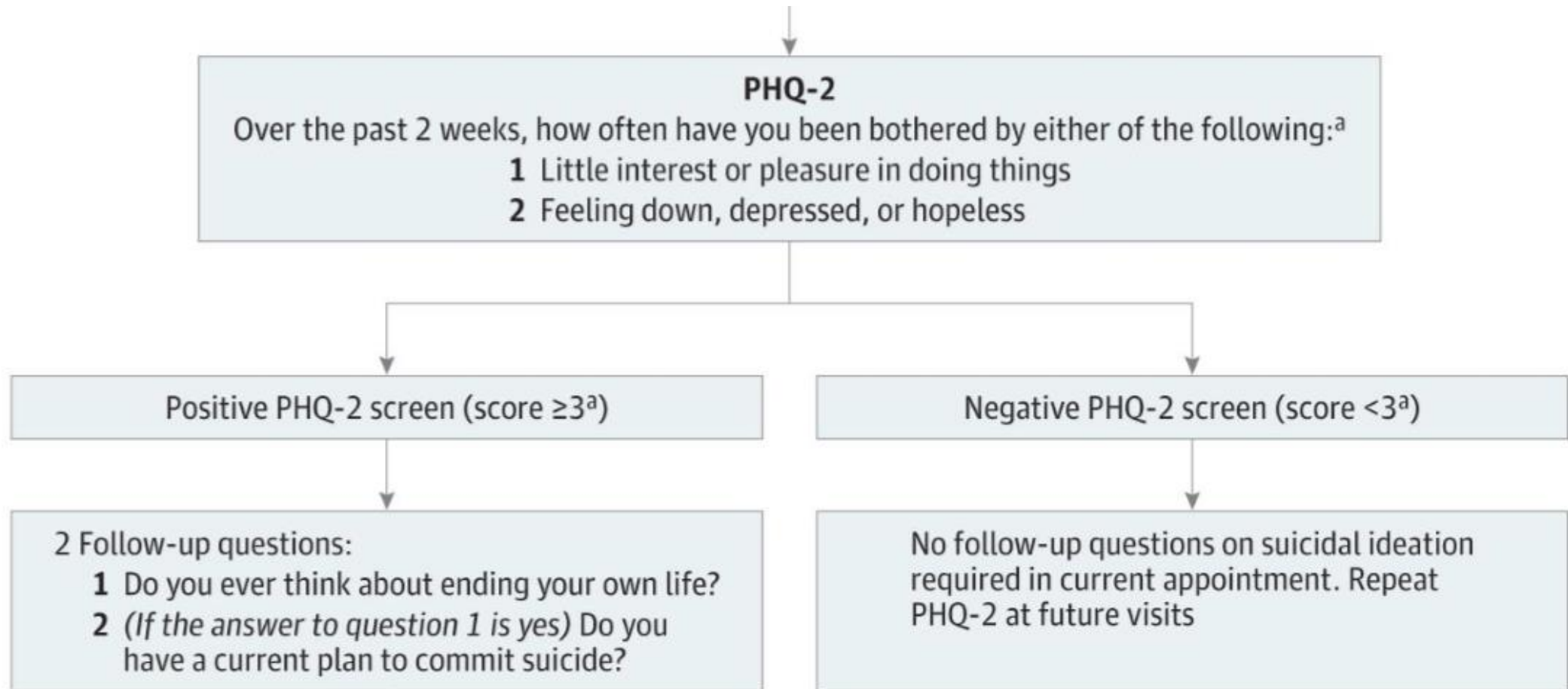


Fig. 1. Prevalence of positive answers to question 9 of the Dermatology Life Quality Index (DLQI) ("Over the last week, how much has your skin caused any sexual difficulties?") **in different skin conditions.** NMSC: non-melanoma skin cancer.

Routine Depression Screening Matters

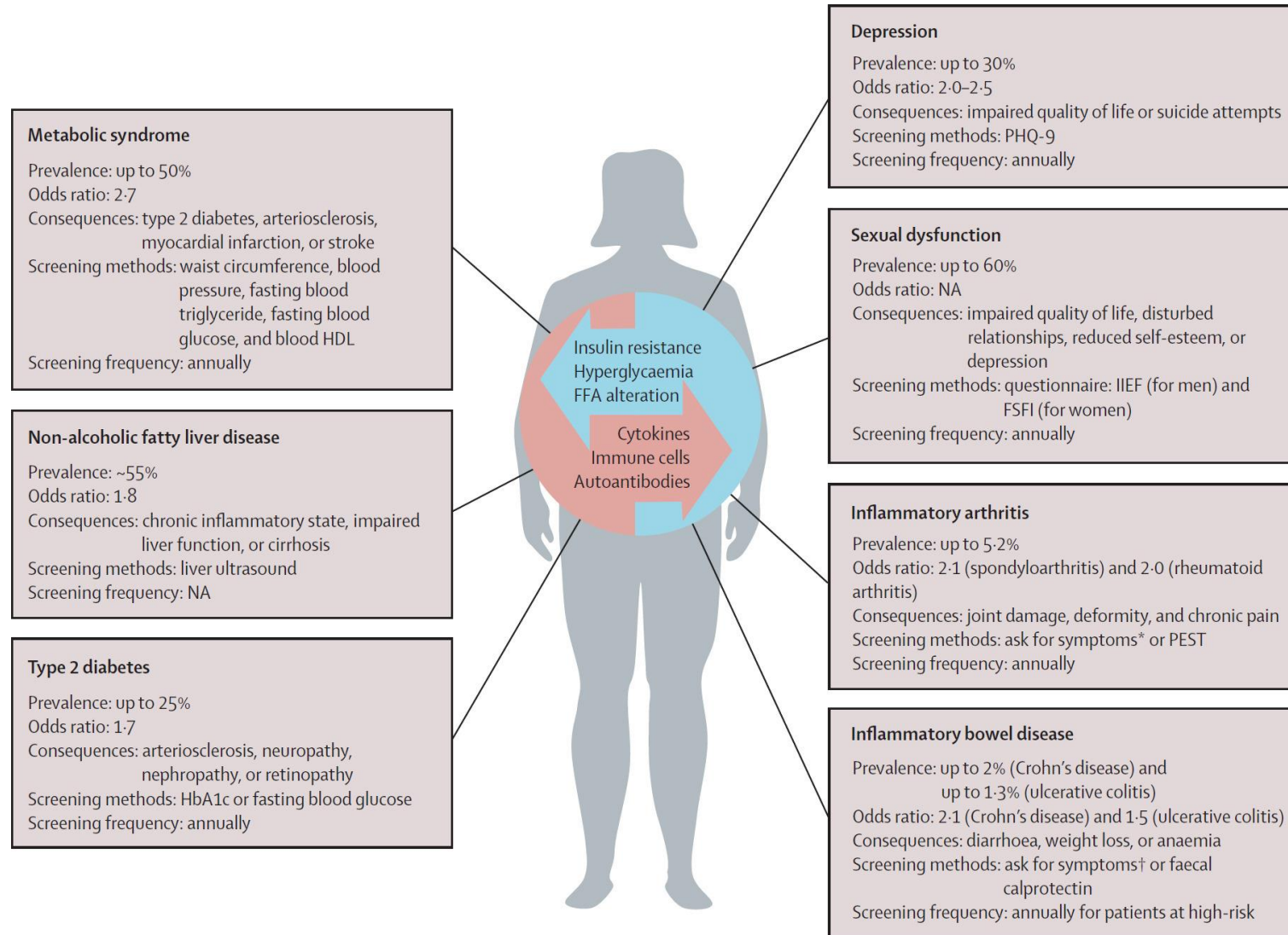
- The US and Canadian HS Foundations recommend routine screening for depression, generalized anxiety disorder, suicide, substance use, and sexual dysfunction in HS
- Screen at diagnosis and periodically using validated tools (eg, PHQ-2/PHQ-9)
- Ask directly about sexual health and relationship impact
- Screen (even with mild disease) adolescents and young adults, in whom psychiatric comorbidity accumulates over time

PHQ-2 Depression Screening



^aEach question should be scored as follows: 0, not at all; 1, several days; 2, more than half the days; 3, nearly every day. A score of 3 or greater is considered positive.
McDonald K. *JAMA Dermatol.* 2018;154(2):139-141.

Comorbid Conditions



IIEF = International Index of Erectile Function; FSFI = Female Sexual Function Index; PEST = Psoriasis Epidemiology Screening Tool.
Sabat R, et al. *Lancet*. 2025;405(10476):420-438.

Comorbidity Screening

TABLE 3. Structured laboratory evaluation in patients with hidradenitis suppurativa

CATEGORY	TESTS/SCREENING	CLINICAL RELEVANCE
General inflammatory evaluation	CBC, CRP, ESR, CMP	Assess systemic inflammation and organ function
Metabolic comorbidities	Fasting glucose, HbA1c, lipid panel	Identify insulin resistance, diabetes, dyslipidemia
Infectious disease screening	HIV, hepatitis B and C serologies	Required before immunosuppressive treatment
Endocrine disorders (PMOS*)	Serum androgens, pelvic ultrasound	Identify PMOS* in appropriate clinical context
Gastrointestinal comorbidities (IBD)	Fecal calprotectin, GI referral	Screen for Crohn's disease or other IBD
Musculoskeletal disorders	HLA-B27, rheumatology referral	Detect seronegative spondyloarthritis

*formerly referred to as polycystic ovarian syndrome (PCOS)

CBC: complete blood count; CMP: comprehensive metabolic panel; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; GI: gastrointestinal; HbA1c: hemoglobin A1C; IBD: inflammatory bowel disease; PMOS: polyendocrine metabolic ovarian syndrome

TABLE 4. Most common comorbid conditions associated with hidradenitis suppurativa

COMORBID CONDITION	LEADS TO	HOW TO SCREEN
Metabolic syndrome	Arteriosclerosis, myocardial infarction, or stroke	Waist circumference, blood pressure, fasting blood lipids, fasting blood glucose
Metabolic dysfunction-associated steatotic liver disease*	Chronic inflammatory state, impaired liver function, or cirrhosis	Blood liver function testing, liver ultrasound
Type 2 diabetes	Arteriosclerosis, neuropathy, nephropathy, or retinopathy	Fasting blood glucose, HbA1C
Polyendocrine metabolic ovarian syndrome*	Hirsutism, amenorrhea, acne, or weight gain	Clinical exam, serum androgen testing, pelvic ultrasound
Depression/anxiety	Impaired quality of life including sleep impairment, altered moods, mood swings, irritability, social isolation, loss of work or school, consideration of self-harm, or suicidal ideation/behavior	History questioning, PHQ-9
Inflammatory bowel disease	Diarrhea, weight loss, or anemia	History of symptoms ^a , fecal calprotectin
Inflammatory arthritis	Joint damage, deformity, and chronic pain	History of symptoms ^b , PEST
Sexual impairment	Impaired quality of life, disturbed relationships, reduced self-esteem, depression	History questioning (distinguish if physical cause due to lesion-associated pain/discomfort or if primary erectile dysfunction), IIEF (men), FSFI (women)

^a Have you had abdominal pain at least 3 times a week for at least 4 weeks; bloody stools and/or diarrhea (more than 3 bowel movements daily) for 7 consecutive days; or been awoken from sleep because of abdominal pain or diarrhea?

^b Have you had joint pain, back pain, or back stiffness for at least 3 months that is worse in the morning and gets better throughout the day?

* formerly referred to as nonalcoholic fatty liver disease (NAFLD)

* formerly referred to as polycystic ovarian syndrome (PCOS)

HbA1c: hemoglobin A1C; FSFI: Female Sexual Function Index; IIEF: International Index of Erectile Function; PEST: Psoriasis Epidemiology Screening Tool; PHQ-9: Patient Health Questionnaire-9

Multidisciplinary Referral Coordination



Comorbidity & Symptoms

Comorbidity

-  Cardiovascular Disease
-  Type 2 Diabetes
-  Liver Disease
-  Obesity
-  PCOS
-  Depression & Anxiety
-  Inflammatory Arthritis
-  Inflammatory Bowel Disease
-  Anemia of chronic disease



Multidisciplinary Referral

Referral

-  Cardiology
-  Endocrinology
-  Internal Medicine/Gastroenterology
-  Weight Wellness/ Nutrition
-  OBGYN
-  Psychiatry
-  Rheumatology
-  Gastroenterology
-  Hematology

Symptom-Based Referral Coordination



Symptom



Pain & Sexual Dysfunction



Limited Range of Motion



Ulcerative wounds & Drainage



Smoking & Substance use



Referral



Pain Management



Physical & Occupational Therapy



Wound Care



Nicotine Cessation Program

Surgical Referral Coordination



Anatomic Site Involved



Head & Neck



Axilla, Trunk, & Groin



Buttock & Perineal



Vulvar



Scrotal



Referral



Plastic Surgery



General Surgery



Colorectal Surgery



Gynecology-Oncology



Urology

Practical Approach to HS

1. Assess severity (Hurley/IHS4) AND patient-reported burden (HiSQOL, DLQI, Pain VAS)
2. Screen for depression, smoking, metabolic and inflammatory comorbidities
3. Integrate patient preferences, prior treatment history, and comorbidities
4. Share decision-making in treatment approach (medical vs surgical), risk perceptions of therapy, goals, and expectations
5. Coordinate multidisciplinary care (mental health, primary care, surgery, gynecology)
6. Reassess disease and psychosocial status at follow-up and adjust

The Role of a Sub-Investigator in Clinical Trials

- Patient identification and eligibility — assist in screening and assess patients against inclusion/exclusion criteria
- Education and informed consent — educate participants and obtain/document informed consent
- PI collaboration — partner with the principal investigator on trial conduct and oversight
- Protocol visits and outcomes — conduct scheduled visits and perform outcome assessments
- Safety monitoring — track laboratory results and identify, report, and manage adverse events

Summary: Key Takeaways

DIAGNOSE EARLY

Diagnostic delay is associated with greater disease severity, comorbidity burden, irreversible tissue damage, and reduced quality of life.

ASSESS MORE THAN LESIONS

Evaluate pain, QOL, psychosocial impact, and comorbidities. Ultrasound can identify subclinical tunnels.

TREAT THE WHOLE PATIENT

HS is systemic and multidimensional. Coordinate with specialists based on individual comorbidities.

PERSONALIZE THERAPY

Choose therapy based on shared decision-making, prior treatments, comorbidities, risks, preferences, and expectations.

LEVERAGE THE PA ROLE

PAs can provide access, education, multidisciplinary referral coordination, and clinical trial participation.



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November 14, 2026
December 19, 2026

