American Academy of Dermatology Association

Online Supplement

Guidelines of Care for the Management of Hidradenitis Suppurativa

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Supplemental Appendix 1. Detailed Methodology

Expert Work Group Composition and Disclosures of Interest

The co-chairs of the Work Group (H.N. and C.B.) were reviewed for potential disclosures of interest (DOIs) and approved by the AAD's Clinical Guidelines Committee (CGC). Additional Work Group members were nominated by the co-chairs based on their expertise related to the clinical topic. All Work Group nominees were reviewed for potential DOIs by the CGC. The majority (at least 51%) of the Work Group was required to be free of financial DOIs relevant to the topic of the guideline. Nominees found to have no relevant financial DOIs were approved, whereas nominees found to have potentially relevant financial DOIs were approved with management. Work Group members approved with management were prohibited from discussions on and voting for recommendations in which they had relevant DOIs. Work Group members completed a DOI form that was periodically updated and reviewed for relevant DOIs throughout guideline development and used to ensure management terms were observed. The multidisciplinary Work Group consisted of the co-chairs, 10 members, an additional member serving as a methodologist, and a patient representative. The Work Group was supported by an AAD guidelines staff member (L.F.G) with health research methodology expertise.

Formulation of Questions and Rating the Importance of Outcomes

Based on the aim of the guideline to provide evidence-based recommendations for the management of hidradenitis suppurativa (HS), the expert Work Group identified ten clinical questions, using the Population, Intervention, Comparator, Outcome (PICO) format (**Table I**). Next, the Work Group identified outcomes considered important for making clinical decisions regarding the treatment of HS through discussion and review of the literature (**Table 1**). The Work Group ranked the importance of each primary outcome for decision-making via anonymous online voting using a 9-point scale (a ranking of 7-9 was assigned to outcomes critical for decision-making, 4-6 for outcomes important for decision-making, and 1-3 for outcomes of limited importance for decision-making).[1] Results of voting were used to categorize outcomes as "critical", "important", or "not important".

Table 1. Outcomes

Outcome	**Importance Ranking by PICO**										
	1	**2**	**3**	**4** (non-surgical)	**4** (surgical)	**5**	**6**	**7**	**8**	**9**	**10**
Pain	Critical	Critical	Critical	Critical	Critical	Critical	Critical	Important	Critical	Important	Critical
Change in clinical severity	Critical	Critical	Critical	Critical	Critical	-	Critical	Critical	Critical	Critical	Critical
Quality of life	Critical	Critical	Critical	Critical	Critical	-	Critical	Critical	Critical	Critical	Critical
Global assessment of HS	Critical	Critical	Critical	Critical	Critical	-	-	Critical	Critical	Critical	Critical
Symptoms (drainage, itch, odor, fatigue)	Important	Important	Important	Important	Important	Important	Important	Important	Important	Important	Important
Disease progression/remission	Critical	Critical	Critical	Critical	Critical	-	-	Critical	Critical	Critical	Critical
Patient global assessment	Critical	Critical	Critical	Important	Critical	-	-	Critical	Critical	Critical	Critical
Serious adverse events	Critical	Critical	Critical	Critical	Critical	Critical	Important	-	-	-	Important
Discontinuation due to adverse events	Critical	Critical	Critical	Important	-	Critical	Important	Important	Important	Important	Important
Other adverse events of interest	Important	Important	Important	Important	-	Important	Important	Important	Important	-	Important

Cosmetic outcome	Important	Important	Important	Important	Important	-	-	-	-	-	Important
Surgical complications	-	-	-	-	Critical	-	-	-	-	-	-
Psychological distress/functioning	-	-	-	-	-	Critical	Important	Critical	Critical	Critical	-
Wound recovery time/healing time	-	-	-	-	Critical	-	Critical	-	-	-	-
Patient recovery time	-	-	-	-	Critical	-	-	-	-	-	-
Reduction in opioid morbidity or other substance use	-	-	-	-	-	Critical	-	-	-	-	-
Healthcare utilization	-	-	-	-	-	Critical		-	-	-	-
Physical functioning	-	-	-	-	-	Critical	Critical	-	-	-	-
Addiction	-	-	-	-	-	Critical	-	-	-	-	-
Hypergranulation tissue/scar/keloid	-	-	-	-	-	-	Important	-	-	-	-
Treatment burden	-	-	-	-	-	-	Critical	-	-	-	-
Wound size	-	-	-	-	-	-	Critical	-	-	-	-
Clinical appearance wound bed	-	-	-	-	-	-	Critical	-	-	-	-
Food medication tradeoff	-	-	-	-	-	-	-	Critical	-	-	-
Nutritional deficits	-	-	-	-	-	-	-	Important	Important	-	-
Adherence	-	-	-	-	-	-	-	Critical	Critical	Critical	-

Evidence Search and Review

A systematic review was commissioned from the Cochrane Skin group to address questions 1-4 (pending publication). Searches of the literature for all other PICO questions using MEDLINE (via PubMed) and the Cochrane Library were conducted in September 2024 and periodically updated through September 2025. All systematic reviews supporting this analysis met or followed standard methodology including development of PICO questions, explicit inclusion criteria, systematic literature searches, and vetted risk of bias assessment procedures.

For all systematic reviews, the following hierarchical evidence inclusion schema was used: randomized controlled trials (RCTs) that assess the effects of interventions for HS at 8 to 16 weeks and/or at 48 to 52 weeks were prioritized. When there are no relevant RCTs for an intervention or comparison of interest, non-randomized studies of interventions (NRSI) including prospective and retrospective cohort studies were included. NRSIs were also included in the evidence base in addition to RCTs if : 1) the available RCT(s) are small (<50 participants) and provide only low or very low certainty evidence for critical outcomes; or 2) The NRSIs provide data on critical outcomes not reported in RCTs. In these situations, NRSIs were included in a step-wise manner: open-label trials→prospective/retrospecitve cohorts→case-control/case series. All studies were required to include at least 5 patients and have a follow-up of at least 8 weeks.

For all reviews, studies retrieved by the literature searches were reviewed for relevance over two rounds of study selection. Two reviewers independently screened citations. All citations deemed relevant by one or both reviewers were obtained as full text. Two independent reviewers screened full text citations against a priori established eligibility criteria; discrepancies were resolved through discussion. Data extraction using structured data abstraction spreadsheets was initially performed by an independent reviewer with subsequent quality control performed by a second reviewer. Risk of bias was assessed for all included studies using the Cochrane Collaboration's tool for assessing risk of bias in randomized trials (ROB2), the Newcastle-Ottawa Scale for cohort studies, cross-sectional studies, or case-control studies, or the Murad, et al. 2018 tool for case reports based on study design.[2-5]

Assessing the Overall Certainty of the Body of Evidence

The GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) approach was used to assess the overall certainty of the evidence from systematic reviews for each critical or important outcome.[6] The GRADEPro Guideline Development Tool was used to create evidence profiles that categorized the overall certainty of the body of evidence for each outcome into one of four categories: high, moderate, low, or very low. Each category represents the confidence in the estimate of effect for an outcome (**Table 2**).

Table 2. Certainty of Evidence Ratings

Certainty of the Evidence	Confidence in the Estimate of Effect
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect
Very Low	We have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

Formulating and Grading Recommendations

The Work Group drafted recommendations using the evidence profiles and considering the following: the balance of desirable and undesirable consequences of an intervention, the overall certainty of the evidence, patient values and preferences, and feasibility.[7] GRADE evidence-to-decision (EtD) frameworks were compiled for each clinical question to facilitate recommendation drafting. Structured searches were conducted for evidence of patient values and preferences, resource use, and feasibility to inform the EtD process. The workgroup also included a patient representative to provide input on preferences and values.

In accordance with the GRADE approach, recommendations were either "strong" or "conditional".[8] The implications of each strength of recommendation are summarized in **Table 3**. Recommendations were also graded according to the GRADE approach.[8] In situations in which the supporting evidence for a recommendation was indirect only, but the certainty surrounding an intervention's impact was high and the benefits of the intervention clearly outweigh the harms (or vice versa), a Good Practice Statement was developed.[9] Good Practice Statements are strong recommendations as the certainty surrounding the impact of the recommended intervention is high.

Table 3. Strength of Recommendation Implications

Strength	Implication
Strong	Net benefit clearly favors one option over another

Conditional	Net benefit closely balanced; or net benefit clearly favors one option but the certainty of the evidence is low or very low

Manuscript Review and Currency Statement

This guideline was developed in accordance with the AAD/AAD Association Administrative Regulations for Evidence-Based Clinical Practice Guidelines (March 2021), which includes the opportunity for review and comment by the entire AAD membership and final review and comment by the AAD Board of Directors.[10] This guideline will be considered current for a period of 5 years from the date of publication unless reaffirmed, updated, or retired before that time.

1. Guyatt GH, Oxman AD, Kunz R, Atkins D, Brozek J, Vist G et al. GRADE guidelines: 2. Framing the question and deciding on important outcomes. J Clin Epidemiol 2011;64:395-400.
2. Sterne JAC, Savovic J, Page MJ, Elbers RG, Blencowe NS, Boutron I et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019;366:l4898.
3. Murad MH, Sultan S, Haffar S , Bazerbachi F. Methodological quality and synthesis of case series and case reports. BMJ Evid Based Med 2018;23:60-3.
4. Wells G, Shea B, O'Connell D, Peterson j , Welch V. The Newcastle-Ottawa Scale (NOS) for assessing the quality of case-control studies in meta-analyses. Eur J Epidemiol 2011;25:603-5.
5. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M , Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2000.
6. Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J et al. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 2011;64:401-6.
7. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y et al. GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. J Clin Epidemiol 2013;66:719-25.
8. Andrews JC, Schunemann HJ, Oxman AD, Pottie K, Meerpohl JJ, Coello PA et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. J Clin Epidemiol 2013;66:726-35.
9. Guyatt GH, Alonso-Coello P, Schunemann HJ, Djulbegovic B, Nothacker M, Lange S et al. Guideline panels should seldom make good practice statements: guidance from the GRADE Working Group. J Clin Epidemiol 2016;80:3-7.
10. American Academy of Dermatology. Administrative regulation–evidence-based clinical practice guidelines. Accessed November, 2021. Available at: https://server.aad.org/Forms/Policies/Uploads/AR/AR%20-%20Evidence-Based%20Clinical%20Practice%20Guidelines.pdf.

Topical Agents Summary of Findings Tables

Contents

e-Table 1. Topical clindamycin solution vs placebo

Topical clindamycin solution compared to placebo for hidradenitis suppurativa

Patient or population: hidradenitis suppurativa
Intervention: Topical clindamycin hydrochloride 1% for 12 weeks (assume daily application)
Comparison: placebo (vehicle of isopropanol 80%, propyleneglycol 10%, and water 9%)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	**Risk with topical clindamycin solution**				
Clinical severity assessed with: number of abscesses/inflammatory nodules/pustules	Mean number of abscesses/inflammatory nodules/pustules baseline → week 12 -Topical clindamycin: 1.15/1.43/8.9 → 0.46/0.14/0.38 (p<0.01) -Placebo: 1.14/1.46/9.9 → 1.50/0.77/18.0			27 (1 RCT)[1]	⨁⨁◯◯ Low[a]	
Non-serious adverse events follow-up: 12 weeks	214 per 1000	**154 per 1000** (30 to 780)	**RR 0.72** (0.14 to 3.64)	27 (1 RCT)[1]	⨁⨁◯◯ Low[b]	
Achieving improvement in participant global self-assessment (PGSA) follow-up: 12 weeks	286 per 1000	**614 per 1000** (243 to 1000)	**RR 2.15** (0.85 to 5.48)	27 (1 RCT)[1]	⨁⨁◯◯ Low[b]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded two levels due to very serious imprecision: very small sample.
[b]Downgraded by two levels due to very serious imprecision: very small sample size and the ratio of the upper to the lower boundary of the CI was > 3.

1. Clemmensen OJ. Topical treatment of hidradenitis suppurativa with clindamycin. Int J Dermatol 1983;22:325-8.

e-Table 2. Clindamycin lotion 1% twice daily versus clindamycin 1% with benzoyl peroxide 5% gel twice daily

Clindamycin 1% with benzoyl peroxide 5% gel compared to clindamycin lotion 1% for hidradenitis suppurativa

Patient or population: Adults with mild to moderate hidradenitis suppurativa
Intervention: clindamycin 1% with benzoyl peroxide 5% gel bid for 12 weeks
Comparison: clindamycin lotion 1% bid for 12 weeks

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with clindamycin lotion 1%	**Risk with clindamycin 1% with benzoyl peroxide 5% gel**				
Pain NRS Scale from: 0 to 10 follow-up: 16 weeks	Significant decrease in the median pain score from baseline to week 16 was observed in the clindamycin lotion group (from 7 to 3, P < 0.05) but not in the clindamycin-benzoyl peroxide gel (6.5 to 4.5, not significant)			20 (1 RCT)[1]	⨁⨁◯◯ Low[a]	
Achieving IHS4 55 at week 16	600 per 1000	**600 per 1000** (294 to 1000)	**RR 1.00** (0.49 to 2.05)	20 (1 RCT)[1]	⨁⨁◯◯ Low[b]	
Itch NRS median change	Baseline → week 16: -Clindamycin lotion: 6 [IQR: 3.8 to 6.3] → 3.5 [IQR: 0.8 to 6] -Clindamycin-benzoyl peroxide gel: 5 [IQR: 2 to 7] → 4.5 [IQR: 1.5 to 6.3]			20 (1 RCT)[1]	⨁⨁◯◯ Low[a]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two levels due to very serious imprecision: Small sample size.
[b]Downgraded by two levels due to imprecision: small sample size and the 95% CI crossed both the conventional upper and lower thresholds of MID (0.75 and 1.25).

1. Aarts P, Reeves JL, Ardon CB, van der Zee HH , Prens EP. Clindamycin-Benzoyl Peroxide Gel Compared with Clindamycin Lotion for Hidradenitis Suppurativa: A Randomized Controlled Assessor-Blinded Intra-Patient Pilot Study. Dermatology 2023;239:670-4.

e-Table 3. Topical clindamycin vs topical resorcinol vs no treatment

Topical resorcinol or clindamycin compared to no treatment for hidradenitis suppurativa

Patient or population: Adults with Hurley stage I and IHS4 ≤10 hidradenitis suppurativa
Intervention: Topical resorcinol 10% cream twice daily for 24 weeks
Comparison: Topical clindamycin 1% lotion twice daily for 24 weeks

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with resorcinol	**Risk with clindamycin**				
Clinical severity Assessed with: mean IHS4 score follow-up: 24 weeks	Baseline → week 24: -Resorcinol 10%: 5.65 → 2.5 -Clindamycin 1%: 5 → 4.2 -No treatment 5.3 →8 .5			40 (1 RCT)[1]	⨁⨁◯◯ Very Low[ab]	
Quality of Life Assessed with: Mean DLQI score follow-up: 24 weeks	Baseline → week 24: -Resorcinol 10%: 9.6 → 4.8 -Clindamycin 1%: 8.85 → 8.4 -No treatment 6.85→ 11.5			40 (1 RCT)[1]	⨁⨁◯◯ Very Low[ab]	
Adverse events leading to discontinuation of intervention - follow-up: 24 weeks	0/20	0/20	Not estimable	40 (1 RCT)[1]	⨁⨁◯◯ Very Low[ab]	No adverse events reported with either active treatment

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a] Downgraded one level for RoB: incomplete outcome reporting.
[b] Downgraded by two levels due to imprecision: very small sample n=40

1. Katoulis A, Efthymiou O, Liakou A, Pappa G, Kanelleas A, Koumaki D et al. Resorcinol 10% as a Promising Therapeutic Option for Mild Hidradenitis Suppurativa: A Prospective, Randomized, Open Study. Skin Appendage Disord 2023;9:438-43.

e-Table 4. Topical clindamycin 1%solution + bi-weekly LAight therapy vs topical clindamycin 1% solution

LAight therapy plus topical clindamycin compared to topical clindamycin for hidradenitis suppurativa

Patient or population: Adults with Hurley stage I or II hidradenitis suppurativa
Intervention: topical clindamycin 1% solution combined with 8 additional bi-weekly treatments with LAight® therapy (intense pulsed light + radiotherapy) for 16 weeks
Comparison: topical clindamycin 1% solution

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with topical clindamycin	**Risk with LAight therapy plus topical clindamycin**				
Change in pain NRS Scale from: 0 to 10 follow-up: 16 weeks	The mean change in pain NRS was **-0.9**	MD **1.4 lower** (2.87 lower to 0.07 higher)	-	71 (1 RCT)[1]	⨁⨁⨁◯ Moderate[a]	
Achieving HiSCR follow-up: 16 weeks	359 per 1000	**625 per 1000** (381 to 1000)	**RR 1.74** (1.06 to 2.86)	71 (1 RCT)[1]	⨁⨁⨁◯ Moderate[c]	
Change in IHS4 follow-up: 16 weeks	The mean change in IHS4 was **-1.8**	MD **5.4 lower** (8.31 lower to 2.49 lower)	-	71 (1 RCT)[1]	⨁⨁⨁◯ Moderate[b]	
Change in DLQI Scale from: 0 to 30 follow-up: 16 weeks	The mean change in DLQI was **-1.6**	MD **3 lower** (5.54 lower to 0.46 lower)	-	71 (1 RCT)[1]	⨁⨁⨁◯ Moderate[d]	
Adverse events leading to discontinuation of intervention follow-up: 16 weeks	0 per 1000	**0 per 1000** (0 to 0)	Not estimable	71 (1 RCT)[1]	⨁⨁◯◯ Low[e]	No adverse events in either arm, but very small sample concerning for precision.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by one level due to imprecision: small sample size and the 95% CI crossed the conventional lower thresholds of MID of 30% for NRS.
[b]Downgraded by one level due to imprecision: small sample size and the 95% CI crossed the conventional lower thresholds of MID of 55% for ISH4.
[c]Downgraded by one level due to imprecision: small sample size and the 95% CI crossed the conventional lower thresholds of MID (25%).
[d]Downgraded by one level due to imprecision: small sample size and the 95% CI crossed the conventional lower thresholds of MID of 4 for DLQI.
[e]Downgraded by two levels due to imprecision: zero events with very small sample size.

1. Schultheis M, Staubach P, Nikolakis G, Grabbe S, Ruckes C, von Stebut E et al. LAight® Therapy Significantly Enhances Treatment Efficacy of 16 Weeks of Topical Clindamycin Solution in Hurley I and II Hidradenitis Suppurativa: Results from Period A of RELIEVE, a Multicenter Randomized, Controlled Trial. Dermatology 2022;238:476-86.

e-Table 5. Topical clindamycin vs oral tetracycline

Oral tetracycline compared to topical clindamycin for hidradenitis suppurativa

Patient or population: Adults with Hurley stage I or II hidradenitis suppurativa
Intervention: Oral tetracycline 500 mg twice daily for 16 weeks
Comparison: topical clindamycin phosphate 1% lotion twice daily for 16 weeks

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with topical clindamycin	Risk with oral tetracycline				
Change in pain VAS Scale from: 0 to 100 follow-up: 16 weeks	The mean change in pain VAS was **-18**	MD **2 higher** (47.38 lower to 51.38 higher)	-	34 (1 RCT)[1]	⨁◯◯◯ Very low[a,b]	
Change in physician Global Assessment VAS Scale from: 0 to 100 follow-up: 16 weeks	The mean change in physician Global Assessment VAS was **-17**	MD **5 higher** (14.02 lower to 24.02 higher)	-	34 (1 RCT)[1]	⨁◯◯◯ Very low[a,c]	
Adverse events follow-up: 16 weeks	227 per 1000	**125 per 1000** (34 to 464)	**RR 0.55** (0.15 to 2.04)	46 (1 RCT)[1]	⨁◯◯◯ Very low[a,d]	
Change in patient global assessment VAS Scale from: 0 to 100 follow-up: 16 weeks	The mean change in patient global assessment VAS was **-8**	MD **15 lower** (32.02 lower to 2.02 higher)	-	34 (1 RCT)[1]	⨁◯◯◯ Very low[a,c]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded due to high risk of bias
[b]Downgraded by two levels due to very serious imprecision (small sample size and The 95% CI crossed the MID of VAS30 (30% reduction = 8.4 in this trial).).
[c]Downgraded by two levels due to very serious imprecision due to very small sample size.
[d]Downgraded by two levels due to very serious imprecision (very small sample size and the ratio of the upper to the lower boundary of the CI was > 3).

1. Jemec GB , Wendelboe P. Topical clindamycin versus systemic tetracycline in the treatment of hidradenitis suppurativa. J Am Acad Dermatol 1998;39:971-4.

e-Table 6. Topical resorcinol vs placebo

Topical resorcinol vs placebo for hidradenitis suppurativa

Patient or population: Adults with Hurley stage I and IHS4 ≤10 hidradenitis suppurativa
Intervention: Topical resorcinol 10% cream twice daily for 24 weeks
Comparison: No treatment for 24 weeks

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with resorcinol	**Risk with clindamycin**				
Clinical severity Assessed with: mean IHS4 score follow-up: 24 weeks	Baseline → week 24: -Resorcinol 10%: 5.65 → 2.5 -No treatment 1%: 5.3 → 8.5			40 (1 RCT)[1]	⨁⨁◯◯ Very Low[ab]	
Quality of Life Assessed with: Mean DLQI score follow-up: 24 weeks	Baseline → week 24: -Resorcinol 10%: 9.6 → 4.8 -Clindamycin 1%: 6.85 → 11.5			40 (1 RCT)[1]	⨁⨁◯◯ Very Low[ab]	
Adverse events leading to discontinuation of intervention - follow-up: 24 weeks	0/20	0/20	Not estimable	40 (1 RCT)[1]	⨁⨁◯◯ Very Low[ab]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
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Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
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Explanations

[a] Downgraded one level for RoB: incomplete outcome reporting.
[b] Downgraded by two levels due to imprecision: very small sample n=40

1. Katoulis A, Efthymiou O, Liakou A, Pappa G, Kanelleas A, Koumaki D et al. Resorcinol 10% as a Promising Therapeutic Option for Mild Hidradenitis Suppurativa: A Prospective, Randomized, Open Study. Skin Appendage Disord 2023;9:438-43.

e-Table 7. Topical resorcinol (case series)

Case series n=5, 229 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control groups. The individual studies included very small samples, increasing concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Boer 2010[1] Case series N=12	• Age (year, mean) 37.8 • 12 F • Smoking status: n=12 • Hurley stage I or II: n=12 • Mean BMI: NR • Prior treatment: antibiotics (n=8), surgery (n=10), etanercept (n=1), isotretinoin (n=1)	topical 15% resorcinol applied once daily (Resorcinol cream twice daily when flares occurred)	NR	NR	Duration of pain	mean =3.7 days (range 2-14 days) with treatment; 5 days to permanent pain without treatment	Selection N Ascertainment Y Causality N Reporting Y
					VAS (pain), 10-cm 0=least pain, 10=worst pain ever	Pretreatment, mean (SD): 7.2 (2.5)* Post treatment, mean (SD): 2.4 (1.8)* *values calculated from individual data reported in table 1	
					AEs	Desquamation in all patients, 4/12 patients experienced reversible brown discoloration	

Cordero-Ramos 2022[2] N=32	• Age (mean, 40.1 years [95% confidence interval, 35.7-44.4] • 20 F, 12 M • Mean BMI: 27.4 • Hurley I, 17 (53.1%); Hurley II, 15 (46.9%) • Smoking status: 75% yes • Prior treatment: NR	topical 15% resorcinol applied twice a day for 16 weeks	None	16 weeks	IHSA4, mean	Basal: 4.5 (2.95-6.05) Week 16: 2.03 (0.86-1.18)	Selection N Ascertainment Y Causality Y Reporting Y
					Total number of lesions, n	Basal: 2.63 (1.99-3.26) Week 16: 0.97 (0.51-1.43)	
					DLQR, mean	Basal: 16.44 (13.93-18.94) Week 16: 4.04 (2.41-5.67)	
					NRS odor, mean	Basal: 4.66 (3.54-5.77) Week 16: 1.48 (0.98-1.98)	
					NRS pain, mean	Basal: 7.44 (6.46-8.42) Week 16: 2.13 (1.31-2.95)	
					NRS drainage, mean	Basal: 6.84 (5.78-7.90) Week 16: 2.22 (1.20-3.24)	
					AEs, patients with any event	N=14	
					SAEs	N=0	
					AEs leading to discontinuation	N=0	
Docampo-Simon 2022[3] N=92	• Age, years [mean, (SD)]: 35.5 (12.5) • 24 M, 68 F • Smoking status: active smoker n=62, former smoker n=2, never a smoker n=28 • BMI: ≥25 n=72, <25 n=20 • Eighty-five out of 92 (92.4%) were Hurley II and 7 Hurley I	topical 15% resorcinol applied twice a day during flare-ups and once a day for maintenance	-Metformin n=30 -Rifampicin plus clindamycin n=22	NR	Side effects	N= 27 (reported as 65 patients having no side effects)	Selection N Ascertainment Y Causality N Reporting N

Molinelli 2020[4] N=61	61 males and females ≥ 18 years old affected by Hurley stage I and II HS	topical 15% resorcinol applied once daily	NR	12 weeks	IHS4 mean ± SD	T0: 3.9 ± 1.4 T4: 2.7 ± 1.4 T12: 3.3 ± 2.8	Selection N Ascertainment Y Causality Y Reporting Y
					Pain VAS	T0: 6.7 ± 1.8 T4: 1.9 ± 1.4 T12: 0.4 ± 0.7	
					DLQI	T0: 16.8 ± 4.8 T4: 6.0 ± 3.2 T12: 1.5 ± 2.1	
					Patients who achieved HiSCR, Hurley I: n (%)	T4:15 (62.5) T12: 22 (91.7)	
					Patients who achieved HiSCR, Hurley II: n (%)	T4:17 (45.9) T12: 30 (81.1)	
					AEs	Mild irritation: n=21 Desquamation: n=39 Reversible brown discoloration: n=25	
Pascual 2017[5] N=32	• Age, years [mean, (SD)]: 35.9 (12.2) • 10 M, 22 F • Smokers, n (%): 17 (53.1) • Overweight/obese, n (%): 25 (78.1) • Eighty-five out of 92 (92.4%) were Hurley II and 7 Hurley I	topical 15% resorcinol applied twice a day	NR	Median duration of lesion treated (IQR) [range], d 30.0 (10-132.5) [7-365]	Clinical resolution, n (%)	Day 7: 6 (18.8) Day 30: 27 (84.4)	Selection N Ascertainment Y Causality N Reporting Y
					Ultrasonographic resolution, n (%)	Day 7: 4 (12.5) Day 30: 21 (65.5)	
					Mean pain score on 10-cm VAS 6 SD	Baseline: 4.6 ± 3.2 Day 7: 1.8 ± 2.4 Day 30: 0.5 ± 1.4	

1. Boer J , Jemec GB. Resorcinol peels as a possible self-treatment of painful nodules in hidradenitis suppurativa. Clin Exp Dermatol 2010;35:36-40.
2. Cordero-Ramos J, Barros-Tornay R, Toledo-Pastrana T, Ferrándiz L, Calleja-Hernández MÁ , Moreno-Ramírez D. Effectiveness and safety of topical 15% resorcinol in the management of mild-to-moderate hidradenitis suppurativa: A cohort study. J Dermatol 2022;49:459-62.

3. Docampo-Simón A, Beltrá-Picó I, Sánchez-Pujol María J, Fuster-Ruiz-de-Apodaca R, Selva-Otaolaurruchi J, Betlloch I , Pascual José C. Topical 15% Resorcinol Is Associated with High Treatment Satisfaction in Patients with Mild to Moderate Hidradenitis Suppurativa. Dermatology 2021;238:82-5.
4. Molinelli E, Brisigotti V, Simonetti O, Campanati A, Sapigni C, D'Agostino GM et al. Efficacy and safety of topical resorcinol 15% as long-term treatment of mild-to-moderate hidradenitis suppurativa: a valid alternative to clindamycin in the panorama of antibiotic resistance. British Journal of Dermatology 2020;183:1117-9.
5. Pascual JC, Encabo B, Ruiz de Apodaca RF, Romero D, Selva J , Jemec GB. Topical 15% resorcinol for hidradenitis suppurativa: An uncontrolled prospective trial with clinical and ultrasonographic follow-up. J Am Acad Dermatol 2017;77:1175-8.

e-Table 8. Ruxolitinib cream vs placebo

Ruxolitinib compared to placebo for hidradenitis suppurativa[1]

Patient or population: Adults with Hurley stage I or II hidradenitis suppurativa
Intervention: ruxolitinib 1.5% cream bid for 16 weeks
Comparison: vehicle cream bid for 16 weeks

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with vehicle	**Risk with ruxolitinib**				
Change in NRS for pain follow-up: 16 weeks	The mean change in NRS for pain : **-2.09**	MD **0.19 higher** (1.24 lower to 1.62 higher)	-	69 (1 RCT)	⨁⨁◯◯ Low[a]	
Achieving HiSCR 50 follow-up: 16 weeks	914 per 1000	**704 per 1000** (558 to 896)	**RR 0.77** (0.61 to 0.98)	69 (1 RCT)	⨁⨁◯◯ Low[a]	
Change in IHS4 follow-up: 16 weeks	The mean change in IHS4: **-2.76**	MD **0.82 lower** (2.16 lower to 0.52 higher)	-	68 (1 RCT)	⨁⨁◯◯ Low[a]	
Treatment-emergent adverse events (TEAEs） follow-up: 16 weeks	429 per 1000	**384 per 1000** (194 to 618)	**OR 0.83** (0.32 to 2.16)	69 (1 RCT)	⨁⨁◯◯ Low[a]	
≥ Grade 3 TEAE follow-up: 16 weeks	57 per 1000	**11 per 1000** (1 to 203)	**OR 0.19** (0.01 to 4.20)	69 (1 RCT)	⨁⨁◯◯ Low[a]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **OR:** odds ratio; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two level due to imprecision: small sample size

1. Porter ML, Ferreira-Cornwell MC, Wang M, Nawaz H , Gooderham MJ. Efficacy and safety of ruxolitinib cream in patients with mild to moderate hidradenitis suppurativa: Results from a randomized, double-blind, vehicle-controlled phase 2 study. J Am Acad Dermatol 2025.

e-Table 9. Ruxolitinib Cream (non-comparative studies)

Open label trial n=1, 6 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The individual studies included very small sample sizes, increasing concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Schell 2025[1] Open-label trial N=6	-Mean age 33 y (range 23-44) -6F, 0M -	Topical ruxolitinib 1.5% twice daily for 16 weeks	Systemic maintenance medications	16 weeks	HiSCR50	5/6 (83.3%)	Moderate

1. Schell SL, Sennett ML, Feehan RP, Wallace TE, Meiszberg EC, Longenecker AL et al. Pilot study of topical ruxolitinib demonstrates efficacy and blunting of heterogeneous inflammatory processes in mild hidradenitis suppurativa. Br J Dermatol 2025;192:845-56.

Systemic Antibiotics Summary of Findings

Contents

Doxycycline

e-Table 10. Modified-release doxycycline vs regular-release doxycycline

Modified-release doxycycline (MR-DC) compared to regular-release doxycycline (RR-DC) for hidradenitis suppurativa

Patient or population: hidradenitis suppurativa
Intervention: Modified-release Doxycycline (MR-DC) 40 mg once daily for a period of 12 weeks
Comparison: Regular-release Doxycycline (RR-DC) 100 mg twice daily for a period of 12 weeks.

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with regular-release doxycycline (RR-DC)	**Risk with modified-release doxycycline (MR-DC)**				
Change in IHS4 follow-up: 12 weeks	The mean change in IHS4 was **-5.7**	MD **2 lower** (4.55 lower to 0.55 higher)	-	49 (1 RCT)[1]	⨁⨁◯◯ Low[a]	
Achieving HiSCR follow-up: 12 weeks	625 per 1000	**638 per 1000** (419 to 981)	**RR 1.02** (0.67 to 1.57)	49 (1 RCT)[1]	⨁⨁◯◯ Low[a]	
Change in DLQI Scale from: 0 to 30 follow-up: 12 weeks	The mean change in DLQI was **-4.4**	MD **0.2 lower** (3.19 lower to 2.79 higher)	-	49 (1 RCT)[1]	⨁⨁◯◯ Low[a]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two levels due to imprecision: small sample size

1. Kontochristopoulos G, Tsiogka A, Agiasofitou E, Kapsiocha A, Soulaidopoulos S, Liakou AI et al. Efficacy of Subantimicrobial, Modified-Release Doxycycline Compared to Regular-Release Doxycycline for the Treatment of Hidradenitis Suppurativa. Skin Appendage Disord 2022;8:476-81.

e-Table 11. Doxycycline monotherapy vs metformin combination therapy

Doxycycline compared to doxycycline + metformin for HS[1]

Patient or population: mild to moderate HS (age not reported)
Intervention: doxycycline 100 mg QD for 6 months
Comparison: doxycycline 100 mg QD + uptitrated from 500 mg to 1500 mg daily fro 6 months

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with doxycycline + metformin	**Risk with doxycycline**				
Change in IHS4 assessed with: change from baseline follow-up: 24 weeks	Median (IQR) change from baseline: Doxycycline -2 (-4.8 to -1.0) Doxycycline + metformin -3 (-4.5 to -1.0) p=0.596			57 (1 RCT)	⊕⊕◯◯ Low[a,b]	
HiSCR50 follow-up: 24 weeks	517 per 1,000	**248 per 1,000** (517 to 119)	**RR 0.48** (0.23 to 1.00)	57 (1 RCT)	⊕⊕◯◯ Low[a,c]	
Change in DLQI assessed with: 0 to 30 follow-up: 24 weeks	Median (IQR) change from baseline: Doxycycline -5 (-7.0 to 0.3) Doxycycline + metformin -5 (-10 to 0.0) p=0.485			57 (1 RCT)	⊕◯◯◯ Very low[a,d]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Variable missing data across outcomes, with up to 11 missing in the doxycycline monotherapy group vs 6 in the combination therapy group. While ITT approach was used, differential missingness could introduce bias, and the reasons for loss to follow up are not specified. Adverse events are mentioned as assessed but not reported. The scales/processes used to assess other reported outcomes are not cited or described (flares, pain, etc.).
b. The very small sample and wide, overlapping confidence intervals are concerning for precision, downgraded one level instead of two as study is "powered" for this outcome.
c. CI consistent with meaningful harm and no difference.
d. Very small sample; Wide, overlapping IQRs spanning from substantial improvement to minimal/no change in both arms; Effect estimates compatible with clinically important benefit or no benefit for either intervention.

1. Aarts P, Koerts NDK, van Huijstee JC, van der Zee HH, Driessen RJB, Horváth B et al. Metformin in conjunction with doxycycline is not superior to doxycycline monotherapy for hidradenitis suppurativa; results of a phase III double-blinded randomized placebo- controlled trial. Br J Dermatol 2025;193:1262-4.

Tetracycline

e-Table 12. Systemic tetracycline vs topical clindamycin

Oral tetracycline compared to topical clindamycin for hidradenitis suppurativa

Patient or population: hidradenitis suppurativa
Intervention: Oral tetracycline 500 mg twice daily for 16 weeks
Comparison: topical clindamycin phosphate 1% lotion twice daily for 16 weeks

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with topical clindamycin	Risk with oral tetracycline				
Change in pain VAS Scale from: 0 to 100 follow-up: 16 weeks	The mean change in pain VAS was **-18**	MD **2 higher** (47.38 lower to 51.38 higher)	-	34 (1 RCT)[1]	⨁◯◯◯ Very low[a,b]	
Change in physician Global Assessment VAS Scale from: 0 to 100 follow-up: 16 weeks	The mean change in physician Global Assessment VAS was **-17**	MD **5 higher** (14.02 lower to 24.02 higher)	-	34 (1 RCT)[1]	⨁◯◯◯ Very low[a,c]	
Adverse events follow-up: 16 weeks	227 per 1000	**125 per 1000** (34 to 464)	**RR 0.55** (0.15 to 2.04)	46 (1 RCT)[1]	⨁◯◯◯ Very low[a,d]	
Change in partient global assessment VAS Scale from: 0 to 100 follow-up: 16 weeks	The mean change in partient global assessment VAS was **-8**	MD **15 lower** (32.02 lower to 2.02 higher)	-	34 (1 RCT)[1]	⨁◯◯◯ Very low[a,c]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded due to high risk of bias
[b]Downgraded by two levels due to very serious imprecision (small sample size and The 95% CI crossed the MID of VAS30 (30% reduction = 8.4 in this trial).).
[c]Downgraded by two levels due to very serious imprecision small sample size.
[d]Downgraded by two levels due to very serious imprecision (small sample size and the ratio of the upper to the lower boundary of the CI was > 3).

1. Jemec GB , Wendelboe P. Topical clindamycin versus systemic tetracycline in the treatment of hidradenitis suppurativa. J Am Acad Dermatol 1998;39:971-4.

Doxycycline vs Tetracycline Vs Lymecycline

e-Table 13. Comparison of doxycycline, tetracycline, and lymecycline

Doxycline compared to lymecycline or tetracycline for HS[1]

Patient or population: HS Hurely stages I-III
Intervention: tetracycline 500 mg twice daily mean duration 4.3 months
Comparison: doxycycline 100 mg twice daily mean duration 4.3 months
Comparison: lymecycline 300 mg twice daily mean duration 4.3 months

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)
Hidradenitis Suppurativa Score (Sartorius) assessed with: Mean decrease in HSS score from baseline follow-up: mean 4.3 months	Tetracycline (n=32) 9.94 (3.03, 16.85) p=0.006Doxycycline (n=31) 6.23 (1.83, 10.62) p=0.007Lymecycline (n=45) 8.16 (4.32, 11.99) p<0.001 Between groups: p=0.609	(1 non-randomised study)	⨁◯◯◯ Very low[a]
Quality of life assessed with: Mean DLQI reduction from baseline follow-up: mean 4.3 months	Tetracycline (n=32) 2.7 (0.2, 5.3) p=0.038 Doxycycline (n=31) 1.4 (-1.2, 4.0) p=0.273 Lymecycline (n=45) 4.3 (2.2, 6.4) p<0.0001	(1 non-randomised study)	⨁◯◯◯ Very low[a]
Disease-related distress assessed with: Mean (SD) reduction in NRS distress score follow-up: mean 4.3 months	Tetracycline (n=32) 1.6 (0.5, 2.7)) p=0.007 Doxycycline (n=31) 1.9 (0.6, 3.2) p=0.005 Lymecycline (n=45) 2.1 (1.1, 3.1) p<0.0001	(1 non-randomised study)	⨁◯◯◯ Very low[a]
Adverse events follow-up: mean 4.3 months	Tetracycline 7/26 (26.9%) Doxycycline 8/19 (42.1%) Lymecycline 16/34 (24.4%) p=0.282	(1 non-randomised study)	⨁◯◯◯ Very low[a]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded 2 levels for imprecision: very small sample.

1. Jørgensen AHR, Yao Y, Thomsen SF , Ring HC. Treatment of hidradenitis suppurativa with tetracycline, doxycycline, or lymecycline: a prospective study. International Journal of Dermatology 2021;60:785-91.

Clindamycin & Rifampicin

e-Table 14. Clindamycin+rifampicin vs lymecycline

Clindamycin+rifampicin compared to lymecycline for HS[1]

Patient or population: moderate to severe HS
Intervention: clindamycin 600mg + rifampicin 600mg qd for 10 weeks
Comparison: lymecycline 300mg qd for 10 weeks

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with lymecycline	Risk with clinda+rifam				
HiSCR follow-up: 10 weeks	577 per 1,000	**540 per 1,000** (283 to 777)	**OR 0.86** (0.29 to 2.56)	52 (1 non-randomised study)	⊕◯◯◯ Very low[a]	
Disease re-lapse assessed with: HS flare follow-up: 10 weeks	769 per 1,000	**694 per 1,000** (388 to 885)	**OR 0.68** (0.19 to 2.32)	52 (1 non-randomised study)	⊕◯◯◯ Very low[a]	
Pain assessed with: Mean(SD) VAS 10 pain scores follow-up: 10 weeks	Clinda+rifam: 6.0(2.1) to 4.2(3.4)Lymecycline: 6.7(1.7) to 3.4(1.2)			52 (1 non-randomised study)	⊕◯◯◯ Very low[b]	
Quality of life assessed with: Mean(SD) DLQI score follow-up: 10 weeks	Clinda+rifam: 13.4(8.1) to 6.9(6.6) Lymecycline: 14.5(5.7) to 8.7(7.3)			52 (1 non-randomised study)	⊕◯◯◯ Very low[b]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **OR:** odds ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded 2 levels for imprecision: Wide CI consistent with equal benefit, harm and no difference; very small sample.
b. Downgraded 2 levels for imprecision: very small sample.

1. Caposiena Caro RD, Molinelli E, Brisigotti V, Offidani A , Bianchi L. Lymecycline vs. clindamycin plus rifampicin in hidradenitis suppurativa treatment: clinical and ultrasonography evaluation. Clinical and Experimental Dermatology 2021;46:96-102.

e-Table 15. Clindamycin & rifampicin (case series & non comparative cohort studies)

Case series/cohort studies n= 392 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The individual studies included small sample sizes, increasing

concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murrad tool
Bettoli 2021[1] Pilot study N=20	-Mean age 15.05 (range 10-16) -12F, 8M -Overweight/obese n=16/20 -Smokers n=4 -Hurley stage I n=5, II n=11, III n=4	600 mg daily of both clindamycin & rifampin for 10 wks	NR	10 weeks	Sartorius score mean reduction	52.8% (range 28.2-83.7)	Selection N Ascertainment Y Causality N Reporting Y
					Exacerbations (mean number)	3.6 (range 1-10)	
					Safety	3/20 experienced mild gastrointestinal side-effects	
Bettoli 2014[2] Prospective cohort N=23	-Mean age 37.52 (range 16-62) -16F, 7M -Mean BMI 28.59 -Smokers n=16/23	600 mg daily of both clindamycin & rifampin for 10 wks	NR	10 weeks	Sartorius score mean reduction	45.85% (range 5.41 to 81.95%)	Selection N Ascertainment Y Causality N Reporting Y
					Exacerbations (mean number)	6.00 (range 1-20)	
					Safety	3/23 experienced Aes : nausea, vomiting	
Dessinioti 2016[3] Prospective cohort N=26	-Mean age 34 -18F, 8M -Overweight/obese n=19 -Median disease duration 6.5yrs -Hurley stage I 15%, II 62%, III 23% -Previous treatments : topical n=3, systemic abx n=8, isotretinoin n=2, surgery n=2, multiple n=9	Oral clindamycin 600mg +rifampicin 600 mg qd for 12 weeks	None	12 weeks & 1 yr	Clinical response (≥50% improvement from baseline) at 12 wks	19/22 (73%)	Selection N Ascertainment Y Causality N Reporting N
					Recurrence at 1 year	10/17 (59%)	
					Adverse events at 12 wks	8/26(31%) ; diarrhea & vomiting	
					Discontinuation due to AE	1/26 (4%)	
Gener 2009[4] Retrospective cohort	- Mean age 33 - 85F, 31M - -Mean BMI 27 - Smokers n=92	Clindamycin 300 mg twice daily 600 my rifampicin for 10 weeks	NR	10 weeks	Sartorius score (median score baseline to week 10) n=70	29 → 14.5 p<0.001	Selection N Ascertainment Y Causality N Reporting Y

N=116	- -Median Sartorius score 28				Pain score (median mx VAS score at baseline to week 10) n=70	7→3 p<0.001	
					Complete remission (Sartorius score=0)	8/70 (11%)	
					Safety	10/70 had Aes 8/70 discontinued due to AE	
Mendonça 2006 [5] case series N = 14	- Age (year, mean, SD): 40, 13.3) - 9 F, 5 M - Duration of disease (year, mean, SD): 10.5, 8.5 - Previous treatments, n (%): - Erythromycine: 8 (50%) - Minocycline: 3 (21%) - Co-cyprindiol: 2 (14%) - Flucloxacillin: 3 (21%) - Lymecycline: 1 (7%) - Penicillin: 1 (7%) - Isotretinoin: 4 (29%) - Oxytetracycline: 1 (7%) - Topical clindamycin: 2 (14%) - Ampicillin: 1 (7%) - Excision: 1 (7%) - Cefalexin: 1 (7%) - Mean BMI: NR - Hurley I n=9, II n=5, III n=3 - Baseline severity : NR - Baseline DLQI score : NR Smoking status: NR	rifampicin 300 mg twice daily and clindamycin 300 mg twice daily	NR	NR Treatment length: 10 weeks	Complete remission	N = 10/14 (71.4%)	Selection N Ascertainment N Causality N Reporting N

Van der Zee 2009[6] Case series N=34	-Mean age 39.9 -29F, 5M -Hurley stage I n=4, II n=20, III n=10 -Mean disease duration 17.8yr -Previous treatments :Oral antibiotics 23 (67.6) Surgery 22 (64.7) Isotretinoin 12 (35.3) Resorcinol 10 (29.4) Topical antibiotics 9 (26.5) Acitretin 3 (8.8) Infliximab 1 (2.9) Prednisone 1 (2.9)	Oral clindamycin+rifampicin -5 different dsing régimes used with clindamycin 300 mg twice daily and rifampicin 300 mg twice daily for 10 weeks most common	NR	10 weeks	Total remission at ≥10 weeks (undefined)	10/21 (47.6%)	Selection N Ascertainment Y Causality N Reporting N
					Adverse events	13/34 (38.2%), diarrhea most common	
					Discontinuation due to AE	9/34(26%)	
Van Straalen 2021[7] Prospective cohort N=103	-Median age 36 [IQR 27-45] -56F, 47M -BMI 29.21 -Smoker 56/103 -Hurely stage I n=14, II n=58, III n=31	clindamycin 300 mg twice daily + rifampicin 600 mg a day for 12 weeks	None (topical therapy allowed but not recorded)	12 weeks	HiSCR	40/83 (48.2%)	Selection N Ascertainment Y Causality N Reporting Y
					DLQI ≥4 point reduction from baseline	44/93 (47.3%)	
					NRS Pain (≥30% and ≥1 point reduction from baseline)	51/80 (63.8%)	
					Safety	10/103 GI AEs 16/101 discontinued due to AE	
Yao 2021[8] Prospective cohort N=56	-Mean age 39.1 -31F, 25M	clindamycin 300 mg + rifampicin 300 mg twice daily for 6 months	Topical therapies allowed	6 months	Median HSS change from baseline	35.5 →23.5 p< 0.001	Selection N Ascertainment Y Causality N Reporting Y
					Median DLQI change from baseline	14.5 → 10.0 p<0.001	
					PGA cateogries at 6 months	Clear n=9 Large improvement n=12 Small improvement n=12 Unchanged n=17 Worsened n=4	

					Safety	30/56 had side effects ; 5/56 discontinued due to AE	

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Ertapenem

e-Table 16. Ertapenem (case series & non-comparative cohort studies)

Case series/cohort studies n=4, 179 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control groups and randomization. The individual studies included very small samples, increasing concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of Bias

Braunberger 2018[1] Retrospective Case series N=36	-Mean age 43 -Mean BMI 35 -Hurely stages II (n = 5)III (n = 28) Unknown (n = 3) -Previous treatments : Adalimumab (n = 7), infliximab (n = 6), infliximab and adalimumab (n = 3)	Ertapenem via PICC IV Mean duration 59.1 days	Benzoyl peroxide wash or hibiclens (n = 17), topical antibiotics (n = 15), prednisone (n = 5), biologics (n = 4), systemic antibiotics (n = 4), spironolactone (n = 3), topical silver nitrate (n = 1), nystatin powder (n = 1)	NR	Disease improvement via patient evaluation (undefined)	35/36 (97.2%) reported improvement	Selection N Ascertainment N Causality N Reporting Y
					Improvement in pain via pain report (undefined)	Moderate improvement 11/36 Significant improvement 12/36	
					Adverse events	PICC line thrombosis (n = 4) diarrhea or loose stools (n = 4), vaginitis (n = 3), vaginal discharge (n = 2), elevated liver transaminases (n = 1), Clostridium difficile colitis (n = 1), nausea (n = 1), and worsening of pre-existing depression (n = 1)	
Joint-Lambert 2016[2] Retrospective Case series N=30	-Mean age 34 -Mean BMI26.3 -Hurkey stages : I (n = 2) II (n = 11) III (n = 8) Unknown (n = 9) -Previous treatment : Antibiotics (n = 30), wide surgery (n = 21), NSAIDs (n = 14), biologics (n = 2), systemic steroids (n = 4), topical steroids (n = 1), tacrolimus, steroids, and mycophenolate mofetil for kidney transplant (n = 1)	Eratpenem via PICC IV (n=29) or peripheral catheter (n=1) for 6 weeks	None	6 weeks	Median(IQR) Sartorius score	Baseline: 49.5 (28–62) 6 weeks: 19.0 (12–28) (p<0.0001)	Selection N Ascertainment N Causality N Reporting Y
					Median (IQR) VAS 10 for pain	Baseline : 6 (5–8) 6 weeks : 0 (0–2) (p<0.0001)	
					Adverse events	Oral and vaginal candidiasis (n = 8), transient abdominal pain or diarrhea (n = 6), minor headaches during infusions (n = 4) and asthenia (n = 5), lymphangitis (n = 1)	
Nosrati 2024[3] Retrospective case series N=98	-Mean age 35.8 -BMI 33.2 -Hurley stage NR -Previous treatments NR	Ertapenem via PICC IV Mean duration 13.1 weeks	Topical antibiotics (n = 97), spironolactone (n = 44), finasteride (n = 31), oral contraceptive pill	Mean 13.1 weeks	Mean(SD) HS Physician Global Assessment scores (6-point scale clear to very severe)	Baseline: 3.9 (1.0) Post-treatment: 2.7 (1.2) (p<0.001)	Selection N Ascertainment N Causality N Reporting Y
					Mean(SD) NRS pain scores (0-10 ; no pain to worst possible pain)	Baseline : 4.2 (3.3) Post-treatment : 1.8 (2.7) (p<0.001)	

			(n = 25), infliximab (n = 78), adalimumab (n = 9), surgery during course of ertapenem (n = 2)		Adverse events	Diarrhea (n = 8), nausea (n = 5), headaches (n = 2), candidiasis (n = 1), syncope (n = 1), dermatitis from PICC adhesives (n = 7), PICC-line associated infections (n = 2)	
Segura Palacios 2023[4] Case series N=15	-Median age 51 -Median BMI 30.1 -Hurley stage:II (n = 3) III (n = 15) -Previous treatments: Adalimumab (n = 14), 2 or 3 biologics (n = 8)	Ertapenem Intramuscular n=9 via IV n=5, both n=1 For 6 weeks	None	6 weeks	Median IHS4 score	Baseline 28 6 weeks: 18 P=0.008	Selection N Ascertainment N Causality N Reporting N
					Median VAS 10 pain score	Baseline : 9 6 weeks : 2 P=0.004	
					Adverse events	0/15	

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Clindamycin Monotherapy

e-Table 17. Clindamycin monotherapy vs clindamycin & rifampicin

Clindamycin compared to Clindamycin + rifampicin for mild to moderate HS[1]

Patient or population: Adults with mild to moderate HS
Intervention: oral clindamycin, 150 mg 4 times a day for 8 weeks
Comparison: oral clindamycin, 150 mg 4 times a day, plus oral rifampicin, 300 mg 2 times a day for 8 weeks

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Clindamycin + rifampicin	Risk with Clindamycin				
HiSCR assessed with: proportion of patients achieving HiSCR follow-up: 8 weeks	567 per 1,000	**635 per 1,000** (419 to 958)	**RR 1.12** (0.74 to 1.69)	60 (1 non-randomised study)	⨁◯◯◯ Very low[a]	

Clindamycin compared to Clindamycin + rifampicin for mild to moderate HS[1]

Patient or population: Adults with mild to moderate HS
Intervention: oral clindamycin, 150 mg 4 times a day for 8 weeks
Comparison: oral clindamycin, 150 mg 4 times a day, plus oral rifampicin, 300 mg 2 times a day for 8 weeks

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Clindamycin + rifampicin	Risk with Clindamycin				
Recurrence assessed with: Average disease-free survival in weeks follow-up: 1 years	Mean disease-free survival was **12.4 weeks**	MD **0.8 weeks more** (4.27 fewer to 5.87 more)	-	60 (1 non-randomised study)	⨁◯◯◯ Very low[b]	
Pain assessed with: Average VAS 10 pain score post-treatment follow-up: 8 weeks	The mean pain was **4.2**	MD **1.7 lower** (3.57 lower to 0.17 higher)	-	60 (1 non-randomised study)	⨁◯◯◯ Very low[c]	
Quality of Life assessed with: Average DLQI score post-treatment follow-up: 8 weeks	The mean DLQI was **9.9**	MD **1.7 lower** (6.82 lower to 3.42 higher)	-	60 (1 non-randomised study)	⨁◯◯◯ Very low[d]	
Serious adverse events assessed with: proportion of patients experiencing the event follow-up: 8 weeks	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	60 (1 non-randomised study)	⨁◯◯◯ Very low[e]	
Adverse event: diarrhea assessed with: proportion of patients experiencing the event follow-up: 8 weeks	200 per 1,000	**134 per 1,000** (42 to 426)	**RR 0.67** (0.21 to 2.13)	60 (1 non-randomised study)	⨁◯◯◯ Very low[b]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded one level for imprecision: CI consistent with meaningful benefit and trivial harm (based on MID of 25%).
b. Downgraded two levels for imprecision: CI consistent with large benefit and large harm.
c. Downgraded one level for imprecision: CI consistent with meaningful benefit and trivial difference (MID 30% difference)
d. Downgraded one level for imprecision: CI consistent with meaningful benefit and no important difference (MID 4 units).
e. Downgraded two levels for imprecision: the number of events is 0 in a very small sample the CI around the effect estimate would be too wide to exclude important harms or benefits.

1. Caposiena Caro RD, Cannizzaro MV, Botti E, Di Raimondo C, Di Matteo E, Gaziano R , Bianchi L. Clindamycin versus clindamycin plus rifampicin in hidradenitis suppurativa treatment: Clinical and ultrasound observations. Journal of the American Academy of Dermatology 2019;80:1314-21.

e-Table 18. Clindamycin monotherapy (case series & non comparative cohort studies)

Non-comparative cohort studies n=2, 65 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from single cohort studies, which are inherently limited due to the lack of control groups. The individual studies included very small sample sizes, increasing concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murrad tool
An 2021[1] Retrospective cohort N=34	-19F, 34M -Mean age 28.64 years (range 14-56) -Smokers n=9 -Mean BMI 26.66 -Hurley Stage I n=4, II n=15, III n=34 *Demographics of entire cohort only 34/53 had outcome data.	Clindamycin monotherapy for 10 weeks (dose not reported)	None	8 weeks	HiSCR at wk 8	21/34 (61.76%)	Selection N Ascertainment Y Causality N Reporting Y
					HS-PGA mean score change from baseline n=34	3.24→2.15, p=0.001	
					Safety	14/53 had an AE ; 9/53 discontinued due to AE 12/53 diarrhea	
Rosi 2018[2] Retrospective cohort N=31	-Mean age 32.3 -22F, 9M -Mean BMI 26.9 -Smokers n=20 -Hurely stage I n=13, II n=15, III n=3	300 mg clindamycin bid for 12 weeks	None	12 weeks	HS-PGS (median score from baseline to week 12)	4 → 3 p< 0.01	Selection N Ascertainment Y Causality N Reporting Y
					VAS pain (median score from baseline to week 12)	8 → 5 p< 0.01	
					Safety	3/31 diarrhea	

1. An JH, Moon SJ, Shin JU, Kim DH, Yoon MS , Lee HJ. Clindamycin Mono-Therapy of Hidradenitis Suppurativa Patients: A Single-Center Retrospective Study. Ann Dermatol 2021;33:515-21.
2. Rosi E, Pescitelli L, Ricceri F, Di Cesare A, Novelli A, Pimpinelli N , Prignano F. Clindamycin as unique antibiotic choice in Hidradenitis Suppurativa. Dermatol Ther 2019;32:e12792.

Ofloxacin + Clindamycin

e-Table 19. Ofloxacin + clindamycin (case series)

Case series n=1, 65 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from a single case series is inherently limited due to the lack of control group and randomization. The study sample is very small, increasing concern about random error and imprecision.

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murrad tool
Delaunay 2018[1] Case series N=65	-Age NR -37F, 28M -Mean duration of disease 14.8yrs -Hurley stage I n=21, II n=21, III n=23 -Previous antibiotics n=38	Ofoxacin 200 or 400 mg + clidamycin 600-1800mg adapted to patients' weight Mean duration 4.3 months (range 1-20)	NR	NR	Complete clinical response (no flares) during treatment	25/65 (34%)	Selection N Ascertainment Y Causality N Reporting N
					Mean reduction in flares	84%	
					Adverse events	18/65 (28%)	
					Discontinuation due to AE	11/65 (16.9%)	

1. Delaunay J, Villani AP, Guillem P, Tristan A, Boibieux A , Jullien D. Oral ofloxacin and clindamycin as an alternative to the classic rifampicin–clindamycin in hidradenitis suppurativa: retrospective analysis of 65 patients. British Journal of Dermatology 2018;178:e15-e6.

Dapsone

e-Table 20. Dapsone (case series)

Case series Dapsone n=5, 226 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control group. Most individual studies included very small sample sizes, increasing concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murrad tool
Baroudi 2023[1] Monocentric retrospective case series N=19	- Age (year, range): 42 range 17-59 - 13 F, 6 M - Previous treatments: n =8 antibiotics, isotretinoin, adalimumab, etanercept, methotrexate, spironolactone - Mean BMI: 36 range 27.1-46.2 - Hurley II n=2, III n=17 - Smoking status: current smokers n=8	Dapsone 25 to 100 mg per day	spironolactone n=4, adalimumab n=6, atb n=5, isotretinoin n=1, prednisolone n=2, methotrexate n=1	NR Mean treatment duration 9.6 months	physician assessment no specific scale or instrument used no definition	-clinically significant improvement n=3 -slight improvement n=10 -no change n=6	Selection Y Ascertainment N Causality N Reporting N
					Safety	Nausea, fatigue n=4	
Lopez-Llunell 2021[2] Monocentric retrospective case series N=56	- Age (year, median (IQR): 33.0 (23.0–43.0) - M 37 F 19 - Age at onset (year, median, IQR): 17.0 (15.0–21.0) - Previous treatments: oral antibiotics, isotretinoin, surgery, colchicine - BMI Median (IQR): 29.1 (25.1–32.6) - Hurley I n=30 (53.6%)II n=13 (23.2%) III n=13 (23.2%) - Smokers n= 35 (62.5%)	50 mg daily. at least 4 weeks, then was titrated up to 150 mg, according to the treatment response and tolerability	isotretinoin n=1, acitretin n=3	Week 12 Median duration of treatment was 8 months (IQR, 3–14)	HiSCR therapeutic objective	62.5% (35/56)	Selection N Ascertainment Y Causality N Reporting Y
					IHS4	4.0 (1.0–10.0)	
					Safety	28.6% of patients Most frequent: anemia, nausea, diarrhea, headache. Withdrawal for AE n=5	

Yazdanyar 2011[3] Retrospective case series N=24	- Age: 44.1 years (range: 27–64) - 22 F, 2 H - Duration of disease (year): 20.2 (n=21) - Previous treatments, n: NR - Obesity: n=17 - Hurley I n=8, II n=12, III n=4 - Smoker n=19	Dapsone 50mg/j n=2 100mg/j n=20 100-200 mg/j n= 21	NR	NR Mean treatment duration 4.4 months (range 0.5-48)	Physician assessment no specific outcome	-Clinically significant improvement n=6 -Slight improvement n=3 -No change n=13 -Deterioration n=2	Selection N Ascertainment N Causality N Reporting Y
					Safety	9 pts experienced AE: Nausea n=3 Dizzy n=2 Headache n= 2 Anemia n=2 Tired n=3 2 withdrawals because of AE	
Kaur 2006[4] Retrospective case series N=5	- Age (year, mean, SD): 49 range 37-73) - 3 F, 2 H - Previous systemic treatments: oral ATB n=5, isotretinoin n=5, prednisolone n=3 - Mean BMI: NR - Baseline disease severity: NR - Smoking status, n (%): NR	Dapsone dose range 25-150)	no concomitant treatment	NR Mean treatment duration 24 months	no specified outcome	improvement in disease activity, n=5	Selection N Ascertainment N Causality N Reporting Y
					Safety	Hemolysis, n=2	
Steyn 2023[5] Retrospective chart review N=122	- Age mean 36 years (SD 11) -99F, 23M -Mean Hurley stage 2 (SD 1) -Most moderate to severe disease -Mean BMI 33.7 (SD 8) -Smoker 50 (41%)	Dapsone mean dose 1.04 mg/kg-1; n=69 received sub-therapeutic doses	N=57 concomitant pharmacologic interventions; N=32 had surgery during treatment	Mean 14 months: n=91 3 months; n=46 12 months; n=20 24 months	HSPGA improvement	Average improvement of one severity category by 3 months (p<0.01)	Selection N Ascertainment N Causality N Reporting Y
					DLQI change	Mean 4-point improvment by 6 months (19 to 15, p<0.01)	
					Adverse events	N=52 discontinued due to AEs (n=28) & lack of efficacy (n=24 ; Headache (n=5) ; « feeling	

						unwell » n=7 ; blood count abnormalities n=9 ; mood changes n=4 ; shortness of breath n=3 ; hypersensitivity n=2	

NR: Not reported; NA: Not applicable

1. Baroudi B, Bashyam AM, Feldman SR , Pichardo RO. Dapsone to Treat Moderate-to-Severe Hidradenitis Suppurativa: A Retrospective Case-Series. J Drugs Dermatol 2023;22:e12-e6.
2. López-Llunell C, Riera-Martí N, Gamissans M , Romaní J. Dapsone in hidradenitis suppurativa: A case series of 56 patients. Dermatol Ther 2021;34:e15161.
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5. Steyn M, Ayis S, O'Connor J, Lakhan MK, Ferguson F, Shah A , Rashidghamat E. Dapsone therapy for hidradenitis suppurativa: a retrospective review of characteristics and treatment outcomes in a cohort of 122 patients in a tertiary dermatology setting. Br J Dermatol 2023;188:573-4.

Dalbavancin

e-Table 21. Dalbavancin (case series)

Case series n=1, 8 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from a single case series is inherently limited due to the lack of control group. The study sample is very small, increasing concern about random error and imprecision.

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of Bias
Molinelli 2022[1] Case series N=8	•Age range 17-59 •6F •Moderate to severe HS with frequent exacerbations	100mg dalbavancin IV slow infusion	Adalimumab n=3	12 & 24 weeks	HiSCR	12wks : 6/8 (75%) 24wks :3/8(37.5%)	Selection N Ascertainment N Causality N Reporting Y
					Mean pain VAS 10 score	Baseline 8 12wk 2 24wks 3	
					Mean DLQI score	Baseline 26 12wk 8 24wks 10	

					Mean Disease free survival at 24 wks	15 wks	

1. Molinelli E, Sapigni C, D'Agostino GM, Brisigotti V, Rizzetto G, Bobyr I et al. The Effect of Dalbavancin in Moderate to Severe Hidradenitis Suppurativa. Antibiotics (Basel) 2022;11.

Comparison of multiple antibiotic & procedural interventions

e-Table 22. Doxycycline; clindamycin and rifampicin; laser; deroofing; and conventional surgery (cohort)

Cohort n=1, 149 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from a single non-randomized, uncontrolled cohort study which is inherently limited due to the lack of control group and randomization. The study sample is very small, increasing concern about random error and imprecision.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	GRADE
Ingram 2024[1] Cohort N = 149	Age (year, mean (SD)): 36 (10.5) 121 F, 28 H Duration of disease (year, mean): NR Previous treatments, n(%): - Tetracycline: 39 (26.4)	- oral doxycycline 200 mg /d - oral clindamycin	NR	36 weeks (6 months) Follow-up: 12 months	HiSCR, n (%), 50% or more reduction in inflammatory lesion count	at 6 months - Doxycycline: 6/19 (31.6) - Clindamycin & rifampicin: 6/18 (33.3)	**Very Low Certainty** • **Risk of bias** -Serious • **Inconsistency** -NA

	- Clindamycin: 19 (12.8) - Rifampicin: 16 (10.8) - Other oral antibiotic: 47 (32.0) - Dapsone: 1 (0.7) - Isotretinoin: 3 (2.0) - Etanercept: 1 (0.7) - Infliximab: 1 (0.7) - Anakinra: 1 (0.7) - Other biologic 1 (0.7) • Mean BMI (SD): 33.0 (7.9) • Hurley I, n = 19, Hurley II, n = 102, Hurley III n = 28 • IHS4, median (IQR) 11 (4–21) • Smoking status: o current smokers n = 63 o former smokers n = 32	and rifampicin, both 300 mg X2 /d 10 weeks - laser treatment targeting the hair follicle (Nd: YAG, diode or alexandrite) - deroofing - conventional surgery with the procedure and closure method determined by the operating surgeon			and no increase in abscesses or draining tunnels between each review and baseline	- Laser: 11/33 (33.3) - Deroofing: 11/30 (36.7) - Conventional surgery: 1/7 (14.3) Number analysed: 107	• **Indirectness** -Serious • **Imprecision** -Serious • **Publication bias** -Serious • **Large effect** -No • **Plausible confounding** -Would reduce demonstrated effect • **Dose response gradient** -No
					DLQI (Median (IQR) change	Change from baseline to 6 months - Doxycycline: -2 (-6, 0) - Clindamycin & rifampicin: -6.5 (-12, -2) - Laser: -3 (-11, 0) - Deroofing: 0 (-7, 2) Conventional surgery: -2.5 (-9, 0) Number analysed: 119	
					Patient Global Assessment (PtGA, answers on a 5-point Likert	Change from baseline to 6 months - Doxycycline: -1 (-1, 0)	

					scale) (Median (IQR) change	- Clindamycin & rifampicin: -1 (-2, 0) - Laser: -0.5 (-1, 0) - Deroofing: 0 (-1, 1) Conventional surgery: 1 (-2, 2) Number analysed: 96	
					Adverse events	At 12 months follow up - Doxycycline: N = 9 - Clindamycin & rifampicin: N = 12 - Laser: N = 3 - Deroofing: N = 12 Conventional surgery: N = 1 Number analysed:NR	
					Serious adverse events	At 12 months follow up N = 0 Number analysed:NR	

1. Ingram JR, Bates J, Cannings-John R, Collier F, Evans J, Gibbons A et al. Treatment of Hidradenitis Suppurativa Evaluation Study (THESEUS): a prospective cohort study. Br J Dermatol 2024;190:382-91.

Systemic Antibiotic Combination Therapies

e-Table 23. Systemic antibiotic combination therapies (case series)

Case series/cohort studies n=4, 91 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control group. The individual studies included very small sample sizes, increasing concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Armyra 2017[1] Prosepctive case series N=20	-Age range 21-61 -10F, 10M -Disease duration 1-21 yrs -Hurely stage I n=1 II n=14, III n=4	Oral minocycline 100mg qd +0.5 mg of colchicine bid for 6 mos. Maintenance : 0.5mg colchicine bid for 3 mos	None	3, 6, 9 mos	Physician's global assessment of excellent/good	3mos : 13/20 (65%) 6mos : 17/20 (85%) 9mos : 19/20 (95%)	Selection N Ascertainment Y Causality N Reporting N
					Adverse events	3/20 (15%)	
Delage 2023[2] Monocentric prospective case series N = 28	- Age (year, median (IQR)): 31.5 (25-41) - 21 F, 7 M - Duration of disease (year, median (IQR)): 14.5 (9.5-23) - Previous treatments, n (%) • Antibiotics : 25 (89) • Rifampicin-clindamycin : 8 (29) • Pristinamycin : 14 (50) • Tetracycline : 11 (39) • nonsteroidal anti-inflammatory drugs: 23 (82) - Mean BMI, median (IQR): 26 (21-29) - Baseline Sartorius score, median (IQR) : 14 (12-19)	<u>induction</u> • 6 weeks rifampicin (10 mg/kg /d, moxifloxacin (400 mg /d), metronidazole (500 mg 3 time/d, half dosing < 60 kg), • 4 weeks rifampicin + moxifloxacin <u>maintenance</u> cotrimoxazole (400 mg/d or 800	NR	12 weeks. 52 weeks Maintenance: 1 year Relapse: 3 weeks	Sartorius Score, week 12	At week 12: Median = 0 (0-2) At week 52: Median = 0 (0-9)	Selection N Ascertainment Y Causality N Reporting Y
					Pain (VAS)	Week 12: Median = 0 (0-1) Week 52: Median = 0 (0-2)	

	- Skindex France score, median (IQR) : 93 (78-115) - Smoking status: current smokers n=26	mg/d if > 90kg) or doxycycline (200 mg /d) <u>flare</u> pristinamycin 1 gX3 /d for 3 weeks. If did not regress after a week, metronidazole added for 2 weeks.			Number of flares/year Week 52	Median = 1 (0-16)	
Molinelli 2023[3] Rospective case series N=15	- Mean age 42.3 - 4F, 11M - Mean disease duration 20 years - Hurley stage II n=13, III n=2 - -Previous treatments :Tetracyclines 11 (73.3) Rifampicin/clindamycin 11 (73.3) Oral zinc 5 (33) Isotretinoin 5 (33) Adalimumab 4 (26.7) Golimumab 1 (7)"	azithromycin 500 mg daily for 3 consecutive days for 4 weeks and concomitant acitretin 25– 35 mg (mean 0.44 mg/kg/day) once daily as maintenance therapy after the combination treatment	None	6 months	Mean(SD) IHS4 score	Baseline : 8(2.9) 8wks : 4.6(2.6) 24wks : 3.3(3.7)	Selection N Ascertainment Y Causality N Reporting Y
					Mean(SD) VAS10 pain scores	Baseline : 6.0(1.95) 8wks : 2.1(1.3) 24wks : 0.8(1.1)	
					Mean(SD) DLQI score	Baseline : 16(5.7) 8wk : 4.4(3) 24wk : 2.6(5.7)	
					Adverse events with azithromycin	2/15 (13.3%) GI issues	
Join-Lambert 2011[4] Retrospective case series N=28	- Median age 30 - -20F, 8M - Median disease duration 13.5yrs - Hurley stages I n=6, II n=10, III n=12 - Refractory disease	rifampin 10 mg/kg once daily, moxifloxacin 400 mg daily, and metronidazole 500 mg three times daily for 6	secondary prophylaxis consisting in trimethoprim-sulfamethoxazole (400 mg/80 mg daily) or	2-12 months	Complete remission (absence of any persisting active clinical lesions)	16/28 (57%)	Selection N Ascertainment Y Causality N Reporting Y
					Flare in those with complete remission	7/14 (50%)	

	- Previous treatments: antibiotics 93%, drainage 86%, wide excision 35%	weeks, then metronidazole stopped	doxycycline (100 mg/day)		Adverse events	18/28 (64%) GI issues	

1. Armyra K, Kouris A, Markantoni V, Katsambas A , Kontochristopoulos G. Hidradenitis suppurativa treated with tetracycline in combination with colchicine: a prospective series of 20 patients. Int J Dermatol 2017;56:346-50.
2. Delage M, Jais JP, Lam T, Guet-Revillet H, Ungeheuer MN, Consigny PH et al. Rifampin-moxifloxacin-metronidazole combination therapy for severe Hurley stage 1 hidradenitis suppurativa: prospective short-term trial and 1-year follow-up in 28 consecutive patients. J Am Acad Dermatol 2023;88:94-100.
3. Molinelli E, Sapigni C, Simonetti O, D'Agostino GM, Brisigotti V, Rizzetto G , Offidani A. Acitretin plus macrolides and acitretin monotherapy in the management of hidradenitis suppurativa. Journal of the European Academy of Dermatology and Venereology 2023;37:e392-e4.
4. Join-Lambert O, Coignard H, Jais J-P, Guet-Revillet H, Poirée S, Fraitag S et al. Efficacy of Rifampin-Moxifloxacin-Metronidazole Combination Therapy in Hidradenitis Suppurativa. Dermatology 2010;222:49-58.

e-Table 24. Hyperbaric oxygen plus clindamycin & rifampicin vs clindamycin & rifampicin

Hyperbaric oxygen plus clindamycin & rifampicin compared to clindamycin & rifampicin for hidradenitis suppurativa

Patient or population: hidradenitis suppurativa
Intervention: Clindamycin 300mg + Rifampicin 300mg twice daily, plus hyperbaric oxygen therapy 20 sessions 5 days/week for 4 weeks (2.4 atmospheres for 3 periods of 25 mins in each session)
Comparison: Clindamycin 300mg + Rifampicin 300mg twice daily for 10 weeks

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with clindamycin & rifampicin	Risk with hyperbaric oxygen plus clindamycin & rifampicin				
Achieving pain VAS50 follow-up: 10 weeks	714 per 1000	**993 per 1000** (750 to 1000)	**RR 1.39** (1.05 to 1.83)	43 (1 RCT) [1]	⨁⨁◯◯ Low[a,b]	
Change in pain VAS Scale from: 0 to 10 follow-up: 10 weeks	The mean change in pain VAS was **-4.19**	MD **1.62 lower** (2.7 lower to 0.54 lower)	-	43 (1 RCT) [1]	⨁⨁◯◯ Low[a,c]	
Achieving DLQI 50 follow-up: 10 weeks	619 per 1000	**953 per 1000** (675 to 1000)	**RR 1.54** (1.09 to 2.18)	43 (1 RCT)[1]	⨁⨁◯◯ Low[a,b]	
Change in DLOI at week 10 Scale from: 0 to 30 follow-up: 10 weeks	mean change in DLOI **-9.28**	MD **3.49 lower** (7.31 lower to 0.33 higher)	-	43 (1 RCT)[1]	⨁⨁◯◯ Low[a,d]	
Achieving Hidradenitis Suppurativa Severity Index (HSSI) 50 for pain follow-up: 10 weeks	714 per 1000	**993 per 1000** (750 to 1000)	**RR 1.39** (1.05 to 1.83)	43 (1 RCT)[1]	⨁⨁◯◯ Low[a,b]	

Hyperbaric oxygen plus clindamycin & rifampicin compared to clindamycin & rifampicin for hidradenitis suppurativa

Patient or population: hidradenitis suppurativa
Intervention: Clindamycin 300mg + Rifampicin 300mg twice daily, plus hyperbaric oxygen therapy 20 sessions 5 days/week for 4 weeks (2.4 atmospheres for 3 periods of 25 mins in each session)
Comparison: Clindamycin 300mg + Rifampicin 300mg twice daily for 10 weeks

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with clindamycin & rifampicin	**Risk with hyperbaric oxygen plus clindamycin & rifampicin**				
Change in Hidradenitis Suppurativa Severity Index (HSSI) Scale from: 0 to 9 follow-up: 10 weeks	mean change in HSSI: **-8.57**	MD **1.66 lower** (3.92 lower to 0.6 higher)	-	43 (1 RCT)[1]	⨁◯◯◯ Very low[a,e]	
Achieving modified Sartorius scale follow-up: 10 weeks	762 per 1000	**990 per 1000** (777 to 1000)	**RR 1.30** (1.02 to 1.67)	43 (1 RCT)[1]	⨁⨁◯◯ Low[a,b]	
Change in Modified Sartorius score at week 10 follow-up: 10 weeks	mean change in Modified Sartorius score: **-10.26**	MD **3.3 lower** (8.63 lower to 2.03 higher)	-	43 (1 RCT)[1]	⨁◯◯◯ Very low[a,e]	
Serious adverse events follow-up: 10 weeks	0 per 1000	**0 per 1000** (0 to 0)	Not estimable	43 (1 RCT)[1]	⨁◯◯◯ Very low[a,f]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded due to high risk of bias
[b]Downgraded by one level due to serious imprecision: The 95% CI crossed either the conventional upper or lower threshold of MID (0.75 or 1.25).
[c]Downgraded by one level due to serious imprecision: The 95% CI crossed the MID of VAS30 (30% reduction = 2 in this trial).
[d]Downgraded by one level due to serious imprecision: The 95% CI crossed the MID of 4 for DLQI.
[e]Downgraded by two levels due to very serious imprecision small sample size.
[f]Downgraded by two levels due to very serious imprecision: zero events with small sample size.

1. Yildiz H, Senol L, Ercan E, Bilgili ME , Karabudak Abuaf O. A prospective randomized controlled trial assessing the efficacy of adjunctive hyperbaric oxygen therapy in the treatment of hidradenitis suppurativa. Int J Dermatol 2016;55:232-7.

Hormonal Medications & Oral Retinoids Summary of Findings

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Hormonal Medications

e-Table 25. Spironolactone

Case series, n=5, 323 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series/retrospective cohorts, which are inherently limited due to the lack of control groups and randomization. The individual studies primarily included small sample sizes, increasing concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murrad tool
Lee 2015[1] Monocentric retrospective case series N=20	• Age (year, mean): 31.7, range 14-59 • 20 F, 0 M • Previous treatments: antibiotic therapy, n=11, antivirals, n=2, isotretinoin, n=1, antifungal, n=1 • Obesity: n=8 • Baseline disease severity: mild n=5 • moderate n=12, severe n=3 • Smoking status: n=4	Spironolactone: • 100 mg /d, n=18 • 125 mg/d, n=1 • 150mg/d, n=1	• minocycline 100 mg daily, n=5 • oral contraceptive pill, n=9	3-months Mean follow-up: 23.2 months, range 4-54	PGA	• Severe to moderate, n=2 • Severe to mild, n=1 • Moderate to clear, n=7 • Moderate to mild, n=3 • Moderate to moderate, n=2 • Mild to clear, n=4 • Mild to mild, n=1	Selection N Ascertainment Y Causality N Reporting Y
					Safety	Mood and dizziness, n=1	
Golbari 2019[2] retrospective single-center chart review	• Age (year, mean): 35.1, SD 10.3 • Age at disease onset (year, mean): 21.4, SD 10.1	Spironolactone: • Average dose 75mg/d Patients categorized by <75mg/d (n=25) or	• Tetracyclines (n=14) • Clindamycin and rifampin (n=1) • Clindamycin (n=1)	Mean follow up: 7.1 months, range 0.75-28 months	PGA	• PGA score (-0.6 [P < .001] • No significant PGA scores between lower dose (<75mg/d)	Selection N Ascertainment Y Causality N Reporting Y

N= 67	• Age at diagnosis (year, mean): 31.1, SD 9.4 • 46 F, 0 M Family history of HS: n=6 (13%) • Baseline disease severity: Hurley stage I n=3 (7%), Hurley stage II n=34 (74%), Hurley stage III n=5 (11%) • Mean HS-PGA score: 2.6, SD 0.9 • Previous treatments: systemic treatment n=38 (83%), antibiotics n=38 (83%), biologic agents n=2 (4%), retinoids n=1 (2%)	>100mg/d (n=21)	• Hormonal contraceptives (n=14) • Retinoids (n=1) • Biologics (n=1) • Systemic steroids (n=1)			and higher dose (>100mg/d)	
Quinlan 2020[3] Retrospective study N = 26	• Age (year, mean): 33, range 20-56 • 26 F, 0 M • Hurley stage I n=4 (15%), Hurley stage II n=20 (77%), Hurley stage III n=2 (8%) • Mean lesion count (pre-treatment): 2, range 0-5 • Mean DLQI (pre-treatment): 13, range 1-23 • Previous treatments: rifampicin and	• 100mg/d: n=22 (85%) • 50mg/d: n=4 (15%)	• Metformin (n=17)	Mean follow up: 6 months, range 2-17 months	Lesion count, DLQI	Mean lesion count (post-treatment): 1, range 0-5 Patients with DLQI reduction of 5: n=9 (35%)	Selection N Ascertainment Y Causality N Reporting Y

	clindamycin n=15 (58%), tetracyclines n=9 (35%), others included metformin, dapsone, liraglutide, intralesional steroids and surgery						
Masson 2024[4] Retrospective N=53	-Age (years, mean ± SD): 31 ± 9.1, range 18-56 -Sex: 53 F, 0 M -Age at HS onset (mean ± SD): 19.2 ± 9.0, range 7-52 -Age at HS diagnosis (mean ± SD): 25.1 ± 7.9, range 12-46 -Body mass index (mean ± SD): 32.4 ± 9.2, range 19-60 -Hurley stage (n=52):I n=10 (19.2%); II n=33 (63.5%); III n=9 (17.3%)	Spironolactone Mean dose: 104.3 mg/day, range 50-200 mg/day	-Antibiotics: n=31 (58.5%) -Oral contraceptive pills: n=27 (50.9%) -Other birth control methods: n=10 (18.9%) -Adalimumab (n=4) -Apremilast (n=2) -secukinumab (n=2) Infliximab (n=1) guselkumab (n=1)	3-6 months	Improvement (undefined) Discontinuation due to adverse events Adverse events	3 months: 37/44 (84.1%) 6 months: 27/33 (81.8%) N=5 Irregular bleeding (n=3) Lethargy, limb heaviness, shortness of breath (n=1) Mental fogginess, confusion (n=1) Breast swelling/tenderness (n=1) Urinary tract infection (n=1) Dehydration, muscle spasm (n=1) Stomach upset (n=1) Dizziness, cramping (n=1) Night sweats (n=1)	

Gangidi 2024[5] Retrospective cohort N=157	-Age (years, median, IQR): 36.5, IQR 10.4 -Age at HS diagnosis (years, median, IQR): 22.8, IQR 10.3 (overall) -Sex: 157 F, 0 M -Hurley stage (n=152): 1 n=42 (28%); 2 n=66 (43%); 3 n=44 (29%) -Obesity n=124 (81%)	Spironolactone Median dose: 100 mg daily Minimum treatment duration: 3 months	-Oral antibiotics: n=81 (52%) -Topical antibiotics: n=110 (70%) -Topical wash: n=139 (89%) -Biologics: n=40 (25%) Humira (adalimumab) n=29 (18%) Stelara (ustekinumab) n=6 (3.8%) Remicade (infliximab) n=4 (2.5%) Other n=4 (2.5%) -Intralesional steroids: n=29 (18%) -Topical steroids: n=8 (5.1%) -Systemic steroids: n=9 (5.7%) -Metformin: n=13 (8.3%) -Zinc: n=12 (7.6%) -Oral contraceptives (OCPs): n=6 (3.8%) -isotretinoin: n=2 (1.3%)	Minimum follow up 3 months	“Improvement” based on "objective clinician assessments" involving review of medical records, physical examinations, and evaluation of treatment response based on patients' assessment of symptoms, pain, and lesion count. "Improvement" was based on documented reductions in these parameters, while "no improvement" was determined by increased lesion count, pain, or clinical indicators of HS progression.	Improvement n=31 (20%) No improvement n=126 (80%)	

1. Lee A , Fischer G. A case series of 20 women with hidradenitis suppurativa treated with spironolactone. Australas J Dermatol 2015;56:192-6.
2. Golbari NM, Porter ML , Kimball AB. Antiandrogen therapy with spironolactone for the treatment of hidradenitis suppurativa. J Am Acad Dermatol 2019;80:114-9.
3. Quinlan C, Kirby B , Hughes R. Spironolactone therapy for hidradenitis suppurativa. Clin Exp Dermatol 2020;45:464-5.
4. Masson R, Park SE, Shih T, Hogeling M, Shi VY , Hsiao JL. Spironolactone in hidradenitis suppurativa: a single-center. Int J Womens Dermatol 2024;10:e135.
5. Gangidi SV, Greene RK, Olsen E, Jackson S , Nakamura M. Efficacy of spironolactone in treating hidradenitis suppurativa in women of childbearing age: a single-center retrospective analysis. Int J Womens Dermatol 2024;10:e159.

e-Table 26. Metformin

Case series, n=3, 94 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control groups and randomization to treatment. The individual studies included very small sample sizes, increasing concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Moussa 2020[1] Monocentric retrospective case series N=16	• Age (year, mean): 13.7, SD=3 • 12 F, 4 M • Mean BMI: NR • Hurley I n=11, II n=5 • Smoking status: NR • Obesity: n=15	Metformin, 500 mg daily for first week, then increased to 500 mg twice daily, with a maximum dose of 1000mg twice daily	NA	NR	Hurley score	- Visit follow-up 1: Hurley I n=7/10, II n=3/10	Selection N Ascertainment Y Causality N Reporting Y
					Safety	Withdrawal for AE, n=2 (gastrointestinal distress and mood changes)	

Verdolini 2013[2] Prospective study N=25	• Age (year, mean): 31.48 • 22 F, 3 M • Smoking status: NR • Obesity: NR • Hurley stage: NR	Metformin, 1000–1700 mg/d three times a day over 24 weeks	NR	24 weeks	Sartorius score	Baseline: 34.40 (SD 12.46) 12 weeks: 26.76 (SD 11.22) 24 weeks: 22.391 (11.30)	Selection N Ascertainment Y Causality Y Reporting Y
					DLQI	Baseline: 15.0 (SD 4.9581) 12 weeks: 10.08 (SD 5.9576) 24 weeks: 7.65217 9SD 7.1198)	
					Quality of Life	Number of work days lost reduced from 1.5 to virtually zero (0.4). Depression, previously ranked as 'severe' for 11 patients, became non-severe for all except four patients	
Jennings 2020[3] Retrospective chart review N=53	• Age, year, mean (range): 37 (19-62) • 45 F, 5 M • Weight, mean, kg (range): 102 (67-160) • Smoking status: 65% • Hurley stage I: 4% • Hurley stage II: 72% • Hurley stage III: 24% • Smoking status: 65%	mean dose was 1.5 g/days	NR	mean duration of metformin was 11.3 months	subjective clinical response	subjective clinical response in 68%; complete remission of inflammatory skin lesions in 19%	Selection N Ascertainment N Causality Y Reporting Y
					AEs	Gastrointestinal side effects were experienced by 11%, 3 discontinued	

1. Moussa C, Wadowski L, Price H, Mirea L , O'Haver J. Metformin as Adjunctive Therapy for Pediatric Patients With Hidradenitis Suppurativa. J Drugs Dermatol 2020;19:1231-4.

2. Verdolini R, Clayton N, Smith A, Alwash N , Mannello B. Metformin for the treatment of hidradenitis suppurativa: a little help along the way. J Eur Acad Dermatol Venereol 2013;27:1101-8.
3. Jennings L, Hambly R, Hughes R, Moriarty B , Kirby B. Metformin use in hidradenitis suppurativa. J Dermatolog Treat 2020;31:261-3.

Oral retinoids

e-Table 27. Acitretin

Case series, n=5, 120 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control groups and randomization to treatment. The individual studies included very small sample sizes, increasing concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murrad tool
Boer 2011[1] Monocentric retrospective case series N=12	• Age (year, mean): 44.6, range 31-63 • 4 F, 9 M • Previous treatments: • Antibiotics n=12, Isotretinoin n=5, Other oral (zinc, dexamethasone, methotrexate, dapsone, anti TNF) n= 5 • Hurley stage II or III • Mean BMI: 27, range 22.7–33.4 • Smoking status: current smokers n=11	Acitretin (mean dose 0.59 mg/kg per day)	No concomitant systemic treatment	NR mean treatment 10.8 months, range 6-12	PGA: Partial improvement < 75% from baseline, total remission > 75%	- Marked or complete remission n=9 - Improvement n=3	Selection N Ascertainment N Causality N Reporting Y
					VAS from baseline	Mean -5.7, range -2 to -10	
					Safety	Cheilitis n=12, Hair loss n=3, Photosensitivity n=2, Withdrawal for AE n=1	

Matusiak 2014[2] Prospective case series N=17	• Age (year, mean ± SD): 36 ± 10.75 • 6 M, 11 F • BMI, mean ± SD: 31.84 ± 6.99 • Smoking status: 82% active or ex-smoker • Hurley stage I: n=2 • Hurley stage II: n=8 • Hurley stage III: n=7	Acitretin (mean dose 0.59 mg/kg ± 0.08 per day)	NR	9 months	Hurley stage	Baseline mean: 2.29 End of treatment mean: 1.65	Selection N Ascertainment N Causality Y Reporting Y
					HSSI	Baseline mean: 13.06 End of treatment mean:7.35	
					DLQI	Baseline mean: 14.8 End of treatment mean: 7.4	
					GQ indexing	Baseline mean: 2.82 End of treatment mean: 2	
					PGA (0=minimal improvement, +5= complete remission)	End of treatment mean: +2.29	
					Dropout rate	47% drop-out rate, 4 patients dropped out due to ineffectiveness of treatment, 1 patient was diagnosed with sigmoid colon tumor, 1 patient experienced worsening visual acuity, 1 patient experienced severe	

						symptoms of retinoid dermatitis	
Tan 2016[3] Retrospective study N=14	• Age, year, mean (range): 48 (32-64) • Hurley stage II or II: 86% • Smoking status: n=7 current smoker • BMI: NR	Acitretin (range 10-50 mg/d)	8 patients received other standard systemic medications	Mean 10 months (range 1-42 months)	Side effects	N=5 patients (xerostomia most commonly reported)	Selection N Ascertainment N Causality Y Reporting N
					Clinical improvement	no patient under acitretin monotherapy achieved clinical response compared to 87.5% in combination group	
Sanchez-Diaz 2022[4] Retrospective cohort study N=62	• Age, year, mean (SD): 44.48 (12.41) • 31 M, 32 F • BMI, mean (SD): 30.31 (8.68) • Hurley stage I: n=25 • Hurley stage II: n=30 • Hurley stage III: n=8 • Tobacco consumption, cig/day (SD): 12 (9.11) • AN score, mean (SD): 3.32 (5.24)	Acitretin (mean 18.17 mg/day (SD 5.55)) N=18 took 10 mg/day N=32 took 20 mg/day N=25 mg/day	6.3% of patients co-treated with oral antibiotics, 12.7% co-treated with biologic drugs	Treatment time, months 4.98 (SD 1.28)	ISHA score	Basal mean: 7.28 (SD 7.14) 12 weeks: 5.17 (SD 6.48) 24 weeks: 4.32 (SD 5.82)	Selection N Ascertainment N Causality N Reporting Y
					AEs	73% experienced no AEs 9/17 who experienced an AE discontinued treatment	
Molinelli 2023[5] Retrospective case series N=15	-Mean age 42.3 (11.6) years -4F, 11M -Mean BMI 25.4 (4.3) -Smokers n=7 (46.7%) -Mean HS duration 20 (12.1) years -Hurley stage II n=12; III n=2	Acitretin 25-35 mg (mean 0.44mg/kg/day) QD. Median duration 18 months (range 9-28)	Azithromycin 500 mg daily for 3 day for 4 weeks	24 weeks	Mean IHS4 score	8.1 (2.9)→3.3 (3.7)	Selection N Ascertainment N Causality N Reporting Y
					Mean VAS 10 pain score	6 (1.95)→0.8 (1.1)	
					Mean DLQI score	16 (5.7)→2.6 (5.7)	
					Mean Flare count over 24 wks	2.1 (1.6)	

					Adverse events	N=15 xerosis; n=11 cheilitis; n=1 discontinuation due to AE	

1. Boer J , Nazary M. Long-term results of acitretin therapy for hidradenitis suppurativa. Is acne inversa also a misnomer? Br J Dermatol 2011;164:170-5.
2. Matusiak L, Bieniek A , Szepietowski JC. Acitretin treatment for hidradenitis suppurativa: a prospective series of 17 patients. Br J Dermatol 2014;171:170-4.
3. Tan MG, Shear NH, Walsh S , Alhusayen R. Acitretin:Monotherapy or Combined Therapy for Hidradenitis Suppurativa? Journal of Cutaneous Medicine and Surgery 2017;21:48-53.
4. Sanchez-Diaz M, Diaz-Calvillo P, Rodriguez-Pozo JA, Arias-Santiago S , Molina-Leyva A. Effectiveness and Safety of Acitretin for the Treatment of Hidradenitis Suppurativa, Predictors of Clinical Response: A Cohort Study. Dermatology 2023;239:52-9.
5. Molinelli E, Sapigni C, Simonetti O, D'Agostino GM, Brisigotti V, Rizzetto G , Offidani A. Acitretin plus macrolides and acitretin monotherapy in the management of hidradenitis suppurativa. J Eur Acad Dermatol Venereol 2023;37:e392-e4.

e-Table 28. Isotretinoin

Case series, n=1, 68 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from a single, small case series, which is inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The very small sample size increases concern about random error and imprecision.

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murrad tool

Boer 1999[1] Monocentric retrospective case series N=68	• Age (year, mean): 32.6, range 15-54 • 59 F, 9 M • Mean duration of HS (year): 4.8, range 1-30 • No. of patients with HS alone: n=60 • No. of patients with HS and acne conglobata: n=8 • Affected areas: Genitocrural n=45, Axillary n=6, Axillary and genitocrural n=17 • Baseline disease severity: Mild n=6, Moderate n=25, Severe n=17	• Isotretinoin, low-dose (mean daily dose: 0.56 mg/kg body weight, range 0.50-0.81)	• intralesional corticosteroid injection (n=6)	4 months Mean follow-up: 46 months, range 6-107	Clearance score (0 to +3 scale; +3 clear to 0=no change)	• 16 (23.5%) of the 68 patients achieved a score of +3 (clear) at the end of treatment • 14 (20.6%) of the 68 scored +2 • 11 (16.2%) scored +1 • 7 (10.3%) scored 0 • 20 (29%) of patients did not complete full treatment (4 months)	Selection N Ascertainment Y Causality N Reporting Y

1. Boer J , van Gemert MJ. Long-term results of isotretinoin in the treatment of 68 patients with hidradenitis suppurativa. J Am Acad Dermatol 1999;40:73-6.

Biologics & Small Molecules Summary of Findings Tables

Contents

Adalimumab

e-Table 29. Adalimumab every other week vs placebo

Adalimumab every other week compared to placebo for hidradenitis suppurativa[1-3]

Patient or population: hidradenitis suppurativa
Intervention: Adalimumab 40mg every other week (subcutaneous)
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with Adalimumab				
Achieving in pain VAS 30 at week 16	271 per 1000	**363 per 1000** (198 to 658)	**RR 1.34** (0.73 to 2.43)	95 (1 RCT)	⨁⨁◯◯ Low[a]	
Mean change in VAS of pain at week 12 Scale from: 0 to 100	Mean change **3.17**	MD **16.57 lower** (55.28 lower to 22.14 higher)	-	21 (1 RCT)	⨁⨁◯◯ Low[b]	
Change in DLQI score (LOCF) ; Scale from: 0 to 30 follow-up: range 12 weeks to 16 weeks		MD **2.07 lower** (5.49 lower to 1.35 higher)	-	124 (2 RCTs)	⨁⨁⨁◯ Moderate[c]	
Achieving Physician Global Assessment (2-grade improvement) follow-up: 16 weeks	39 per 1000	**96 per 1000** (20 to 473)	**RR 2.45** (0.50 to 12.07)	103 (1 RCT)	⨁⨁◯◯ Low[d]	
Serious adverse events follow-up: range 12 weeks to 16 weeks	35 per 1000	**52 per 1000** (9 to 296)	**RR 1.47** (0.26 to 8.44)	124 (2 RCTs)	⨁⨁◯◯ Low[d]	
Discontinuation due to adverse event follow-up: range 12 weeks to 16 weeks	0 per 1000	**0 per 1000** (0 to 0)	**RR 4.91** (0.24 to 99.74)	124 (2 RCTs)	⨁⨁◯◯ Low[d]	
Other adverse events: infectious follow-up: range 12 weeks to 16 weeks	333 per 1000	**533 per 1000** (190 to 1000)	**RR 1.60** (0.57 to 4.53)	124 (2 RCTs)	⨁⨁◯◯ Low[a]	
Change in modified Sartorius scale score (LOCF) follow-up: range 12 weeks to 16 weeks	-	SMD **0.42 lower** (1.22 lower to 0.37 higher)	-	124 (2 RCTs)	⨁⨁◯◯ Low[e]	
Achieving HiSCR follow-up: 16 weeks	256 per 1000	**297 per 1000** (153 to 568)	**RR 1.16** (0.60 to 2.22)	88 (1 RCT)	⨁⨁◯◯ Low[a]	
Achieving HS-PGA follow-up: 16 weeks	23 per 1000	**41 per 1000** (6 to 287)	**RR 1.77** (0.26 to 12.32)	88 (1 RCT)	⨁⨁◯◯ Low[a]	

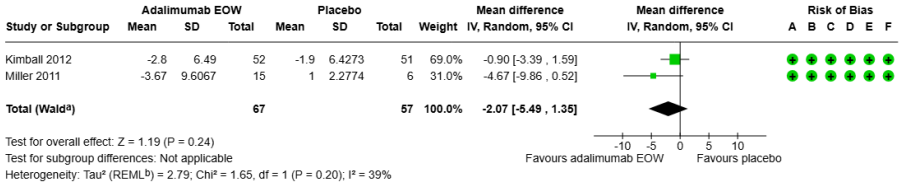
***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardised mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two levels due to very serious imprecision: the 95% CI crossed both the conventional upper and lower thresholds of MID (25).
[b]Downgraded by two level due to very serious imprecision: The 95% CI crossed both upper and lower thresholds of the MID of VAS30 (30% reduction = 14.1 in this trial).
[c]Downgraded by one level due to serious imprecision: The 95% CI crossed the MID of 4 for DLQI.
[d]Downgraded by two levels due to very serious imprecision: the ratio of the upper to the lower boundary of the CI was > 3.
[e]Downgraded by two levels due to very serious imprecision: small sample size.
[f]Downgraded by two levels due to very serious imprecision: zero events with small sample size.

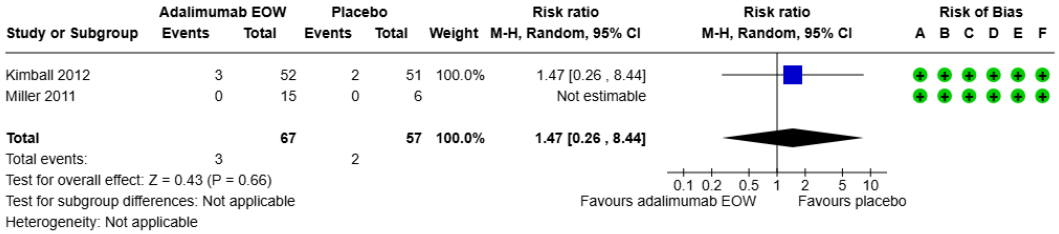
Outcome 3: Change in DLQI score (LOCF) at week 12-16



Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

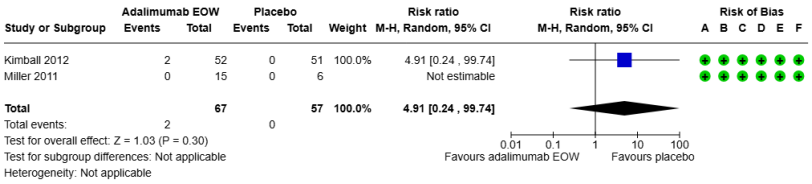
Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Outcome 5: Serious adverse events through week 12-16



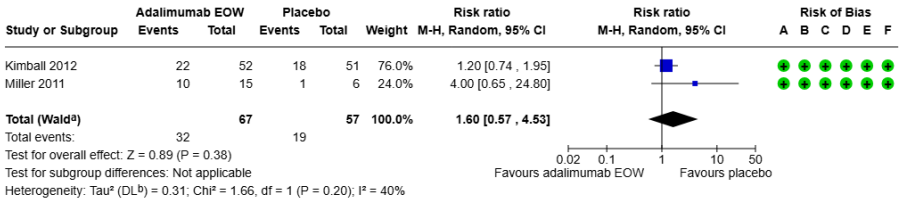
Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Outcome 6: Adverse events leading to discontinuation of intervention through week 12-16



Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

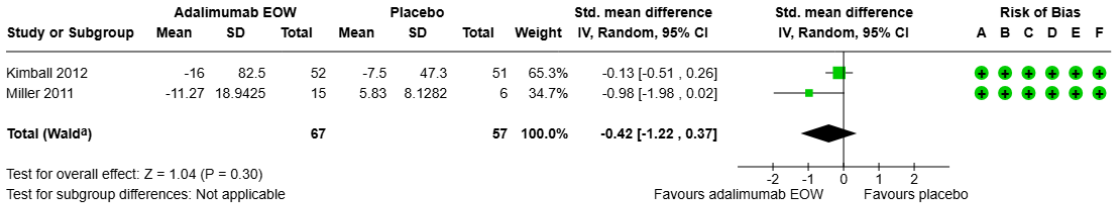
Outcome 7: Other adverse events: infectious through week 12-16



Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Outcome 8:Change in modified Sartorius scale score (LOCF) at week 12-16



Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

1. Kimball AB, Kerdel F, Adams D, Mrowietz U, Gelfand JM, Gniadecki R et al. Adalimumab for the treatment of moderate to severe Hidradenitis suppurativa: a parallel randomized trial. Ann Intern Med 2012;157:846-55.
2. Kimball AB, Okun MM, Williams DA, Gottlieb AB, Papp KA, Zouboulis CC et al. Two Phase 3 Trials of Adalimumab for Hidradenitis Suppurativa. N Engl J Med 2016;375:422-34.
3. Miller I, Lynggaard CD, Lophaven S, Zachariae C, Dufour DN , Jemec GB. A double-blind placebo-controlled randomized trial of adalimumab in the treatment of hidradenitis suppurativa. Br J Dermatol 2011;165:391-8.

e-Table 30. Adalimumab weekly versus placebo

Adalimumab weekly compared to placebo for hidradenitis suppurativa[1-7]

Patient or population: hidradenitis suppurativa
Intervention: adalimumab 40mg weekly (subcutaneous)
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with adalimumab weekly				
Pain VAS30 follow-up: 16 weeks	271 per 1000	**479 per 1000** (276 to 831)	**RR 1.77** (1.02 to 3.07)	96 (1 RCT)	⊕⊕⊕◯ Moderate[c]	
HiSCR50 follow-up: 12 weeks	269 per 1000	**516 per 1000** (422 to 634)	**RR 1.92** (1.57 to 2.36)	669 (3 RCTs)	⊕⊕⊕◯ Moderate[c]	
IHS4-55 follow-up: 12 weeks	295 per 1000	**533 per 1000** (433 to 657)	**RR 1.81** (1.47 to 2.23)	578 (1 RCT)	⊕⊕⊕⊕ High	
Change in DLQI (LOCF) score ; Scale from: 0 to 30 follow-up: range 12 weeks to 16 weeks		MD **2.82 lower** (3.69 lower to 1.96 lower)	-	724 (3 RCTs)	⊕⊕⊕⊕ High	
Serious adverse events follow-up: range 12 weeks to 16 weeks	27 per 1000	**25 per 1000** (10 to 62)	**RR 0.90** (0.36 to 2.28)	733 (3 RCTs)	⊕⊕⊕◯ Moderate[d]	
Discontinuation due to AE follow-up: range 12 weeks to 16 weeks	22 per 1000	**17 per 1000** (1 to 291)	**RR 0.76** (0.04 to 13.32)	733 (3 RCTs)	⊕⊕⊕◯ Moderate[d]	
Other adverse events: headache follow-up: range 12 weeks to 16 weeks	104 per 1000	**120 per 1000** (28 to 515)	**RR 1.16** (0.27 to 4.96)	733 (3 RCTs)	⊕⊕⊕◯ Moderate[e]	
Other adverse events: infectious through week 12-16	311 per 1000	**262 per 1000** (209 to 330)	**RR 0.84** (0.67 to 1.06)	733 (3 RCTs)	⊕⊕⊕◯ Moderate[e]	
30% improvement in PGA-Skin Pain (PGA-SP) follow-up: 12 weeks	263 per 1000	**450 per 1000** (345 to 587)	**RR 1.71** (1.31 to 2.23)	433 (1 RCT)	⊕⊕⊕⊕ High	
The number of days on flare follow-up: 12 weeks	Mean days **29.9**	MD **13.9 lower** (24.02 lower to 3.78 lower)	-	596 (1 RCT)	⊕⊕⊕⊕ High	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

Adalimumab weekly compared to placebo for hidradenitis suppurativa[1-7]

Patient or population: hidradenitis suppurativa
Intervention: adalimumab 40mg weekly (subcutaneous)
Comparison: placebo

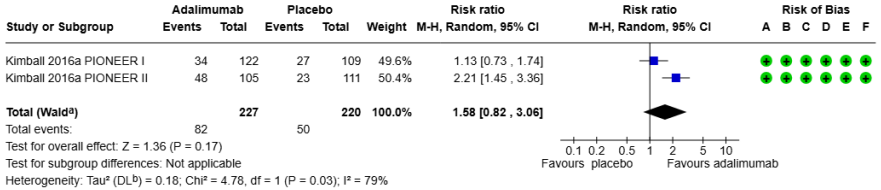
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with adalimumab weekly				

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by one level due to heterogeneity (I-squared value 79%) with no subgroup analysis possible
[b]Downgraded by one level due to serious imprecision: The 95% CI crossed the MID of NRS30 (30% reduction = 1.8 in this trial).
[c]Downgraded by one level due to serious imprecision: The 95% CI crossed either the conventional upper or lower threshold of MID (25).
[d]Downgraded by one level due to serious imprecision: Although the CI is consistent with both meaningful benefit and harm, the overall event rates were very low and comparable between groups, suggesting that adalimumab is likely safe in this population.
[e]Downgraded by one level due to serious imprecision: Although the CI is consistent with both meaningful benefit and harm, the overall event rates were modest and, more importantly, comparable between groups, suggesting that adalimumab likely does not increase the risk of this event in the short term.
[f]Downgraded by one level due to serious imprecision: The CI is consistent with meaningful benefit and trivial harm, the overall event rates were modest to high, but, more importantly, comparable between groups, suggesting that adalimumab likely does not increase the risk of this event and may reduce the risk in the short term.

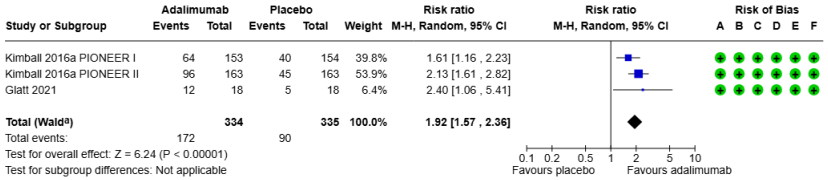
Outcome 1: Achieving NRS30 of pain (≥ 30% and ≥ 1 point reduction) at week 12



Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Outcome 3: Achieving HiSCR50 at week 12



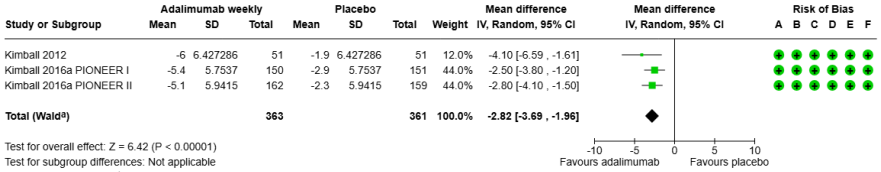
Footnotes

[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Outcome 5: Change in DLQI (LOCF) score at week 12-16



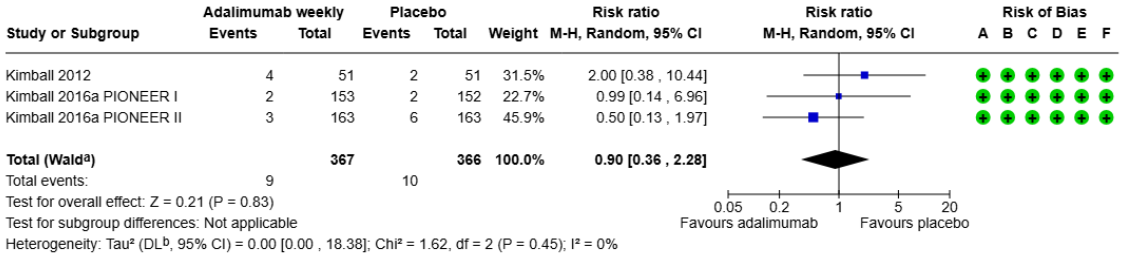
Footnotes

[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Outcome 7: Serious adverse events through week 12-16



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Bias arising from the randomization process

(B) Bias due to deviations from intended interventions

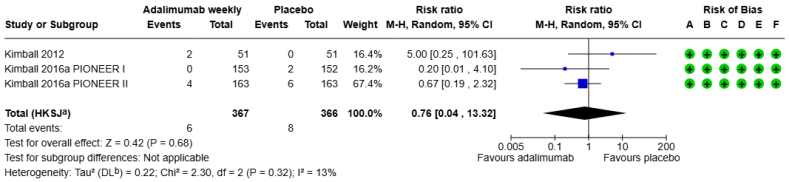
(C) Bias due to missing outcome data

(D) Bias in measurement of the outcome

(E) Bias in selection of the reported result

(F) Overall bias

Outcome 8: Adverse events leading to discontinuation of intervention through week 12-16



Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Bias arising from the randomization process

(B) Bias due to deviations from intended interventions

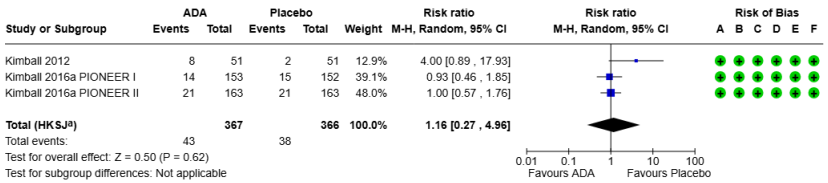
(C) Bias due to missing outcome data

(D) Bias in measurement of the outcome

(E) Bias in selection of the reported result

(F) Overall bias

Outcome 9: Other adverse events: headache through week 12-16



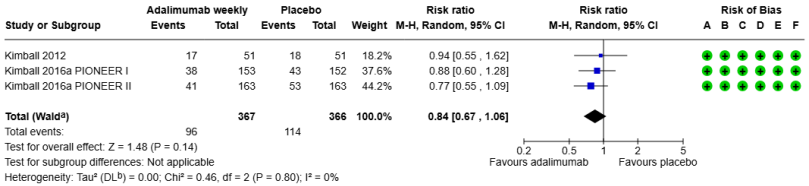
Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Outcome 10: Other adverse events: infectious through week 12-16



Footnotes

[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

1. Forman SB BD, Gu Y, & Teixeira HD. Risk of flare in patients with hidradenitis suppurativa treated with adalimumab for 12 weeks during PIONEER I and PIONEER II: Two phase 3, randomized, placebo-controlled trials. Journal of the American Academy of Dermatology 2016;74:AB71.
2. Glatt S, Jemec GBE, Forman S, Sayed C, Schmieder G, Weisman J et al. Efficacy and Safety of Bimekizumab in Moderate to Severe Hidradenitis Suppurativa: A Phase 2, Double-blind, Placebo-Controlled Randomized Clinical Trial. JAMA Dermatol 2021;157:1279-88.
3. Kimball AB, Kerdel F, Adams D, Mrowietz U, Gelfand JM, Gniadecki R et al. Adalimumab for the treatment of moderate to severe Hidradenitis suppurativa: a parallel randomized trial. Ann Intern Med 2012;157:846-55.
4. Kimball AB, Okun MM, Williams DA, Gottlieb AB, Papp KA, Zouboulis CC et al. Two Phase 3 Trials of Adalimumab for Hidradenitis Suppurativa. N Engl J Med 2016;375:422-34.

5. Kimball AB, Sobell JM, Zouboulis CC, Gu Y, Williams DA, Sundaram M et al. HiSCR (Hidradenitis Suppurativa Clinical Response): a novel clinical endpoint to evaluate therapeutic outcomes in patients with hidradenitis suppurativa from the placebo-controlled portion of a phase 2 adalimumab study. J Eur Acad Dermatol Venereol 2016;30:989-94.
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7. Tzellos T, van Straalen KR, Kyrgidis A, Alavi A, Goldfarb N, Gulliver W et al. Development and validation of IHS4-55, an IHS4 dichotomous outcome to assess treatment effect for hidradenitis suppurativa. J Eur Acad Dermatol Venereol 2023;37:395-401.

e-Table 31. Adalimumab plus surgery versus Adalimumab

Adalimumab plus surgery compared to Adalimumab for hidradenitis suppurativa[1]

Patient or population: Adults with moderate-to-severe HS
Intervention: Adalimumab 40mg weekly (subcutaneous) & surgery
Comparison: Adalimumab 40mg weekly (subcutaneous)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Adalimumab	Risk with Adalimumab + surgery				
≥ 2 reduction in pain follow-up: 12 months	97 per 1000	**258 per 1000** (75 to 883)	**RR 2.67** (0.78 to 9.12)	62 (1 RCT)	⨁⨁◯◯ Low[a]	
Achieving HiSCR50 follow-up: 12 months	194 per 1000	**323 per 1000** (134 to 778)	**RR 1.67** (0.69 to 4.02)	62 (1 RCT)	⨁⨁◯◯ Low[a]	
Achieving IHS4-55 follow-up: 12 months	323 per 1000	**871 per 1000** (513 to 1000)	**RR 2.70** (1.59 to 4.58)	62 (1 RCT)	⨁⨁⨁⨁ High	
Change in DLQI ; Scale from: 0 to 30 follow-up: 12 months	Mean change in DLQI **-4.0**	MD **4.2 lower** (7.68 lower to 0.72 lower)	-	62 (1 RCT)	⨁⨁⨁◯ Moderate[b]	
≥ 2 reduction in HS-PGA follow-up: 12 months	129 per 1000	**581 per 1000** (222 to 1000)	**RR 4.50** (1.72 to 11.78)	62 (1 RCT)	⨁⨁⨁⨁ High	
Serious adverse events follow-up: 12 months	65 per 1000	**65 per 1000** (10 to 430)	**RR 1.00** (0.15 to 6.66)	62 (1 RCT)	⨁⨁◯◯ Low[a]	
Discontinuation due to AE follow-up: 12 months	97 per 1000	**32 per 1000** (4 to 293)	**RR 0.33** (0.04 to 3.03)	62 (1 RCT)	⨁⨁◯◯ Low[a]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

Adalimumab plus surgery compared to Adalimumab for hidradenitis suppurativa[1]

Patient or population: Adults with moderate-to-severe HS
Intervention: Adalimumab 40mg weekly (subcutaneous) & surgery
Comparison: Adalimumab 40mg weekly (subcutaneous)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Adalimumab	**Risk with Adalimumab + surgery**				

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two levels due to serious imprecision (small sample size and the ratio of the upper to the lower boundary of the CI was > 3)
[b]Downgraded by one level due to serious imprecision: The 95% CI crossed the MID of 4 for DLQI.
[c]Downgraded by one level due to serious imprecision: The 95% CI crossed either the conventional upper or lower threshold of MID (0.75 or 1.25)

1. Aarts P, van Huijstee JC, van der Zee HH, van Doorn MBA, van Straalen KR , Prens EP. Adalimumab in conjunction with surgery compared with adalimumab monotherapy for hidradenitis suppurativa: A Randomized Controlled Trial in a real-world setting. J Am Acad Dermatol 2023;89:677-84.

e-Table 32. Adalimumab plus surgery versus placebo plus surgery

Adalimumab plus surgery compared to placebo plus surgery for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: adalimumab 40mg weekly (subcutaneous) & surgery
Comparison: placebo & surgery

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo plus surgery	**Risk with adalimumab plus surgery**				
Change in pain NRS at week 12	mean change in pain NRS: **-0.9**	MD **1 lower** (1.77 lower to 0.23 lower)	-	177 (1 RCT)	⨁⨁⨁◯ Moderate[a]	
HiSCR50 at week 12	301 per 1000	**506 per 1000** (355 to 716)	**RR 1.68** (1.18 to 2.38)	206 (1 RCT)	⨁⨁⨁◯ Moderate[b]	
Change in DLQI (LOCF) at week 12	mean change in DLQI (LOCF) score: **-3.1**	MD **2.3 lower** (4.12 lower to 0.48 lower)	-	175 (1 RCT)	⨁⨁⨁◯ Moderate[c]	

Adalimumab plus surgery compared to placebo plus surgery for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: adalimumab 40mg weekly (subcutaneous) & surgery
Comparison: placebo & surgery

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo plus surgery	**Risk with adalimumab plus surgery**				
Serious adverse events through post-surgery week 12	29 per 1000	**68 per 1000** (18 to 256)	**RR 2.33** (0.62 to 8.78)	206 (1 RCT)	⨁⨁◯◯ Low[d]	
Adverse events leading to death at week 12	0 per 1000	**0 per 1000** (0 to 0)	**RR 3.00** (0.12 to 72.80)	206 (1 RCT)	⨁⨁◯◯ Low[d]	
Discontinuation due to AE at week 12	39 per 1000	**39 per 1000** (10 to 151)	**RR 1.00** (0.26 to 3.89)	206 (1 RCT)	⨁⨁◯◯ Low[d]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by one level due to serious imprecision: The 95% CI crossed the MID of NRS30 (30% reduction = 1.5 in this trial).
[b]Downgraded by one level due to serious imprecision: The 95% CI crossed either the conventional upper or lower threshold of MID (0.75 or 1.25).
[c]Downgraded by one level due to serious imprecision: The 95% CI crossed the MID of 4 for DLQI.
[d]Downgraded by two levels due to very serious imprecision (small sample size and the ratio of the upper to the lower boundary of the CI was > 3)

1. Bechara FG, Podda M, Prens EP, Horváth B, Giamarellos-Bourboulis EJ, Alavi A et al. Efficacy and Safety of Adalimumab in Conjunction With Surgery in Moderate to Severe Hidradenitis Suppurativa: The SHARPS Randomized Clinical Trial. JAMA Surg 2021;156:1001-9.

Bimekizumab

e-Table 33. Bimekizumab every 2 weeks versus placebo

Bimekizumab every 2 weeks compared to placebo for hidradenitis suppurativa[1, 2]

Patient or population: moderate to severe **hidradenitis** suppurativa
Intervention: Bimekizumab 320mg every 2 weeks for 16 weeks
Comparison: placebo for 16 weeks

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with Bimekizumab				
HiSCR 50 at week 12-16	305 per 1000	**509 per 1000** (399 to 649)	**RR 1.67** (1.31 to 2.13)	784 (3 RCTs)	⨁⨁⨁⨁ High	
Achieving HiSCR 75 at week 12-16	165 per 1000	**352 per 1000** (245 to 504)	**RR 2.14** (1.49 to 3.06)	784 (3 RCTs)	⨁⨁⨁⨁ High	
Change in DLQI score at week 16 Scale from: 0 to 30	-	MD **1.89 lower** (3.06 lower to 0.72 lower)	-	726 (2 RCT)	⨁⨁⨁⨁ High	
Serious adverse events through week 12-16	12 per 1000	**17 per 1000** (1 to 484)	**RR 1.44** (0.05 to 40.42)	789 (3 RCTs)	⨁⨁⨁◯ Moderate[a]	
Discontinuation due to AE week 12-16	6 per 1000	**17 per 1000** (4 to 74)	**RR 2.86** (0.66 to 12.38)	789 (3 RCTs)	⨁⨁⨁◯ Moderate[b]	
Any TEAE through week 12-16	617 per 1000	**660 per 1000** (574 to 752)	**RR 1.07** (0.93 to 1.22)	789 (3 RCT)	⨁⨁⨁⨁ High	
Hidradenitis suppurativa symptom daily diary (HSSDD) worst skin pain response(≥3 points reduction) follow-up: 16 weeks	82 per 1000	**214 per 1000** (122 to 376)	**RR 2.60** (1.48 to 4.58)	726 (2 RCT)	⨁⨁⨁⨁ High	
Other adverse events: Headache through week 16	68 per 1000	**69 per 1000** (25 to 188)	**RR 1.01** (0.37 to 2.74)	722 (2 RCT)	⨁⨁⨁◯ Moderate[c]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

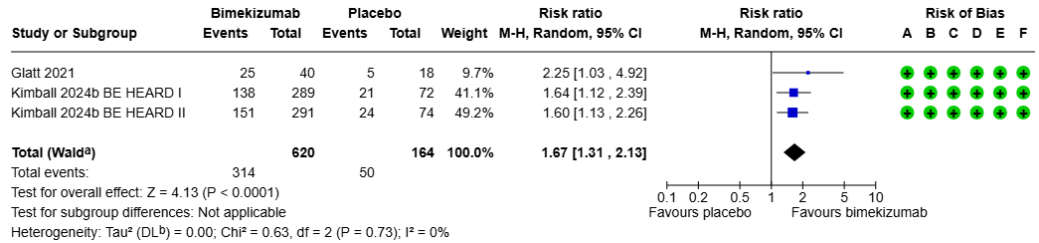
GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a Downgraded by one level due to serious imprecision: Although the CI is consistent with both meaningful benefit and harm, the overall event rates were modest (<3%) and comparable between groups, suggesting that bimekizumab likely does not increase the risk of this event in the short term.

b Downgraded by one level due to serious imprecision: Although the CI is consistent with both meaningful benefit and harm and there is a trend towards more withdrawal with treatment, the overall event rate was modest (<4%), indicating a safety concern.
c. Downgraded by one level due to serious imprecision: The CI is consistent with meaningful benefit and harm, the overall event rates in both groups were moderate but comparable (6.9% vs 6.8%), suggesting that treatment likely does not increase the risk of this event.

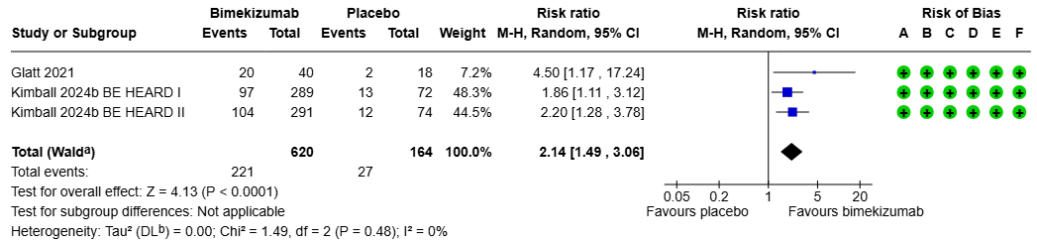
Outcome 1 : Achieving HiSCR 50 at week 12-16



Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

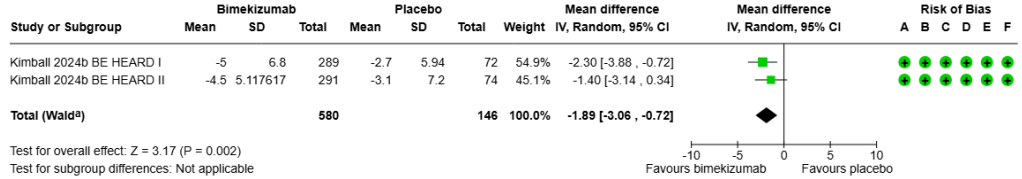
Outcome 2 : Achieving HiSCR 75 at week 12-16



Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Outcome 4 : Change in DLQI score at week 16

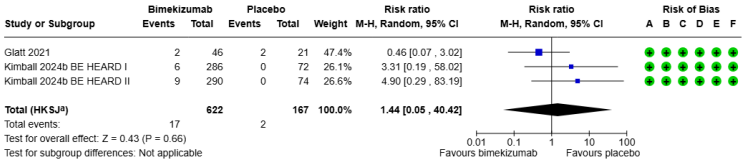


Test for overall effect: Z = 3.17 (P = 0.002)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL[b]) = 0.00; Chi² = 0.56, df = 1 (P = 0.45); I² = 0%

Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Outcome 6 : Serious adverse events through week 12-16

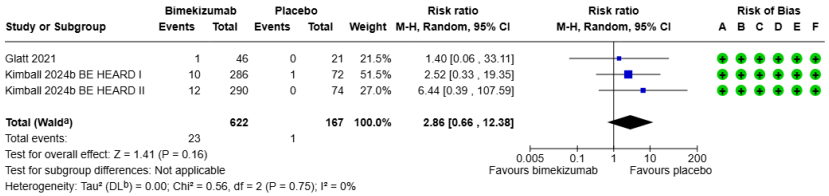


Test for overall effect: Z = 0.43 (P = 0.66)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL[b]) = 0.55; Chi² = 2.67, df = 2 (P = 0.26); I² = 25%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Outcome 7 : Adverse events leading to discontinuation of intervention through week 12-16



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Bias arising from the randomization process

(B) Bias due to deviations from intended interventions

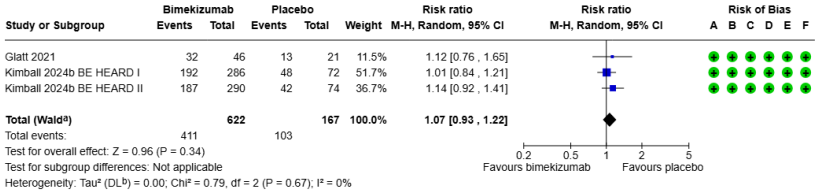
(C) Bias due to missing outcome data

(D) Bias in measurement of the outcome

(E) Bias in selection of the reported result

(F) Overall bias

Outcome 8 : Any TEAE through week 12-16



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Bias arising from the randomization process

(B) Bias due to deviations from intended interventions

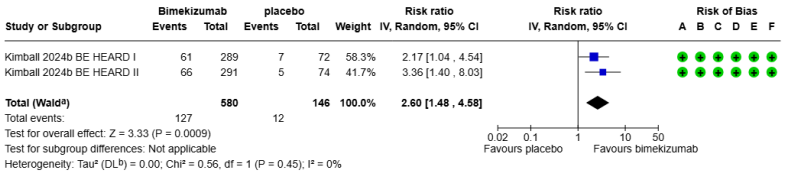
(C) Bias due to missing outcome data

(D) Bias in measurement of the outcome

(E) Bias in selection of the reported result

(F) Overall bias

Outcome 10 : Hidradenitis suppurativa symptom daily diary (HSSDD) worst skin pain response (≥3 points reduction)



Footnotes

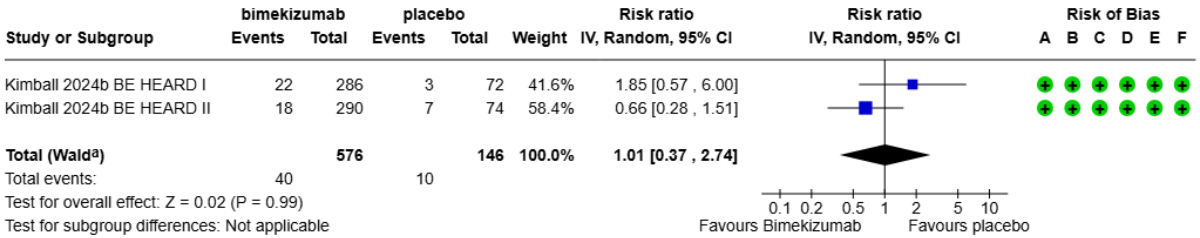
[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Outcome 11 : Other adverse events: Headache through week 16



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

1. Glatt S, Jemec GBE, Forman S, Sayed C, Schmieder G, Weisman J et al. Efficacy and Safety of Bimekizumab in Moderate to Severe Hidradenitis Suppurativa: A Phase 2, Double-blind, Placebo-Controlled Randomized Clinical Trial. JAMA Dermatol 2021;157:1279-88.

2. Kimball AB, Jemec GBE, Sayed CJ, Kirby JS, Prens E, Ingram JR et al. Efficacy and safety of bimekizumab in patients with moderate-to-severe hidradenitis suppurativa (BE HEARD I and BE HEARD II): two 48-week, randomised, double-blind, placebo-controlled, multicentre phase 3 trials. Lancet 2024;403:2504-19.

e-Table 34. Bimekizumab every 4 weeks versus placebo

Bimekizumab every 4 weeks compared to placebo for hidradenitis suppurativa[1]

Patient or population: moderate to severe hidradenitis suppurativa
Intervention: Bimekizumab 320mg every 4 weeks for 16 weeks
Comparison: placebo for 16 weeks

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with Bimekizumab				
HiSCR 50 at week 16	308 per 1000	**493 per 1000** (376 to 647)	**RR 1.60** (1.22 to 2.10)	434 (2 RCT)	⨁⨁⨁◯ Moderate[a]	
HiSCR 75 at week 16	171 per 1000	**293 per 1000** (193 to 440)	**RR 1.71** (1.13 to 2.57)	434 (2 RCT)	⨁⨁⨁◯ Moderate[a]	
Change in DLQI score at week 16; Scale from: 0 to 30	-	MD **1.79 lower** (3.55 lower to 0.04 lower)	-	434 (2 RCT)	⨁⨁⨁⨁ High	
Serious adverse events through week 16	0 per 1000	**0 per 1000** (0 to 0)	**RR 4.10** (0.52 to 32.52)	431 (2 RCT)	⨁⨁◯◯ Low[b]	
Discontinuation due to AE through week 16	7 per 1000	**22 per 1000** (4 to 122)	**RR 3.23** (0.58 to 17.83)	431 (2 RCT)	⨁⨁◯◯ Low[b]	
Any TEAE through week 16	616 per 1000	**586 per 1000** (499 to 690)	**RR 0.95** (0.81 to 1.12)	431 (2 RCT)	⨁⨁⨁⨁ High	
Other adverse events: Headache through week 16	68 per 1000	**52 per 1000** (21 to 130)	**RR 0.76** (0.31 to 1.90)	431 (2 RCT)	⨁⨁◯◯ Low[b]	

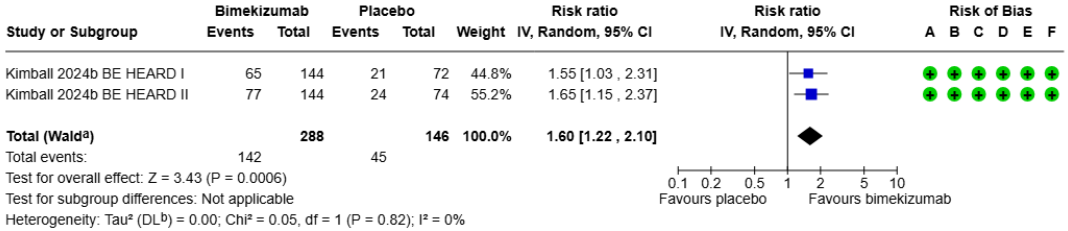
***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by one level due to serious imprecision: The 95% CI crossed either the conventional upper or lower threshold of MID (0.75 or 1.25).
[b]Downgraded by two levels due to very serious imprecision: the ratio of the upper to the lower boundary of the CI was > 3.

Outcome 1: Achieving HiSCR 50 at week 16



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Bias arising from the randomization process

(B) Bias due to deviations from intended interventions

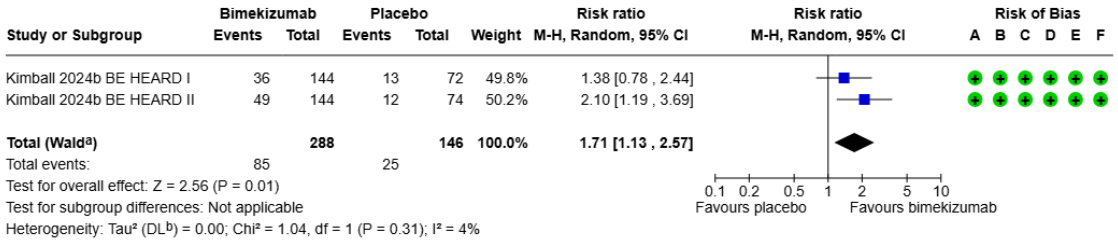
(C) Bias due to missing outcome data

(D) Bias in measurement of the outcome

(E) Bias in selection of the reported result

(F) Overall bias

Outcome 2: Achieving HiSCR 75 at week 16



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Bias arising from the randomization process

(B) Bias due to deviations from intended interventions

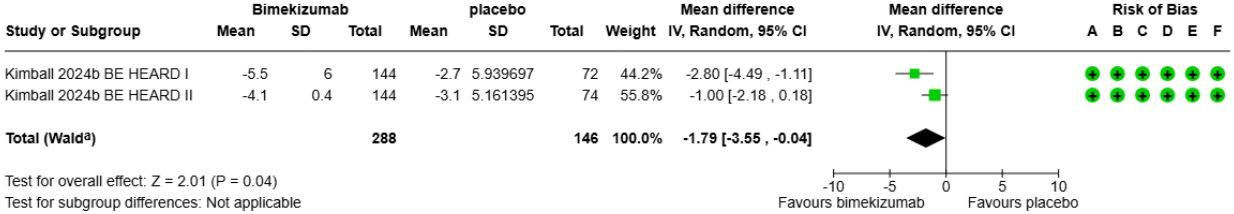
(C) Bias due to missing outcome data

(D) Bias in measurement of the outcome

(E) Bias in selection of the reported result

(F) Overall bias

Outcome 3: Change in DLQI score at week 16

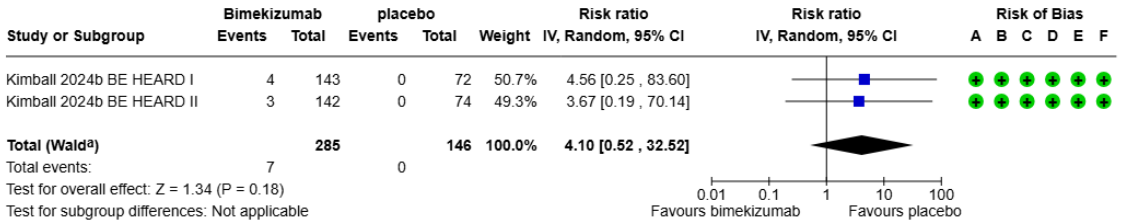


Test for overall effect: Z = 2.01 (P = 0.04)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL[b]) = 1.07; Chi² = 2.94, df = 1 (P = 0.09); I² = 66%

Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Outcome 4: Serious adverse events through week 16

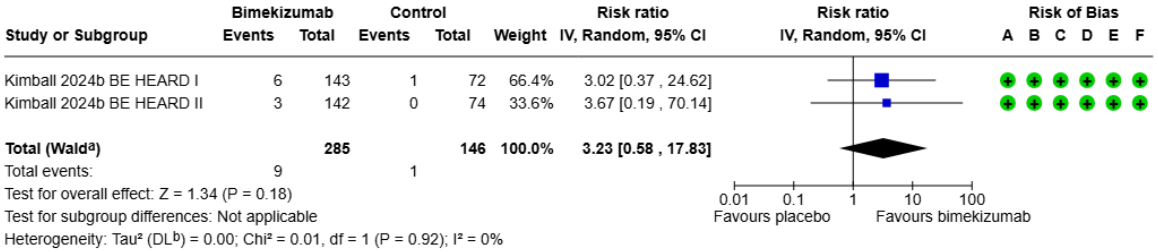


Test for overall effect: Z = 1.34 (P = 0.18)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL[b]) = 0.00; Chi² = 0.01, df = 1 (P = 0.92); I² = 0%

Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Outcome 5: Adverse events leading to discontinuation of intervention through week 16



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Bias arising from the randomization process

(B) Bias due to deviations from intended interventions

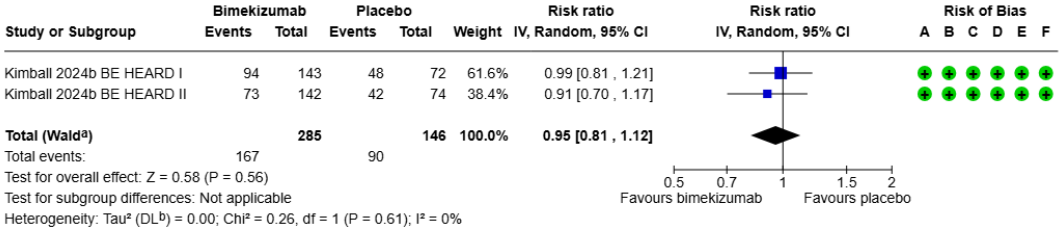
(C) Bias due to missing outcome data

(D) Bias in measurement of the outcome

(E) Bias in selection of the reported result

(F) Overall bias

Outcome 6: Any TEAE through week 16



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Bias arising from the randomization process

(B) Bias due to deviations from intended interventions

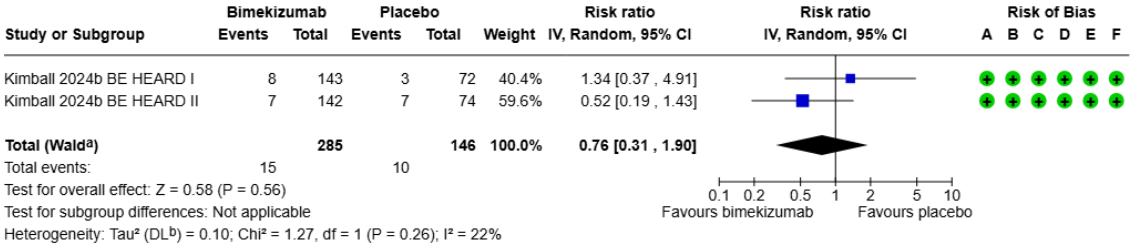
(C) Bias due to missing outcome data

(D) Bias in measurement of the outcome

(E) Bias in selection of the reported result

(F) Overall bias

Outcome 7: Other adverse events: Headache through week 16



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Bias arising from the randomization process

(B) Bias due to deviations from intended interventions

(C) Bias due to missing outcome data

(D) Bias in measurement of the outcome

(E) Bias in selection of the reported result

(F) Overall bias

1. Kimball AB, Jemec GBE, Sayed CJ, Kirby JS, Prens E, Ingram JR et al. Efficacy and safety of bimekizumab in patients with moderate-to-severe hidradenitis suppurativa (BE HEARD I and BE HEARD II): two 48-week, randomised, double-blind, placebo-controlled, multicentre phase 3 trials. Lancet 2024;403:2504-19.

Infliximab

e-Table 35. Infliximab vs placebo

Infliximab compared to placebo for hidradenitis suppurativa[1]

Patient or population: Adults with moderate-to-severe hidradenitis suppurativa
Intervention: infliximab (5 mg/kg) at weeks 0, 2, 6
Comparison: placebo at weeks 0, 2, 6

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with infliximab				
Mean change in pain VAS 100 from baseline to week 8	IFX Mean change 38 Placebo Mean change **0.6 (P<0.001)**		-	33 (1 RCT)[1]	⨁⨁◯◯ Low[a]	
Achieving HSSI 50 at week 8	56 per 1000	**267 per 1000** (33 to 1000)	**RR 4.80** (0.60 to 38.48)	33 (1 RCT)[1]	⨁⨁◯◯ Low[a]	
Decrease from baseline in DLQI	IFX group: 10 Placebo group: 1.6 (P = 0.003)			33 (1 RCT)[1]	⨁⨁◯◯ Low[b]	
Achieving Physician Global Assessment at week 8	167 per 1000	**800 per 1000** (277 to 1000)	**RR 4.80** (1.66 to 13.90)	33 (1 RCT)[1]	⨁⨁◯◯ Low[a]	
Mean Physician Global Assessment (PGA) scores at week 8	IFX group: 1.8 Placebo group: 4.7 (P < 0.001)			33 (1 RCT)[1]	⨁⨁◯◯ Low[b]	
75-99% improvement in PGA ('excellent')	IFX group: 1 (6.7%) Placebo group: 0			33 (1 RCT)[1]	⨁⨁◯◯ Low[b]	
100% improvement in PGA ('clear')	IFX group: 1.8 Placebo group: 4.7 (P < 0.001)			33 (1 RCT)[1]	⨁⨁◯◯ Low[b]	
Serious adverse events through week 8	0 per 1000	**0 per 1000** (0 to 0)	Not estimable	(1 RCT)[1]	⨁⨁◯◯ Low[b]	No events in either arm
Discontinuation due to AE through week 8	0 per 1000	**0 per 1000** (0 to 0)	Not estimable	(1 RCT)[1]	⨁⨁◯◯ Low[b]	No events in either arm

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two levels due to very serious imprecision small sample size.
[b]Downgraded by two levels due to very serious imprecision small sample size.

1. Grant A, Gonzalez T, Montgomery MO, Cardenas V , Kerdel FA. Infliximab therapy for patients with moderate to severe hidradenitis suppurativa: a randomized, double-blind, placebo-controlled crossover trial. J Am Acad Dermatol 2010;62:205-17.

e-Table 36. Infliximab (non-comparative cohort studies)

Prospective cohorts n=7, 132 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from retrospective and prospective cohorts, which are inherently limited due to the lack of control groups and randomization to treatment. The individual studies included small sample sizes, increasing concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias
Ghias 2020[1] Prospective cohort N=42	-Age: Mean 34.5 ± 11.9 years -24F, 18M -Hurley stage II n=1, III n=41 -BMI Mean 34.1 ± 7.1 kg/m^2	Induction dose of 7.5 mg/kg at weeks 0, 2, and 6, followed by maintenance dose of 7.5 mg/kg every 4 weeks Dose escalation to 10 mg/kg every 4 weeks for patients with insufficient disease control on IFX 7.5 (defined as HS-PGA ≥3) (n=16/42)	Topical antibiotics: 98.8% of patients (chlorhexidine wash, clindamycin gel 1%) Oral antibiotics: 91.0% of patients (clindamycin 300 mg and rifampin 300 mg twice daily; or levofloxacin 500 mg daily, rifampin 300 mg twice daily, and metronidazole	Weeks 4 & 12	Clinical response: HS-PGA score 0-2 with at least 2-grade improvement from baseline	Week 4: 20/42 (47.6%) Week 12: 17/24 (70.8%)	NOS Total 8/9
					30% or greater reduction and at least a 1-point decrease in NRS pain scores in pts with baseline NRS score of 3 or more	Week 4: 31/35 (88.6%) Week 12: 21/22 (95.5%)	

			500 mg 3 times per day) Anti-androgen therapy: 85.7% of patients (spironolactone 25-100 mg twice daily or finasteride 5 mg daily)		Safety	Serious AEs: 0/42 1/42 discontinued due to AE (myalgia & influenza-like symptoms)	
Montaudie 2017[2] Prospective cohort N=13	-Age Mean 36.1 (18-59) -9F, 3M -BMI mean 26.8 -Hurley II n=9, III n=4	5mg/kg at week 0, 2 ,6 ,14	NR	Week 14	HS-PGA(≥50%improved)	9/13 (69.2%)	NOS Total 4/9
					Mean VAS 100 from baseline	47.8 (range20-100) → 28.5 (range0-100)	
					Mean DLQI from baseline	15(range6-30)→10.3(range0-30)	
					Adverse events	1/13 (7.7%)	
Lesage 2012[3] Prospective cohort N=10	-Age mean 38.7 (24-54) -5F, 5M -Hurely II n=6, III n=4 -Obesity n=2 -Smoker n=9	5mg/kg at weeks 0, 2, 6, then q4w	Antibiotic therapy for flares	12 months	# of annual flares (mean)	24 to 6 over 12 months (P<0.05).	NOS Total 3/9
					Mean DLQI from baseline	20 (range 9-30) → 6 (range 1-13) p<0.001	
					Infectious episodes	N=4	
					Safety	1/10 keratoacanthoma; 1 urticarial eruption	
Mekkes 2007[4] Prospective cohort N=10	-Age mean 41 (23-53) -6F, 4M -Severe HS(≥5pus-producinglesions and acne severity score>100)	5mg/kg at week 0, 2, 6	NR	Week 2-6, 1 year, and 2 years	Change in mean Sartorius score	164 (SD 50) → 108 (SD 38) at 1 mo →89 (SD 49) at 1 year	NOS Total 4/9
					Change in mean DLQI score	18.4 (SD7.9) → 9.3 (SD 9.1) at 1 year	
					Recurrence	3/10 no recurrence at 2 years; average time to recurrence 8 months	
					Adverse events	3/10	
	-Age mean 37.9 (23-60)		NR		HSS ≥50%decrease	8/10 (80%)	

Paradela 2012[5] Prospective cohort N=10	-6F, 4M -Hurley stage II or III (ns not reported)	5mg/kg at weeks 0, 2, 6, then q8w Median of 7.5 doses over 49 weeks		Mean 42.7 weeks (range 3-181 weeks)	Recurrence	4/8 (50%) Time to recurrence 29-45 weeks	NOS Total 3/9
					Serious adverse events (life threatening)	0/10	
Westerkam 2021[6] Retrospective cohort N=20	-Mean age 42.2 (13.2) years -17F, 3M - Mean MBI37.20 -Hurley stage II n=2; III n=18	Continuous dose of infliximab for at least 10 weeks	NR	Up to 4 years	HiSCR50	12/20 (60%)	NOS Total 4/9
					Mean VAS 10 pain score change	6.12 →4.00 p=0.03	
					Mean DLQI score change	22.19→16.38 p=0.02	
					Adverse events	3/20 (15%)	
Islam 2025[7] Retrospective cohort N=27	-Mean age 34.74 years -Mean BMI 32.42 -15F, 12M -Hurley stage III n=24; Mean 2.88 -Smoker n=2	Infliximab at 3 week intervals (high frequency) IFX dosing included 7.5 mg/kg (3.7%), 10 mg/kg (51.9%), and 12.5 mg/kg (44.4%)	NR	Median 582 days	Mean HS-PGA change from dosing 4 wks to 3 wks	3.59 (1.18)→2.70 (1.06) p<0.001	NOS Total 3/9
					Minimum mean NRS pain score change from dosing 4 wks to 3 wks	1.80(2.57)→0.64(1.52) p=0.47	

1. Ghias MH, Johnston AD, Kutner AJ, Micheletti RG, Hosgood HD , Cohen SR. High-dose, high-frequency infliximab: A novel treatment paradigm for hidradenitis suppurativa. J Am Acad Dermatol 2020;82:1094-101.
2. Montaudié H, Seitz-Polski B, Cornille A, Benzaken S, Lacour J-P , Passeron T. Interleukin 6 and high-sensitivity C-reactive protein are potential predictive markers of response to infliximab in hidradenitis suppurativa. J Am Acad Dermatol 2017;76:156-8.
3. Lesage C, Adnot-Desanlis L, Perceau G, Bonnet M, Palot JP, Bernard P , Reguiaï Z. Efficacy and tolerance of prolonged infliximab treatment of moderate-to-severe forms of hidradenitis suppurativa. Eur J Dermatol 2012;22:640-4.
4. Mekkes JR , Bos JD. Long-term efficacy of a single course of infliximab in hidradenitis suppurativa. Br J Dermatol 2008;158:370-4.
5. Paradela S, Rodríguez-Lojo R, Fernández-Torres R, Arévalo P , Fonseca E. Long-term efficacy of infliximab in hidradenitis suppurativa. J Dermatolog Treat 2012;23:278-83.
6. Westerkam LL, Tackett KJ , Sayed CJ. Comparing the Effectiveness and Safety Associated With Infliximab vs Infliximab-abda Therapy for Patients With Hidradenitis Suppurativa. JAMA Dermatol 2021;157:708-11.

7. Islam Z, Wong JH, Alicea DS, Choi S, Andriano TM , Campton K. Three-week infliximab dosing is associated with improved disease control in severe hidradenitis suppurativa: A retrospective study. J Am Acad Dermatol 2025.

Secukinumab

e-Table 37. Secukinumab versus placebo

Secukinumab 300 mg compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: secukinumab 300 mg once weekly for four weeks followed by secukinumab 300 mg every two weeks or every four weeks
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with secukinumab 300 mg				
Achieving pain NRS 30 at week 16 - Q2W	231 per 1000	**365 per 1000** (277 to 481)	**RR 1.58** (1.20 to 2.08)	517 (2 RCTs)	⨁⨁⨁◯ Moderate[a]	
Achieving pain NRS 30 at week 16 - Q4W	231 per 1000	**333 per 1000** (250 to 444)	**RR 1.44** (1.08 to 1.92)	503 (2 RCTs)	⨁⨁⨁◯ Moderate[a]	
Achieving HiSCR 50 at week 16 - Q2W	325 per 1000	**439 per 1000** (361 to 530)	**RR 1.35** (1.11 to 1.63)	724 (2 RCTs)	⨁⨁⨁◯ Moderate[a]	
Achieving HiSCR 50 at week 16 - Q4W	325 per 1000	**439 per 1000** (364 to 530)	**RR 1.35** (1.12 to 1.63)	723 (2 RCTs)	⨁⨁⨁◯ Moderate[a]	
DLQI ≥ 5 point reduction from baseline in DLQI at week 16 -Q2W	304 per 1000	**426 per 1000** (307 to 590)	**RR 1.40** (1.01 to 1.94)	551 (2 RCTs)	⨁⨁⨁◯ Moderate[a]	
DLQI ≥ 5 point reduction from baseline in DLQI at week 16-Q4W	304 per 1000	**477 per 1000** (383 to 593)	**RR 1.57** (1.26 to 1.95)	543 (2 RCTs)	⨁⨁⨁⨁ High	
Serious adverse events (non-fatal) at 16 weeks – Q2W	30 per 1000	**25 per 1000** (10 to 62)	**RR 0.84** (0.34 to 2.03)	724 (2 RCTs)	⨁⨁⨁◯ Moderate[b]	
Serious adverse events (non-fatal events) through 16 weeks-Q4W	30 per 1000	**25 per 1000** (10 to 62)	**RR 0.84** (0.34 to 2.04)	723 (2 RCTs)	⨁⨁⨁◯ Moderate[b]	
Discontinuation due to AE through 16 weeks – Q2W	14 per 1000	**16 per 1000** (1 to 288)	**RR 1.13** (0.06 to 20.90)	724 (2 RCTs)	⨁⨁⨁◯ Moderate[b]	
Discontinuation due to AE through 16 weeks – Q4W	14 per 1000	**14 per 1000** (4 to 48)	**RR 1.01** (0.30 to 3.46)	723 (2 RCTs)	⨁⨁⨁◯ Moderate[b]	

Secukinumab 300 mg compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: secukinumab 300 mg once weekly for four weeks followed by secukinumab 300 mg every two weeks or every four weeks
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with secukinumab 300 mg				
Adverse events at 16 weeks – Q2W	650 per 1000	**650 per 1000** (585 to 722)	**RR 1.00** (0.90 to 1.11)	724 (2 RCTs)	⨁⨁⨁⨁ High	
Adverse events at 16 weeks -Q4W	650 per 1000	**644 per 1000** (579 to 715)	**RR 0.99** (0.89 to 1.10)	723 (2 RCTs)	⨁⨁⨁⨁ High	
Proportion of patients experiencing flares through 16 weeks - Secukinumab Q2W	281 per 1000	**177 per 1000** (132 to 242)	**RR 0.63** (0.47 to 0.86)	724 (2 RCTs)	⨁⨁⨁◯ Moderate[a]	
Proportion of patients experiencing flares through 16 weeks - Secukinumab Q4W	281 per 1000	**194 per 1000** (138 to 273)	**RR 0.69** (0.49 to 0.97)	723 (2 RCTs)	⨁⨁⨁◯ Moderate[a]	

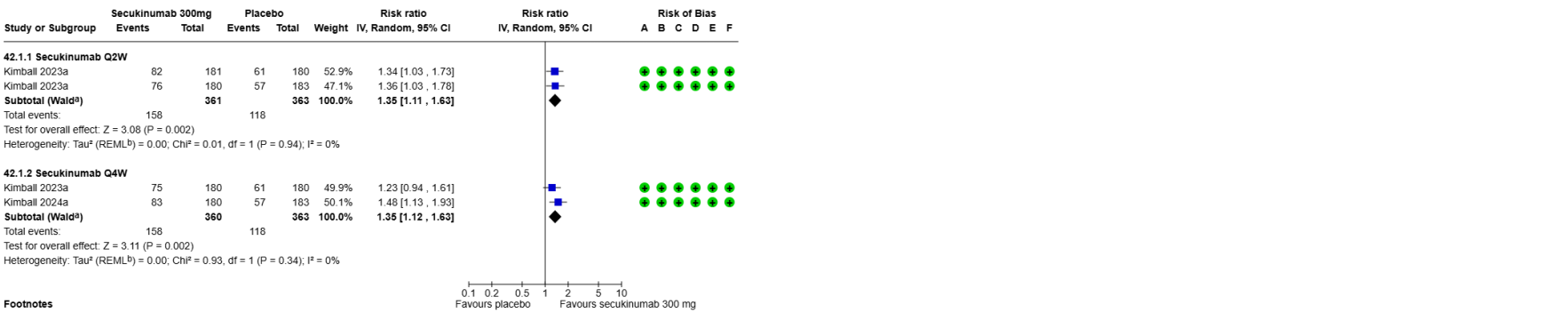
***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by one level due to serious imprecision: The 95% CI crossed either the conventional upper or lower thresholds of MID (0.75 or 1.25).
[b]Downgraded by one level due to serious imprecision: Although the CI is consistent with both meaningful benefit and harm, the overall event rates were low and comparable between groups, suggesting that secukinumab likely does not increase the risk of this event in the short term.

Outcome 2: Achieving HiSCR 50 at week 16



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend

(A) Bias arising from the randomization process

(B) Bias due to deviations from intended interventions

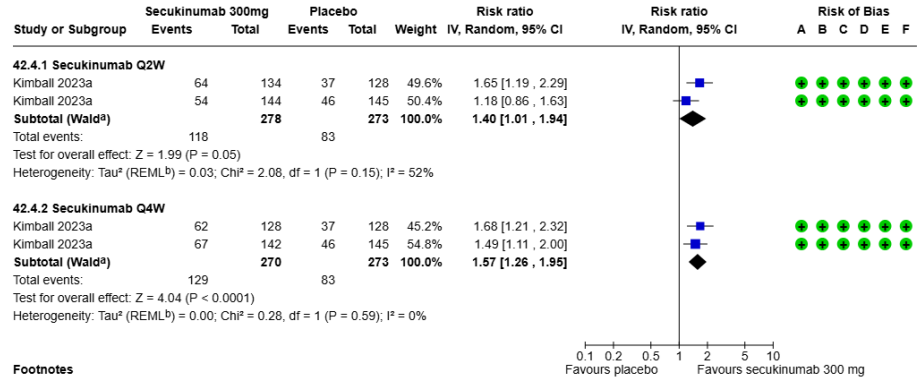
(C) Bias due to missing outcome data

(D) Bias in measurement of the outcome

(E) Bias in selection of the reported result

(F) Overall bias

Outcome 3: Achieving ≥ 5 point reduction from baseline in DLQI at week 16



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend

(A) Bias arising from the randomization process

(B) Bias due to deviations from intended interventions

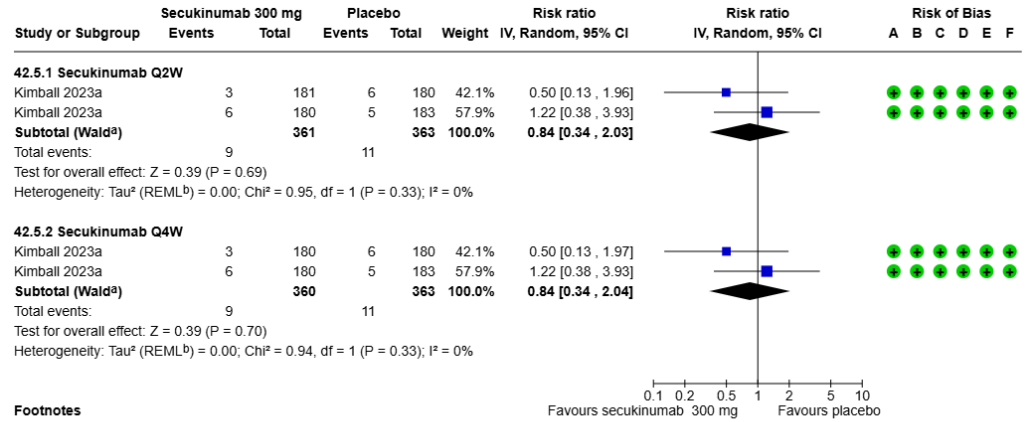
(C) Bias due to missing outcome data

(D) Bias in measurement of the outcome

(E) Bias in selection of the reported result

(F) Overall bias

Outcome 4: Serious adverse events (non-fatal events) through 16 weeks



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend

(A) Bias arising from the randomization process

(B) Bias due to deviations from intended interventions

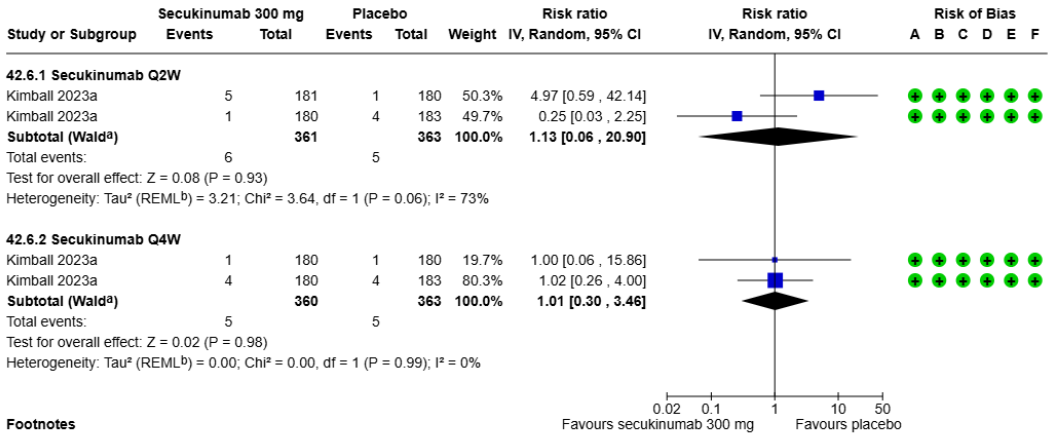
(C) Bias due to missing outcome data

(D) Bias in measurement of the outcome

(E) Bias in selection of the reported result

(F) Overall bias

Outcome 5: Adverse events leading to discontinuation through 16 weeks



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend

(A) Bias arising from the randomization process

(B) Bias due to deviations from intended interventions

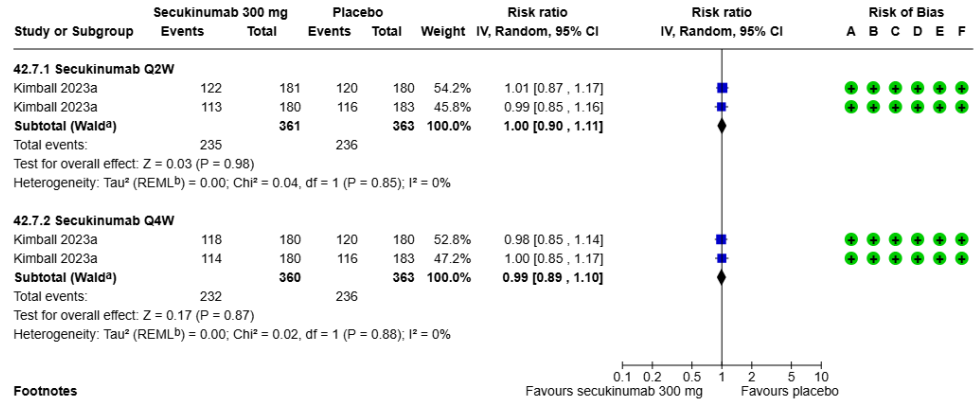
(C) Bias due to missing outcome data

(D) Bias in measurement of the outcome

(E) Bias in selection of the reported result

(F) Overall bias

Outcome 6: Any adverse events through 16 weeks



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend

(A) Bias arising from the randomization process

(B) Bias due to deviations from intended interventions

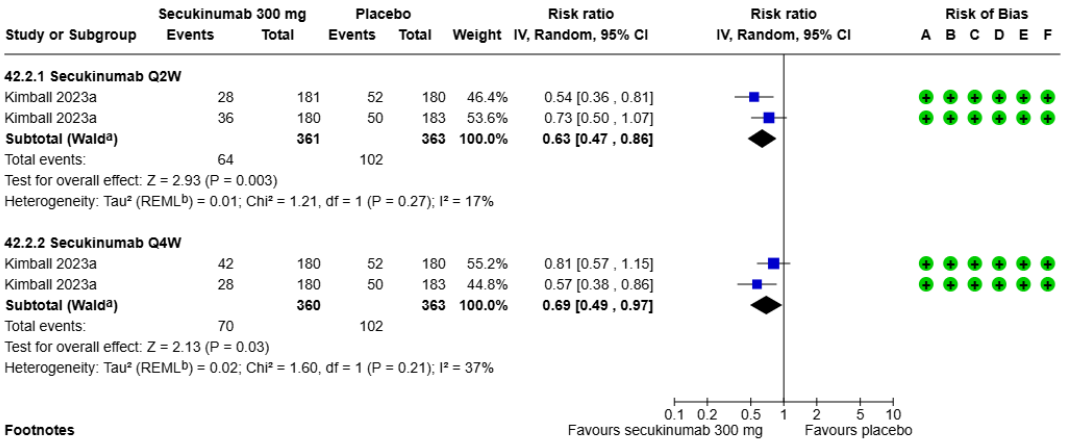
(C) Bias due to missing outcome data

(D) Bias in measurement of the outcome

(E) Bias in selection of the reported result

(F) Overall bias

Outcome 7: Proportion of patients experiencing flares through 16 weeks



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend

(A) Bias arising from the randomization process

(B) Bias due to deviations from intended interventions

(C) Bias due to missing outcome data

(D) Bias in measurement of the outcome

(E) Bias in selection of the reported result

(F) Overall bias

1. Kimball AB, Jemec GBE, Alavi A, Reguiai Z, Gottlieb AB, Bechara FG et al. Secukinumab in moderate-to-severe hidradenitis suppurativa (SUNSHINE and SUNRISE): week 16 and week 52 results of two identical, multicentre, randomised, placebo-controlled, double-blind phase 3 trials. Lancet 2023;401:747-61.

e-Table 38. Secukinumab every 2 weeks versus placebo based on biologic exposure status (biologic-experienced vs. biologic-naïve)

Secukinumab 300 mg every 2 weeks compared to placebo for hidradenitis suppurativa (biologic exposure)[1]

Patient or population: hidradenitis suppurativa (biologic exposure)
Intervention: secukinumab 300 mg every 2 weeks
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with secukinumab				
Achieving pain NRS30 - Biologic experienced follow-up: 16	129 per 1000	**328 per 1000** (163 to 661)	**RR 2.55** (1.27 to 5.14)	137 (1 RCT)	⨁⨁◯◯ Low[a]	
Achieving pain NRS30 - Biologic naive follow-up: 16 weeks	271 per 1000	**382 per 1000** (284 to 514)	**RR 1.41** (1.05 to 1.90)	380 (1 RCT)	⨁⨁⨁◯ Moderate[b]	
Achieving HiSCR 50 - Biologic experienced follow-up: 16 weeks	277 per 1000	**376 per 1000** (243 to 578)	**RR 1.36** (0.88 to 2.09)	174 (1 RCT)	⨁⨁⨁◯ Moderate[b]	
Achieving HiSCR 50 - Biologic naive follow-up: 16 weeks	342 per 1000	**455 per 1000** (369 to 561)	**RR 1.33** (1.08 to 1.64)	550 (1 RCT)	⨁⨁⨁◯ Moderate[c]	
Achieving HiSCR 75 - Biologic experienced follow-up: 16 weeks	145 per 1000	**223 per 1000** (113 to 438)	**RR 1.54** (0.78 to 3.03)	155 (1 RCT)	⨁⨁◯◯ Low[a]	
Achieving HiSCR 75 - Biologic naive follow-up: 16 weeks	166 per 1000	**264 per 1000** (186 to 375)	**RR 1.59** (1.12 to 2.26)	493 (1 RCT)	⨁⨁⨁◯ Moderate[c]	
Achieving IHS4-55 - Biologic experienced follow-up: 16 weeks	241 per 1000	**306 per 1000** (183 to 513)	**RR 1.27** (0.76 to 2.13)	155 (1 RCT)	⨁⨁⨁◯ Moderate[b]	
Achieving IHS4-55 - Biologic naive follow-up: 16 weeks	349 per 1000	**457 per 1000** (366 to 569)	**RR 1.31** (1.05 to 1.63)	493 (1 RCT)	⨁⨁⨁◯ Moderate[c]	
Achieving EQ-5D VAS score - Biologic experienced follow-up: 16 weeks	608 per 1000	**657 per 1000** (505 to 851)	**RR 1.08** (0.83 to 1.40)	132 (1 RCT)	⨁⨁⨁◯ Moderate[b]	
Achieving EQ-5D VAS score - Biologic naive follow-up: 16 weeks	645 per 1000	**691 per 1000** (607 to 787)	**RR 1.07** (0.94 to 1.22)	457 (1 RCT)	⨁⨁⨁⨁ High	
Proportion of patients experiencing flares - Biologic experienced follow-up: 16 weeks	277 per 1000	**263 per 1000** (160 to 429)	**RR 0.95** (0.58 to 1.55)	174 (1 RCT)	⨁⨁◯◯ Low[d]	
Proportion of patients experiencing flares - Biologic naive follow-up: 16 weeks	283 per 1000	**153 per 1000** (110 to 215)	**RR 0.54** (0.39 to 0.76)	550 (1 RCT)	⨁⨁⨁◯ Moderate[c]	

Secukinumab 300 mg every 2 weeks compared to placebo for hidradenitis suppurativa (biologic exposure)[1]

Patient or population: hidradenitis suppurativa (biologic exposure)
Intervention: secukinumab 300 mg every 2 weeks
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with secukinumab				
Achieving ≥ 5 point reduction from baseline in DLQI - Biologic experienced follow-up: 16 weeks	309 per 1000	**435 per 1000** (272 to 695)	**RR 1.41** (0.88 to 2.25)	121 (1 RCT)	⨁⨁⨁◯ Moderate[b]	
Achieving ≥ 5 point reduction from baseline in DLQI - Biologic naive follow-up: 16 weeks	303 per 1000	**422 per 1000** (325 to 549)	**RR 1.39** (1.07 to 1.81)	421 (1 RCT)	⨁⨁⨁◯ Moderate[c]	
Serious adverse events (death) through - Biologic experienced follow-up: 16 weeks	0 per 1000	**0 per 1000** (0 to 0)	Not estimable	174 (1 RCT)	⨁⨁⨁◯ Moderate[e]	No events in either arm
Serious adverse events (death) - Biologic naive follow-up: 16 weeks	0 per 1000	**0 per 1000** (0 to 0)	Not estimable	550 (1 RCT)	⨁⨁⨁◯ Moderate[e]	No events in either arm
Serious adverse events (non-fatal events)- Biologic experienced follow-up: 16 weeks	32 per 1000	**50 per 1000** (11 to 217)	**RR 1.57** (0.36 to 6.79)	174 (1 RCT)	⨁⨁◯◯ Low[a]	
Serious adverse events (non-fatal events) - Biologic naive follow-up: 16 weeks	30 per 1000	**18 per 1000** (6 to 54)	**RR 0.60** (0.20 to 1.81)	550 (1 RCT)	⨁⨁◯◯ Low[a]	
Adverse events leading to discontinuation - Biologic experienced follow-up: 16 weeks	32 per 1000	**50 per 1000** (11 to 217)	**RR 1.57** (0.36 to 6.79)	174 (1 RCT)	⨁⨁◯◯ Low[a]	
Adverse events leading to discontinuation - Biologic naive follow-up: 16 weeks	7 per 1000	**7 per 1000** (1 to 50)	**RR 0.96** (0.14 to 6.75)	550 (1 RCT)	⨁⨁◯◯ Low[a]	
Any adverse events - Biologic experienced follow-up: 16 weeks	617 per 1000	**636 per 1000** (506 to 802)	**RR 1.03** (0.82 to 1.30)	174 (1 RCT)	⨁⨁⨁◯ Moderate[b]	
Any adverse events - Biologic naive follow-up: 16 weeks	662 per 1000	**655 per 1000** (582 to 741)	**RR 0.99** (0.88 to 1.12)	550 (1 RCT)	⨁⨁⨁⨁ High	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two levels due to imprecision: small sample size (the ratio of the upper to the lower boundary of the CI was > 3).
[b]Downgraded by one level due to imprecision: small sample size and the 95% CI crossed either the conventional upper or lower thresholds of MID (25&).
[c]Downgraded by two levels due to imprecision: the ratio of the upper to the lower boundary of the CI was > 3.
[d]Downgraded by one level due to imprecision: the 95% CI crossed either the conventional upper or lower thresholds of MID (25%).

[e]Downgraded by one level due to imprecision: small sample size.

1. Zouboulis CC, Passeron T, Pariser D, Wozniak MB, Li X, Uhlmann L et al. Secukinumab in patients with moderate-to-severe hidradenitis suppurativa based on prior biologic exposure: an efficacy and safety analysis from the SUNSHINE and SUNRISE phase III trials. Br J Dermatol 2024;190:836-45.

e-Table 39. Secukinumab every 4 weeks versus placebo based on biologic exposure status (biologic-experienced vs. biologic-naïve)

Secukinumab 300 mg every 4 weeks compared to placebo for hidradenitis suppurativa (biologic exposure)[1]

Patient or population: hidradenitis suppurativa (biologic exposure)
Intervention: secukinumab 300 mg every 4 weeks
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with secukinumab				
Achieving NRS 30 at week 16 - Biologic experienced	129 per 1000	**339 per 1000** (167 to 687)	**RR 2.64** (1.30 to 5.34)	129 (1 RCT)	⨁⨁◯◯ Low[a]	
Achieving NRS 30 at week 16 - Biologic naive	271 per 1000	**336 per 1000** (246 to 460)	**RR 1.24** (0.91 to 1.70)	374 (1 RCT)	⨁⨁⨁◯ Moderate[b]	
Achieving HiSCR 50 at week 16 - Biologic experienced	277 per 1000	**382 per 1000** (249 to 586)	**RR 1.38** (0.90 to 2.12)	175 (1 RCT)	⨁⨁⨁◯ Moderate[b]	
Achieving HiSCR 50 at week 16 - Biologic naive	342 per 1000	**455 per 1000** (369 to 561)	**RR 1.33** (1.08 to 1.64)	548 (1 RCT)	⨁⨁⨁◯ Moderate[c]	
Achieving HiSCR 75 at week 16 - Biologic experienced	145 per 1000	**230 per 1000** (117 to 448)	**RR 1.59** (0.81 to 3.10)	157 (1 RCT)	⨁⨁⨁◯ Moderate[a]	
Achieving HiSCR 75 at week 16 - Biologic naive	166 per 1000	**285 per 1000** (202 to 403)	**RR 1.72** (1.22 to 2.43)	491 (1 RCT)	⨁⨁⨁◯ Moderate[c]	
Achieving IHS4 55 at week 16 - Biologic experienced	241 per 1000	**337 per 1000** (205 to 557)	**RR 1.40** (0.85 to 2.31)	157 (1 RCT)	⨁⨁⨁◯ Moderate[b]	
Achieving IHS4 55 at week 16 - Biologic naive	349 per 1000	**464 per 1000** (373 to 579)	**RR 1.33** (1.07 to 1.66)	491 (1 RCT)	⨁⨁⨁◯ Moderate[c]	

Secukinumab 300 mg every 4 weeks compared to placebo for hidradenitis suppurativa (biologic exposure)[1]

Patient or population: hidradenitis suppurativa (biologic exposure)
Intervention: secukinumab 300 mg every 4 weeks
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with secukinumab				
Achieving EQ-5D VAS score at week 16 - Biologic experienced	608 per 1000	**657 per 1000** (511 to 845)	**RR 1.08** (0.84 to 1.39)	141 (1 RCT)	⨁⨁⨁◯ Moderate[b]	
Achieving EQ-5D VAS score at week 16 - Biologic naive	645 per 1000	**684 per 1000** (600 to 781)	**RR 1.06** (0.93 to 1.21)	451 (1 RCT)	⨁⨁⨁⨁ High	
Proportion of patients experiencing flares through 16 weeks - Biologic experienced	277 per 1000	**260 per 1000** (158 to 423)	**RR 0.94** (0.57 to 1.53)	175 (1 RCT)	⨁⨁◯◯ Low[d]	
Proportion of patients experiencing flares through 16 weeks - Biologic naive	283 per 1000	**175 per 1000** (127 to 240)	**RR 0.62** (0.45 to 0.85)	548 (1 RCT)	⨁⨁⨁◯ Moderate[c]	
Achieving ≥ 5 point reduction from baseline in DLQI at week 16 - Biologic experienced	309 per 1000	**491 per 1000** (315 to 763)	**RR 1.59** (1.02 to 2.47)	127 (1 RCT)	⨁⨁⨁◯ Moderate[b]	
Achieving ≥ 5 point reduction from baseline in DLQI at week 16 - Biologic naive	303 per 1000	**464 per 1000** (361 to 598)	**RR 1.53** (1.19 to 1.97)	412 (1 RCT)	⨁⨁⨁◯ Moderate[c]	
Serious adverse events (death) through 16 weeks - Biologic experienced	0 per 1000	**0 per 1000** (0 to 0)	Not estimable	175 (1 RCT)	⨁⨁◯◯ Low[e]	
Serious adverse events (death) through 16 weeks - Biologic naive	0 per 1000	**0 per 1000** (0 to 0)	**RR 2.89** (0.12 to 70.70)	548 (1 RCT)	⨁⨁◯◯ Low[f]	
Serious adverse events (non-fatal events) through 16 weeks - Biologic experienced	32 per 1000	**62 per 1000** (15 to 250)	**RR 1.93** (0.48 to 7.84)	175 (1 RCT)	⨁⨁◯◯ Low[a]	
Serious adverse events (non-fatal events) through 16 weeks - Biologic naive	30 per 1000	**14 per 1000** (4 to 47)	**RR 0.48** (0.15 to 1.58)	548 (1 RCT)	⨁⨁◯◯ Low[a]	
Adverse events leading to discontinuation through 16 weeks - Biologic experienced	32 per 1000	**12 per 1000** (1 to 116)	**RR 0.39** (0.04 to 3.65)	175 (1 RCT)	⨁⨁◯◯ Low[a]	
Adverse events leading to discontinuation through 16 weeks - Biologic naive	7 per 1000	**14 per 1000** (3 to 78)	**RR 1.93** (0.36 to 10.44)	548 (1 RCT)	⨁⨁◯◯ Low[f]	
Any adverse events through 16 weeks - Biologic experienced	617 per 1000	**654 per 1000** (524 to 821)	**RR 1.06** (0.85 to 1.33)	175 (1 RCT)	⨁⨁⨁◯ Moderate[b]	
Any adverse events through 16 weeks - Biologic naive	662 per 1000	**642 per 1000** (569 to 728)	**RR 0.97** (0.86 to 1.10)	548 (1 RCT)	⨁⨁⨁⨁ High	

Secukinumab 300 mg every 4 weeks compared to placebo for hidradenitis suppurativa (biologic exposure)[1]

Patient or population: hidradenitis suppurativa (biologic exposure)
Intervention: secukinumab 300 mg every 4 weeks
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	**Risk with secukinumab**				

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two levels due to imprecision: small sample size and the 95% CI crossed both the conventional upper and lower thresholds of MID (0.75 and 1.25).
[b]Downgraded by two levels due to imprecision: small sample size (the ratio of the upper to the lower boundary of the CI was > 3).
[c]Downgraded by one level due to imprecision: small sample size and the 95% CI crossed either the conventional upper or lower thresholds of MID (0.75 or 1.25).
[d]Downgraded by two levels due to imprecision: the ratio of the upper to the lower boundary of the CI was > 3.
[e]Downgraded by one level due to imprecision: the 95% CI crossed either the conventional upper or lower thresholds of MID (0.75 or 1.25).
[f]Downgraded by two levels due to imprecision: small sample size.
[g]Downgraded by two levels due to imprecision: the 95% CI crossed both the conventional upper and lower thresholds of MID (0.75 and 1.25).

1. Zouboulis CC, Passeron T, Pariser D, Wozniak MB, Li X, Uhlmann L et al. Secukinumab in patients with moderate-to-severe hidradenitis suppurativa based on prior biologic exposure: an efficacy and safety analysis from the SUNSHINE and SUNRISE phase III trials. Br J Dermatol 2024;190:836-45.

Etanercept

e-Table 40. Etanercept vs placebo

Etanercept compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: Etanercept 50mg subcutaneous injection twice weekly
Comparison: Placebo subcutaneous injection twice weekly

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Placebo	**Risk with Etanercept**				
Physician-assessed Pain	No significant difference (P = 0.78 at 12 weeks; P = 0.53 at 24 weeks)			17 (1 RCT)[1]	⨁⨁◯◯ Low[a]	

Patient Pain Assessment	No significant difference at 12 (P = 0.77) or 24 weeks (P > 0.99)			17 (1 RCT)[1]	⨁⨁◯◯ Low[a]	
Dermatology Life Quality Index (DLQI)	No significant difference at 12 weeks (P = 0.12) or 24 weeks (P = 0.47)			17 (1 RCT)[1]	⨁⨁◯◯ Low[a]	
Physician global assessment of HS as clear or mild at week 12	No significant difference between treatment and placebo groups at 12 or 24 weeks (P > 0.99)			17 (1 RCT)[1]	⨁⨁◯◯ Low[a]	
Physician-assessed Erythema	No significant difference (P > 0.99 at 12 weeks; P = 0.33 at 24 weeks)			17 (1 RCT)[1]	⨁⨁◯◯ Low[a]	
Serious adverse events through week 24 follow-up: 24 weeks	Not pooled	Not pooled	Not pooled	17 (1 RCT)[1]	⨁⨁◯◯ Low[a]	No serious adverse events occurred in either arm.
Patient Global Assessment	No significant difference between groups (P = 0.41 at 12 weeks)			17 (1 RCT)[1]	⨁⨁◯◯ Low[a]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations
[a]Downgraded by two levels due to very serious imprecision: very small sample.

1. Adams DR, Yankura JA, Fogelberg AC , Anderson BE. Treatment of hidradenitis suppurativa with etanercept injection. Arch Dermatol 2010;146:501-4.

e-Table 41. Etanercept (non-comparative studies)

Open-label trials n=3, 31 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from non-randomized, uncontrolled, open-label trials. The individual studies included small sample sizes, increasing concern about random error and imprecision. Varied outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias
Cusack 2006[1]	-Mean age 32.3 y (range 16-42) -6F, 0M -Hurley stage II or III	Etanercept 25mg subcutaneously twice weekly	None	12 to 40 weeks	Mean Patient-reported % clinical	61% (range 50-70)	Moderate

Open-label trial N=6		N=2 increased to 50mg after 2 months Duration varied			improvement at 24 weeks		
					Mean reduction in DLQI at 24 weeks	64% (range 44-73)	
					Average relapse frequency	6 → 2	
					Adverse reactions	0/6	
Giamarellos-Bourboulis 2008[2] Pelekanou 2010[3] Open-label trial N=10	-Aged 18-59y -7F, 3M -HS activity index >20	Etanercept 50mg subcutaneously once weekly for 12 weeks 2nd course in 7/10 pateints	None	24 weeks long-term f/u through 144 weeks	>30% decrease from baseline in Sartorius score	8/10 (80%)	Moderate
					Infection	1/10 (10%)	
					Serious adverse events	0/10	
					Recurrence	6/7 (85.7%) had no recurrence through week 144	
Lee 2009[4] Open-label trial N=15	-Mean age 42y -13F, 2M -Hurley stage II or III -Mean BMI 35.1	Etanercept 50 mg subcutaneously once weekly for 12 weeks At week 12, etanercept was tapered to 25 mg/wk over a 2-week period	None	12 weeks	Median PGA score from baseline	4.35 →3.5 p=0.14	Moderate
					Median DLQI from baseline	19→15 p=0.02	
					Median VAS 100 pain score from baseline	6.4→4.1 p=0.08	
					Adverse events	14/15 (93.3%)	

1. Cusack C , Buckley C. Etanercept: effective in the management of hidradenitis suppurativa. Br J Dermatol 2006;154:726-9.
2. Giamarellos-Bourboulis EJ, Pelekanou E, Antonopoulou A, Petropoulou H, Baziaka F, Karagianni V et al. An open-label phase II study of the safety and efficacy of etanercept for the therapy of hidradenitis suppurativa. Br J Dermatol 2008;158:567-72.

3. Pelekanou A, Kanni T, Savva A, Mouktaroudi M, Raftogiannis M, Kotsaki A , Giamarellos-Bourboulis EJ. Long-term efficacy of etanercept in hidradenitis suppurativa: results from an open-label phase II prospective trial. Exp Dermatol 2010;19:538-40.
4. Lee RA, Dommasch E, Treat J, Sciacca-Kirby J, Chachkin S, Williams J et al. A prospective clinical trial of open-label etanercept for the treatment of hidradenitis suppurativa. J Am Acad Dermatol 2009;60:565-73.

Guselkumab

Table 42. Guselkumab versus placebo

Guselkumab compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: guselkumab 200mg every 4 weeks (SC) or guselkumab 1200mg every 4 weeks (IV) for initial dosing (0-12 weeks)
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with guselkumab				
Achieving HiSCR50 - Guselkumab subcutaneous (SC) follow-up: 16 weeks	387 per 1000	**507 per 1000** (341 to 759)	**RR 1.31** (0.88 to 1.96)	121 (1 RCT)	⨁⨁⨁◯ Moderate[a]	
Achieving HiSCR50 - Guselkumab intravenously (IV) follow-up: 16 weeks	387 per 1000	**449 per 1000** (294 to 685)	**RR 1.16** (0.76 to 1.77)	122 (1 RCT)	⨁⨁⨁◯ Moderate[a]	
Achieving DLQI 0/1 - Guselkumab subcutaneous (SC) follow-up: 16 weeks	48 per 1000	**90 per 1000** (22 to 357)	**RR 1.85** (0.46 to 7.37)	118 (1 RCT)	⨁⨁◯◯ Low[b]	
Achieving DLQI 0/1 - Guselkumab intravenously (IV) follow-up: 16 weeks	48 per 1000	**50 per 1000** (11 to 238)	**RR 1.03** (0.22 to 4.92)	122 (1 RCT)	⨁⨁◯◯ Low[b]	
Serious adverse events - Guselkumab subcutaneous (SC) follow-up: 16 weeks	48 per 1000	**17 per 1000** (2 to 158)	**RR 0.35** (0.04 to 3.27)	121 (1 RCT)	⨁⨁◯◯ Low[b]	
Serious adverse events - Guselkumab intravenously (IV) follow-up: 16 weeks	48 per 1000	**16 per 1000** (2 to 156)	**RR 0.34** (0.04 to 3.22)	122 (1 RCT)	⨁⨁◯◯ Low[b]	
Discontinuation due to AE - Guselkumab subcutaneous (SC) follow-up: 16 weeks	0 per 1000	**0 per 1000** (0 to 0)	**RR 3.15** (0.13 to 75.82)	121 (1 RCT)	⨁⨁⨁◯ Moderate[c]	1/59 with guselkumab vs 0/62 with placebo
Discontinuation due to AE - Guselkumab intravenously (IV) follow-up: 16 weeks	0 per 1,000	0 per 1000	Not pooled	121 (1 RCT)	⨁⨁⨁◯ Moderate[c]	No adverse events occurred in either arm

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

Guselkumab compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: guselkumab 200mg every 4 weeks (SC) or guselkumab 1200mg every 4 weeks (IV) for initial dosing (0-12 weeks)
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with guselkumab				

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by one level due to serious imprecision: The 95% CI crossed either the conventional upper or lower threshold of MID (0.75 or 1.25).
[b]Downgraded by two levels due to very serious imprecision: the 95% CI crossed both the conventional upper and lower thresholds of MID (0.75 and 1.25).
[c]Downgraded by two levels due to serious imprecision: small sample size.

1. Kimball AB, Podda M, Alavi A, Miller M, Shen YK, Li S et al. Guselkumab for the treatment of patients with moderate-to-severe hidradenitis suppurativa: A phase 2 randomized study. J Eur Acad Dermatol Venereol 2023;37:2098-108.

Risankizumab

e-Table 43. Risankizumab versus placebo

Risankizumab (RZB) compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: Risankizumab (RZB) 180mg or 360mg at 0, 1, 2, 4 and 12 weeks
Comparison: Placebo

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Certainty	What happens
		Placebo	Risankizumab (RZB)	Difference		
Achieving HiSCR 50 at week 16 - RZB 180 mg № of participants: 162 (1 RCT)	**RR 1.12** (0.79 to 1.58)	41.5%	**46.4%** (32.8 to 65.5)	**5.0% more** (8.7 fewer to 24 more)	⊕⊕⊕◯ Moderate[a]	
Achieving HiSCR 50 at week 16 - RZB 360 mg № of participants: 163 (1 RCT)	**RR 1.04** (0.73 to 1.49)	41.5%	**43.1%** (30.3 to 61.8)	**1.7% more** (11.2 fewer to 20.3 more)	⊕⊕◯◯ Low[b]	

Risankizumab (RZB) compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: Risankizumab (RZB) 180mg or 360mg at 0, 1, 2, 4 and 12 weeks
Comparison: Placebo

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Certainty	What happens
		Placebo	**Risankizumab (RZB)**	**Difference**		
Change in DLQI at week 16 - RZB 180 mg № of participants: 162 (1 RCT)	-	mean change in DLQI: **-2.1**	-	MD **1.4 lower** (3.62 lower to 0.82 higher)	⊕⊕⊕⊕ High	
Change in DLQI at week 16 - RZB 360 mg № of participants: 163 (1 RCT)	-	mean change in DLQI: **-2.1**	-	MD **1.6 lower** (3.82 lower to 0.62 higher)	⊕⊕⊕⊕ High	
DLQI score 0/1 at week 16 - RZB 180 mg № of participants: 162 (1 RCT)	**RR 0.68** (0.20 to 2.33)	7.3%	**5.0%** (1.5 to 17)	**2.3% fewer** (5.9 fewer to 9.7 more)	⊕⊕◯◯ Low[c]	
DLQI score 0/1 at week 16 - RZB 360 mg № of participants: 163 (1 RCT)	**RR 1.01** (0.34 to 3.01)	7.3%	**7.4%** (2.5 to 22)	**0.1% more** (4.8 fewer to 14.7 more)	⊕⊕◯◯ Low[c]	
Serious adverse events through 16 weeks - RZB 180 mg № of participants: 162(1 RCT)	**RR 1.54** (0.26 to 8.96)	2.4%	**3.8%** (0.6 to 21.9)	**1.3% more** (1.8 fewer to 19.4 more)	⊕⊕◯◯ Low[c]	
Serious adverse events through 16 weeks - RZB 360 mg № of participants: 162 (1 RCT)	**RR 1.03** (0.15 to 7.10)	2.4%	**2.5%** (0.4 to 17.3)	**0.1% more** (2.1 fewer to 14.9 more)	⊕⊕◯◯ Low[c]	
Adverse events leading to discontinuation of intervention through 16 weeks - RZB 180 mg № of participants: 162 (1 RCT)	**RR 1.37** (0.32 to 5.91)	3.7%	**5.0%** (1.2 to 21.6)	**1.4% more** (2.5 fewer to 18 more)	⊕⊕◯◯ Low[c]	
Adverse events leading to discontinuation of intervention through 16 weeks - RZB 360 mg № of participants: 162 (1 RCT)	**RR 0.68** (0.12 to 3.98)	3.7%	**2.5%** (0.4 to 14.6)	**1.2% fewer** (3.2 fewer to 10.9 more)	⊕⊕◯◯ Low[c]	
Treatment-emergent adverse event (TEAE) through 16 weeks - RZB 180 mg № of participants: 162 (1 RCT)	**RR 1.09** (0.86 to 1.37)	61.0%	**66.5%** (52.4 to 83.5)	**5.5% more** (8.5 fewer to 22.6 more)	⊕⊕⊕◯ Moderate[a]	
Treatment-emergent adverse event (TEAE) through 16 weeks - RZB 360 mg № of participants: 162 (1 RCT)	**RR 0.98** (0.77 to 1.26)	61.0%	**59.8%** (47 to 76.8)	**1.2% fewer** (14 fewer to 15.9 more)	⊕⊕⊕◯ Moderate[a]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

Risankizumab (RZB) compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: Risankizumab (RZB) 180mg or 360mg at 0, 1, 2, 4 and 12 weeks
Comparison: Placebo

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Certainty	What happens
		Placebo	Risankizumab (RZB)	Difference		

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by one level due to serious imprecision: The 95% CI crossed either the conventional upper or lower threshold of MID (0.75 or 1.25).
[b]Downgraded by two levels due to very serious imprecision: The 95% CI crossed both the conventional upper and lower thresholds of MID (0.75 and 1.25).
[c]Downgraded by two levels due to very serious imprecision: Small sample size and the ratio of the upper to the lower boundary of the CI was > 3.

1. Kimball AB, Prens EP, Passeron T, Maverakis E, Turchin I, Beeck S et al. Efficacy and Safety of Risankizumab for the Treatment of Hidradenitis Suppurativa: A Phase 2, Randomized, Placebo-Controlled Trial. Dermatol Ther (Heidelb) 2023;13:1099-111.

Vilobelimab

e-Table 44. Vilobelimab (IFX-1) vs placebo

Vilobelimab (IFX-1) compared to placebo for hidradenitis suppurativa[1, 2]

Patient or population: severe hidradenitis suppurativa refractory to adalimumab
Intervention: Vilobelimab (IFX-1) 400mg Q4W or 800mg Q4W or 800mg Q2W or 1200mg Q2W
Comparison: placebo

Outcomes	Results	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
HiSCR50 at 16 weeks	- Placebo: 16/36 (47.1%) - IFX-1 400mg Q4W: 12/34 (40%) - IFX-1 800mgQ4W: 17/35 (51.5%) - IFX-1 800mg Q2W: 12/36 (38.7%) - IFX-1 1200mg Q2W: 15/36 (45.5%)	(p: 0.85 vs placebo)	177 (1 RCT)	⨁⨁◯◯ Low[a]	

Decrease of IHS4, week 16	- - - - -	Placebo: 19.8% IFX-1 400mg Q4W: 24.6% IFX-1 800mgQ4W: 41.1% IFX-1 800mg Q2W: 38.4% IFX-1 1200mg Q2W: 51.4%	(p: 0.020 vs placebo	177 (1 RCT)	⊕⊕◯◯ Low[b]
Flares at week 16	- - - - -	Placebo: 6/34 (18%) IFX-1 400mg Q4W: 3/30 (10%) IFX-1 800mgQ4W: 1/32 (3%) IFX-1 800mg Q2W: 0/30 IFX-1 1200mg Q2W: 1/32 (3%)	(p: 0.04 vs placebo)	158 (1 RCT)	⊕⊕◯◯ Low[b]
Absolute change from baseline in average global assessment of skin pain at 16 weeks Median(IQR)	- - - - -	Placebo: -0.9 (-2.4, 0.7) IFX-1 400mg Q4W: -0.2 (-0.9, 2.0) IFX-1 800mgQ4W: -0.6 (-1.9, 0.8) IFX-1 800mg Q2W: -1.1 (-1.9, 0.2) IFX-1 1200mg Q2W: -0.8 (-2.3, 0.0)	(p: 0.23 vs placebo)	177 (1 RCT)	⊕⊕◯◯ Low[b]
Absolute change from baseline in DLQI at 16 weeks Median(IQR)	- - - - -	Placebo: -1.5 (-5.0, 3.0) IFX-1 400mg Q4W: -1.0(-3.0, 5.0) IFX-1 800mgQ4W: -3.0 (-6.0, 1.0) IFX-1 800mg Q2W: -6.0 (-9.0, 1.0) IFX-1 1200mg Q2W: -1.5(-5.5, 2.5)	(p: 0.05 vs placebo)	177 (1 RCT)	⊕⊕◯◯ Low[b]
Decrease of AN count, week 16	- - - - -	Placebo: 25.9% IFX-1 400mg Q4W: 32.3% IFX-1 800mgQ4W: 53.7% IFX-1 800mg Q2W: 43.9% IFX-1 1200mg Q2W: 48.4%	-	177 (1 RCT)	⊕⊕◯◯ Low[b]
Decrease of Draining tunnels count, week 16	- - - - -	Placebo: 17.9% IFX-1 400mg Q4W: 14.5% IFX-1 800mgQ4W: 14.9% IFX-1 800mg Q2W: 28% IFX-1 1200mg Q2W: 63.2%	(p: 0.0001 vs placebo)	177 (1 RCT)	⊕⊕◯◯ Low[b]
Decrease of AN and draining tunnels count together, week 16	- - - - -	Placebo: 25.3% IFX-1 400mg Q4W: 29.4% IFX-1 800mgQ4W: 48.4% IFX-1 800mg Q2W: 40.9% IFX-1 1200mg Q2W: 50.4%	(p: 0.028 vs placebo)	177 (1 RCT)	⊕⊕◯◯ Low[b]
Decreases of AN, mean, week 16	- - - - -	Placebo: 25.9% IFX-1 400mg Q4W: 32.3% IFX-1 800mgQ4W: 53.7% IFX-1 800mg Q2W: 43.9% IFX-1 1200mg Q2W: 47.8%	-	177 (1 RCT)	⊕⊕◯◯ Low[b]
Serious Treatment-related AEs 16 weeks	- - - - -	Placebo: 0/36 IFX-1 400mg Q4W: 0/34 IFX-1 800mgQ4W: 0/35 IFX-1 800mg Q2W: 1/36 (2.8%) IFX-1 1200mg Q2W: 0/36	-	177 (1 RCT)	⊕⊕◯◯ Low[b]

Treatment-related AEs 16 weeks	- - - - -	Placebo: 15/36 (41.7%) IFX-1 400mg Q4W: 13/34 (38.2%) IFX-1 800mgQ4W: 9/35 (25.7%) IFX-1 800mg Q2W: 10/36 (27.8%) IFX-1 1200mg Q2W: 10/36 (27.8%)	-	177 (1 RCT)	⨁⨁◯◯ Low[b]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Rated down twice for imprecision based on small sample and imprecise findings when comparing placebo to most effective active dose.
b. The sample size per arm is very small which is concerning for precision.

1. Giamarellos-Bourboulis EJ JG, Prens EP, Riedemann N, Szepietowski JC, Van Der Zee HH, Zouboulis CC, & Sayed CJ Outcome measures for moderate and severe hidradenitis suppurativa: lessons learned from the SHINE study. Exp Dermatol 2022;31:44.
2. Giamarellos-Bourboulis EJ, Jemec GBE, Prens EP, Riedemann NC, Otto I, Weisman J et al. Vilobelimab to improve clinical outcomes of moderate-to-severe hidradenitis suppurativa through an adjunctive effect on draining tunnels: Results of the SHINE double-blind, placebo-controlled randomised trial. Br J Dermatol 2025.

Anakinra

e-Table 45. Anakinra versus placebo

Anakinra compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: anakinra 100mg once daily (subcutaneous)
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with anakinra				
Achieving HiSCR50 at week 12	300 per 1000	**777 per 1000** (285 to 1000)	**RR 2.59** (0.95 to 7.11)	19 (1 RCT)	⨁⨁◯◯ Low[a]	

Anakinra compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: anakinra 100mg once daily (subcutaneous)
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with anakinra				
Serious adverse events through week 24	0 per 1000	**0 per 1000** (0 to 0)	Not estimable	19 (1 RCT)	⨁⨁◯◯ Low[b]	No events in either arm
Adverse events through week 24	100 per 1000	**333 per 1000** (42 to 1000)	**RR 3.33** (0.42 to 26.58)	19 (1 RCT)	⨁⨁◯◯ Low[a]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two levels due to very serious imprecision (small sample size and the ratio of the upper to the lower boundary of the CI was > 3).
[b]Downgraded by two levels due to very serious imprecision: zero events with small sample size

1. Tzanetakou V, Kanni T, Giatrakou S, Katoulis A, Papadavid E, Netea MG et al. Safety and Efficacy of Anakinra in Severe Hidradenitis Suppurativa: A Randomized Clinical Trial. JAMA Dermatol 2016;152:52-9.

e-Table 46. Anakinra (non-comparative studies)

Open-label trial n=1, 6 patients

Overall Certainty of the Evidence: Very Low (The evidence comes a single, small non-randomized, uncontrolled trial, increasing concern about random error and imprecision.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias
Leslie 2014[1]	-Mean age 36.8 -4F, 2M		Oral or topical antibiotics	8 weeks	Sartorius Score mean decrease from baseline n=5	34.8	Moderate

Open-label trial N=6	-Moderate to severe HS	100 mg anakinra subcutaneous once daily			DLQI mean decrease from baseline n=5	8.4	
					VAS 100 mean decrease from baseline n=5	10.2	
					Adverse events n=5	0	
					Injection site reactions	5/5	

1. Leslie KS, Tripathi SV, Nguyen TV, Pauli M , Rosenblum MD. An open-label study of anakinra for the treatment of moderate to severe hidradenitis suppurativa. J Am Acad Dermatol 2014;70:243-51.

Spesolimab

e-Table 47. Spesolimab versus placebo

Spesolimab compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: Spesolimab 1200mg every other week (subcutaneous)
Comparison: Placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Placebo	Risk with Spesolimab				
Achieving pain NRS30 at week 12	59 per 1000	**229 per 1000** (31 to 1000)	**RR 3.89** (0.53 to 28.61)	52 (1 RCT)	⨁⨁◯◯ Low[a]	
Achieving HiSCR50 at week 12	176 per 1000	**314 per 1000** (101 to 979)	**RR 1.78** (0.57 to 5.55)	52 (1 RCT)	⨁⨁◯◯ Low[a]	
Change in IHS4 at week 12	mean change in IHS4: **4.9**	MD **13.9 lower** (25.04 lower to 2.76 lower)	-	44 (1 RCT)	⨁⨁◯◯ Low[b]	
Change in DLQI score at week 12	mean change in DLQI: **-2.8**	MD **0** (4.24 lower to 4.24 higher)	-	44 (1 RCT)	⨁⨁◯◯ Low[c]	
Change in HiSQOL at week 12	mean change in HiSQOL: **-4.5**	MD **1.3 lower** (9.14 lower to 6.54 higher)	-	39 (1 RCT)	⨁⨁◯◯ Low[b]	
Change in Hidradenitis Suppurativa Area and Severity Index Revised (HASI-R) at week 12	mean change in HASI-R: **-3.8**	MD **19.8 lower** (36.16 lower to 3.44 lower)	-	44 (1 RCT)	⨁⨁◯◯ Low[b]	
Proportion of patients with ≥1 flare at week 12	176 per 1000	**86 per 1000** (19 to 381)	**RR 0.49** (0.11 to 2.16)	52 (1 RCT)	⨁⨁◯◯ Low[a]	

Spesolimab

e-Table 47. Spesolimab versus placebo

Spesolimab compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: Spesolimab 1200mg every other week (subcutaneous)
Comparison: Placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Placebo	Risk with Spesolimab				
Serious adverse events through week 12	63 per 1000	**9 per 1000** (1 to 223)	**RR 0.15** (0.01 to 3.57)	52 (1 RCT)	⨁⨁◯◯ Low[a]	
Adverse events leading to treatment discontinuation through week 12	63 per 1000	**9 per 1000** (1 to 223)	**RR 0.15** (0.01 to 3.57)	52 (1 RCT)	⨁⨁◯◯ Low[a]	
Drug-related adverse events through week 12	188 per 1000	**416 per 1000** (141 to 1000)	**RR 2.22** (0.75 to 6.61)	52 (1 RCT)	⨁⨁◯◯ Low[a]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

[a]Downgraded by two levels due to very serious imprecision: Small sample size and the ratio of the upper to the lower boundary of the CI was > 3.
[b]Downgraded by two levels due to very serious imprecision: Small sample size.
[c]Downgraded by two levels due to very serious imprecision: Small sample size and the 95% CI crossed the MID of 4 for DLQI.

1. Alavi A, Prens EP, Kimball AB, Frew JW, Krueger JG, Mukhopadhyay S 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. British Journal of Dermatology 2024;191:508-18.

Ustekinumab

e-Table 48. Ustekinumab (case series)

7 open-label trials/case series, including 79 patients

Outcome	Absolute Effect (95% CI)	Certainty of Evidence (GRADE)	Notes/Rationale

HiSCR50 response **3 studies; 47 pts**	**Overall: 31/47 (66%)** (Range: 21.4% to 90% across studies)	⊕◯◯◯ Very Low	Wide variation likely due to different dosing regimens, follow-up duration, and patient populations. Higher rates with longer treatment and IV loading.
HS-PGA/IHS4 improvement/PGA "improvement" **3 studies; 32 pts**	HS-PGA ≥1 point reduction: 70% (7/10); IHS4 reduction: 36.1% (95% CI: 70.9% to 1.3%); PGA improvement: 12/16 (75%)	⊕◯◯◯ Very Low	Limited data from small studies; consistent with clinical improvement signal.
Pain improvement (VAS/NPRS) **3 studies; 37 pts**	Mean VAS reductions: 5.8→4.6 (Blok); -2.5 points (Jiang); 100% improvement (Romani). NPRS ≥20% reduction: 80% (8/10)	⊕◯◯◯ Very Low	Consistent pain improvement across studies; clinically meaningful reductions reported.
DLQI improvement **3 studies; 47 pts**	Meaningful response rates: 41.2% (Blok) to 91.6% (Romani). Mean reductions: 16.6→10.25 (Hollywood). DLQI ≥4 point reduction: 91.6% (11/12)	⊕◯◯◯ Very Low	Consistent quality of life improvements across studies; most showing clinically meaningful changes.
Any adverse events **3 studies; 39 pts**	Range: 0% to 6.3%. Blok 2016: 5.9% (1/17); Hollywood 2022: 6.3% (1/16) infections	⊕◯◯◯ Very Low	Generally well-tolerated; limited safety data from small studies.
Treatment-related adverse events **2 studies; 24 pts**	0% across reporting studies (Montero-Vilchez, Romani, Jiang)	⊕◯◯◯ Very Low	No treatment-related AEs reported but studies underpowered for safety assessment.

Prospective trials/Case series n=7, 79 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from uncontrolled, open-label trials or case series, which are inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The individual studies included small sample sizes, increasing concern about random error and imprecision. Varied interventions and outcome reporting with limited poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias
Blok 2016[1]	-Mean age 35 (range 20-53) -13F, 4M -Obesity n=7	Ustekinumab 45 mg SC (90 mg SC for	topical resorcinol (n =	40 weeks	HiSCR50	8/17 (41.5%)	Moderate
					DLQI improvement	7/17 (41.2%)	

Prospective trial N=17	-Hurley stage II or III	pts > 100 kg) at 0, 4, 16, 28w	4); ILK (n = 2); I&D (n = 1)		VAS pain mean score	5.8 → 4.6	
					Adverse events	1/17 (5.9%)	
Hollywood 2022[2] Case series N=16	- Mean age 37 (range 22-70) - -12F, 4M - Hurley stage II n=4; III n=12 -	Ustekinumab dosing not specified mean duration 16 months	None	Mean 16 months	Physician assessment improved or unchanged	Improved 12/16 (75%) Unchanged 4/16 (25%)	Selection Y Ascertainment Y Causality N Reporting N
					Mean DLQI	16.6 (1–25) → 10.25 (range 1–27)	
					Infections	1/16 (6.3%)	
Jiang 2022[3] Monocentric retrospective case series N=6	- Age (year, mean, SD): 53.5 (10.2) - Sex: 5 F, 1 M - Previous treatments: adalimumab n=6 infliximab n=4 - Mean BMI: 38.0 (SD 10.1) - Hurley III n=6 - Smoking status: NR	Ustekinumab 90 mg every 4 weeks, n=5 90 mg every 8 weeks, n=1	Systemic antibiotics	weeks 8–12	mean percentage change in IHS4 from baseline	36.1% (95% CI 70.9% to 1.3%)	Selection Y Ascertainment Y Causality N Reporting Y
					VAS pain score compared with baseline	-2.5 (95% CI 5.5 to 0.5)	
					Safety	No adverse events	
Montero-Vilchez 2022[4] Bicentric retrospective case series N=10	- Age: median 44 years (range 34-55) - 4 F, 6 M - Previous treatments: Systemic antibiotics n=8 Acitretin n=1 Isotretinoin n=1 Infliximab n=3 Adalimumab n=7 Ciclosporin n=1 Corticosteroids n=5 - Mean BMI: NR (obesity n=3) - Hurley: II n=2, III n=8 - Smoker: n=7	Ustekinumab Induction dose: 45 mg or 90 mg (weight-based) SC → 45 mg q12w SC Median duration 48 weeks	NR	Mean follow up 92.8 weeks (range 22-232)	reduction of ≥ 1 point in the HS-PGA	n=7 (70%)	Selection N Ascertainment N Causality N Reporting N
					Decrease of ≥20% in the NPRS (Numerical Pain Rating Scale.)	n=8 (80%)	
					Treatment-related AEs	0/10	
Romani 2019[5] Case series	- Ages 19-63 - -Hurley II n=2; III n=12	Ustekinumab IV loading dose (≤ 55 kg:	oral/intralesional corticosteroids	8 & 16 weeks	HiSCR50	At 8wks 3/14 (21.4%) 16 wks 8/14 (57.1%)	Selection Y Ascertainment Y Causality N

N=14		260 mg; > 55 to ≤ 85 kg: 390 mg; > 85 kg: 520 mg) → 90 mg q8w SC	or abx for flares (n = 4)		VAS pain improvement	At 8 & 16 wks 11/11 (100%)	Reporting Y
					DLQI reduction of ≥4	11/12 (91.6%)	
					Treatment-related AEs	0/14	
Sanchez-Martinez 2020[6] Case series N=6	- Median age 47 (range 31-59) - -3F, 3M - Hurley III n=6	IV loading dose (weight adjusted) → 90 mg q8w SC	ILK, abx, retinoids (n = 2); surgery (n = 1)	12 weeks	HiSCR50	3/6 (50%)	Selection Y Ascertainment Y Causality N Reporting N
Valenzuela-Ubina 2022[7] Retrospective case series N=10	- Age (year, mean):42.9 (range 26-53) - 6F, 4M - Previous treatments : Systemic ATB n=10, Corticosteroids n=7, Dapsone n=6, Adalimumab n=8, Infliximab n=6, Azathioprine n=2, Anakinra n=4, Methotrexate n=5, Isotretinoin n=3, Sulfasalazine n=1, Acitretin n=2, Cyclosporine n=3 - Hurley II n=1, Hurley III n= 9 - Smoking status: Current n= 4, Former n=4	Ustekinumab subcutaneously 90 mg every 2 months n=9 45 mg every 3 months n=1 Mean treatment duration 17.6 months	NR	Mean treatment duration 17.6 months	HiSCR50	n= 9/10 (90%)	Selection N Ascertainment Y Causality N Reporting Y

1. Blok JL, Li K, Brodmerkel C, Horvátovich P, Jonkman MF , Horváth B. Ustekinumab in hidradenitis suppurativa: clinical results and a search for potential biomarkers in serum. Br J Dermatol 2016;174:839-46.
2. Hollywood A, Murray G, Fleming S, Kirby B , Hughes R. Ustekinumab in the Management of Hidradenitis Suppurativa: A Retrospective Study. J Drugs Dermatol 2022;21:319-20.
3. Jiang SW, Kwock JT, Liu B, Petty AJ, Zhao AT, Green CL , Jaleel T. High-dose, high-frequency ustekinumab therapy for patients with severe hidradenitis suppurativa. Br J Dermatol 2022;187:417-9.

4. Montero-Vilchez T, Pozo-Román T, Sánchez-Velicia L, Vega-Gutiérrez J, Arias-Santiago S , Molina-Leyva A. Ustekinumab in the treatment of patients with hidradenitis suppurativa: multicenter case series and systematic review. J Dermatolog Treat 2022;33:348-53.
5. Romaní J, Vilarrasa E, Martorell A, Fuertes I, Ciudad C , Molina-Leyva A. Ustekinumab with Intravenous Infusion: Results in Hidradenitis Suppurativa. Dermatology 2020;236:21-4.
6. Sánchez-Martínez EM, García-Ruiz R, Moneva-Léniz LM , Mateu-Puchades A. Effectiveness and safety of ustekinumab in patients with hidradenitis suppurativa using intravenous induction. Dermatol Ther 2020;33:e14054.
7. Valenzuela-Ubiña S, Jiménez-Gallo D, Villegas-Romero I, Rodríguez-Mateos ME , Linares-Barrios M. Effectiveness of ustekinumab for moderate-to-severe hidradenitis suppurativa: a case series. J Dermatolog Treat 2022;33:1159-62.

Ixekizumab

e-Table 49. Ixekizumab (case series)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murrad tool
Esme 2022[1] Monocentric retrospective case series N=5	- Age (year, mean): 43.8 (range 29-56) - 5 M - Mean BMI: NR - Hurley III n=5 - Smoking: packet-years mean 14.2	Ixekizumab 160 mg once, then 80 mg Q2W	NR	12 weeks	HiSCR	80% (n=4)	Selection Y Ascertainment Y Causality N Reporting Y
					DLQI from baseline	Mean – 9.2 (range – 4 to -15)	
					VAS from baseline	Mean – 5.6 (range -2 to -8)	
					Safety	No adverse évents	

NR: Not reported; 1. Esme P, Botsali A, Akoglu G , Caliskan E. An Anti-Interleukin-17A Monoclonal Antibody, Ixekizumab, in the Treatment of Resistant Hidradenitis Suppurativa: A Case Series. Skin Appendage Disord 2022;8:342-5.

Upadacitinib

e-Table 50. Upadacitinib versus placebo

Upadacitinib compared to placebo for hidradenitis suppurativa[1]

Patient or population: Adults with moderate-to-severe HS with inadequate response to oral antibiotics
Intervention: upadacitinib 30mg once daily (oral) for 12 weeks
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with upadacitinib				
Pain NRS 30 follow-up: 12 weeks *In-trial placebo group*	333 per 1000	**363 per 1000** (147 to 910)	**RR 1.09** (0.4 to 2.73)	45 (1 RCT)	⨁⨁◯◯ Low[a]	Per study : adjusted Δ 2.2% p=0.421
Pain NRS 30 follow-up: 12 weeks *Historical controls*	225 per 1,000	**364 per 1,000** (225 to 589)	**RR 1.62** (1.0 to 2.62)	482 (1 RCT)	⨁⨁◯◯ Low[b, c]	Per study : Δ 13.9% p=0.028
HiSCR50 follow-up: 12 weeks *In-trial placebo group*	238 per 1000	**383 per 1000** (164 to 893)	**RR 1.61** (0.69 to 3.75)	68 (1 RCT)	⨁⨁◯◯ Low[a]	Per study : adjusted Δ of 14.7% p=0.087 adjusted for strata (baseline Hurley stage and prior TNFi use)
HiSCR50 follow-up: 12 weeks *Historical controls*	249 per 1,000	**384 per 1,000** (257 to 569)	**RR 1.54** (1.03 to 2.28)	496 (1 RCT)	⨁⨁◯◯ Low[b, d]	Per study : Δ 13.3% p=0.18
Serious adverse events follow-up: 12 weeks	0 per 1000	**0 per 1000** (0 to 0)	**RR 3.21** (0.17 to 59.48)	68 (1 RCT)	⨁⨁◯◯ Low[a]	Upadacitnib 3/47 vs Pbo 0/21
Treatment-emergent AEs follow-up: 12 weeks *In-trial placebo group*	381 per 1000	**510 per 1000** (290 to 975)	**RR 1.34** (0.76 to 2.56)	68 (1 RCT)	⨁⨁◯◯ Low[a]	
Discontinuation due to AE follow-up: 12 weeks *in-trial placebo group*	48 per 1,000	**7 per 1,000** (0 to 171)	**RR 0.15** (0.007 to 3.60)	68 (1 RCT)	⨁⨁◯◯ Low[a]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two levels due to imprecision: small sample size and the ratio of the upper to the lower boundary of the CI was > 3.

b. Downgraded by one level for risk of bias: No randomization between upadacitinib and historical controls with some baseline characteristics noted to differ; historical control data from two different studies; methodological limitations to cross-study comparisons.
c. Downgraded one level for imprecision: CI consistent with meaningful benefit and no difference.
d. Downgraded one level for imprecision: CI consistent with meaningful and trivial benefit.

1. Ackerman LS, Schlosser BJ, Zhan T, Prajapati VH, Fretzin S, Takahashi H et al. Improvements in moderate-to-severe hidradenitis suppurativa with upadacitinib: Results from a phase 2, randomized, placebo-controlled study. J Am Acad Dermatol 2025.

Systemic Steroids, DMARDs, and PDE4i Summary of Findings

Note: Intralesional steroids are covered in the procedural interventions document

Contents

Disease-Modifying Antirheumatic Drugs (conventional synthetic)

Systemic Steroids

e-Table 51. Oral prednisone adjunctive therapy

Case series n=3, 73 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control group. The individual studies included small sample sizes, increasing concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Duarte 2020[1] Monocentric retrospective case series N=16; 20 systemic steroid cycles	•Mean Age 45 •9F, 7M •Moderate to severe HS (severe n=10)	Systemic prednisolone median maximum prednisolone dose 0.44 mg/kg (0.28-1); median duration 30 days (10-90) •n=3 >1 cycle •Initiated for disease cooling (n=9), symptom relief (n=2), acute flare (n=5)	Doxycycline (9 cycles) Adalimumab (8 cycles) Isotretinoin (1 cycle) Clindamycin + rifampin (3 cycle) Ertapenem (1 cycle) Infliximab (1 cycle) Acitretin (1 cycle)	Median 30 days (range 10-90)	Clinical response via achievement of HiSCR	14/20 (70%) cycles resulted in the achievement of HiSCR	Selection N Ascertainment Y Causality N Reporting Y
					Pain via NRS % reduction from baseline	Median pain NRS reduced 74% p=0.0007	
					Quality of life via DLQI % reduction from baseline	Median DLQI reduced 19% p=0.003	
					Adverse events	0/20 cycles	
Gibson 2024[2] Monocentric prospective case series	•Mean age 37.1 •29F, 14M, 1 Transgender M •Acute HS flare	Amoxicillin/ clavulanic acid of 875 to 125 mg bid for 10 days + 40 mg prednisone taper	Amoxicillin/ clavulanic acid of 875 to 125 mg bid for 10 days	14 days	Clinical severity via patient global impression of change (very much improved	Very much improved n=12 Much improved n=13 Minimally improved n=5 No change n=1	Selection N Ascertainment Y Causality N Reporting Y

N=44	•Mean Hurley stage 2.2(0.7) •Obesity n=21	(decreasing by 10 mg every 3 days)			to very much worse) n=31	A little worse n=0 Much worse n=0 Very much worse n=0	
					Pain via HS Pain scale (0-10; higher score indicates greater pain)	<u>Baseline→14 days:</u> 6.4 → 3.1 p<0.001	
					Quality of life via mean DLQI	<u>Baseline→14 days:</u> 16.3 →8.6 p<0.001	
Wong 2016[3] Monocentric prospective case series N=13	•Mean age 42.5 •recalcitrant HS •Hurley stage: I n=1, II n=7, III n=5	Low-dose oral prednisone 10mg/day combination therapy (immediate prior treatment)	•Rifampin +clindamycin n=2 •Acitretin n=1 •Dapsone n=2 •Adalimumab n=5 •Doxycycline n=3 •Isotretinoin n=1	4-12 weeks	Clinical response	11/13 patients showed a clinical response to low-dose systemic prednisone as adjunct therapy	Selection N Ascertainment Y Causality N Reporting Y
					PGA (Good, Partial, No response) Categories undefined	Good 5/13 Partial 6/13 No 2/13	
					Adverse events	3/13; minor hyperglycemia, sleep disturbance, psychomotor agitation	

1. Duarte B, Cunha N, Lencastre A , Cabete J. Systemic Steroids in the Management of Moderate-to-severe Hidradenitis Suppurativa. Actas Dermosifiliogr (Engl Ed) 2020;111:879-83.
2. Gibson RS, Snyder CL, Porter ML , Kimball AB. Prednisone and amoxicillin/clavulanic acid for the treatment of hidradenitis suppurativa flares: a prospective observational study. Int J Womens Dermatol 2024;10:e162.
3. Wong D, Walsh S , Alhusayen R. Low-dose systemic corticosteroid treatment for recalcitrant hidradenitis suppurativa. J Am Acad Dermatol 2016;75:1059-62.

e-Table 52. Methotrexate

Case series n=1, 15 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from a single, small case series, which is inherently limited due to the lack of control group. The very small sample size increases concern about random error and imprecision.

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Savage 2020[1] Monocentric retrospective case series N=15	•Mean age 43.8 years •1, 5M •Mean BMI 31.4 •Severe HS	Methotrexate mean dose 10mg/week; cumulative dose 520.1 mg (range 30-1665mg)	Biologics n=8 Oral antibiotics n=9	Mean length of treatment 11.7 months (range 1-38 months)	Clinical characteristics Mean #	<u>Baseline→Follow up</u> *MTX+biologics (n=8)* Inflammatory nodules 5.63→6.50 Fistulas 3.75→3.00 Abscesses 0.63→1.75 *MTX w/o biologics (n=7)* Inflammatory nodules 3.57→1.86 Fistulas 1.5→1.00 Abscesses 0.57→0.00	Selection N Ascertainment Y Causality N Reporting Y
					Mean HSPGA	<u>Baseline→Follow up</u> *MTX+biologics (n=8)* 4.25→4.50 *MTX w/o biologics (n=7)* 3.86→3.00	

1. Savage KT, Brant EG, Rosales Santillan M, Morss PC, Salian P, Flood KS et al. Methotrexate shows benefit in a subset of patients with severe hidradenitis suppurativa. Int J Womens Dermatol 2020;6:159-63.

e-Table 53. Azathioprine

Case series n=2, 20 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The individual studies included small sample sizes, increasing concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Lopez Riquelme 2023[1] Monocentric retrospective case series N=11	•Age •f,M •Moderate-to-severe HS	Azathioprine monotherapy	None	12-16 weeks	Significant Clinical improvement (reduction in iHS4 and DLQI scores and achieving HiSCR)	6/11 (54.5%)	Selection N Ascertainment Y Causality N Reporting Y
					iHS4 (Median[Q3, Q1])	Baseline→Follow up 6[12, 6]→4[6, 2]	
					Quality of life (Median[Q3, Q1])	Baseline→Follow up 17[23, 11] → 14 [18, 9] p=0.099	
					Discontinuation due to adverse events	2/11 (18.2%); anemia (n=1) & abdominal pain (n=1)	
Nazary 2016[2] Monocentric retrospective case series N=9	•Mean Age 40.4 years •6F, 3M •Moderate-to-severe HS •Failed standard treatment (abx,	azathioprine (50–100 mg per day) monotherapy for a duration of 1–7.5 months (mean 2.4)	None	Mean 2.4 months; range 1-7.5	Physician's Global Assessment: 'worsening', 'no change' 'slight improvement' or 'clinically significant improvement'	Worsening 0/9 No change 5/9 Slight improvement 4/9 Clinically significant improvement 0/9	Selection N Ascertainment Y Causality N Reporting Y

	surgery, isotretinoin, acitretin, cyclosporine)				Adverse events	6/9 (66.7%); decreased hemoglobin, nausea, tiredness, arthralgia, hematuria	
					Discontinuation due to adverse events	5/9 (55.6%) hematuria; hypatic dysfunction, diarrhea, pancreatitis	

1. López Riquelme I, Fernández Ballesteros MD, Perea Polak A, Serrano Ordoñez A , Martínez Pilar L. Azathioprine in hidradenitis suppurativa with inflammatory phenotype: a case series of 11 patients. Int J Dermatol 2023;62:1300-3.
2. Nazary M, Prens EP , Boer J. Azathioprine lacks efficacy in hidradenitis suppurativa: a retrospective study of nine patients. Br J Dermatol 2016;174:639-41.

Avacopan

e-Table 54. Avacopan 10mg vs placebo

Avacopan 10 mg twice daily compared to placebo for hidradenitis suppurativa[1]

Patient or population: Adults with Hurely stage II or II hidradenitis suppurativa
Intervention: avacopan 10 mg twice daily
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with avacopan				
Achieving HiSCR follow-up: 12 weeks	308 per 1000	**225 per 1000** (148 to 335)	**RR 0.73** (0.48 to 1.09)	264 (1 RCT)	⊕⊕◯◯ Low[a]	
Achieving NRS 30 for pain follow-up: 12 weeks	248 per 1000	**220 per 1000** (136 to 362)	**RR 0.89** (0.55 to 1.46)	209 (1 RCT)	⊕⊕◯◯ Low[a]	
Change in IHS4 follow-up: 12 weeks	The mean change: **-6.4**	MD **1.5 lower** (6.72 lower to 3.72 higher)	-	220 (1 RCT)	⊕⊕◯◯ Low[b]	
Serious adverse events follow-up: 12 weeks	23 per 1000	**22 per 1000** (5 to 109)	**RR 0.96** (0.20 to 4.68)	263 (1 RCT)	⊕⊕◯◯ Low[c]	

Avacopan 10 mg twice daily compared to placebo for hidradenitis suppurativa[1]

Patient or population: Adults with Hurely stage II or II hidradenitis suppurativa
Intervention: avacopan 10 mg twice daily
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with avacopan				
Adverse events leading to discontinuation follow-up: 12 weeks	31 per 1000	**45 per 1000** (13 to 155)	**RR 1.46** (0.42 to 5.04)	264 (1 RCT)	⨁⨁◯◯ Low[c]	
Other adverse events follow-up: 12 weeks	171 per 1000	**135 per 1000** (75 to 239)	**RR 0.79** (0.44 to 1.40)	263 (1 RCT)	⨁⨁◯◯ Low[a]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two levels due to imprecision: small sample size
[b]Downgraded by two levels due to imprecision: small sample size and the 95% CI crossed the MID of 55% for IHS
[c]Downgraded by two levels due to imprecision: small sample size and the 95% CI crossed both the conventional upper and lower thresholds of MID (0.75 and 1.25)

1. Kirby JS, Prens E, Jemec GB, v M, Prasad S, Schall T et al. LB791 Avacopan, a highly selective small molecule inhibitor of c5a receptor, in patients with Hidradenitis Suppurativa: Initial results from a randomized, double-blind, placebo-controlled, phase 2 study (aurora). Journal of Investigative Dermatology 2021;141:B19.

e-Table 55. Avacopan 30mg vs placebo

Avacopan 30 mg twice daily compared to placebo for hidradenitis suppurativa[1]

Patient or population: Adults with Hurely stage II or II hidradenitis suppurativa
Intervention: avacopan 30 mg twice daily
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with avacopan				
Achieving HiSCR follow-up: 12 weeks	308 per 1000	**351 per 1000** (249 to 495)	**RR 1.14** (0.81 to 1.61)	264 (1 RCT)	⨁⨁◯◯ Low[a]	
Achieving NRS30 for pain follow-up: 12 weeks	248 per 1000	**163 per 1000** (94 to 282)	**RR 0.66** (0.38 to 1.14)	209 (1 RCT)	⨁⨁◯◯ Low[a]	

Avacopan 30 mg twice daily compared to placebo for hidradenitis suppurativa[1]

Patient or population: Adults with Hurely stage II or II hidradenitis suppurativa
Intervention: avacopan 30 mg twice daily
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	**Risk with avacopan**				
Change in IHS4 follow-up: 12 weeks	mean change: **-6.4**	MD **3.4 lower** (7.72 lower to 0.92 higher)	-	220 (1 RCT)	⨁⨁◯◯ Low[b]	
Serious adverse events follow-up: 12 weeks	23 per 1000	**7 per 1000** (1 to 70)	**RR 0.32** (0.03 to 3.02)	264 (1 RCT)	⨁⨁◯◯ Low[c]	
Adverse events leading to discontinuation follow-up: 12 weeks	31 per 1000	**30 per 1000** (8 to 117)	**RR 0.97** (0.25 to 3.80)	264 (1 RCT)	⨁⨁◯◯ Low[c]	
Other adverse events follow-up: 12 weeks	171 per 1000	**111 per 1000** (60 to 205)	**RR 0.65** (0.35 to 1.20)	264 (1 RCT)	⨁⨁◯◯ Low[d]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two levels due to imprecision:small sample size and the 95% CI crossed either the conventional upper or lower thresholds of MID (0.75 or 1.25)
[b]Downgraded by two level due to imprecision: small sample size and the 95% CI crossed the MID of 55% for IHS
[c]Downgraded by two levels due to imprecision: small sample size and the 95% CI crossed both the conventional upper and lower thresholds of MID (0.75 and 1.25)
[d]Downgraded by two level due to imprecision: small sample size

1. Kirby JS, Prens E, Jemec GB, v M, Prasad S, Schall T et al. LB791 Avacopan, a highly selective small molecule inhibitor of c5a receptor, in patients with Hidradenitis Suppurativa: Initial results from a randomized, double-blind, placebo-controlled, phase 2 study (aurora). Journal of Investigative Dermatology 2021;141:B19.

e-Table 56. Colchicine

Case series n=3, 72 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control groups. The individual studies included small sample sizes, increasing concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Armyra 2017[1] Monocentric prospective case series N=20	•Age range 21-61 •10F, 10M •BMI range 19.0 to 36.2 kg/m2 •Hurley stage: I n=1, II n=15, III n=4		0.5mg colchicine bid + 100 mg minocycline qd for 6 months Maintenance 0.5mg colchicine bid for 3 months	9 months	PGA (0-25% poor, 25-50% fair, 50-75% good, 75-100% excellent response)	<u>3 months→6 months→9 months</u> Poor 1→0→0 Fair 6→3→1 Good 10→9→11 Excellent 3→8→8	Selection N Ascertainment Y Causality N Reporting Y
					Hurley stage (individual scores)	<u>Baseline→9 months</u> I 1→20 II 15→0 III 4→0	
					Quality of life via DLQI (individual scores)	<u>Baseline→9 months</u> DLQI 0-1 0→0 DLQI 2-5 0→8 DLQI 6-10 1→12 DLQI 11-20 18→0 DLQI 21-30 1→0	
					Adverse events	3/20; nausea and diarrhea	
Liakou 2021[2] Monocentric, retrospective case series N=44	•Mean Age 41.8 (14.2) years •23F, 21M •Hurley stages: I n=11, II n=26, III n=7	Colchicine 1mg/d monotherapy (n=15) Colchicine 1mg/d+	None (3 month washout period)	12 weeks	Clinical severity via IHS4 Mean (SD)	<u>Baseline→12 wks</u> Colchicine 7.7 (3.3)→ 2.8(1.4) p<0.001 Colchicine+ Doxy 100 11.1(2.9)→5.8(1.9) p<0.001 Colchicine+ Doxy 40 9.9(3.6)→4.5(2.5) p<0.001	Selection N Ascertainment Y Causality N Reporting Y

		doxycycline 100mg/d (n=14) Colchicine 1mg/d + doxycycline 40mg/d (n=15)			Quality of life via DLQI Mean (SD)	<u>Baseline→12 wks</u> Colchicine 9.8 (4.2)→ 3.4(2.3) p<0.001 Colchicine+ Doxy 100 13.0(3.9)→6.3(3.2) p=0.001 Colchicine+ Doxy 40 11.6(4.8)→4.5(2.2) p<0.001	
					Discontinuation due to adverse events	0/44	
Van der Zee 2011[3] Monocentric prospective case series N=8	•Mean age • 6F, 2M •Moderate to severe HS refractory to standard therapies •	0.5 mg colchicine b.i.d. orally up to 4 months; option for dose escalation to t.id. at 1 month (n=2)	None	1 month	PGA (–2 clear worsening, –1 slight worsening, 0 no change, 1 slight improvement, 2 clear improvement and 3 total clearance of inflammatory lesions)	Baseline to: 1 month (n=8): 2/8 slight improvement; 6/8 no change 2 months (n=6): 3/6 slight improvement; 1/6 worsening; 2/6 no change 4 months (n=2): ½ slight improvement; ½ deteriorated	Selection N Ascertainment Y Causality N Reporting Y
					Adverse events	3/8; nausea and diarrhea	

1. Armyra K, Kouris A, Markantoni V, Katsambas A , Kontochristopoulos G. Hidradenitis suppurativa treated with tetracycline in combination with colchicine: a prospective series of 20 patients. Int J Dermatol 2017;56:346-50.
2. Liakou AI, Kontochristopoulos G, Agiasofitou E, Tsantes AG, Papadakis M, Marnelakis I et al. Colchicine Improves Clinical Outcomes and Quality of Life in Hidradenitis Suppurativa Patients: A Retrospective Study. J Clin Med 2021;10.
3. van der Zee HH , Prens EP. The Anti-Inflammatory Drug Colchicine Lacks Efficacy in Hidradenitis Suppurativa. Dermatology 2011;223:169-73.

e-Table 57. Cyclosporine

Case series n=1, 18 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from a single small case series, which is inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The very small sample size, increases concern about random error and imprecision.

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Anderson 2016[1] Multicentric retrospective case series N=18	•Mean age 42.8 years • F, M •Hurley stage: I n=0, n= II n=13, III n=5 •Refractory to standard therapies	CsA at a dose of 2.0–3.5 mg/kg/day for 0.5 to 24+ months	Clavulenic acid and Amoxicillin n=1 Minocin 100mg/d n=1 Clindamycin+rifampicin n=1	2 weeks to 24 months	Clinical improvement (“worsening”, “no change”, “slight improvement”= “clinically significant improvement”= obvious reduction of symptoms and inflammation noticed by patients and physicians alike and leading to continued treatment)	Clinically significant improvement: 2*/18 (11.1%) Slight improvement: 7/18 (38.9%) No change: 9/18 (50%) *After concomitant therapy initiated	Selection N Ascertainment Y Causality N Reporting Y
					Adverse events	10/18 (55.6%); GI, headache, hirsutism, increased BP, heart palpitations	
					Discontinuation due to adverse events	2/18 (11.1%)	

1. Anderson MD, Zauli S, Bettoli V, Boer J , Jemec GB. Cyclosporine treatment of severe Hidradenitis suppurativa--A case series. J Dermatolog Treat 2016;27:247-50.

E-Table 58. Hydroxychloroquine

Case series n=1, 17 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from a single small case series, which is inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The very small sample size, increases concern about random error and imprecision.

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool

Brant 2023[1]
 	
Monocentric prospective case series
 	
N=17
	- Age (year, mean): 39
	- 14 F, 3 M
	- Previous treatments:
	  - oral antibiotics n=25, adalimumab n=1, isotretinoin n=3, spironolactone n=2
	  - intralesional triamcinolone n=1
	- Mean BMI: NR
	- Hurley I n=9, II n=5, III n=3
	- Smoking status: current smokers n=8, never smokers n=7, former smokers n=2
		200 mg of hydroxychloroquine twice daily for 6 months	NA	3 and 6 months	Hurley stage	- At 3 months (n=7):
						Hurley I n= 4,
						II n=3
						- At 6 months (n=3):
						Hurley I n= 1,
						II n=2
							Selection Y
							Ascertainment N
							Causality N
							Reporting Y

					DLQI	Baseline to 3 months: 14.7± 11 to 4.4 ± 5.2 (7 patients analysed)	
					Sartorius score	Baseline to 3 months: 23.3± 16.2 to 13 ± 6.6 (7 patients analysed)	
					Safety	No persistent side effects	

1. Brant EG , Akilov O. Hydroxychloroquine for the treatment of hidradenitis suppurativa. JAAD Case Rep 2023;37:64-7.

Phosphodiesterase 4 (PDE4) inhibitors

e-Table 59. Apremilast vs placebo

Apremilast compared to placebo for hidradenitis suppurativa[1]

Patient or population: Adults with moderate (HS-PGA score of 3) hidradenitis suppurativa
Intervention: Apremilast 30 mg twice daily, dose escalation in first week (10 mg on day 1, with 10 mg/day increases) for 16 weeks
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	**Risk with apremilast**				
Change in numeric rating scale (NRS) for pain Scale from: 0 to 10 follow-up: 16 weeks	mean change in NRS for pain: **2.2**	MD **3 lower** (5.07 lower to 0.93 lower)	-	20 (1 RCT)	⊕⊕⊕◯ Moderate[a]	
HiSCR follow-up: 16 weeks	0 per 1000	**533 per 1000** (*Not estimable*)	**RR 6.37** (0.43 to 94.24)	20 (1 RCT)	⊕⊕◯◯ Low[b]	No HiSCR in placebo; small sample; wide CI; external placebo risk needed for absolute difference
Change in DLQI Scale from: 0 to 30 follow-up: 16 weeks	mean change in DLQI: **4.2**	MD **6.5 lower** (11.81 lower to 1.19 lower)	-	20 (1 RCT)	⊕⊕⊕◯ Moderate[c]	
Serious adverse events follow-up: 16 weeks	0 per 1000	**0 per 1000** (0 to 0)	Not estimable	20 (1 RCT)	⊕⊕⊕◯ Moderate[d]	
Other adverse events: Headache follow-up: 16 weeks	200 per 1000	**466 per 1000** (74 to 1000)	**RR 2.33** (0.37 to 14.61)	20 (1 RCT)	⊕⊕◯◯ Low[b]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by one level due to imprecision: the 95% CI crossed the minimal important difference (MID) of 30% reduction in pain.
[b]Downgraded by two levels due to imprecision: the 95% CI crossed both the conventional upper and lower thresholds of MID (0.75 and 1.25).
[c]Downgraded by one level due to imprecision: the 95% CI crossed the MID of 4 for DLQI.
[d]Downgraded by one level due to imprecision: zero events with small sample size

1. Vossen A, van Doorn MBA, van der Zee HH , Prens EP. Apremilast for moderate hidradenitis suppurativa: Results of a randomized controlled trial. J Am Acad Dermatol 2019;80:80-8.

e-Table 60. Apremilast (non-comparative studies)

Open label trial/Case series n=2, 29 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from a small non-randomized open-label trial & a small case series, which are inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The very small sample sizes increase concern about random error and imprecision.

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias
Kerdel 2019[1] Open-label trial N=20	-Mean age 32.5y -Mile-to-moderate HS	Apremilast 30mg twice daily for 24 weeks after a 5-day titration period	NR	24 weeks	Mean change Sartorius score	-21.7; p<0.001	Moderate
					Mean change VAS 100 pain	-16.8; p<0.05	
					Mean change in DLQI	-6.2; p<0.01	
					Mean change PGA	-1.1; p<0.01	
					Adverse events	Diarrhea 4/20 Nausea 3/20 Depression 2/20 SAEs 0/20	
Weber 2017[2] Case series N=9	-Age range 26-63 y -3F, 5M -Hurley stage II n=3, III n=6	Apremilast 30mg twice daily for 5 to 9 months	NR	2-3 months post induction	Mean Sartorius score n=6	73.17(SD 67.76) → 56.17 (SD 44.89) p=0.028	Serious
					Mean VAS 10 pain score n=6	7.17(SD 0.98) →2.00(SD 2.10) p=0.026	

					Mean change in DLQI n=6	21.33(SD 8.91) → .33 (SD 5.85) p=0.027	

1. Kerdel FR, Azevedo FA, Kerdel Don C, Don FA, Fabbrocini G , Kerdel FA. Apremilast for the Treatment of Mild-to-Moderate Hidradenitis Suppurativa in a Prospective, Open-Label, Phase 2 Study. J Drugs Dermatol 2019;18:170-6.
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Brepocitinib

e-Table 61. Brepocitinib vs placebo

Brepocitinib compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: brepocitinib 45mg once daily (oral)
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI) Risk with placebo	Risk with brepocitinib	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Percentage of participants achieving pain NRS30 follow-up: 16 weeks		MD **6.5 % more** (10.4 less to 23.4 more)	-	100 (1 RCT)	⨁⨁◯◯ Low[a]	
Achieving HiSCR 50 follow-up: 16 weeks	333 per 1000	**520 per 1000** (323 to 837)	**RR 1.56** (0.97 to 2.51)	100 (1 RCT)	⨁⨁⨁◯ Moderate[b]	
Percentage change in IHS4 follow-up: 16 weeks		MD **14.9 % lower** (36.7 lower to 7.8 higher)	-	100 (1 RCT)	⨁⨁◯◯ Low[c]	
Serious adverse events (all causality) follow-up: 16 weeks	0 per 1000	**0 per 1000** (0 to 0)	Not estimable	100 (1 RCT)	⨁⨁◯◯ Low[d]	
Serious adverse events (treatment-related) follow-up: 16 weeks	0 per 1000	**0 per 1000** (0 to 0)	Not estimable	100 (1 RCT)	⨁⨁◯◯ Low[d]	
Adverse events (all causality) leading to discontinuation of intervention through 16 weeks	0 per 1000	**20 per 1000** (1 to 42)	**RR 2.77** (0.12 to 66.49)	100 (1 RCT)	⨁⨁◯◯ Low[e]	
Adverse events (treatment-related) leading to discontinuation of intervention follow-up: 16 weeks	0 per 1000	**20 per 1000** (1 to 42)	**RR 2.77** (0.12 to 66.49)	100 (1 RCT)	⨁⨁◯◯ Low[e]	
Cumulative flare rate follow-up: 16 weeks		MD **22.3 % lower** (36.7 lower to 7.9 lower)	-	100 (1 RCT)	⨁⨁◯◯ Low[d]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

Brepocitinib compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: brepocitinib 45mg once daily (oral)
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with brepocitinib				

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by one level due to serious imprecision: Small sample size and the 95% CI crossed either the conventional upper or lower thresholds of MID (0.75 or 1.25).
[b]Downgraded by two levels due to very serious imprecision: Zero events with small sample size.
[c]Downgraded by two levels due to very serious imprecision: Small sample size and the ratio of the upper to the lower boundary of the CI was > 3.
[d]Downgraded by two levels due to very serious imprecision: Small sample size and the 95% CI crossed the MID of 55% for HIS.
[e]Downgraded by two levels due to very serious imprecision: Small sample size and the 95% CI crossed the MID of 30% for NRS.

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Surgical Interventions Summary of Findings

Contents

Deroofing

e-Table 62. Deroofing (case series & non-comparative cohort studies)

Case series/cohorts n=9, 899 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series and non-comparative cohorts, which are inherently limited due to the lack of control groups. The individual studies generally included small sample sizes, increasing concern about random error and imprecision. Varied outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Time of outcome assessment	Outcome	Results
Dahmen 2019[1] Prospective cohort N=45pts ; 87 lesions	•Mean age 39 •40%F •Hurley stage II-III •Multiple anatomic locations	Median 28+ mos	Mean healing time (complete healing & re-epitheliazation	5.2 weeks (range 2.3, 8)
			Recurrence rate	12/87 (14%)
			Mean VAS 10 pain score	Baseline Axilla 3.2 Inguinal 3.8 1 day post-op Axilla 4.1 Inguinal 4.5 6 weeks post-op Axilla 0 Inguinal 0
			Complications	7/87 (8%) bleeding
Kohorst 2016[2] Case series N=168	•Age 13+ •42.9%F *For enitre study cohort, not specific to deroofing	Range 1-6,691 days	Risk of recurrence	HR 1.0 (0.6, 1.4) compared to wide excision
Krajewski 2024[3] Prospective cohort N=79	•Mean age 36.3 •48.1%F •Multiple anatomic locations	NR	Mean(SD) time to closure	4.4(1.9) wks
			Mean (SD) pain at 24 hr post-op (scale 0-10)	0.7(1.2)
			Mean(SD) Satisfaction (scale 0-10)	9.9(0.4)
			Achieve HiSCR	71/79 (89.9%)
			Complications	1/79 (1.3%)
Pham 2024[4] Retrospective case series	•Median age 32 •63.3%F •Hurely stage II-III	NR	Median Time to wound healing	9.6 weeks (95%CI 9, 10)

N=270				
Ravi 2022[5] Retrospective cohort N=129 procedures	•Mean age 35.1 yrs •83%F •Hurley stage II n=77 ; III n=117 •Multiple anatomic locations	Median 13 mos	Recurrence rate	43/129 (33%)
Sechi 2025[6] Retrospective cohort N=10	•Mean age 24.9yrs •60%F •Mean IHS4 4.3 •Multiple anatomic locations	6 mos	Mean time to complete healing	10.9(4.) weeks
			Mean VAS 10 pain at 1st dressing change	4.9(1.7)
			Cosmesis via Vancouver Scar Scale at 6 months	3.4(1.1)
			Complications	3/10 (30%)
Van Der Zee 2010[7] Propsective cohort N=44 pts ; 88 lesions	•Mean age 35 •93.2%F •Multiple anatomic locations •Hurley stage I-II	Median 5 years	Reurrence rate	15/73 (20.5%) lesions
			Complications	1/44 (2.3%) bleeding
Vu 2025[8] Prospective cohort N=44 pts ; 115 lesions	•Mean age 37 •84% F •Hurley stage I-III •Multiple anatomic locations	3 & 12 mos	Recurrence rate	3 mos 12/115(10.4%) 12mo 13/108 (12.0%)
			Mean(SD) change in VAS 10 pain	Baseline 7.7(2.1) 3mo 0.7(1.4) 12mo 0.05 (0.2)
			Mean(SD) change in DLQI	Baseline 15.7(8.3) 3mo 8.8(8.2) 12mo 7.7 (7.8)
			Complications	1/44 (2.3%) infection
Mortimore 2025[9] Retrospective cohort N=119	•Mean age 73 •73F, 46M •-Hurley stage I n=24; II n=32; III n=41; NR n=22 •-Concomitant biologic n=34	3-6 months	Mean NRS pain score from baseline to day 7 to 1-3 mos, to 4-6 mos, 6 mos post procedure	6.61(2.41)→3.37(3.08)→1.06(1.91)→0.50(1.37)→0.45(1.50)
			Recurrence rate	1-year 6/189 procedures 5-year 4/189
			Complications	Infection 3/189 procedures Hypergranulation tissue 3/189 Bleeding 1/189

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Incision & Drainage

e-Table 63. Incision & drainage (Case series)

Case series n=3, 256 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control groups and selection bias. The individual studies included very small sample sizes, increasing concern about random error and imprecision. Varied outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Kohorst 2016[1] Case series N=17	•Age 13+ •42.9%F *For entire study cohort, not specific to I&D	Incision & drainage	NR	Mean 632.9 days	Recurrence	HR 3.5(1.2, 10.7) Compare to wide excision & deroofing	Selection N Ascertainment Y Causality N Reporting N
Revankar 2023[2] Case series N=233	•Majority aged 24-54 yrs •Varied anatomic locations	Incision & drainage	NR	NR	Complete resolution	60/233 (25.8%)	Selection N Ascertainment Y Causality N Reporting N
					Failed to improved	154/233 (66.1%)	
					Percieved benefits over drawbacks (self-reported VAS 0-10 scale) mean (SD)	6.4 (2.8)	
Ritz 1998[3] Case series N=6	NR	Incision & drainage	NR	Mean 72 months	Recurrence	6/6(100%) vs 6/14 local excision vs 3/11 radical excision	Selection N Ascertainment Y Causality N Reporting Y

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Surgical Excision

Wide Excision

e-Table 64. Wide surgical excision (case series)

Case series/cohorts n=33, 1338 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series and non-comparative cohorts, which are inherently limited due to the lack of control groups and selection bias. The individual studies included small sample sizes, increasing concern about random error and imprecision. Varied patient populations, procedural techniques, and outcome assessment and reporting make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.) Most studies do not report the majority of patient-important outcomes of interest (i.e pain reduction, clinical severity changes, etc.)

Study details	Baseline characteristics	Closure	Time of outcome assessment	Outcome	Results
Alharbi 2012[1] Case series N=32	•Mean age 31.43 •62.5% F	Primary, Flap, And Graft	2 yr	Recurrence rate	6/32 (18.8%)
				Average hospital stay	5 days
Altmann 2004[2] Case series	•Mean age 36	Flap	5 mos	Recurrence rate	3/15 (15%)
				Average hospital stay	8 days

N=20	•70%F			Complications	1/20 epitheliolysis 3/20 fistula 1/20 lymphedema
Balik 2009[3] Case series N=15	•Mean age 42.5 •0%F •Perineal/Perianal, gluteal HS	Secondary Intention, Graft, Flap	5 yrs	Recurrence rate	0/15 (0%)
				Average healing time	8 weeks
				Complications	1/20 diverting colostomy
Brierley 2017 Case series N=41	•Chronic, severe HS	Graft	At least 6 mos	Healing time	< 2 weeks
				Recurrence rate	0/41 (0%)
				Cosmesis & function (undefined)	Excellent 41/41 (100%)
				Complications	0/41
Burney 2017[4] Case series N=122	•Mean age 38 •54.1%F	Secondary Intention, Primary, Graft	5.6 yrs	Median time to heal	60 days
				Median hospital LOS	5.5 days
				Recurrence	"common" (no data)
				Pain	" Pain free after first 2-3 weeks"
Butron-Bris 2023[5] Case series N=17	•Mean age 44 yrs •11F, 6M •Obesity n=12 •Smoker n=14 •Hurley stage II n=10 ; III n=7 •20 excisions		Mean 11.65 mos	Recurrence rate	2/20 (10%)
Busnardo 2011[6] Case series N=12	•Mean age 46.6 •Severe bi-lateral axillary HS	Flap	25.4 mos	Recurrence rate	2/12 (16.7%)
				Complications	1/12 (8.3%)
Cuenca-Barrales 2023[7] Case series N=63	•Mean age 36.18 years •82 procedures •Hurely stage II n=65; III n=17 •Smoker n=46 •Obesity n=38	Second intention	68 weeks	Recurrence	Tunnel recurrence 7/82 (8.5%) AN recurrence 13/82 (15.8%)
Chen 2014[8] Case series N=21	•Mean age 38 •70.4%F	Primary Intention, Wound Vac Delayed Primary Intention	2.3 mos	Average healing time	Vacuum-assisted 2.2mos Without vacuum-assistance 2.7 mos
				Recurrence rate	0/21 (0%)
Deckers 2018[9]	•Mean age NR		3 yrs	Recurrence rate	95/253(37.6%) procedures

Case series N=84; 253 procedures	•42.9%F	Secondary intention		Total remission in treatment area	124/253 (49%) procedures
Humphries 2015[10] Case series N=17	•Mean age 36.8 •76.5%F	Secondary intention	1.02 yrs	Healing time range	8 weeks to 16 months
				Average hospital LOS	6 days (range 1-18)
				Recurrence rate	2/17 (11.8%)
				Complications	1/17 DVT 2/17 severe nausea/vomitting 1/17 dysthymia 2/17 blood transfusion 1/17 polyarthralgia 2/17 wound infections
Keles 2018[11] Case series N=20	•Mean age 40.3 •45%F	Graft, Flap, Primary Closure	22 mos	Recurrence rate	1/20 (5.0%)
				Complications	2/20 wound dehiscence
Kuo 2003[12] Case series N=6	•Mean age 32.7 •33.3%F •Gluteal HS	Graft	Median 21 mos (range 8-36)	Recurrence rate	0/6 (0%)
				Severe complications	1/6(16.7%) graft necrosis & wound infection
Maeda 2015[13] Case series N=18	•Mean age 41.7 •0%F •Chronic gluteal HS	Graft	63.1 mos	Recurrence rate	0/18 (0%)
Maghsoudi 2018[14] Case series N=21	•Mean age 47.4 •9.5%F	Primary Graft, Flap	2yrs	Average hospital LOS	5 days
				Recurrence rate	0/21 (0%)
				Complications	2/21 (9.5%)
Mandal 2005[15] Case series N=106	•Mean age 36 •88.7%F	Primary Closure, Graft, Flap	4yrs	Recurrence rate	74/106 (69.9%)
Michelucci 2025[16] Michelucci 2025[17] Prospective cohort N=40	•Mean age 39 years •26F, 14M •Smoker n=26 •Mean(SD) BMI 26(1.7) •Moderate HS n=29 ; Severe n=11	Second intention	22 mos	Recurrence rate	4/40 (10%)
				Mean VAS 10 pain from baseline to week 4	5.1→1.0
				Mean healing time	41.8 days
				Mean change in Skindex-16 scores	57.92→16.03
Mirza 2012[18]			1yr	Average hospital LOS	7 days (range 0-17)

Case series N=22	•Mean age 37 •27%F	Primary closure, Graft		Recurrence rate	0/22 (0%)
				Complications	Major : 1/22 (2.3%) ; graft loss Minor : 7/22 (16.7%) partial graft loss & wound dehiscence
Mutfa 2014[19] Case series N=16	•Mean age NR •25%F •Sacroccygeal HS	Flap	3yrs	Hospital stay	Range 3-4 days
				Recurrence	0/16 (0%)
				Complications	2/16 (12.5%) tip necrosis
Nail-Barthelemy 2019[20] Case series N=13	•Mean age 37.2 •61.5%F •Axillary HS	Flap	Mean 279.1 days	Mean(SD) hospital LOS	5.1(3.1) days
				Mean time to complete healing	20.5(13.5) days
				Recurrence	0/13 (0%)
				Complications	6/13 (35%) ; hematoma, infection, wound dehiscence, necrosis
Ocker 2025[21] Prospective cohort N=82	•Mean age 37.5 (12.7) •42F, 40M •Mean BMI 30.2 (6.8) kg/m2 •Smokers n=50 •Hurley stage II n=66 ; III n=16 •116 excisions	Secondary intention n=64 ; Skin graft n=18	3-6 mos	Change in mean (SD) HSS from baseline to months 3 and 6	50.3(49.3)→10.6(16.8)→8.61(10.8)
				Change in mean (SD) pain NRS-11 from baseline to months 3 and 6	3.01(3.04)→1.46(2.42)→1.07(2.02)
				Change in mean (SD) DLQI from baseline to months 3 and 6	11.66(8.28)→8.26(7.37)→4.65(4.87)
Posch 2017[22] Case series N=74	•Mean age 37.8 •45.9%F •Hurley stage III	Secondary intention	7.42 yrs	Recurrence rate	14/74 (18.9%)
				Mean(SD) hospital LOS	9.0 (6.2) days
				Mean change in DLQI at least 6 mos post-surgery	Pre-surgery : 27.89(5.3) Post-surgery : 51 (7.38)
				Cosmesis (pts satisfaction with cosmetic outcome)	Very satisfied 37.8% Satisfied 32.4% Neutral 10.8% Unsatisfied 14.9% Very Unsatisfied 4.1%
				Complications	35/74 (43%)
Romanowski 2017[23] Case series N=98	•Mean age 36 •66%F	Graft	1 yr	Mean(SD) Hospital LOS	6.3(5.6) days
				% of wounds fully grafted & closed at 30 days	94.7%
Sirvan 2019[24] Case series N=14	•Mean age 31.1 •35.7%F •Axillary HS	Flap	6 mos	Recurrence rate	1/14(7.1%)
				Complications	2/14 (14.3%) ; wound dehiscence, marginal necrosis

Soldin 2000[25] case series N=29	•Mean Age 32 •71.2%F •Axillary HS	NR	NR	Recurrence rate	0/29(0%)
Tchero 2018[26] Case series N=31	•Mean age 37.8 •61.3%F	Artificial dermis graft	1yr	Mean hospital LOS	4.8 days
				Recurrence	0/31 (0%)
				Complications	6/31(19.4%) infections
Unal 2011[27] Case series N=12	•Mean age 44.4 •0%F •Gluteal & perianal/perineal HS	Flap	20 mons	Mean hospital LOS	6 days
				Recurrence	0/12 (0%)
				Complications	2/12 (16.7%) ; flap necrosis & suture detachment
Varkarakis 2010[28] Case series N=15	•Age range 16-65 yr •80%F •Axillary HS	Flap	1yr	Residual disease requiring re-excision	1/15(6.7%)
				Complications	3/15 (20%) flap necrosis, delay of return of shoulder mobility
Walter 2018[29] Case series N=48	•Mean age 39.3 •60.4%F •Hurley stage III	Secondary intention, Graft	3.81 yrs	Complete recovery (undefined) at least 1 yr post-treatment	22/48 (45.8%)
				Active HS symptoms local/distant at least 1 yr post-surgery	26/48 (54.2%)
				Local recurrence rate	22/48 (45.8%)
Wollina 2012[30] Case series N=67	•Mean age 38.6 •46.3%F •Severe anogenital HS	Primary Intention, Graft, Secondary Intention, Transdermal CO2, Wound Vac	Mean 56.9 mos f/u; 10-12 wks post-op for clinical outcomes	Mean(SD) HS-LASI score at 10-12wks post-op	Pre-surgery 41.8(21.3) Post-op 2.4 (2.8)
				Mean(SD) hospital LOS	12.6(11.2) days
				Mean (SD) VAS pain scores at 10-12 wks post-op	Pre-surgery 6.3(1.5) Post-op 0.8(0.7)
				Mean (SD) patient global assessment at 10-12 wks post-op	Pre-surgery 7.3(1.2) Post-op 1.1(0.5)
				Recurrence	4/67 (6%)
				Complications	7/67 (10.4%) ; bleeding, fever, erysipelas, wound dehiscence, anemia
Wollina 2017[31] Case series N=117	•Mean age 40.6 •46.2%F •Severe anogenital HS	Secondary Intention, Graft, Wound Vac, Topical CO2	NR	Mean(SD) hospital LOS	Primary closure 38(7.1) days Secondary intention 13.5(16.9) days
				Mean(SD) time to complete healing	Primary closure 14(6.6) days Secondary intention 13.6(9.8) weeks
				Recurrence rate	11/117 (9.4%)
				Mean(SD) Pain VAS 10 score 10-12 wks post-op	Pre-surgery 7.9(3.4) Post-op 1.1 (2.9)
				Complications	15 complications ; bleeding, anemia, suture dehiscence, abcess, infection, erysipelas, scar contracture, thrombophlebitis

Wormald 2014[32] Case series N=27	•Mean age 34.7 •70.4%F •Hurley stage 3	Graft, Flap	1yr	Mean hospital LOS	Flap: 4.7 days Graft:6.7 days
				Mean time to complete healing (return to pre-op activity)	Flap : 5.4wks Graft :16.1wks
				Mean Pain VAS 10 scores reduction	Flap : -5 Graft :-3.92
				Mean DLQI scores reduction	Flap : -23.1 Graft : -19.3
				Recurrence rate	2/27 (7.4%)
				Complications	Flap :3 events Graft :9 events
Yamashita 2014[33] Case series N=18	•Mean age 40.6 •11.1%F	Artificial Dermis Graft, then Graft	1yr	Recurrence rate	1/18 (5.6%)
				Complications	10/18 (55.6%) local infections 1/18(5.6%) skin graft loss

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e-Table 65. Radical surgical excision (case series)

Case series/cohorts n=17, 627 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series and non-comparative cohorts, which are inherently limited due to the lack of control groups and selection bias. The individual studies generally included small sample sizes, increasing concern about random error and imprecision. Varied patient populations, procedural techniques, and outcome assessment and reporting make it difficult to assess consistency across studies and preclude pooling. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.) The studies do not report the majority of patient-important outcomes of interest (i.e pain reduction, clinical severity changes, etc.)

Study details	Baseline characteristics	Closure	Time of outcome assessment	Outcome	Results
Bieniek 2025[1] Case series N=12	•Mean age 32(12.1) years •12M •Hurley stage II n=6 ; III n=6 •Obesity n=4 •Smokers n=8	Flap	6 months	Recurrence rate	1/12 (8.3%)
				Bleeding	0/12
Bohn 2001[2]	•Median age 33	Graft		Recurrence rate	38/116(33%)

Case series N=116	•Sex NR		3-21 yr follow up	Complications	0/116 (0%)
Buyukasik 2011[3] Case series N=15 patients; 36 sites	•Mean age 41.8 •31.3%F	Primary, Flap, Graft	3.67 yrs	Recurrence rate	2/36 (5.6%)
				Complications	9/36(25%) sites
Chang 2024[4] Retrospective cohort N=136	•Median (IQR) age 24.1 (18.7-33.1) years •Obesity n=65 •Smokers n=47 •Hurley stage I n=28 ; II n=89 ; III n=19 •284 excisions	Primary closure n=215 ; STSG closure n=50; Flap n=19	Median 2.5 (1.2, 4.0) years	Recurrence rate	31.0%; median time to recurrence 6.9 months
				Complication rate	Overall 35.9% Dehiscence 13.7% Hypertrophic scare 13.4% Infections 12.7% Skin graft failure 3.5% Hematoma 2.8%
DeFazio 2016[5] Case series N=10	•Mean age 32 •67%F •Hurley stage III	Delayed primary closure	Mean 20.5 mos	Recurrence rate	38.5%
				Disease progression (development of new lesions)	5/10 (50%)
				Complications	3/10 (30%) wound dehiscence, infections
Egemen 2013[6] Case series N=11	•Mean age 39.3 •0%F	Flap	11.5 mos	Recurrence rate	0/11 (0%)
				Complications	3/11 (27.3%) ; marginal necrosis, infections
Elboraey 2019[7] case series N=6	• Mean age 30 •33.3%F •Hurley III	Flap	NR	Mean hosptial LOS	4 days
				Recurrence rate	1/6(16.7%)
				Complications	1/6(16.7%)
Elgohary 2018[8] Case series N=20	•Mean age 29.3 •10%F •Axillary Hurley Stage II/III HS	Flap	Mean 30 mos	Complete remission	20/20 (100%)
				Recurrence rate at 30 mos	0/20 (0%)
				Mean (SD) hospital LOS	6(3) days
				Mean(SD) DLQI scores 1 yr post-op	Hurley II Pre 11.6(2.82) Post 3.25(1.77) p<0.001 Hurley III Pre 21.5(3.32) Post 2.9(1.65) p<0.001
				Pt satisfaction with cosmesis at 1 yr	18/20 (90%) satisfied
				Complications	7/28 operations
Judge 2024[9]		Complete closure n=9;	NR	Recurrence	2/71 (2.8%)
				Mean hospital LOS	8.5 (2.9) days

Retrospective cohort N=71	•Mean age 34.6 (11.2) years •Hurely stage II n=14; III n=57 •Mean 3.7(2.3) surgeries per person •71 failed medical management	Partial closure n=8; Staged reconstruction n=54		Complications	Dehiscence 34/71 (48%) Infection 10/71 Hematoma 3/71 Necrosis 3/71 Pulmonary embolism 1/71 DVT 1/71 Abcess 1/71
Marchesi 2018[10] Case series N=12	•Mean age 32.6 •66.7%F •Hurley stage III	Flap	Range 6-22 mos	Hospital LOS	Range 1-5 days
				Mean(SD) time to complete healing	20(9) days
				Recurrence rate	0/12 (0%)
				Complications	Early (undefined) 29% ; wound dehiscence, hematoma, venous congestion Late (undefined) 35% ; scarring, flap bulkiness
Mendes 2018[11] Case series N=19 pts; 34 lesions	•Mean age 32 •Sex NR	Primary Closure, Graft, Flap	≥1 yr	Complete healing by 12 wks	25/34 (73.5%)
				Recurrence rate	16/34 (47%)
				Complications	22/34 (64.5%) lesions
Nesmith 2013[12] Case series N=11 pts; 15 lesions	•Mean age 30.3 •81.8%F	Flap	4.3yrs	Recurrence rate	0/15 (0%)
				Complications	0/15 (0%)
Ortiz 2010[13] Case series N=16	•Mean age 39.8 •62.5%F	Flap	NR	Mean Hospital LOS	5 days (range 4-7)
				Complications	3/16 (18.8%) ; hypertrophic scare & hematoma
Prandl 2008[14] Case series N=30	•Mean age 40 •4F •Anogenital HS	Graft, Flap	4.5 yrs	Recurrence rate	0/30(0%)
				Infections	0/30(0%)
Romanowski 2023[15] Prospective cohort N=16	•Median(IQR) age 38.2(34.2, 54.5) •9F, 7M •Median(IQR) BMI 39.7(28.4, 50.6) •Hurley stage II or III	Graft	1 yr	Median(IQR) change in DLQI from baseline to 6 and 12 months	6 months : 15.5 [12–21.8] vs 10 [4–20], P = .036 12 months : 15.5 [12–21.8] vs 12 [3–26.3], P = .311
Rompel 2000[16] Case series N=106	•Mean age 33.6 •57.5%F	Graft, Flap, Primary closure	36 mos	Recurrence rate	2.5%
				Complications	19/106 (17.8%)

Schmidt 2015[17] Case series N=20 pts; 31 lesions	•Mean age 37.75 •50%F •Axillary HS	Flap	NR	Revisions required during 5 yr study period	3/31 (9%)
				Complications	7/31 (22.6%)

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e-Table 66. Local surgical excision (case series)

Case series/cohorts n=5, 317 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series and non-comparative cohorts, which are inherently limited due to the lack of control groups and selection bias. The individual studies included small to very sample sizes, increasing concern about random error and imprecision. Varied patient populations, procedural techniques, and outcome assessment and reporting make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.) Most studies do not report the majority of patient-important outcomes of interest (i.e pain reduction, clinical severity changes, etc).

Study details	Baseline characteristics	Closure	Time of outcome assessment	Outcome	Results
Aksakal 2008[1] Case series N=12 pts; 30 lesions	•Mean age 34 •66.7%F •Hurley stage I-II	Secondary intention	2 mos	Complete lesion cure	26/30 (86%) lesions
				Mean time to complete healing	16 days (range 15-21)
				Complications	4/30 (13.3%) infections
Bienek 2010[2] Case series N=57	•Mean age 38.3 •52.6%F	Primary, Graft, Flap, Secondary Intention	2 yrs	Complete lesion cure	34/57 (59.7%
				Post-operative pain	19/57 (30%)
				Complications	14 events ; infection, contractures, bleeding, granulation tissue
Blok 2015[3] Case series	•Mean age 23.1	Secondary intention	3.6 yrs	Disease remission	132/363 (36.4%)
				Recurrence rate	230/363 (63.4%)

N=113pts; 363 lesions	•68.2%F			Satisfaction with medical and cosmetic outcomes (0-10 scale ; 10=very satisfied)	Medical : Median 8 Cosmetic : Median 6
				Complications	58/363 (16%)
Ravi 2022[4] Retrospective cohort N=65 procedures	•Mean age 35.1 yrs •83%F •Hurley stage II n=77 ; III n=117 •Multiple anatomic locations	With closure (n=53) ; without closure (n=12)	Median 13 mos	Recurrence rate	36/65 (55%)
Van Rappard 2012[5] Case series N=57	•Mean age 42.5 •82.5%F	Primary closure	27 mos	Successful treatment without recurrence	38/57 (66.7%)
				Mean time to wound healing	3.2 wks
				Recurrence rate	13/57 (23%)
				Postoperative pain requiring medication	35/57 (61.4%)
				Complications	17/57 (29.8%)

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e-Table 67. Other surgical interventions (Case series)

Case series n=9, 121 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control groups and selection bias. The studies included small sample sizes, increasing concern about random error and imprecision. Varied patient populations, procedural techniques, and outcome assessment and reporting make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.) Most studies do not report the majority of patient-important outcomes of interest (i.e pain reduction, clinical severity changes, etc).

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Yildirim 2022[1] Monocentric retrospective case series N=11	- Age (year, mean, SD): 33.9 (10.3) - 1 F, 10 M - Previous treatments: NR - Mean BMI: 27.2 (SD 3.5) - Hurley III n=11 - Smoking status: 6/11	propeller parascapular flap surgery	antibiotics no precision	NR	Recurrence	N=0	Selection N Ascertainment Y Causality N Reporting Y
					Mean hospital stay	4 days (from 3 to 6 days)	
					Safety	Dehiscence occurrence: n= 1 Infection n=0 Partial necrosis n=0 flap loss n=0	
Bu 2022[2] Multicentric:3 centers retrospective case series N=35	- Age (year, mean, SD): 23.6 (7.9) - 5 F, 30 M - Previous treatments: 35(100%) No precision - Mean BMI: NR -Hurley: II n=15/35 (42.9%), III n=20 (57.1%) -Smoker: n= 12/35 (34%)	•modified excision combined with bidirectional PDT	NR	1 year	Clearance rate	100%: 31/35(88.6%) 75%: 4/35 (11.4%)	Selection N Ascertainment Y Causality N Reporting y
					Modified Vancouver Scar Scale	Hurley II: - None: 12/15 - Mild: 3/15 Hurley III: - None: 8/20 - Mild: 10/20 - Moderate: 2/10	
					Patient satisfaction	Very satisfied: 30/35 (85.7%) Satisfied: 5/35 (14.3%)	

					Safety	N=6 (small patchy blackness, necrosis, or ulcer in the tip of the flap)	
Karabay 2020[3] Retrospective case series N=14	- Age (year, mean): 40.3 (8.4) - 2F, 12M -Previous treatments: NR - Mean BMI: NR - Hurley II n=9 Hurley III n= 5 - Smoking status: NR	•Surgery with Fistula-tract Laser Closure (FiLaCTM)	All patients were discharged on the same day of surgery with antibiotics (ciprofloxacin plus metronidazole)	NR	"Complete response" (wound healing without drainage and closure of all external orifices at the 3rd month control) "Partial response" (Slight drainage with minimal symptoms)	complete response: n=4 partial response n= 8 no response n=2	Selection Y Ascertainment Y Causality N Reporting Y
					Safety	No intraoperative or postoperative complications were observed	
Chaffin 2020[4] Prospective case series N=6	-Age (year, mean, SD): 32 (SD = 5.0) -4 F 2M -Previous treatments: NR -Mean BMI: NR -Hurley Stage: NR -1 active smoker	•decellularized ovine forestomach matrix (OFM) extracellular matrix (ECM) graft for soft tissue regeneration as part of surgical reconstruction of stage III HS of the axilla	NR	Short-term outcomes were measured between 1 and 3 months.	Time to complete healing of surgical site	1 to 3 months	Selection NR Ascertainment Y Causality Y Reporting N
					Recurrences at the last postoperative visit at 3-12 months	N=0	
					Safety	mild wound dehiscence N=1	

Young Sing 2019[5] Retrospective monocentric case series N=9	-Age (year, mean, range): 29 (24 to 48) - Sex:NR -Previous treatments n (%):NR -Mean BMI:NR -Hurley Stage: NR -Smoking status: NR	•The Modified Skoog approach for the management of axillary HS as a skin sparing technique.	All severe active infection was completely treated with antibiotics prior to the surgery	Day 7 post surgery	Good wound healing with minimal local discomfort Recurrences at a 6-month and 3-year	N=7 N=0	Selection N Ascertainment N Causality N Reporting Y
STOŠIĆ 2016[6] Retrospective monocentric case series N=8	-Age (year, mean, range): 42 (30 to 73) -8M -Previous treatments:antibiotics -Mean BMI:NR -Hurley Stage III n=8 -Smoking status: NR	•Surgery excision to the fascia or to leave a thin layer of adipose tissue.	NR	NR	HS relapse Hospital stays Time to dressing free Functional satisfaction Aesthetic dissatisfaction	1/8 7 to 14 days 2 months 8/8 1/8	Selection N Ascertainment Y Causality Y Reporting N
Janse 2016[7] Prospective monocentric case series N=16	-Age (year, mean, SD):42.2(10.5) -6F; 10M -Previous treatments (n): Adalimumab 1,Doxycycline 2 Infliximab 5 -Mean BMI(SD):27.4(4.8) -Hurley Stage II and III -Smoking status n : Active 10; Former 4	•STEEP Procedure	Anti-inflammatory agents=8 -Infliximab n=16	- Patient satisfaction was measured 8 weeks postoperatively	Time to complete wound closure Recurrence Safety	53.1 days (SD 24.0) N=8 hyper granulation n= 10	Selection Y Ascertainment Y Causality Y Reporting N

Mutaf 2014[8] Retrospective monocentric case series N=16	-Age 18 to 52 years - 4F 12M -Previous treatments: NR -Mean BMI:NR -Hurley Stage: NR -Smoking status n (%) Smokers:13(81.25)	•Mutaf Triangular closure procedure	NR	NR	Hospital stay	3 to 4 days	Selection N Ascertainment Y Causality Y Reporting Y
					Long-term recurrence	N=0	
					Safety	Partial flap necrosis n=2	
Amarante 1996[9] Retrospective monocentric case series N=6	-Age (year, mean, SD): 31.1 (8.7) -4F, 2M -Previous treatments: NR -Mean BMI:NR -Hurley Stage: NR -Smoking status: NR	•Scapular island flaps	NR	NR	Outcome: complications	0/6	Selection NR Ascertainment Y Causality N Reporting Y

NR: Not reported

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e-Table 68. Carbon dioxide laser excision (case series)

Case series n=3, 77 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series/cohorts, which are inherently limited due to the lack of control groups and selection bias. The individual studies included very small sample sizes, increasing concern about random error and imprecision. Varied populations, interventions and outcome assessment and reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Finley 1996[1] Monocentric prospective case series N=7; 12 procedures	•Ages 20-46 •7F, 0M •Duration of disease 1-10 years	CO2 laser excision 40 W, 0.1 mm spot size, continuous-wave	Oral contraceptives n=1 Cleansing with hydrogen peroxide & bacitracin-polymyxin B antibiotic ointment & Telfa dressing.	10-27 months follow up	Local recurrence (# of pts with lesion recurrences in treated area)	1/7 (14.3%)	Selection N Ascertainment Y Causality N Reporting N
					Healing time	Range 4-8 weeks	
					Adverse events	1/7 paresthesias 2/7 infection 0/7 hypertrophic scar	
Hazen 2010[2] Monocentric prospective case series	•Mean age 38.5 •42F, 19M •Obese n=8 •Misease duration 8.5 years	CO2 laser excision 8-30 W Spot size 0.22 mm	Bacitracin/polymyxin B ointment & hydrocolloid dressing for 2 days	Range 12-228 months of follow up	Local recurrence (# of pts with lesion recurrences in treated area)	2/61 (3.3%) Mean 4.1 years without disease recurrence	Selection N Ascertainment Y Causality N Reporting N
					Healing time	Mean 8.8 weeks for secondary-intention healing	

N=61; 185 treated sites		Average 2.5 treatments per patient	Petroleum jelly & Telfa dressing until reepithlialization		Adverse events	Hypergranulation 17/61 (28.0) Cellulitis 3/61 (4.9) Fever 1/61 (1.6)	
Madan 2008[3] Monocentric prospective case series N=9	•Mean Age 39 •8F, 1M •Mean disease duration 9.3 years •Refractory HS	Co2 laser excision		12 months	Healing time mean	2 weeks (range 1, 4)	Selection N Ascertainment Y Causality N Reporting Y
					Local recurrences (# of pts with lesion recurrences in treated area) at 12 months	0/9	
					Adverse events	1/9 wound dehiscence 0/9 infections	

1. Finley EM , Ratz JL. Treatment of hidradenitis suppurativa with carbon dioxide laser excision and second-intention healing. J Am Acad Dermatol 1996;34:465-9.
2. Hazen PG , Hazen BP. Hidradenitis Suppurativa: Successful Treatment Using Carbon Dioxide Laser Excision and Marsupialization. Dermatologic Surgery 2010;36.
3. Madan V, Hindle E, Hussain W , August PJ. Outcomes of treatment of nine cases of recalcitrant severe hidradenitis suppurativa with carbon dioxide laser. Br J Dermatol 2008;159:1309-14.

e-Table 69. Carbon dioxide laser vaporization (case series)

Case series n=5, 133 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series/cohorts, which are inherently limited due to the lack of control groups and selection bias. The individual studies included very small sample sizes, increasing concern about random error and imprecision. Varied populations, interventions and outcome assessment and reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Dalrymple 1987[1]	•Ages 20-34 •5F, 1M	Co2 laser vaporization 1-4 sessions	None	9 months & 3 years	Healing time	3-7 weeks by granulation	Selection N Ascertainment Y Causality N Reporting N
					Local recurrence (# of pts with lesion recurrences in	0/6	

Monocentric retrospective case series N=6					treated area) at 3 years		
					Adverse events	0/6 infections	
Lapins 1994[2] Monocentric prospective case series N=24; 33 operating sites	•Mean age 36 •21F, 3M •Mean disease duration 13 years •Hurley stage II •3+ recurrences of suppurating lesions in past year	CO2 laser vaporization 30 W, defocused to 2 mm	NR	Mean 27 months follow-up (range 15-47)	Healing time mean weeks	4 weeks (range 3-5 weeks)	Selection N Ascertainment Y Causality N Reporting Y
					Local recurrence (# of pts with lesion recurrences in treated area)	2/24 (8.3%)	
					Adverse events	2/24 (8.3%) infection 1/24 (2.9%) hypertrophic scar	
Lapins 2002[3] Monocentric prospective case series N=34	•Mean age 33.9 •31F, 3M •Hurley stage II •Mean disease duration 13.4 years •3+ recurrences of suppurating lesions in past year	CO2 laser vaporization Scanner- assisted 20-30 W, spot size 3-6 mm, focal length setting 12.5-18 cm	NR	Mean 34.5 months follow-up (range 8.8-60)	Healing time mean weeks	4 weeks (range 3-5 weeks)	Selection N Ascertainment Y Causality N Reporting Y
					Local recurrences (# of pts with lesion recurrences in treated area)	4/34 (11.8%)	
					Post-operative pain via scale 0-3; higher score indicates greater pain	0 n=6 1 n=9 2 n=15 3 n=4	
					Adverse events	0/34 infections 1/34 (2.9%) hypertrophic scar	
Mikkelsen 2015[4] Monocentric retrospective case series N=58	•Mean age 37.8 •48F, 10M •Mean BMI 29.8 •Mean disease duration 18.1 years •	CO2 laser vaporization Scanner- assisted 20-35 W, spot size 4 mm	Mepilex border dressing, ibuprofen 400mg qd for 1 week	Mean 20.6 months follow up (range 1-47)	Local recurrences (# of pts with lesion recurrences in treated area)	17/58 (29.3%) Recurrence at a mean 12.2 months	Selection N Ascertainment Y Causality N Reporting Y
					Patient satisfaction (unchanged, small improvement, great improvement)	Unchanged n=3 Small improvement n=11 Great improvement n=44	

					Adverse events	Contracture of the scar 1/58 (1.7) Bleeding 1/58 (1.7)	
Sherman 1991[5] Monocentric case series N=11	•Mean age 33 •11F, 0M •Vulvar & anogenital lesions •Mean disease duration 10.8 years	CO2 laser vaporization -n=2 required 2 operations	NR	8 years follow up	Successful treatment (eradicating the suppurative sinus tracts and the infected apocrine glands)	9/11 (81.8%)	Selection N Ascertainment Y Causality N Reporting N

1. Dalrymple JC , Monaghan JM. Treatment of hidradenitis suppurativa with the carbon dioxide laser. Br J Surg 1987;74:420.
2. Lapins J, Marcusson JA , Emtestam L. Surgical treatment of chronic hidradenitis suppurativa: CO2 laser stripping-secondary intention technique. Br J Dermatol 1994;131:551-6.
3. Lapins J, Sartorius K , Emtestam L. Scanner-assisted carbon dioxide laser surgery: a retrospective follow-up study of patients with hidradenitis suppurativa. J Am Acad Dermatol 2002;47:280-5.
4. Mikkelsen PR, Dufour DN, Zarchi K , Jemec GBE. Recurrence Rate and Patient Satisfaction of CO2 Laser Evaporation of Lesions in Patients With Hidradenitis Suppurativa: A Retrospective Study. Dermatologic Surgery 2015;41:255-60.
5. Sherman AI , Reid R. CO2 laser for suppurative hidradenitis of the vulva. J Reprod Med 1991;36:113-7.

Procedural & Intralesional Interventions Summary of Findings

Contents

e-Table 70. Alexandrite laser hair removal vs no laser hair removal

Alexandrite laser hair removal compared to no laser hair removal for HS[1]

Patient or population: mild to HS
Intervention: 755-nm alexandrite laser hair removal series of 4 monthly sessions
Comparison: no laser hair removal on the contralateral side

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no laser hair removal	Risk with alexandrite laser hair removal				
Clinical severity assessed with: HiSCR response follow-up: 24 weeks	333 per 1,000	**750 per 1,000** (407 to 1,000)	**RR 2.25** (1.22 to 4.15)	48 (1 RCT)	⨁⨁◯◯ Low[a]	
Pain assessed with: Pain score 0-3; higher score indicates greater pain follow-up: 24 weeks	Average pain score across all treatment sites at baseline vs week 24: Treatment: 1.2 vs 0.63 Control: 1.2 vs 0.96			(1 RCT)	⨁⨁◯◯ Low[b]	
Discontinuation due to adverse events follow-up: 16 weeks	No patients discontinued treatment due to side effects.			(1 RCT)	⨁⨁◯◯ Low[b]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded 2 levels for very serious imprecision: very small sample with ratio of upper to lower CI bounds >3.
b. Downgraded 2 levels for very serious imprecision: very small interindividual sample

1. Sidhom S, Petry SU, Ward R , Daveluy S. Treatment of hidradenitis suppurativa with 755-nm alexandrite laser hair removal: A randomized controlled trial. JAAD Int 2024;16:239-43.

e-Table 71. Alexandrite laser hair removal adjuvant therapy

Alexandrite laser hair removal adjuvant therapy compared to chlorhexidine wash+ zinc 90mg for mild to moderate HS[1]

Patient or population: Females with mild to moderate (Hurley stages I-II) HS
Intervention: alexandrite hair removal laser 755 nm for 5 sessions at 6-week intervals + antiseptic chlorhexidine washes and oral gluconate zinc 90 mg daily for 30 weeks
Comparison: antiseptic chlorhexidine washes and oral gluconate zinc 90 mg daily for 30 weeks

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with chlorhexidine wash+ zinc 90mg	Risk with alexandrite laser hair removal adjuvant therapy				
HiSCR response follow-up: 30 weeks	200 per 1,000	**700 per 1,000** (278 to 1,000)	**RR 3.50** (1.39 to 8.80)	40 (1 non-randomised study)	⨁◯◯◯ Very low[a]	
Pain (end score) assessed with: Mean VAS 10mm follow-up: 30 weeks	The mean pain (end score) was 3.9	MD **1.5 lower** (3.48 lower to 0.48 higher)	-	40 (1 non-randomised study)	⨁◯◯◯ Very low[b]	
Flares assessed with: Mean # of acute disease flares follow-up: 30 weeks	The mean # of flares was 6.4	MD **4.3 fewer** (5.37 fewer to 3.23 fewer)	-	40 (1 non-randomised study)	⨁◯◯◯ Very low[c]	
Quality of life assessed with: Mean DLQI end score follow-up: 30 weeks	The mean DLQI was 12.7	MD **8.2 lower** (11.69 lower to 4.71 lower)	-	40 (1 non-randomised study)	⨁◯◯◯ Very low[c]	
Adverse events follow-up: 30 weeks	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	40 (1 non-randomised study)	⨁◯◯◯ Very low[d]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded 2 levels due to very serious imprecision: small sample (ratio of upper and lower CI bounds >3)
b. Downgraded 2 levels due to very serious imprecision: CI consistent with meaningful difference (3+ points) and no difference; the sample is <30% of optimal information size.
c. Downgraded 2 levels for serious imprecision: CI consistent with meaningful difference but the sample is <30% of optimal information size.
d. Downgraded 2 levels due to very serious imprecision: no events in a very small sample.

1. Molinelli E, Sapigni C, Simonetti O, Brisigotti V, Giuliodori K , Offidani A. Alexandrite laser as an adjuvant therapy in the management of mild to moderate hidradenitis suppurativa: A controlled prospective clinical study. J Am Acad Dermatol 2022;87:674-5.

e-Table 72. Nd:YAG laser hair removal vs no hair removal

Nd:YAG laser hair removal compared to control for hidradenitis suppurativa

Patient or population: hidradenitis suppurativa
Intervention: Neodymium:yttrium-aluminium-garnet (Nd:YAG) laser hair removal 4 treatments at 6-week intervals
Comparison: No laser hair removal on contralateral side

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with topical control	**Risk with Nd:YAG laser**				
Achieving HiSCR50 follow-up: 30 weeks	526 per 1000	**526 per 1000** (289 to 963)	**RR 1.00** (0.55 to 1.83)	38 (1 RCT)[1]	⊕⊕◯◯ Low[a]	
Disease flares Mean±SD # of flares follow-up: 30 weeks	Treated(n=36): 1.97±3.16 Untreated(n=36): 2.42±3.7 p=0.378			36 (1 RCT)[1]	⊕⊕◯◯ Low[b]	
Pain during treatments 0-10 scale; Higher score worse pain During treatment	Mean pain during laser sessions 5.4			38 (1 RCT)[1]	⊕⊕◯◯ Low[b]	
Serious adverse events through 30 weeks follow-up: 30 weeks	0 per 1000	**0 per 1000** (0 to 0)	Not estimable	38 (1 RCT)[1]	⊕⊕◯◯ Low[b]	No SAEs reported
Adverse events During treatment	1/36 burning sensation & irritation			36 (1 RCT)[1]	⊕⊕◯◯ Low[b]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two levels due to serious imprecision (small sample size and the ratio of the upper to the lower boundary of the CI was > 3)
[b]Downgraded by two levels due to very serious imprecision: very small sample/# of events

1. Naouri M, Maruani A, Lagrange S, Cogrel O, Servy A, Collet Vilette AM et al. Treatment of hidradenitis suppurativa using a long-pulsed hair removal neodymium:yttrium-aluminium-garnet laser: A multicenter, prospective, randomized, intraindividual, comparative trial. J Am Acad Dermatol 2021;84:203-5.

e-Table 73. Laser hair removal (case series)

Case series n=2, 29 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from two case series, which are inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The individual studies included very small sample sizes, increasing concern about random error and imprecision. Varied interventions and outcome assessment and reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Fradet 2021[1] Monocentric retrospective case series N=14	•Mean Age 33.3 •F •Hurley stage I-II	Hair removal using Long-pulsed 755 nm Alexandrite Skin types II and III: F = 18 J/cm2 and PD = 20 ms. Skin types IV: F = 15 J/cm2 and PD = 30 ms. SS = 15mm for all skin types At least 2 treatments; intervals <10 weeks	doxycycline (n=5), rifampicin/clindamycin (n=3), secukinumab (n=1), infliximab (n=1), and cyclosporine (n=1)	1& 3 months post-treatment	Mean # abscesses/nodules and draining fistulas	<u>Baseline→1 month→3 months</u> Abscesses/nodules 5.3→1.6 (p=0.038)→2 (p=0.043) Fistulas 0.5→0.5 (no 3 month data)	Selection N Ascertainment Y Causality N Reporting Y
					HiSCR50 (patients achieving)	9/14 (64%)	
					Mean pain NRS score during treatment	6.0	
					Localized flares (≥25% increase in abscess/nodule count or new draining fistulas)	3/14 localized flares	
Vossen 2018[2] Monocentric retrospective case series	•Mean age 34.1 •5F, 10M •Mean BMI 25.1 •Hurley stage I	Laser hair removal using long-pulsed Nd:YAG laser Fluence 30-60 J/cm 2 , Spot size 7–12	Clindamycin 300mg bid+rifampicin 600mg qd (n=1)	Mean 14.9 (14.1) months	Flares per month (# of patients with reported # of flares)	<u>Pre-treatment→Post-treatment</u> <1 4→8 1 2→0 2 1→3 3 3→3	Selection N Ascertainment Y Causality N Reporting Y

N=15		mm, pulse duration 20-40 ms, 2 passes(n = 13), 1 pass (n = 2) Mean of 9.8 (±9.4) treatments, intervals 5.6 ±0.1 wk	Minocycline 100 mg qd (n=1) Acitretin 25mg qd (n=1)			>3 5→1 P=0.019	
					Mean(SD) HS disease severity via NRS	<u>Pre-treatment→Post-treatment</u> 6.4(2.8) → 3.6(3.5) p=0.010	
					Mean(SD) pain due to laser treatment via NRS	5.4(2.6)	

1. Fradet M, Bulai Livideanu C, Katoulis A, Hegazy S, Bouznad A, Jendoubi F et al. Efficacy and tolerability of long-pulse Alexandrite laser hair removal for hidradenitis suppurativa. Eur J Dermatol 2021.
2. Vossen ARJV, van der Zee HH, Terian M, van Doorn MBA , Prens EP. Laser hair removal alters the disease course in mild hidradenitis suppurativa. JDDG: Journal der Deutschen Dermatologischen Gesellschaft 2018;16:901-3.

Botulinum Toxin

e-Table 74. Intralesional botulinum toxin B vs placebo

Botulinum toxin-B (BTX-B) compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: botulinum toxin-B (BTX-B) intradermal injections maximum dose limits were set at 150 U per armpit, 200 U per groin area, and 600 U in perianal/perigenital areas, with a total maximum dose of 4000 U per treatment session for 1 session
Comparison: placebo (normal saline)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	**Risk with botulinum toxin-B (BTX-B)**				
Change in pain VAS Scale from: 0 to 10 follow-up: 3 months	The mean change **0.4**	MD **2.7 lower** (4.64 lower to 0.76 lower)	-	20 (1 RCT)	⨁⨁⨁◯ Low[a]	
Change in DLQI Scale from: 0 to 30 follow-up: 3 months	The mean change **-0.1**	MD **6 lower** (11.75 lower to 0.25 lower)	-	20 (1 RCT)	⨁⨁⨁◯ Moderate[b]	
Change in total number of lesions follow-up: 3 months	The mean change **-0.6**	MD **3.3 fewer** (8.91 fewer to 2.31 higher)	-	20 (1 RCT)	⨁⨁◯◯ Low[c]	
Change in number of nodules of lesions at month 3 follow-up: 3 months	The mean change **-0.1**	MD **3.8 fewer** (9.06 fewer to 1.46 higher)	-	20 (1 RCT)	⨁⨁◯◯ Low[c]	
Adverse events follow-up: 3 months	0 per 1000	**0 per 1000** (0 to 0)	Not estimable	20 (1 RCT)	⨁⨁◯◯ Low[d]	No adverse events occurred in either group.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two levels due to serious imprecision: The 95% CI crossed the MID of VAS30 (30% reduction), and the total sample is very small, suggesting fragility.

[b]Downgraded by one level due to serious imprecision: The 95% CI crossed the MID of 4 for DLQI, and the total sample is very small, suggesting fragility.
[c]Downgraded by two levels due to very serious imprecision small sample size.
[d]Downgraded by two levels due to very serious imprecision: zero events with small sample size.

1. Grimstad Ø, Kvammen B , Swartling C. Botulinum Toxin Type B for Hidradenitis Suppurativa: A Randomised, Double-Blind, Placebo-Controlled Pilot Study. Am J Clin Dermatol 2020;21:741-8.

e-Table 75. Botulinum toxin (case series)

Case series n=1, 8 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series/non-comparative cohort studies, which are inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The individual studies included small sample sizes, increasing concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data makes it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of Bias
Goandal 2025[1] Retrospective cohort N=8	-Mean age 38.25y -6F, 2M -Hurley stage I n=1, III n=5, III n=2 -Mean BMI 36.01 -Smoker n=3	Botulinium toxin A (no dosing or duration details); adjunctive to other therapies	Topical resorcinol n=6; azelaic acid n=1; metformin n=6; secukinumab n=2; isotretinoin n=1	NR	Median pain reduction (Likert scale -3 to 3; -3 was worsening)	2.50 (IQR 0.00-3.00)	Serious

1. Goandal NF, Jemec GBE , Saunte DML. Botulinum toxin type A efficacy on pain and suppuration in hidradenitis suppurativa. J Eur Acad Dermatol Venereol 2025.

Intralesional Triamcinolone

e-Table 76. Intralesional triamcinolone vs placebo

Triamcinolone compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa with an inflammatory lesion
Intervention: triamcinolone 10 mg/mL or 40 mg/mL
Comparison: placebo (normal saline)

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	**Risk with triamcinolone**				
Pain-Triamcinolone 10mg Mean pain score reduction Scale from: 1 to 10 follow-up: 5 days	Mean pain score reduction: **-2.63**	MD **0.63 lower** (1.07 lower to 2.33 higher)	-	36 (1 RCT)	⊕⊕◯◯ Low[a]	
Pain- Triamcinolone 40mg Mean pain score reduction Scale from: 1 to 10 follow-up: 5 days	Mean pain score reduction: **-2.63**	MD **0.33 lower** (1.25 lower to 1.91 higher)	-	39 (1 RCT)	⊕⊕◯◯ Low[a]	
Clinical severity-Triamcinolone 10 mg Average days to lesion resolution follow-up: 14 days	Mean days to lesion resolution: **9.35**	MD **1.43 more** (1.93 fewer to 4.79 more)	-	38 (1 RCT)	⊕⊕◯◯ Low[a]	
Clinical severity-Triamcinolone 40 mg Average days to lesion resolution follow-up: 14 days	Mean days to lesion resolution: **9.35**	MD **1.5 higher** (1.5 lower to 4.5 higher)	-	40 (1 RCT)	⊕⊕◯◯ Low[a]	
Serious adverse events-Triamcinolone 10mg follow-up: 14 days	0/20	0/18	Not estimable	38 (1 RCT)	⊕⊕◯◯ Low[a]	No serious adverse events occurred in either group.
Serious adverse events-Triamcinolone 40mg follow-up: 14 days	0/20	0/20	Not estimable	40 (1 RCT)	⊕⊕◯◯ Low[a]	No serious adverse events occurred in either group.
Adverse events- Triamcinolone 10mg follow-up: 14 days	0/20	0/18	Not estimable	38 (1 RCT)	⊕⊕◯◯ Low[a]	No adverse events occurred in either group.

Triamcinolone compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa with an inflammatory lesion
Intervention: triamcinolone 10 mg/mL or 40 mg/mL
Comparison: placebo (normal saline)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	**Risk with triamcinolone**				
Adverse events- Triamcinolone 40mg follow-up: 14 days	0/20	0/20	Not estimable	40 (1 RCT)	⨁⨁◯◯ Low[a]	No adverse events occurred in either group.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two levels due to very serious imprecision: very small sample.

1. Fajgenbaum K, Crouse L, Dong L, Zeng D , Sayed C. Intralesional Triamcinolone May Not Be Beneficial for Treating Acute Hidradenitis Suppurativa Lesions: A Double-Blind, Randomized, Placebo-Controlled Trial. Dermatol Surg 2020;46:685-9.

e-Table 77. Intralesional corticosteroids (case series/uncontrolled cohort studies)

Case series/non-comparative cohorts n=10, 473 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series/non-comparative cohort studies, which are inherently limited due to the lack of control groups and risk of selection bias. The individual studies included small sample sizes, increasing concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data makes it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Alvarez 2020[1] Prospective case series N=53	•Mean(SD) Age 34.5(12.1) years •36F, 17M •Obese/overweight n=36 •Hurley stage II 100% •HS with a single lesions with fistulous tracts	Single injection of 0.5 mL triamcinolone 40 mg/ml in fistulous tracts	None	90 days	Clinical characteristics mean (SD)	<u>Baseline→90 days:</u> Size in mm: 17.0(5.1)→5.1(8.5) p<0.0001 Erythema: 2.1(0.9) Suppuration: 1.6(1.1)	Selection N Ascertainment Y Causality N Reporting Y
					Pain VAS 10cm Mean (SD)	<u>Baseline→90 days:</u> 3.1(3.1)→0.7(2.1) p<0.0001	
					Pruritus VAS 10cm Mean(SD)	<u>Baseline→90 days:</u> 2.0(3.0)→0.4(1.4) p<0.0001	
					Adverse events	26 AEs in 46 lesions: Pigmentary Changes: n=25 Yellowish Depositions: N=6 Atrophy: n=17 (mild in most cases)	
Benesh 2023[2] Monocentric retrospective case series N=45	•Age •Acute severe HS flare	Intramuscular and intralesional triamcinolone 1.1–1.4 mg/kg for IMTAC and 40 mg/mL for ILTAC	NR	Mean 6.77 (4.45) weeks	HS-PGA Mean(SD)	<u>Baseline→Follow up:</u> 4.19(0.86)→3.62(1.15) p<0.001	Selection N Ascertainment Y Causality N Reporting Y
					Pain scale (0-10) Mean(SD)	<u>Baseline→Follow up:</u> 6.55(3.18)→3.37(3.07) p<0.001	
					Adverse events	1/45; aggravation of lesion	
Fania 2020[3] Monocentric prospective case series N=36	•Mean (SD) Age: 37.7(13.9) years •23F, 13M •Mean (SD) disease duration: 12.8 (9.4) years •acute HS-related nodules,	Triamcinolone 40 mg plus lincomycin 600 mg diluted in 10 ml saline solution were injected into inflamed Lesions at baseline & week 2	Adalimumab 40 mg, once a week (n=4), doxycycline 200 mg/day (n=3), clindamycin 600 mg/day (n=3), oral acitretin 25	4 weeks	Clinical severity via mean clinical score summing the scores of erythema, edema, suppuration, and size (possible scores from 0 to 16; higher score indicates greater severity	<u>Baseline → 4 weeks</u> 12.2 → 6.8 p<0.001	Selection N Ascertainment Y Causality N Reporting Y

	abscesses, tunnels, lasting for at least 6 months Exclusions •Severe/uncontrolled diabetes •Hypertension •Study drug allergy		mg/day (n=3), oral dapsone 100 mg/day (n=2), treated exclusively with topical antibiotic and corticosteroid therapy (n=10). No concomitant therapy (n=11)		Pain via mean VAS 10mm	<u>Baseline → 4 weeks</u> 4.6 → 1.5 p=0.027	
					Quality of life via mean SKINDEX-17 psychosocial score	<u>Baseline → 4 weeks</u> 50.9 → 43.7 p=0.014	
					Adverse events via # or participants with an AE	3/36; fever, acanthosis nigricans of folds, delayed menstrual cycle	
Giorgio 2025[4] Case series N=30	•Mean age 39.1 years •16F, 14M •Hurley stage II n=15; III n=15 •Had active inflamed lesions at baseline	Per lesion 0.5–1 mL of a 1:1 solution of clindamycin phosphate (150 mg/mL) and triamcinolone acetonide (40 mg/mL) for 4 intralesional injection sessions at 2-week intervals.	NR	8-24 weeks	Mean HiSCR score from baseline to 8 wks to 24 wks	30→8→10	Selection N Ascertainment Y Causality N Reporting N
					Recurrence rate at 24 weeks	13%	
					Adverse events	Systemic 0/30 Skin atrophy and pigment changes were "infrequent and self-limiting"	
Iannone 2021[5] Monocentric prospective case series N= 31	•Mean age 33 (DS 13) years •20 F, 11 M •Hurley stage: I n=9, II n=21, III n=1 •≤3 acute lesions (inflammatory nodules, abscesses, draining-inflamed fistulae), which	Ultrasound-guided injection of intralesional triamcinolone 40 mg/ml with dilutions of 1:4 or 1:2	NR	30 days	Pain via mean(SD) VAS 10mm at 30 days	<u>Baseline → 30 days</u> -triamcinolone dilution 1:4 (n=14): 4.1(3.2) → 2.3 (2.6) p=0.035 -triamcinolone dilution 1:2 (n=17): 4.5 (2.9) → 3.4 (2.9) p=0.114	Selection N Ascertainment Y Causality N Reporting N
					Quality of life via DLQI at 30 days	<u>Baseline → 30 days</u> -triamcinolone dilution 1:4 (n=14): 8.9(9.0) → 7.4 (8.2) p=0.043 -triamcinolone dilution 1:2 (n=17): 9.8 (7.8) → 6.9 (7.2) p=0.007	

	appeared in the previous 4 weeks prior to the baseline and did not respond to topical therapy.				Clinical severity via Hidradenitis Suppurativa Severity Index [HSSI]) at 30 days	<u>Baseline → 30 days</u> -triamcinolone dilution 1:4 (n=14): 2.1(1.0) → 1.5 (1.0) p=0.014 -triamcinolone dilution 1:2 (n=17): 2.1(1.0) → 1.4 (0.7) p=0.001	
Garcia-Martinez 2021[6] Multicenter Retrospective cohort N=98 patients; 135 lesions	•Mean Age 34.98(SD 12.36) •60F, 38M •Hurley stage for lesions: I n=19, II 95, III 21 •Lesion types: ○Non-inflammatory (n=5) ○Inflammatory (n=50) ○Abscesses (n=56) ○Fistulous tracts (n=24)	Intralesional corticosteroids q4w for up to 3 sessions: •Triamcinolone 40mg/ml mean dose 33.72 (n=109) •Betamethasone 3mg/ml mean dose 5.43 n=26 •Ultrasound guided n=41 •Dilution: none=18; mepivacaine 2% n=114' Lidocaine 2% n=3 •125 lesions (92.5%) were infiltrated only once, 14 (10.3%) twice and only one (0.74%) required three ICI to achieve a clinical response during the follow-up period	NR	12 weeks	Clinical response at 12 weeks (Complete=significant clinical improvement or clearance of lesions on sonogram; Partial response= relapse after clinical improvement; Null response= worsening or absence of improvement	Complete response: 95 (70.4%); Partial response 34 (25.2%); Null response 6 (4.4%)	NOS for cohort studies: Representativeness: * Non-exposed: - Ascertainment of exposure: * Outcome of interest no present at start of study: * Comparability: N/A Outcome assessment: * Follow up: * Adequacy: *
					HS-PGA (0-5 scale); Proportion of lesion at each score	<u>Baseline→12 weeks:</u> 0: 0.0% → 11.1% 1: 2.2%→31.9% 2: 35.6%→27.8% 3: 40.0%→8.3% 4: 13.3%→13.9% 5: 8.9%→6.9% P<0.001	
					VAS 10mm pain (Median [IQR])	<u>Baseline→12 weeks:</u> 4[2-6] → 0 [0-1] p<0.001	
					Adverse events	4/135 (2.9%); atrophic scar, local hypopigmentation, lesion aggravation (n=2)	
Licata 2025[7] Case series N=15	Mean age 34.2y 10F, 5M Hurley stage I-II	6 bi-weekly treatments of 0.5 ml of rifampin (600 mg/10 ml sterile water) and 0.3 ml of triamcinolone	NR	12-24 weeks	% reduction in lesion count at week 12	36.1%	Selection N Ascertainment Y Causality N Reporting Y
					Mean change in VAS 10 pain score at week12	-4.1 points	

		acetonide (40 mg/ml, undiluted), delivered using a 30-gauge needle into either the dermis or the subcutis, depending on lesion depth -Max cumulative volume per session 3mL rifampin and 2 mL triamcinolone			Patients with sustained remission at treatment sites at 24 week	10/15 (66.7%)	
					Adverse events	Mild localized dermal atrophy in 3 patients (resolved within 8 weeks); no systemic side effects observed	
Riis 2016[8] Multicenter prospective Case series N=36	•Age NR •acute HS-related nodules/abscesses	Intralesional triamcinolone 10 mg/mL into inflamed lesions associated with HS flares. Nodules/abscesses were injected with a mean of 0.75 mL triamcinolone 10 mg/ mL (range 0.2–2.0 mL)	NR	7 days	Clinical severity via clinician assessment of redness, edema, and suppuration on 0-4 scale; Higher score indicates greater severity	<u>Baseline → 7 days:</u> Redness: 2 (2) → 1(1) Suppuration: 2 (2)→ 1(1) Size: 3 (3)→ 1(1) Edema: 2 (2)→ 1(1) P=0.001 for all	NOS for cohort studies: Representativeness: * Non-exposed: - Ascertainment of exposure: * Outcome of interest no present at start of study: * Comparability: N/A Outcome assessment: * Follow up: * Adequacy: *
					Pain via mean (SD) VAS 10mm	<u>Baseline → 7 days:</u> 5.5(2.3)→1.1 (1.8) p=NS	
Sechi 2022[9] Retrospective case series N=13	•Mean age 33.1 •10F, 3M •Hurley stage II or III	Ultrasound guided Intralesional TCA 20mg/mL diluted 1:2 with either lidocaine 1% or sodium chloride.	Adalimumab (n=3) Methotrexate (n=2) clindamycin (n=4)	Follow up mean 23 weeks post-treatment range (11-34 weeks)	Lesion response post-treatment(marked reduction of fibrotic scarring or no improvement from baseline undefined)	Marked reduction of fibrotic scarring: 9/13 (69.2%) No improvement: 4/13 (30.8)	

		Max 40mg per session Topical abx for 3 days post treatment Mean 2.5 injection sessions	Oral zinc (n=2) doxycycline (n=1) rifampicin +clindamycin (n=1) minocycline (n=1)		Adverse events	4/13(30.8%) skin atrophy 1/13 (7.7%) Hypopigmentation 2/13 (15.4%) Both	
Salvador-Rodriguez 2020[10] Monocentric Prospective cohort N=116 patients; 247 infiltrated lesions; 172 non-infiltrated lesions	•Mean age 33.3 years •Mild to severe HS with one or more inflammatory lesions	Ultrasound-assisted intralesional infiltration of triamcinolone acetonide 40 mg/ml (max 40 mg per session); 54.5%, only had one infiltration session, 28.6% of patients had two infiltration sessions, 11.7% of patients had three sessions, 3.9% of patients four sessions, and 1.3% five sessions	43.1% (56/130) of infiltrations were performed without associated anti inflammatory treatment; 35.4% (46/130) were performed in the presence of systemic antibiotics; 8.4% (11/130) with systemic retinoids (acitretin); 7.7% (10/130) in the presence of biological treatment and 5.4% (7/130) in combination with two anti-inflammatory treatments	12 weeks	Complete response rate (lesions completely resolved at follow up)	- 81.1% (30/37) of infiltrated nodules vs 69.1% (47/68) of non-infiltrated inflammatory nodules (p = 0.18) - 72.0% (108/150) of infiltrated abscesses vs 54.3% (38/70) of non-infiltrated abscesses (p = 0.009) - 53.33% (32/60) of infiltrated fistulas vs 35.3% (12/34) of non-infiltrated draining fistulas (p = 0.09)	NOS for cohort studies: Representativeness: * Non-exposed: - Ascertainment of exposure: * Outcome of interest no present at start of study: * Comparability: N/A Outcome assessment: * Follow up: * Adequacy: *
					Clinical severity via mean (SD) International Hidradenitis Suppurativa Severity Scoring System (IHS4)	<u>Baseline</u> Infiltrated 5.7(0.4) Non-infiltrated 7.4 (0.6) <u>Reduction at 12 weeks:</u> 2.2 (3.6) p<0.001	
					Pain mean (SD) via NRS (0-10)	<u>Baseline</u> Not reported <u>Reduction at 12 weeks:</u> 1.5 (4.1) p=NS	

					Adverse events	2/116; glycemic decompensation & behavioral change	

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Radiotherapy

e-Table 78. Radiotherapy (case series)

Case series n=4, 109 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The individual studies included small sample sizes, increasing concern about random error and imprecision. Varied populations, interventions, and outcome assessment and reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Patel 2013[1] Monocentric prospective case series N=5	•Mean age 45 •2F, 3M •Disease duration 2-24 years Hurley II n=2, III n=3	Radiotherapy Electron beam 7.5 Gy/ 2.5 Gy/fraction 3 fractions, daily	None (discontinued 2 weeks prior)	2 months	Response to treatment of lesions (complete or partial response undefined)	Complete response: 0% Partial response(PR): 53% Axillae lesions: 100% PR Infragluteal/buttock lesions: 67% PR Groin lesions: 50% PR Perineum lesions: 0% PR	Selection N Ascertainment Y Causality N Reporting N
					Adverse events	1/5; swelling	
Schenck 1950[2] Monocentric retrospective case series N=54	•Mean age 24 •29F, 25M	Radiotherapy Orthovoltage (180kVp) Hyperacute HS: (1 Gy1, 10–12 Gy1) Per fraction dose increased as	I&D and dry dressing	NR	Treatment response (undefined)	Single abscesses responded after an average of 3 treatments; An average of 7.8 treatments were given to resolve the axilla; All cases responded well with no recurrences	Selection N Ascertainment Y Causality N Reporting N
					Pain (undefined)	Pain mostly resolved after 2–3 treatments	

		severity of disease diminishes Chronic HS: (1.5–2 Gy1, 10–12 Gy1) Course: 3 times a week for 5–10 treatments			Adverse events	Temporary depilatory effect	
Steiner 1950[3] Monocentric retrospective case series N=45	•Overweight n=10 •Acute HS n=23; Chronic n=22	Radiotherapy Radiation dose not mentioned Treated location(s): axilla, groin, generalized (most or all regions with apocrine sweat glands involved	Acute: hot compress locally and systemic antibiotics (NS) Chronic localized: antibiotics (NS), autogenous vaccine, staphylococcus toxoid injections	NR	Treatment response (undefined)	Acute: No response Chronic localized: recurrences expected Chronic generalized: "uniformly poor response"	Selection N Ascertainment Y Causality N Reporting N
Zeligman 1965[4] Monocentric retrospective case series N=5	•Mean age 36.4 •4F, 1M •Obesity n=1	Radiotherapy 1 treatment course 4.5Gy1, 4.5 Gy1 n=4 5Gy1, 5Gy1 n=1	None	9 months to 6 years	Treatment response (no active lesions[NAL] & no recurrence[NR] of lesions)	By patient: 1 NAL at 1 yr; NR at 6 yrs 2 NAL at 3mo; NAL/NR at 4yr 3 NAL at 1 yr 4 NAL at 2wks & 4 yr 5 NAL at 4 & 9 mos	
					Adverse events	5/5; defluvium n=5, hyperpigmentation n=4, scarring n=3	

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Cryotherapy/Cryoinsufflation

e-Table 79. Cryotherapy and cryoinsufflation (case series)

Case series n=3, 33 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The individual studies included very small sample sizes, increasing concern about random error and imprecision. Varied populations, interventions, and outcome assessment and reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Bong 2003[1] Monocentric retrospective case series N=10	•Mean age 32.9 •10F, 0M •Persistent painful nodules resistant to systemic abx •Mean duration of disease 10.2 years	Liquid nitrogen cryotherapy via CRY-AC spray One freeze-thaw cycle until -20C	None	NR	Healing time (mean days)	25 days (range 18-42)	Selection N Ascertainment Y Causality N Reporting N
					Pain (scale 0-4; Higher score indicates greater pain) Mean	During procedure: 2.4 During healing: 2.5	
					Treatment response (3 categories undefined)	Marked improvement n= 4/10 (40%) Improvement n= 4/10 (40%) None n= 2/10 (20%)	
					Complications	8/10 (80%)	
Dell'Antonia 2023[2] Monocentric retrospective case series N=23 patients; 71 nodules	•Mean age 34.6 •17F, 6M •Persistent (no improvement in 16 wks) nodules not responding to medical therapy	Liquid nitrogen cryotherapy 1 session via cryogun one freeze–thaw cycle of variable	Systemic therapy (for at least 12 wks before cryotherapy) Antibiotic n=16 Estroprogestinic pill n=4	3 months & 6 months	Clinical response (0-3 scale; 3= complete response nodule not detectable, 2=partial response volume reduction >50%; 1= volume reduction <50%, 0=no response) at 3 months	3-Complete response n= 63/71 (88.7%) 2-Partial response n=1/71 (1.4%)* 1-Limited response n=1/71 (1.4%)* 0-No response 6/71(8.5%)* *Completely resolved with a 2nd cryotherapy session	Selection N Ascertainment Y Causality N Reporting N

	•Mean disease duration 12.7 years •Hurely I n=8, II n=11, III n=4	duration from 20 to 50 s	Adalimumab n=6		Pain during treatment (scale 1-10; higher score indicates greater pain)	Mean 5 (range 2-9)	
Molina-Leyva 2019[3] Monocentric prospective case series N=10	•Ages 17-46 •9F, 1M •Hurley I n=1, II n=7, III n=2 •1+ fluid collection of 4 weeks or less duration susceptible to I&D treatment	Drainage and punch-trocar-assisted cryoinsufflation (cryopunch) one session	Doxy n=3 Colchi n=2 Adalimumab n=2 Rifamp+clinda n=1 Rescorcinol 15% n=1 Contraceptive pill n=5	24 weeks	Treatment response (complete=no inflammatory signs or fluid collection; No response=inflammation unimproved/partially improved and fluid smaller/equal/greater)	Complete response n=7/10(70%) No response n=3/10 (30%)	Selection N Ascertainment Y Causality N Reporting N
					Pain during procedure (NRS mean score)	Mean 2.4; Median 2 [IQR 1.7, 3.25]	
					Complications	0/10	

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Sclerotherapy

e-Table 80. Sclerotherapy (uncontrolled cohort)

Case series n=1, 21 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from a single, small case series, which is inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The very small sample size increases concern about random error and imprecision.

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	NOS cohort tool
Porter 2022[1] Phase 2 open label N=21	•Mean age 36.85 •16F, 5M •Hurley I n=3, II n=13, III n=4 •	Hypertonic saline (23.4%, up to 0.4mL) sclerotherapy q2w until fistula closure/max 3 injections	Pain medication n=6 Antibiotic n=7 Hormonal n=6 Adalimumab n=2 Contraceptive n=4 Topical n=3 Allergy n=2 Other n=10	4 weeks post final injection	Physician assessed overall Improvement (0-5 scale for pain, fluid leakage, erythema, tenderness, swelling, hardness, hotness, odor)	Drainage (p=0.035), erythema (p=0.008), and swelling (p=0.025) were significantly improved from baseline to 4 weeks post-treatment.	-minimally reported
					DLQI mean(SD)	Baseline→post-treatment 9.14(5.83)→6.0(5.62)p=0.011	
					Pain median score	Baseline→post-treatment <0.4mL (n=9): 3→4 0.4mL (n=4): 4.5→5.5	
					Adverse events	"well tolerated"; draining clotted blood at fistulas	

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Photodynamic therapy

e-Table 81. PDT vs topical clindamycin

PDT compared to topical clindamycin for HS[1]

Patient or population: HS any hurely stage
Intervention: 12 PDT treatments (twice weekly for 6 weeks); Elkofast gel 0.3% under occlusive dressing & RLP068/Cl gel applied 1ml per 25cm2 for 30 mins, then skin irradiated for 8 minutes with 60J/com2 of 630 nm red light
Comparison: topical clindamycin gel 1% BID for 6 weeks

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with topical clindamycin	Risk with PDT				
Complete clinical response assessed with: inflammation & abscesses absent with no reported pain follow-up: 6 weeks	94 per 1,000	**406 per 1,000** (1,000 to 128)	**RR 4.33** (1.36 to 13.77)	64 (1 non-randomised study)	⨁◯◯◯ Very low[a,b]	
Pain assessed with: Mean VAS 10 pain score follow-up: 6 weeks	PDT: 2.7 (0.6) Clindamycin: 4.2(1.1)			(1 non-randomised study)	⨁◯◯◯ Very low[a,b]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. The treatment site was randomized, but selection of patients was not, which is concerning for selection bias; Unblinded with outcomes dependent on subjective patient & provider assessment. Standard HS clinical assessment tools are stated as used, but the primary outcomes are reported by non-standardized measures.
b. Very small sample is concerning for precision.

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e-Table 82. Photodynamic therapy (case series & uncontrolled cohort studies)

Case series n=5, 59 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control groups and selectionbias. The individual studies included small sample sizes, increasing concern about random error and imprecision. Varied interventions (not comparable to variation in photosensitizers, light sources, treatment regimens) and outcome reporting with no poolable outcome data make it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	NOS cohort tool
Andino Navarrette 2014[1] Monocentric prospective case series N=5	•Mean age 26 •4F, 1M •Mean duration of disease 4 years •Hurley stage II or III refractory to at least 2 treatments	PDT with 20% ALA solution for 1.5 h; light (635 nm, 37 J/cm2, 70 mW/cm2) per session Minimum 4 sessions spaced 1-2 wk	NR	8 weeks	Disease severity via Sartorius score Mean(SD)	Baseline→wk 8 35.40(4.98)→18.20(8.11)	Moderate risk
					Pain & activity scale (0-3; no symptoms to serve pain/disease activity) Mean(SD)	Baseline→wk 8 3(0)→0.80(0.45)	
					DLQI score Mean(SD)	Baseline→wk 8 28.80(2.68)→7.49(2.79)	
					Adverse events	2/5 (40%); mild burning during light exposure	
Calzavara-Pinton 2012[2] Multicentric respective cohort N=6	•Mean age 34 •5F, 1M	PDT with MAL cream 3-4 hours under occlusive dressings then irradiation with 37J/cm2 red 635±18 nm light from diode lamp	NR	7-15 days post-treatment for clinical response/AEs Mean follow up 2.6(0.5) months for	Clinical response (Marked=>75% improvement; Moderate 50-75%, No/poor <50%) at 7-15 post-treatment	Marked:2/6 (33%) Moderate: 3/6(50%) No/Poor: 1/6(17%)	
					Excellent cosmesis (no scarring, atrophy, induration, change in pigmentation) &	2/6 (33%)	

		Mean 4.8(2.9) sessions at mean interval of 18.8(8.4) days		persistent response	Marked improvement at 7-15 days post-treatment		
					Persistent marked response at mean follow-up of 2.6 (0.5) months post-treatment	1/6 (17%)	
					Local reactions (marked=persistent erythema with edema and/or erosions; moderate=temporary erythema)	Marked:0/6 Moderate:5/6 (83%) Absent; 1/6 (17%)	
					Pain/burning during treatment	Marked: 0/6 Moderate: 4/6 (67%) Mild: 2/6 (33%) No: 0/6	
Gamissans 2022[3] Case series N=41	•Mean age 33.7(2.2) years •27F, 14M •IMI 27.8(1.01)kg/m2 •Smoker n=23 •Hurely stage I n=16; II n=19; III n=6	PDT with intralesional methylene blue & diode lamp	N=15 concomitant treatment: n=8 topical, n=3 oral antibiotic, n=4 adalimumab	1-6 months	Mean reduction lesion diameter	Reduction ≥75% n=24 (58.5%) Reduction 50-75% n=9 (22%) Reduction >50% n=8 (19.5%)	Moderate risk
					Serious adverse events	1/41 (2.4%)-cellulitis	
					Adverse events	Mild side effects like erythema and local pain were “common”	
Schweiger 2011[4] Monocentric prospective case series N=7	•Mean age NR •9F, 3M •multiple lesions consistent with HS in axillae and/or groin, with a history of no or poor response to at least one treatment	PDT with 20% ALA 45 mins; 417 nm blue light (NA) or 415 nm blue light from a light-emitting diode (NA) weekly for four weeks	NR	8 weeks	Mean(SD) lesion counts	Pre: 11.4 (10.9) Post: 8.1 (8.6)	Moderate risk
					Mean(SD) Physician Global Severity Scores	Pre: 2.1 (0.9) Post: 1.7 (1.3)	
					Mean(SD) DLQI	Pre: 16.7 (7.1) Post: 13.1 (6.0)	

Sotiriou 2009[5] Monocentric prospective case series N=5	•Mean age 33.6 •2F, 3M •Mean disease duration 3.2 years	PDT with 20% ALA 3 ours under occlusive dressing 570–670 nm, noncoherent light source 20 J/cm2 4 sessions at 2 week intervals	NR	2 months post-treatment	Mean Sartorius score	Baseline: 18.8 2 mo: 17.2	Moderate risk
					Mean pain via VAS 10mm	Baseline: 2.4 2 mo: 2.1	
					Mean DLQI reduction at 2 months	6.4%	
					Adverse events	5/5 (100%) pain/burning during treatment 5/5 (100%) erythema lasting up to 1 week 2/5(40%) swelling & blistering lasting 8-10 days	

1. Andino Navarrete R, Hasson Nisis A , Parra Cares J. Effectiveness of 5-aminolevulinic acid photodynamic therapy in the treatment of hidradenitis suppurativa: a report of 5 cases. Actas Dermosifiliogr 2014;105:614-7.
2. Calzavara-Pinton PG, Rossi MT, Aronson E, Sala R , The Italian Group for Photodynamic Therapy. A retrospective analysis of real-life practice of off-label photodynamic therapy using methyl aminolevulinate (MAL-PDT) in 20 Italian dermatology departments. Part 1: Inflammatory and aesthetic indications. Photochemical & Photobiological Sciences 2012;12:148-57.
3. Gamissans M, Riera-Martí N, Romaní J , Gilaberte Y. Ultrasound-guided photodynamic therapy with intralesional methylene blue and a 635 nm light-emitting diode lamp in hidradenitis suppurativa: A retrospective study of 41 patients. Photodermatol Photoimmunol Photomed 2022;38:12-8.
4. Schweiger ES, Riddle CC , Aires DJ. Treatment of hidradenitis suppurativa by photodynamic therapy with aminolevulinic acid: Preliminary results. Journal of Drugs in Dermatology 2011;10:381-6.
5. Sotiriou E, Apalla Z, Maliamani F , Ioannides D. Treatment of recalcitrant hidradenitis suppurativa with photodynamic therapy: report of five cases. Clinical and Experimental Dermatology 2009;34:e235-e6.

e-Table 83. Niosomal methylene blue (NMB) gel PDT vs. free methylene blue (FMB) gel PDT

Niosomal Methylene Blue (NMB) gel compared to free methylene blue (FMB) gel for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa of any severity
Intervention: Niosomal Methylene Blue (NMB) Gel followed by IPL (630 nm filter, pulse duration 20 ms, fluence 25 J/cm 2) once every 2 weeks for up to 6 months
Comparison: Free Methylene Blue (FMB) Gel followed by IPL (630 nm filter, pulse duration 20 ms, fluence 25 J/cm 2) once every 2 weeks for up to 6 months

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with free methylene blue (FMB) gel	**Risk with niosomal Methylene Blue (NMB) gel**				
Change in HS-LASI score follow-up: 6 months	The mean change in HS-LASI score was **-6.1**	MD **5.2 lower** (10.59 lower to 0.19 higher)	-	20 (1 RCT)	⨁⨁◯◯ Low[a]	
Adverse events follow-up: 6 months	0 per 1000	**0 per 1000** (0 to 0)	Not estimable	20 (1 RCT)	⨁⨁◯◯ Low[b]	No events in either arm

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two levels due to very serious imprecision small sample size.
[b]Downgraded by two levels due to very serious imprecision: zero events with small sample size.

1. Fadel MA , Tawfik AA. New topical photodynamic therapy for treatment of hidradenitis suppurativa using methylene blue niosomal gel: a single-blind, randomized, comparative study. Clin Exp Dermatol 2015;40:116-22.

Intense Pulsed Light

e-Table 84. Intense pulsed light vs no treatment

Intense pulsed light compared to no treatment for hidradenitis suppurativa

Patient or population: hidradenitis suppurativa
Intervention: Intense pulsed light two times per week for 4 weeks OR once a month for six months
Comparison: no treatment on contralateral side

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no treatment	**Risk with Intense pulsed light**				
HiSCR follow-up: 24 weeks	444 per 1000	**667 per 1000** (289 to 1000)	**RR 1.50** (0.65 to 3.45)	21 (1 RCT)[1]	⨁⨁◯◯ Low[a]	
Quality of life-DLQI Median[IQR] follow-up 24 weeks	Pre-treatment : 4.0 [2.5-12.0] Post-treatment : 5.0 [2.0-9.5]			17 (1 RCT)[1]	⨁⨁◯◯ Low[b]	
Pain-VAS 10cm Median [IQR] follow-up 24 weeks	PL : 8.0 [1.5-18.0] Control: 13.0 [3.0-46.0]			17 (1 RCT)[1]	⨁⨁◯◯ Low[b]	
Pruritus-VAS 10cm Median [IQR] follow-up 24 weeks	IPL : 12.0 [3.0-25.5] Control : 22.0 [4.0-64.0]			17 (1 RCT)[1]	⨁⨁◯◯ Low[b]	
Participant global assessment: satisfaction with treatment at month 12	0 per 1000	**0 per 1000** (0 to 0)	**RR 6.54** (1.40 to 30.56)	34 (1 RCT)[2]	⨁⨁◯◯ Low[a]	
Adverse event follow-up: 12 weeks	7/32 patients experienced adverse events related to IPL; 1/32 patients withdrew due to pain of IPL			32 (2 RCT)[1, 2]	⨁⨁◯◯ Low[b]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio; **IQR:** Interquartile range

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by two levels due to very serious imprecision: small sample size and the ratio of the upper to the lower boundary of the CI was > 3.
b. Downgraded by two levels due to very serious imprecision: small sample size

1. Andersen PL, Riis PT, Thorlacius L, Sigsgaard V, Nielsen CW, Chafranska L et al. [Intense pulsed light treatment for hidradenitis suppurativa: a within-person randomized controlled trial]. Eur J Dermatol 2020;30:723-9.

2. Highton L, Chan WY, Khwaja N , Laitung JKG. Treatment of hidradenitis suppurativa with intense pulsed light: a prospective study. Plast Reconstr Surg 2011;128:459-66.

e-Table 85. Intense pulsed light (case series)

Case series n=1, 25 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from a single, small case series, which is inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The very small sample size increases concern about random error and imprecision. Outcome assessment relied on unvalidated measures with only two patient-important outcomes assessed.

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Riis 2017[1] Monocentric retrospective case series N=25	•Mean age 39.2 •25F, 0M •Hurley I n=3, II n=21, III n=1 •Fitzpatrick skin type 2 n=17, 3 n=6, 4 n=2	IPL 525-1200 nm; pulse width 20 or 100 nm; 18or 34J/cm fluence 1-10 sessions at 4-6 week intervals	Metformin n=2 Resorcinol n=10 Tetracycline n=6 Skinoren n=3 Dalacin n=6 Rimactan n=1	NR	Disease reduction (reduction in disease activity as "yes" or 'no" based on pt & nurse assessment)	13/25 (52%) had disease reduction	Selection N Ascertainment Y Causality N Reporting N
					Adverse events	7/25 (%); irritation after shaving, minor burn, worsening of HS the day after treatment	

1. Theut Riis P, M. SD, V. S, C. W , and Jemec GBE. Intense pulsed light treatment for patients with hidradenitis suppurativa: beware treatment with resorcinol. Journal of Dermatological Treatment 2018;29:385-7.

Radiofrequency

e-Table 86. Radiofrequency vs no radiofrequency

Fractional needle RF compared to no RF for HS[1]

Patient or population: HS
Intervention: fractional micro-needling radiofrequency for 3 sessions at 2-week intervals
Comparison: no radiofrequency on contralateral side

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no RF	**Risk with fractional needle RF**				
Clinical severity assessed with: Mean HS-PGA (end score) follow-up: 8 weeks	The mean clinical severity was **2.0**	MD **0.8 lower** (1.73 lower to 0.13 higher)	-	10 (1 non-randomised study)	⊕◯◯◯ Very low[a,b]	
Pain during procedure assessed with: Mean VAS 10mm pain score follow-up: 8 weeks	Mean pain during treatment was 4.1			10 (1 non-randomised study)	⊕◯◯◯ Very low[a,b]	
Treatment-emergent adverse events follow-up: 8 weeks	No adverse events from treatment reported.			10 (1 non-randomised study)	⊕◯◯◯ Very low[a,b]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded 1 level for serious RoB: most severe body side selected for treatment leading to baseline imbalances in outcome important factors; intraindividual design; incomplete outcome reporting.
b. Downgraded 2 levels for very serious imprecision: very small intraindividual sample.

1. Yang JH, Cho SI, Kim DH, Yoon JY, Moon J, Kim JW et al. Pilot study of fractional microneedling radiofrequency for hidradenitis suppurativa assessed by clinical response and histology. Clin Exp Dermatol 2022;47:335-42.

e-Table 87. Radiofrequency (uncontrolled cohort studies)

Case series n=1, 10 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from a single, small case series, which is inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The very small sample size increases concern about random error and imprecision.

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	NOS cohort tool
Behrangi 2023[1] Monocentric prospective cohort N=10	•Mean age 30.1 •4F, 6M •Mean BMI 31.3 •Mean disease duration 4.8 years •HS-PGA scores 2 n=3, 3 n=3, 4 n=1, 5 n=3	Radiofrequency with Aphrodite 4 MHZ monopolar 60W 1KΩ heating up to 90C 3 sessions	Antibiotics n=3 Retinoids n=2 Biologics n=5	3 & 6 months	Mean HS-PGA score	Baseline: 3.4 3 months: 2.3	
					Recurrence status	3 months: 4/10 (40%) 6 Months: 2/10 (20%)	
					Adverse events	0/10	

1. Behrangi E, Atefi N, Mireshghollah P, Goodarzi A, Dehghani A, Zare Dehnavi A et al. The efficacy and safety of endo-radiofrequency for the treatment of hidradenitis suppurativa. Skin Res Technol 2023;29:e13450.

Radiofrequency combination therapy

e-Table 88. Topical clindamycin 1%solution + bi-weekly LAight therapy vs topical clindamycin 1% solution

LAight therapy plus topical clindamycin compared to topical clindamycin for hidradenitis suppurativa

Patient or population: hidradenitis suppurativa
Intervention: topical clindamycin 1% solution combined with 8 additional bi-weekly treatments with LAight® therapy (intense pulsed light + radiotherapy) for 16 weeks
Comparison: topical clindamycin 1% solution

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with topical clindamycin	**Risk with LAight therapy plus topical clindamycin**				
Change in pain NRS Scale from: 0 to 10 follow-up: 16 weeks	The mean change in pain NRS was **-0.9**	MD **1.4 lower** (2.87 lower to 0.07 higher)	-	71 (1 RCT)[1]	⨁⨁⨁◯ Moderate[a]	
Achieving HiSCR follow-up: 16 weeks	359 per 1000	**625 per 1000** (381 to 1000)	**RR 1.74** (1.06 to 2.86)	71 (1 RCT)[1]	⨁⨁⨁◯ Moderate[c]	
Change in IHS4 follow-up: 16 weeks	The mean change in IHS4 was **-1.8**	MD **5.4 lower** (8.31 lower to 2.49 lower)	-	71 (1 RCT)[1]	⨁⨁⨁◯ Moderate[b]	
Change in DLQI Scale from: 0 to 30 follow-up: 16 weeks	The mean change in DLQI was **-1.6**	MD **3 lower** (5.54 lower to 0.46 lower)	-	71 (1 RCT)[1]	⨁⨁⨁◯ Moderate[d]	
Adverse events leading to discontinuation of intervention follow-up: 16 weeks	0 per 1000	**0 per 1000** (0 to 0)	Not estimable	71 (1 RCT)[1]	⨁⨁◯◯ Low[e]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by one level due to imprecision: small sample size and the 95% CI crossed the conventional lower thresholds of MID of 30% for NRS.
[b]Downgraded by one level due to imprecision: small sample size and the 95% CI crossed the conventional lower thresholds of MID of 55% for ISH4.
[c]Downgraded by one level due to imprecision: small sample size and the 95% CI crossed the conventional lower thresholds of MID (0.75 or 1.25).
[d]Downgraded by one level due to imprecision: small sample size and the 95% CI crossed the conventional lower thresholds of MID of 4 for DLQI.
[e]Downgraded by two levels due to imprecision: zero events with small sample size.

1. Schultheis M, Staubach P, Nikolakis G, Grabbe S, Ruckes C, von Stebut E et al. LAight® Therapy Significantly Enhances Treatment Efficacy of 16 Weeks of Topical Clindamycin Solution in Hurley I and II Hidradenitis Suppurativa: Results from Period A of RELIEVE, a Multicenter Randomized, Controlled Trial. Dermatology 2022;238:476-86.

e-Table 89. Radiofrequency + IPL vs radiofrequency and IPL monotherapies

Summary of findings:

RF+IPL compared to RF and IPL monotherapies for HS[1]

Patient or population: HS
Intervention: Intense Pulsed Light (IPL) + Radiofrequency (RF) 6 sessions at 2 week intervals
Comparison: RF monotherapy for 6 sessions at 2 week intervals
Comparison: IPL monotherapy for 6 sessions at 2 week intervals

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)
Clinical severity assessed with: Mean change in active lesion count follow-up: 12 weeks	RF+IPL (n=15): -1.3 lesions RF monotherapy (n=15): -0.4 lesions (p=0.118) IPL monotherapy (n=13): +0.8 lesions (p=0.044)	43 (1 RCT)	⊕⊕◯◯ Low[a]
Quality of life assessed with: Mean change in DLQI scores follow-up: 12 weeks	RF+IPL (n=15): -5.1 (44% improvement form baseline p=0.040) RF monotherapy (n=15): -6.6 (45% improvement from baseline p=0.015) IPL monotherapy (n=13): -1.3 (15% improvement from baseline p=0.186)	43 (1 RCT)	⊕⊕◯◯ Low[a]

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded 2 levels for very serious imprecision: very small sample across 3 treatment groups.

1. Wilden S, Friis M, Tuettenberg A, Staubach-Renz P, Wegner J, Grabbe S , von Stebut E. Combined treatment of hidradenitis suppurativa with intense pulsed light (IPL) and radiofrequency (RF). J Dermatolog Treat 2021;32:530-7.

e-Table 90. Radiofrequency + IPL (cohort study)

Cohort n=1, 10 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from a single, small case series, which is inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The very small sample size increases concern about random error and imprecision.

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	NOS cohort tool
Lyons 2022[1] Monocentric prospective cohort^ N=10	•Mean age 42 •7F, 3M •Hurley stage I n=4, II n=5, III n=1 •Bilateral HS	IPL+RF IPL: 420-1200 nm, 4.4-6.0 J/cm2, 4 sub-impulses, 8ms/8ms duration/pause RF: 1MHz 12.2 J/cm2, 1s 9 sessions n=2 10 sessions n=7 At least 2 weeks apart	None	NR	Clinical severity via IHS4 & HS=PGA n=9	No statistically significant difference reported between treated and control sides (no quantitative data)	
					DLQI mean difference from baseline n=9	-2.8 p=0.043	
					Adverse events	0/9	
Strobel 2025[2] Retrospective cohort N=96	•Mean age 15.91(1.64) years •63F, 33M •Obese n=18 •Smoker n=10 •Hurley stage I n=26; II n=58; III n=12	LAight therapy (IPL + radiofrequency)	Median number of therapies at baseline 8	36 weeks	IHS4-55	19.4%	
					NRS pain reduction of 2+ points	40.4%	
					DLQI reduction of 4+ points	54.1%	
					Adverse event rate	16.17%	

^ design was split-body however outcomes of interest were not reported 1) with quantitative data or 2) comparatively between treatment and no treatment sides

1. Lyons A, Narla S, Kohli I, Zubair R, Jacobsen G, Ceresnie M et al. Safety and Efficacy of Intense Pulsed Light With Radiofrequency in United States Hidradenitis Suppurativa Patients. J Drugs Dermatol 2022;21:430-2.
2. Strobel A, Schultheis M, Staubach P, Grabbe S, Hennig K, Szepietowski J et al. LAight Therapy is an Effective and Gentle Treatment in Adolescents Suffering from Hidradenitis Suppurative: Results from 96 Patients Using Real-world Data. Acta Derm Venereol 2025;105:adv43543.

Other Energy Devices

Microwave ablation

e-Table 91. Microwave ablation vs placebo

MiraDry compared to placebo for hidradenitis suppurativa[1]

Patient or population: hidradenitis suppurativa
Intervention: Microwave ablation (MiraDry) (5.8 GHz, energy level 5, manufacturer-recommended settings) one treatment of 1 axilla under tumescent anesthesia
Comparison: placebo on contralateral side

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	**Risk with MiraDry**				
Achieving HiSCR 50 at week 12 follow-up: 12 weeks	250 per 1000	**250 per 1000** (45 to 1000)	**RR 1.00** (0.18 to 5.46)	8 (1 RCT)	⨁◯◯◯ Very low[a,b]	
Pain Median(IQR) NRS score Follow-up: 12 weeks	-MiraDry: 7.0(2.0-8.0) -Control: 0(0-5.0)			8 (1 RCT)	⨁◯◯◯ Very low[a,b]	
Serious adverse event with treatment	1/8(12.5%)			8 (1 RCT)	⨁◯◯◯ Very low[a,b]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by one level due to high risk of bias.
[b]Downgraded by two levels due to very serious imprecision: small sample size and the 95% CI crossed both the conventional upper and lower thresholds of MID (0.75 and 1.25).

1. Vossen A, van Huijkelom M, Nijsten TEC, Bakker EWP, van der Zee HH, van Doorn MBA , Prens EP. Aggravation of mild axillary hidradenitis suppurativa by microwave ablation: Results of a randomized intrapatient-controlled trial. J Am Acad Dermatol 2019;80:777-9.

e-Table 92. Intralesional light-based therapies (case series)

Case series/non-comparative cohorts n=6, 187 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series/non-comparative cohort studies, which are inherently limited due to the lack of control groups and higher risk of bias, as well as the potential for publication bias. The individual studies included small sample sizes, increasing concern about random error and imprecision. Varied interventions and outcome reporting with no poolable outcome data makes it difficult to assess consistency across studies. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	NOS cohort tool
Agut-Busquet 2016[1] Retrospective case series N=7	•Ages 24-49 •3F, 4M •Hurley stage II or II •At least 1 active anatomical site •Failure of other treatment options	IL-PDT free methylene blue 1% injected into abscesses 15min incubation 635nm light-emitting diode lamp One session n=2 Two session with 15 day interval n=5	NR	1,2, 4, 6, 8 months	Clinical response by lesion reduction (Good=>75%, Bad 50-75%, No response <50%) at 1 month	Good: 6/7 (85.7%) Bad: 0 No: 1/7 (14.3%)* Achieved good response by 6 month f/u	Moderate risk
					Recurrence/relapse at 2, 4 and 6 months	2 months: 1/6 (16.7%) 4 months: 1/6 (16.7%) 6 months: 0/6	
					Mean DLQI at 8 months	Pre-treatment: 9.43 8 months: 1.9	
					Pain during treatment via VAS	Low (1-3): 1/7 (14.3%) Moderate (4-6): 6/ (85.7%)	

		Duration 8 months			Adverse events	Any AE 7/7 (100%) Cellulitis 1/7 (14.3%) Erythema/edema 6/7(85.7%)	
Fabbrocini 2018[2] Prospective case series N=20	•Mean age 27 •14F, 6M •Hurley I (16, 39%), II (19, 46%) and III (6, 15%)	4 sessions every 2 weeks of IL 1,064-nm diode laser followed by azithromycin 500 mg/ day for 3 days	None	NR	HiSCR achieved post-treatment	13/20 (65%)	Moderate risk
					Mean final Sartorius score	19.75 (31% reduction)	
					Adverse events	2/20 (10%); postoperative pain, erythema, mild swelling Influenza-like illness 1/20(5%)	
Gamissans 2022[3] Retrospective case series N=41	•Mean age 34 •27F, 14M •Hurley I (16, 39%), II (19, 46%) and III (6, 15%)	15-min incubation of IL methylene blue solution 1%. 635-nm red-light emitting diode lamp. One session n=10 Two session at 15 day interval n=10	Topical ATB (8, 20%), oral ATB (3, 7%), biologic (4, 10%)	1 & 6 months	Reduction in lesion size at 1 month	≥75% 24/41 (59%) 50–75% 9/41 (22%) <50% 8/41(20%)	Moderate risk
					Recurrence of lesions at 6 months in those with ≥75% lesion reduction	3/24 (12.5%)	
					Adverse events	1/41(2%) cellulitis	
Garcia-Ladaria 2021 Retrospective case series N=42 patients; 117 lesions	•Mean age 39 •24F, 18M •Hurley I in 1 lesion 1%), II in 73 (62%), III in 43 (37%)	2-h incubation of IL 5-aminolaevulinic acid gel 2% or solution 1%. Later, IL irradiation with a 630-nm laser diode 1 session per lesion	Biologics in 31 lesions, non-biologic treatment in 25	3 & 6 months	Lesion resolution at 3 & 6 months (resolved, improved in size or symptoms, no change undefined)	<u>3 months:</u> Resolved 26/117 (22%) Improved 73/117 (62%) No change 18/117 (15%) <u>6 months:</u> Resolved 37/117 (35%) Improved 35/117 (33%) No change 33/117 (31%)	Moderate risk
					Adverse events at 3 months	53/117(45%) skin burns 8/117 (7%) abscess formation 3/42(7%) pts fever 1/42 (2%) paresthesia	
	•Mean age 36	2-h incubation of IL	None	Median 26 months	Complete remission (no	29/38 (76%)	Moderate risk

Suarez Valladares 2017[4] Prospective case series N=38 patients; 64 lesions	•18F, 20M •Obese n=20 •Hurley I (4, 11%), II (21, 55%), III (13, 34%)	5-aminolaevulinic acid 5% IL irradiation with a 630-nm laser diode 1 session n=18 2 session at 5-7 week intervals n=20			lesions or symptoms)		
					Median[IQR] HS Severity Score	Pre-treatment 28.5[11.75, 38.5] Post-treatment 0 [0, 45]	
					Median[IQR] DLQI Score	Pre-treatment 10 [7, 17] Post-treatment 1 [0, 2.25]	
					Pain during treatment Median VAS 10	3[2, 5.25]	
					Recurrence	1/38(2.6%)	
Valladres-Narganes 2015[5] Prospective case series N=27	•Mean age 39 •11F, 16M •Longstanding presence of sinus tracts	3-h incubation of IL 5-aminolaevulinic acid in saline at 1% (0.2 mL/cm3); IL irradiation with a 630-nm laser diode 1 session n=18 2 sessions n=9	None	6 months	Clinical response via improvement from baseline in modified Sartorius score	≥75% 10/27 (37%) 50-75% 11/27 (41%) 25-50% 5/27(19%) <25% 1/27 (3%)	Moderate risk
					Pain during treatment via VAS 10	Severe (9-10) 1/27 (3.7%) Moderate (6-9) 4/27 (1%) <6 22/27 (81.5%)	
					Adverse events	1/27 influenza-like illness	
Zerbinati 2017[6] Case series N=12	•Mean age 37 •Sex NR •Hurley stage I	3 sessions every 2 months of IL 1,064-nm diode laser, followed by azithromycin 500 mg/ day for 3 days	None	4 months	Mean % improvement in Sartorius score:	85.3%	Moderate risk

1. Agut-Busquet E, Romaní J, Gilaberte Y, García-Malinis A, Ribera-Pibernat M , Luelmo J. Photodynamic therapy with intralesional methylene blue and a 635 nm light-emitting diode lamp in hidradenitis suppurativa: a retrospective follow-up study in 7 patients and a review of the literature. Photochemical & Photobiological Sciences 2016;15:1020-8.
2. Fabbrocini G, França K, Lotti T, Marasca C, Annunziata MC, Cacciapuoti S et al. Intralesional Diode Laser 1064 nm for the Treatment of Hidradenitis Suppurativa: A Report of Twenty Patients. Open Access Maced J Med Sci 2018;6:31-4.

3. Gamissans M, Riera-Martí N, Romaní J , Gilaberte Y. Ultrasound-guided photodynamic therapy with intralesional methylene blue and a 635 nm light-emitting diode lamp in hidradenitis suppurativa: A retrospective study of 41 patients. Photodermatol Photoimmunol Photomed 2022;38:12-8.
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5. Valladares-Narganes LM, Rodríguez-Prieto MA, Blanco-Suárez MD, Rodriguez-Lage C , García-Doval I. Treatment of hidradenitis suppurativa with intralesional photodynamic therapy using a laser diode attached to an optical cable: a promising new approach. Br J Dermatol 2015;172:1136-9.
6. Zerbinati N, D'Este E, Ini L, Baruffato A, Premoli V, Calligaro A , Paulli M. Clinical and histological changes in Hidradenitis suppurativa following 1064 nm nd:YAG intralesional laser treatment. J Biol Regul Homeost Agents 2017;31:131-40.

Post-Operative Wound Care Summary of Findings Tables

Contents

e-Table 93. Gentamicin sponge vs primary closure

Gentamicin sponge compared to primary closure alone for hidradenitis suppurativa[1]

Patient or population: Adults with hidradenitis suppurativa & one or more active lesions excised
Intervention: Primary closure of the wound over a 5x5cm **g**entamicin-collagen sponge
Comparison: Primary closure of the wound without enclosure of antibiotics

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Primary closure alone	**Risk with Gentamicin sponge**				
Adverse events - complication rate after surgery at week 1	526 per 1000	**411 per 1000** (305 to 553)	**RR 0.78** (0.58 to 1.05)	200 (1 RCT)	⨁⨁⨁◯ Moderate[a]	
Adverse events - complication rate after surgery through 3 months	197 per 1000	**178 per 1000** (99 to 320)	**RR 0.90** (0.50 to 1.62)	200 (1 RCT)	⨁⨁◯◯ Low[b]	
Recurrence rate after surgery through 3 months	421 per 1000	**404 per 1000** (286 to 564)	**RR 0.96** (0.68 to 1.34)	200 (1 RCT)	⨁⨁◯◯ Low[b]	
Healing time- time to complete healing of wound	Mean weeks to healing was 3.35	MD 0.33 weeks fewer (0.78 fewer to 0.12 more)		200 (1 RCT)	⨁⨁⨁◯ Moderate[c]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]Downgraded by one level due to serious imprecision: The 95% CI crossed either the conventional upper or lower threshold of MID (0.75 or 1.25).
[b]Downgraded by two levels due to very serious imprecision: the 95% CI crossed both the conventional upper and lower thresholds of MID (0.75 and 1.25).
c.Downgraded by one level due to serious imprecision: The 95% CI is consistent with a meaningful reduction in healing time and little to no difference.

1. Buimer MG, Ankersmit MF, Wobbes T , Klinkenbijl JH. Surgical treatment of hidradenitis suppurativa with gentamicin sulfate: a prospective randomized study. Dermatol Surg 2008;34:224-7.

e-Table 94. Silver Hydrofiber foam vs olive oil

Silver hydrofiber & polyurethane foam compared to olive oil dressing for HS wound care[1]

Patient or population: Moderate to severe HS resistant to standard therapy treated with wide excision of the entire affected area
Interventions: Silver hydrofiber & polyurethane foam per HS-TIME principles; Oxygen-enriched olive oil gel & olive oil-based dressings; ultraportable Negative pressure wound therapy

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)
Wound size assessed with: mean % reduction in wound size following treatment follow-up: 4 weeks	Mean % reduction in wound size at 4 weeks following: - silver hydrofiber & polyurethane foam per the HS-TIME principle was 79.91%, -Oxygen-enriched olive oil gel & olive oil based dressings was 81.74% -Ultraportable Negative pressure wound therapy was 74.75%	(1 RCT)	⨁◯◯◯ Very low[a,b]
Wound bed score improvement assessed with: WBS 0-16; Higher score indicates greater healing progress follow-up: 4 weeks	Mean % reduction in wound bed score at 4 weeks following: - silver hydrofiber & polyurethane foam per the HS-TIME principle was 22.88%, -Oxygen-enriched olive oil gel & olive oil based dressings was 19.49% -Ultraportable Negative pressure wound therapy was 25.86%	(1 RCT)	⨁◯◯◯ Very low[a,b]
Pain improvement assessed with: NRS scale 0-10; Higher score indicates greater pain intensity follow-up: 4 weeks	Mean % reduction in pain score at 4 weeks following: - silver hydrofiber & polyurethane foam per the HS-TIME principle was 71.19%, -Oxygen-enriched olive oil gel & olive oil based dressings was 75.00% -Ultraportable Negative pressure wound therapy was 73.33%	(1 RCT)	⨁◯◯◯ Very low[a,b]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgrade one level for serious risk of bias: single blind with limited outcome reporting.
b. Downgraded two levels for very serious imprecision as the total sample was 25.

1. Michelucci A, Janowska A, Granieri G, Margiotta FM, Morganti R, Romanelli M , Dini V. Advanced wound management approaches in Hidradenitis Suppurativa postsurgical lesions. Health Sci Rep 2023;6:e1582.

e-Table 95. LNPWT vs conventional foam

LNPWT compared to Conventional foam dressing for HS wound care[1]

Patient or population: Hurley stage II or III undergoing CO2 laser treatment
Intervention: LNPWT for 7 days
Comparison: Conventional foam dressing for 7 days

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)
Healing time assessed with: Median days to complete healing follow-up: median 43 days	Median days [range] to complete healing following 7 days of intervention: LNPWT was 21 [17, 146] vs conventional foam dressing 43 [11, 80];p=0.10	200 (1 RCT)	⨁◯◯◯ Very low[a,b]
Pain assessed with: Median VAS 10mm pain score; Higher score indicates worse pain follow-up: 7 days	Median pain score [range] after 7 days of intervention: LNPWT was 2 [0, 9] vs conventional foam dressing 3.5 [0, 10]; p<0.02	(1 RCT)	⨁◯◯◯ Very low[a,b]
Physical functioning-daily life activities assessed with: Median daily activity score; 0-18 scale scale; presume higher score indicates a greater negative impact on daily functioning follow-up: 7 days	Median daily activity score [range] after 7 days of intervention: LNPWT was 6.5 [2, 11] vs conventional foam dressing 7.2 [2, 11]; p not reported	(1 RCT)	⨁◯◯◯ Very low[a,b]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded one level for serious risk of bias: prospective intra-individual design without randomization of patients or treatment side; minimal outcome reporting
b. Downgraded two levels for very serious imprecision: total sample 12 individuals (24 wounds).

1. Grimstad Ø. Single use negative-pressure wound therapy compared to standard care in patients after carbon dioxide laser surgery for hidradenitis suppurativa. Dermatol Ther 2022;35:e15483.

e-Table 96. Negative-pressure wound therapy (case series)

Case series n=2, 28 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from a small case series, which is inherently limited due to the lack of control groups and selection bias. The very small sample sizes increases concern about random error and imprecision.

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murrad tool
Ezanno 2021[1] Monocentric retrospective Case series N= 20 patients; outcomes reported for 36 wounds	-Age (Mean±SD): 27.1±7.7 -12 F, 8 M -Previous medical treatments: n=15 systemic antibiotics; n=2 Anti-TNF -Mean BMI: 28.2±5 -Hurley II n=10, III n=10 -Smoking status: current n=11	Negative-pressure wound therapy system set at 100mmHg for at least 15 days post-radical wide excision (mean duration 18.5 days)	NR	Mean 412.5±195.2 days	Mean time to complete healing	115±85 days	Selection N Ascertainment Y Causality N Reporting Y
					Wounds reported as painful	4/36 (11.1%)	
					Complications (proportion of wounds)	Complications 5/36 (13.9%) Infection 2/36 (5.6%) Loss of mobility 1/36 (2.8%)	
					Mean hospital stay	3±0.2 days	
					Mean duration of wound care intervention	18.5±9 days	
Madueke 2025[2] Prospective cohort N=8 patients ; 21 wounds	-Mean age 32.6(7.9) years -4F, 4M -Mean BMI 34.6(3.8)	Negativepressure wound therapy applied over synthetic electrospun fiber matrix after radical excision	NR	Mean 3.3 weeks	Mean time to >90% wound bed grannulation	14 (3.2) days	
					Complications	0/21	

1. Ezanno AC, Fougerousse AC , Guillem P. The role of negative-pressure wound therapy in the management of axillary hidradenitis suppurativa. Int Wound J 2022;19:802-10.
2. Madueke M , Lau F. Synthetic Electrospun Fiber Matrix in the Management of Acute Wounds Following Excision of Hidradenitis Suppurativa Lesions: A Prospective Pilot Study. Polymers (Basel) 2025;17.

Pain Management Summary of Findings

No HS-specific studies of pain interventions were identified by the systematic review. In lieu of direct evidence below is 1) a table summarizing recent, existing HS pain management recommendations and 2) a summary of the pain outcomes of studies of HS interventions.

e-Table 97. Summary of hidradenitis suppurativa pain management specific therapies recommendations & treatment algorithms

**Only includes recommendations published within the past 10 years for currency*

Guideline/Consensus Statement/Systematic Review	Specific Pain Therapy Recommendations	Supporting Evidence
Alavi, et al. Consensus Statement 2017[1]	• General recommendation to follow WHO pain ladder • Prescribing pain medications beyond the scope of dermatology	Expert panel of Canadian dermatologists and surgeons developed statements and recommendations via Delphi method
Australasian Guidelines 2025[2]	• Pain control is an essential component to overall management <u>Acute pain:</u> Incision and drainage and ILCS (Intralesional corticosteroids) for acutely painful inflamed lesions	Consensus statement via Delphi method (13 expert panel)
Brazilian Society of Dermatology Association Consensus Statement 2019[3]	<u>Acute Pain:</u> Abscess incision/drainage for symptom relief	Consensus statement via Delphi method (8 dermatologist workgroup)
British Association of Dermatologist Guidelines 2018[4]	• Treat pain if needed (Good Practice Statement) • Intralesional triamcinolone for painful lesions	No pain treatment-specific recommendations due to lack of evidence.
Dagnet 2025[5] Updated Algorithm for HS management	• Disease control is the foundation of pain management • Acute pain can be treated with acetaminophen and NSAIDs • Opioids can be prescribed for severe pain episodes	Based on other Savage 2022

European Guidelines 2016[6]	• Analgesics and corticosteroids can be considered to control pain and reduce inflammation • NSAIDs and opiates recommended for pain control	Expert committee reports or opinion or clinical experience of respected authorities, or both
European S1 Guidelines 2015[7]	<u>Acute Pain:</u> • Use of NSAIDs is recommended in the usual dosage schemas • Ketoprofen topical preparations, especially the patch one, suggested for treating inflammatory pain • Avoid coxibs due to risk of cardiovascular events • Intralesional triamcinolone for painful lesions <u>Chronic pain:</u> • Opioids restricted and limited to cases where all other painkillers have failed • Codeine should be the first treatment option for this drug class. • Hydrocodone may also be an option	No clinical evidence for the use of pain therapies in HS
European S2k Guidelines 2024[8]	• Given the lack of RCT for HS pain management and the disappearance of pain with HS efficient treatments, an early management of HS and a cautious and limited use of all analgesics, weighing their benefits and risks • Acetaminophen should be tried first for pain relief • Restricted use of NSAIDs for pain relief • SSRI/depressants not recommended for pain relief • Pregabalin/gabapentin may be considered for pain relief • Opiates are not recommended for pain relief • Topical analgesics are not recommended for pain relief	No clinical evidence for the use of pain therapies in HS; Consensus recommendations
HS ALLIANCE Guidelines 2019[9]	<u>Acute Pain:</u> • Surgical incision and drainage of tense and painful abscesses, i.e. fluctuant lesions, may be performed • Intralesional triamcinolone for painful lesions	Four manuscripts focused on the surgical management of HS including two retrospective review/cohorts and narrative reviews

Jeha, et al. HS pain algorithm 2021[10]	**eTABLE. Suggested Algorithm for the Treatment of Pain in Hidradenitis Suppurativa**	No direct evidence; review of existing guidance

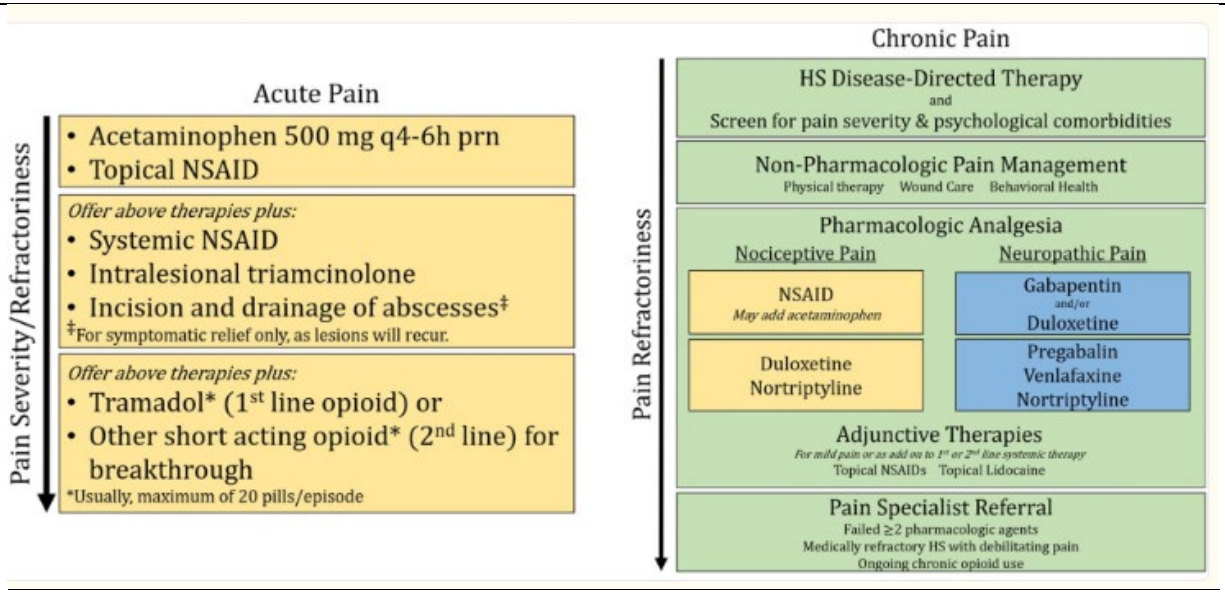
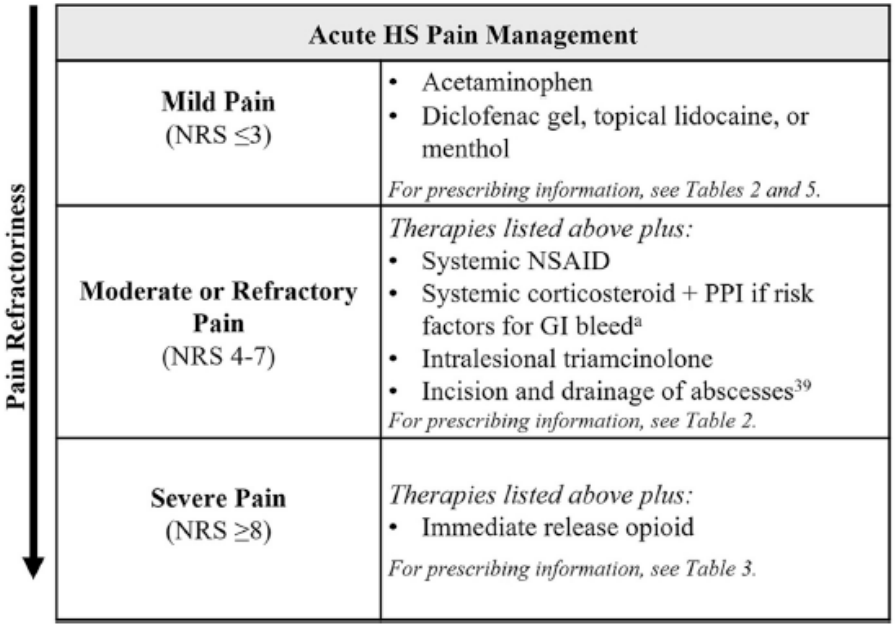
Pain Severity		
Mild localized/mild disseminated	**Moderate**	**Severe**
Lifestyle		
Weight loss, smoking cessation, zinc gluconate, metformin		
Pain management		
Loose clothing; ice packets; topical analgesics; scheduled NSAIDs or acetaminophen; refractory: opioids or anticonvulsants		
Psychosocial		
Disease education, referral to support groups, consider treatment for anxiety		
Procedures		
Localized and recurrent abscesses: drainage, excision, CO_2 or long-pulsed Nd:YAG laser ablation	Sinus tracts: deroofing, STEEP, excision, CO_2 or long-pulsed Nd:YAG laser ablation	Radial wide excision
Topical medications		
Management of new lesions, flares, and preoperative inflammation: clindamycin, resorcinol peels, 2% triclosan; intralesional steroids; botulinum toxin		
Systemic medications		
Antibiotics (12-wk course): tetracycline, doxycycline; refractory: clindamycin and rifampin; antiandrogens: spironolactone, finasteride[a]	Antibiotics; TNF-α inhibitors: adalimumab, infliximab; retinoids: acitretin	Antibiotics; TNF-α inhibitors; retinoids; immune suppressants: cyclosporine, prednisone course

Abbreviations: NSAIDs, nonsteroidal anti-inflammatory drugs; STEEP, skin tissue-sparing excision with electrosurgical peeling; TNF, tumor necrosis factor.

[a]Topical therapy may be adequate for localized disease.

Adapted from Saunte and Jemec.[36]

<table>
<tr>
<td>Li, et al. pain management guide 2022[11]</td>
<td>
TABLE 3 Interdisciplinary team Involved in hidradenitis suppurativa (HS) pain management
<table>
<tr><th>Team member</th><th>Role(s)</th></tr>
<tr><td>Patient</td><td>• Communication about pain symptoms and degree of interference in their life.
• Set priorities and goals for pain management.</td></tr>
<tr><td>Dermatologist</td><td>• Lead role in medical and surgical management of HS.
• Initiate first-line analgesics and provide short courses of medications for acute pain episodes
• Coordinate additional referrals as needed.
• Educate other care team members about HS and advocate for effective pain management.</td></tr>
<tr><td>Primary care provider</td><td>• Initiate first-line analgesics, especially in patients at risk for medication interactions.
• Coordinate and centralize the long-term pain management of the multidisciplinary team, particularly for
suffering from multifactorial pain.
• First-line management of comorbid mental health disorders.</td></tr>
<tr><td>Pain management specialist</td><td>• Analgesia and procedures for refractory pain.
Consider referral if[17]:
Failed ≥2 analgesics
Medically refractory HS with poorly controlled pain
Ongoing chronic opioid use.</td></tr>
<tr><td>Psychiatrist</td><td>• Pharmacologic treatment of comorbid mental health disorders, especially if refractory to first-line therap
• Monitor for safety and interactions in patients on multiple psychotropic agents.</td></tr>
<tr><td>Psychologist</td><td>• Nonpharmacologic management of comorbid mental health disorders.
• Cognitive-behavioral therapy, acceptance commitment therapy, and others for chronic pain.</td></tr>
<tr><td>Palliative care specialist</td><td>• Holistic support for patients and families to cope with suffering caused by HS.
• Medications for HS pain and other symptoms of disease.</td></tr>
<tr><td>Wound care specialist</td><td>• Identify dressing materials and techniques to minimize discomfort from bandage materials, dressing chan
wound exudate.</td></tr>
</table>
</td>
<td>Narrative literature review on HS pain, management of other painful conditions, and expert opinion</td>
</tr>
<tr>
<td>North American HS Foundation Guidelines 2019[12]</td>
<td>
<u>Acute Pain:</u>
• Incision & draining acute abscesses only
• Topical lidocaine, oral acetaminophen, oral NSAIDs
• Short-acting opioids for select cases of severe pain (“carefully prescribed)
• Intralesional triamcinolone
<u>Chronic Pain:</u>
• WHO pain ladder (codeine, hydrocodone, morphine)
• Anticonvulsants used with caution for neuropathic pain (pregabalin, gabapentin)
Multidisciplinary approach with pain specialists
</td>
<td>No HS-specific pain studies Based on a review of pain guidelines, expert opinion, and patient preferences</td>
</tr>
</table>

Savage et al. treatment algorithm 2022[13]		Based on evidence in other diseases and author opinions
Surapaneni et al. algorithm 2024[14]	 **Fig 1.** Medical management of acute HS pain.[53] [a]Risk factors for gastrointestinal bleeding include concomitant NSAID use, smoking, alcohol use, age >65, history of *Helicobacter pylori* infection or peptic ulcer disease. *GI*, Gastrointestinal; *HS*, hidradenitis suppurativa; *NRS*, numerical rating scale, 0 to 10; *NSAID*, nonsteroidal antiinflammatory drug; *PPI*, proton pump inhibitor.	Based on Masson et al. flare management consensus recommendations; studies in other disease states

1. Alavi A, Lynde C, Alhusayen R, Bourcier M, Delorme I, George R et al. Approach to the Management of Patients With Hidradenitis Suppurativa: A Consensus Document. J Cutan Med Surg 2017;21:513-24.
2. Frew J, Smith A, Penas PF, Ellis E, Foley P, Rubel D et al. Australasian hidradenitis suppurativa management guidelines. Australas J Dermatol 2025;66:75-89.
3. Magalhães RF, Rivitti-Machado MC, Duarte GV, Souto R, Nunes DH, Chaves M et al. Consensus on the treatment of hidradenitis suppurativa - Brazilian Society of Dermatology. An Bras Dermatol 2019;94:7-19.
4. Ingram JR, Collier F, Brown D, Burton T, Burton J, Chin MF et al. British Association of Dermatologists guidelines for the management of hidradenitis suppurativa (acne inversa) 2018. Br J Dermatol 2019;180:1009-17.
5. Dagenet CB, Lee KH, Sayed C, Hsiao JL , Shi VY. Comprehensive and Updated Algorithm of Hidradenitis Suppurativa Management from the Experts. Am J Clin Dermatol 2025;26:487-97.
6. Gulliver W, Zouboulis CC, Prens E, Jemec GB , Tzellos T. Evidence-based approach to the treatment of hidradenitis suppurativa/acne inversa, based on the European guidelines for hidradenitis suppurativa. Rev Endocr Metab Disord 2016;17:343-51.
7. Zouboulis CC, Desai N, Emtestam L, Hunger RE, Ioannides D, Juhász I et al. European S1 guideline for the treatment of hidradenitis suppurativa/acne inversa. J Eur Acad Dermatol Venereol 2015;29:619-44.
8. Zouboulis CC, Bechara FG, Benhadou F, Bettoli V, Bukvić Mokos Z, Del Marmol V et al. European S2k guidelines for hidradenitis suppurativa/acne inversa part 2: Treatment. J Eur Acad Dermatol Venereol 2024.
9. Zouboulis CC, Bechara FG, Dickinson-Blok JL, Gulliver W, Horváth B, Hughes R et al. Hidradenitis suppurativa/acne inversa: a practical framework for treatment optimization - systematic review and recommendations from the HS ALLIANCE working group. J Eur Acad Dermatol Venereol 2019;33:19-31.
10. Jeha GM, Kodumudi V, O'Quinn MC, Luckett KO, Dickerson TG, Kaye RJ et al. Management of Acute and Chronic Pain Associated With Hidradenitis Suppurativa: A Comprehensive Review of Pharmacologic and Therapeutic Considerations in Clinical Practice. Cutis 2021;108:281-6.
11. Li YH, Williams MN, Jedrzejczak MJ, Orenstein LAV , Singh V. A practical, comprehensive guide to pain management hidradenitis suppurativa. Dermatological Reviews 2022;3:137-49.
12. Alikhan A, Sayed C, Alavi A, Alhusayen R, Brassard A, Burkhart C et al. North American clinical management guidelines for hidradenitis suppurativa: A publication from the United States and Canadian Hidradenitis Suppurativa Foundations: Part I: Diagnosis, evaluation, and the use of complementary and procedural management. J Am Acad Dermatol 2019;81:76-90.
13. Savage KT, Singh V, Patel ZS, Yannuzzi CA, McKenzie-Brown AM, Lowes MA , Orenstein LAV. Pain management in hidradenitis suppurativa and a proposed treatment algorithm. J Am Acad Dermatol 2021;85:187-99.
14. Surapaneni V, Milosavljevic MV , Orenstein LAV. Pain management in hidradenitis suppurativa. Journal of the American Academy of Dermatology 2024;91:S52-S63.

e-Table 98. Pain outcomes for clinical intervention studies

Intervention	Study design & N	Follow up	Change in NRS or VAS pain severity from baseline				NRS30^ of VAS30^^			Certainty
			Treatment Δ	PBO Δ	MD (95%CI)	p-value	Treatment	PBO	p-value	
Systemic biologic & smaller molecule therapies										
Adalimumab 40 mg q1w	2 RCTs[1] N=447	12w	-	-	-	-	36.1%	22.7%	0.17	⊕⊕◯◯ Low
Adalimumab 40 mg q2w	RCT[2] N=21	12w	-13.4[#]	+3.17	-16.57 (-55.28, 22.14)	0.40	-	-	-	⊕⊕◯◯ Low
Adalimumab 40 mg q2w	RCT[3] N=95	16w	-	-	-	-	36.2%	27.1%	0.34	⊕⊕◯◯ Low
Anakinra 100 mg qd	RCT[4] N=19	12w	5.4 →4.9[$]	6.1→5.8	-	>0.05	-	-	-	⊕◯◯◯ Very Low
Apremilast 30 mg bid	RCT[5] N=20	16w	-0.8	+2.2	-3.00 (-5.07, -0.93)	0.004	-	-	-	⊕⊕⊕◯ Moderate
Avacopan 10 mg bid	RCT[6] N=209	12w	-	-	-	-	22.1%	28%	0.65	⊕⊕◯◯ Low
Avacopan 30 mg bid	RCT[6] N=209	12w	-	-	-	-	16.3%	28%	0.14	⊕⊕◯◯ Low
Bermekimab 800mg LD 400 mg q2w	RCT[7] N=96	16w	-1.8	-1.52	-0.28 (-1.23, 0.67)	0.56				⊕⊕◯◯ Low
Bimekizumab 320 mg q2w	2 RCTs[8] N=726	16w	-1.9* -1.9	-1.1 -0.4	-1.15 (-5.60, 3.30)	0.19	21.9%**	8.2%	0.0009	⊕⊕⊕◯ Moderate
Bimekizumab 320 mg q4w	2 RCTs[8] N=434	16w	-1.7* -1.7	-1.1 -0.4	-0.95 (-5.40, 3.50)	0.22	18.8%**	8.2%	0.25	⊕⊕⊕◯ Moderate
Brepocitinib 45 mg qd	RCT[9] N=100	16w	-	-	-	-	Difference: 6.5% (90%CI -10.4, 23.4)			⊕⊕◯◯ Low
Eltrekibart 600 mg q2w	RCT[10] N=67	16w	-1.83	-1.78	0.05 (-1.41, 1.51)	0.95	-	-	-	⊕⊕◯◯ Low
Guselkumab 200 mg q4w	RCT[11] N=121	16w	-1.6	-0.3	-1.3	0.007	-	-	-	⊕◯◯◯ Very Low
Infliximab 5 mg/kg on wk 0, 2, 6	RCT[12] N=33	8w	-39.8[#]	-0.6	-39.2	<0.001	-	-	-	⊕◯◯◯ Very Low
Ixekizumab LD 160 mg; 80 mgq2w	Case series[13] N=5	12w	-5.6 (range 2, -8)	-	-	-	-	-	-	⊕◯◯◯ Very Low
Izokibep 160 mg q1w	RCT[14] N=60	16w	-	-	-	-	17.2%	16.1%	0.91	⊕⊕◯◯ Low
Izokibep 160 mg q2w	RCT[14] N=60	16w	-	-	-	-	27.6%	16.1%	0.29	⊕⊕◯◯ Low
Povorcitinib 15 mg qd	RCT[15] N= 104	16w	-	-	-	-	44.1%	30.8%	0.11	⊕⊕⊕◯ Moderate
Povorcitinib	RCT[15]	16w	-	-	-	-	51.5%	30.8%	0.08	⊕⊕⊕◯

45 mg qd	N= 104									Moderate
Povorcitinib 75 mg qd	RCT[15] N=105	16w	-	-	-	-	53.3%	30.8%		⊕⊕⊕◯ Moderate
Secukinumab 300 mg q2w	RCT[16] N=517	16w	-	-	-	-	36.5%	23.1%	0.001	⊕⊕⊕◯ Moderate
Secukinumab 300 mg q4w	RCT[16] N=503	16w	-	-	-	-	33.3%	23.1%	0.01	⊕⊕⊕◯ Moderate
Spesolimab 3600mg wks 0, 1, 2 1200 mg wks 4, 6, 10	RCT[17] N=52	12w	-	-	-	-	22.9%	5.9%	0.18	⊕⊕◯◯ Low
Upadacitinib 30mg qd	RCT[18] N=45	12w	-	-	-	-	36.4%	22.5%	0.50	⊕◯◯◯ Very Low
Ustekinumab 90mg q4w or q8w	Case series[19] N=6	8-12w	-2.5 (5.5, 0.5)	-	-	-	-	-	-	⊕◯◯◯ Very Low
Systemic antibiotics										
Clindamycin 300mg + Rifampicin 300mg bid	RCT[20] N=21	10w	6.67 → 2.48	-	-	-	-	-	-	⊕⊕◯◯ Low
Clindamycin+rifampicin 300 mg bid + 600 mg qd	Case series[21] N=69	10w	7.0 → 3	-	-	<0.001	-	-	-	⊕◯◯◯ Very Low
Ertapenam 1g qd	Case series[22] N=98	12-16w	4.2 → 1.8	-	-	<0.001	-	-	-	⊕◯◯◯ Very Low
Lymecycline 300 mg qd	Case series[21] N=26	10w	6.7 → 3.4	-	-	-	-	-	-	⊕◯◯◯ Very Low
Oral retinoids and hormonal medications										
Acitretin 0.59 mg/kg qd (mean)	Case series[23] N=12	24+w	-5.7 (range -2, -10)	-	-	-	-	-	-	⊕◯◯◯ Very Low
Spironolactone 75 mg qd (mean)	Case series[24] N=46	3-112w	2.7 → 1.2	-	-	0.01	-	-	-	⊕◯◯◯ Very Low
Systemic steroids, DMARDs, and PDE4is										
Apremilast 30 mg bid	RCT[5] N=20	16w	-0.8 (-2.2, 0.6)	+2.2 (-0.1, 4.5)	-	0.004	-	-	-	⊕⊕⊕◯ Moderate
Triamcinolone 10 mg/mL	RCT[25] N=36	5 days	-2.0	-2.63	0.63 (-1.07, 2.33)	0.47	-	-	-	⊕⊕◯◯ Low
Triamcinolone 20 mg/mL	Case-control[26] N=31	4w	4.1 → 3.2	-	-	0.035	-	-	-	⊕⊕◯◯ Low
Triamcinolone 40 mg/mL	RCT[25] N=39	5 days	-2.3	-2.63	0.33 (-1.25, 1.91)	0.68	-	-	-	⊕⊕◯◯ Low
Other systemic therapies										
Botulinum toxin B 4000 U max	RCT[27] N=20	12w	-2.3	+0.4	-2.70 (-4.64, -0.76)	0.006	-	-	-	⊕⊕⊕◯ Moderate
Topical therapies										
Topical clindamycin 1%	Case series[28]	12w	7.0 → 5.1	<0.05	-	-	-	-	-	⊕⊕◯◯

bid	N=73									Low
Topical resorcinol 15% qd	Case series[28] N=61	12w	6.7 → 0.4	<.001	-	-	-	-	-	⊕⊕◯◯ Low
Ruxolitinib 1.5% cream bid	RCT[29] N=45	16w	-1.90	-2.09	0.19 (-1.24, 1.62)	0.79	-	-	-	⊕⊕◯◯ Low

^ ≥30% and ≥1 point reduction from baseline
^^30% reduction from baseline and a 10 mm absolute reduction
*HSSDD 11-point numeric rating scale
**Hidradenitis suppurativa symptom daily diary (HSSDD) worst skin pain response (≥3 points reduction among patients with a baseline score of at least 3)
$Data from Surapaneni 2024 as approximated from a figure.
#VAS 100mm

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e-Table 99. Tobacco smoking status and HS clinical severity or treatment response

Overall Certainty of Evidence: Very Low

Limited direct evidence was available (i.e, studies on the impact of tobacco cessation on the patient-important outcomes of interest). To supplement the very limited direct evidence, additional indirect evidence has been summarized. All available studies were of very low certainty due to study design (retrospective single-cohort and survey). Additional evidence indirectly addresses the research question of interest, derived from non-randomized studies, making the overall certainty very low.

Study	Population	Comparison	Impact
Tobacco cessation intervention studies			
Macklis 2022[1] Survey	N=140 -HS of any severity -Member of an online HS support group -Tried a lifestyle modification	Tobacco cessation (no comparative data)	Tobacco cessation resulted in the self-reported improvement of HS in 17% of patients attempting the intervention based on Hurley stage and global assessment of HS using 5-point scale from no disease to very severe disease. However, the symptomatic improvement noted by the 17% of patients were the most significant improvement in subjective and Hurley staging of HS seen with any of the studied interventions, including diet and weight loss.
Siddiquee 2021[2] Retrospective cohort	N=26 -Hurley stage I n=6, II n=12, III n=9 -Using an individualized smoking support intervention -Age: Mean 41 years - 24F, 7M	Tobacco cessation (varied modalities including pharmacotherapy) n=6/26 reported 100% cessation	0/26 patients reported adverse events of smoking cessation interventions. No clinical outcomes were reported.
Clinical severity			
Canoui-Poitrine 2009[3] Case series	N=302 -Age: Mean 30.4 years -Hurley score I n=191, II n=78, III n=11	Smoking status (current, former, non-smoker)	Smoking status was not significantly associated with HS severity per Sartorious score on univariate or multivariate analysis: Univariate results median Sartorious score nonsmoker (n=27) 16, current smoker (n=228) 17 p=0.72, ex-smoker (n=45) 23 p=0.10
Chastagner 2025[4] Retrospective cohort N=1689	-Mean age 32.2 years -1064F, 625M -Mean BMI 27 kg/m2 -Hurley stage I n=876; II n=628; III n=185 -Hx of smoking n=1172	Smoking status (current/former smoker vs never smoker)	Smokers (n=1172) were associated with a more severe disease: the number of affected sites was positively associated with the number of pack-years ($\rho = 0.126$, $p = 0.0002$). There was also a significant association between active smoking and a poorer quality of life ($p < 0.001$), as well as increased pain during HS flares ($p < 0.003$).
Dessinioti 2017[5]	N=133 -Age: Mean 34.5 years	Smoking status (current/former vs never)	Smoking (current or former smoker; n=112) vs never smoking (n=21) causes no change in Hurley staging (stage I vs II or II) (OR = 1.31, 95% CI:

Retrospective cohort	-81 F, 52 M -Hurley score I n=22, II n=84, III n=27		0.37–4.61), but increases number of affected body areas (>2 areas vs 2 or fewer) (OR: 3.56, 95% CI: 1.27–9.96)
Kaya 2025[6] Cross-sectional N=193	-Mean age 34.51 years -72F, 121M -Mean BMI 27.84kg.m2 -Mean pack years 11.39 (11.99) -Hurley stage I n=118; II n=47; III n=28	Pack years of smoking	Pack-years was not associated with higher Hurely stage on multivariate analysis: aOR 1 (0.966, 1.034) p=0.98
Kjaersgaard 2022[7] Prospective cohort	N=430 -Self-reported HS via validated questionnaire in blood donors -Age: Mean 36.4 years - 256 F, 174 M	Smoking status (active smoking vs former or no smoking)	Active smoking was statistically associated with the decreased likelihood of HS remission (HR = 0.49, 95% CI: 0.32-0.76); Median f/u 693 days
Liakou 2021[8] Cross-sectional	N=290 -Hurley stage I n=123, II n=125, III n=42 -Age: Mean 37.3 years - 148 F, 142 M -Active smoking n=164	Smoking status (active smoking n=164 vs no active smoking n=126)	Active smoking was a statistically significant risk factor for higher stage of disease based on Hurley stage (aOR 1.38, 95% CI: 1.11-1.65); Smoking and thyroid disease were the only variables to be significantly associated with higher stage disease (other factors considered dermatopathies, metabolic syndrome, IBD, polycystic oval, BMI, disease duration, age of disease onset)
Omine 2020[9] Case series	N=58 -Hurley stage II n=19, III n=35 -Age: Mean 43.4 years -16F, 42M	Smoking status (current n=31, former n=9, never n=15)	Smoking history was not significantly associated with HS severity: Current smokers had a Sartorius Score of 48 compared to 57 in never smokers (p = 0.53). Ex-smokers had a Sartorius Score of 38 compared to 57 in never smokers (p = 0.35)
Sartorius 2009[10] Case series	N=249 -Median HSS 38[18, 66] -Age: Mean 37.5 years	Smoking status (current n=173, former n=37, never n=39)	Median Hidradenitis Suppurativa Score for smokers was 41 [22, 75.5], former smokers 27 [16, 53], and nonsmokers 22 [10, 57]; Median DLQI was 10[4,16] for smokers, 7[4, 11.5] for former smokers, and 9[4, 12] for non-smokers.
Schrader 2014[11] Retrospective cohort	N=846 -Hurley stage I n=385, II n=351, III n=110 -614F, 232M	Smoking status (current n=5, former n=119, never n=127) -Mean pack years 18.8 (SD 15.6)	HS severity (Hurley stage I vs II or III) was associated with smoking pack-years(number of cigarettes & duration of smoking): **OR 1.02 per pack year; p = 0.001** Smoking status was not a statistically significant risk factor for HS severity based on Hurley stage: **Current smoker aOR 0.94(0.60, 1.47) p=0.78; Former smoker aOR 1.14 (0.64, 2.02) p=0.66**

Vazquez 2013[12] Retrospective cohort	N=268 -Hurley stage I n=160, II n=102, III n=6 -Age: mean 32.9 years -189F, 79M	Smoking status (current n=153, former n=33, never n=79)	On multivariate analysis, smoking was not statistically significantly associated with disease severity (Hurley stages I/II vs III) (data not provided); Univariate analysis **OR 2.0(1.1, 3.5) p=0.016** for past/current smoking vs never smoking
Treatment response			
Abu Rached 2025[13] Retrospective cohort N=42	-Maintenance treatment with 300 mg secukinumab every 4 weeks	Tobacco pack-years	Median tobacco pack-years were significantly lower in patients achieving HiSCR50 at 16 weeks: 8(0-10) vs 20 (12-31.5) in nonresponders; aOR 0.83 (0.71, 0.98) p=0.029.
Denny 2017[14] Retrospective cohort	N=198 -Clinical dx of HS of any severity -Prescribed first-line medical therapy for HS (oral antibiotics, topical antibiotics, intralesional corticosteroids, antimicrobial creams/lotions/washes) -Follow up appointment within 6 months of initial visit	Smoking status (non-smoker/former smoker vs current smoker)	Non-smokers/former smokers had a 2.634 (95% CI = 1.301-5.332, p = 0.007) times increased odds of having improvement in their disease on first line medical therapy compared to current smokers, regardless of amount smoked.
Iannone 2021[15] Retrospective cohort	N=36 -Age: Mean 32.5 years -Hurley stage I n=4, II n=30, III n=2 -Smokers n=28 -On antibiotic therapy: clindamycin+rifampicin n=17, clindamycin monotherapy n=19	Smoking pack years (Median pack years 5)	Smoking was predictive of a poor response to antibiotic treatment: -Smoking pack years were positively correlated with Acne Inversa Severity Index (Spearman's rho = 0.51, p = .036) and DLQI (0.47, p = 0.061) in patients being treated with clindamycin and rifampicin -In patients taking clindamycin monotherapy, a positive correlation was found between smoking pack years and AISI (0.47, p=0.041), while a negative correlation was found with DLQI (-0.44, p=0.61)

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Weight Reduction Summary of Findings

Contents

e-Table 100. Bariatric Surgery for weight reduction

Bariatric surgery compared to standard care/nutritional care for HS

Patient or population: HS with obesity (BMI ≥30kg/m2)
Intervention: bariatric surgery resulting in a mean weight significantly lower than the control group
Comparison: standard care or nutritional care (undefined)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with standard care/nutritional care	**Risk with bariatric surgery**				
Clinical severity assessed with: Mean change in HS activity score: 0-10cm VAS; Higher score indicates greater disease severity follow-up: mean 44.4 months	Bariatric surgery: mean score change -3.3 Nutritional care: mean score change -2 **Difference -1.3 points**			19[1] (1 non-randomised study)	⨁◯◯◯ Very low[a,b]	
Quality of life assessed with: DLQI 0-30; Higher score indicates greater negative impact on QoL follow-up: mean 44.4 months	Bariatric surgery: Mean score 4.25 (range 0, 18) Nutritional care: Mean score 12.29 (3, 26) **Difference -8.04; p=0.04**			19 (1 non-randomised study)[1]	⨁◯◯◯ Very low[a,b]	
Recurrence assessed with: risk of HS recurrence follow-up: 9 years	**Not estimable**		**RR 0.676** (0.369 to 1.238)	4185 (1 non-randomised study)[2]	⨁◯◯◯ Very low[a,c]	
Hospitalization for HS assessed with: Risk of hospitalization for HS symptoms follow-up: 9 years	**Not estimable**		**RR 0.731** (0.390 to 1.371)	4185 (1 non-randomised study)[2]	⨁◯◯◯ Very low[a,c]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded one level for risk of bias: retrospective data collection & minimal outcome reporting.
b. Downgraded two levels for very serious imprecision: total sample size is 19.
c. Downgraded one level for serious imprecision: CI is consistent with risk reduction and increase; limited outcome reporting precluded calculation of the absolute effect.

1. Canard C, Diaz Cives A, Gaubil-Kaladjian I, Bertin E , Viguier M. Impact of Bariatric Surgery on Hidradenitis Suppurativa. Acta Derm Venereol 2021;101:adv00471.
2. Chierici A, Bulsei J, Alromayan M, Alamri A, Pavone G, Fontas E , Iannelli A. Bariatric surgery reduces the incidence of hidradenitis suppurativa in individuals with obesity: results of a nationwide administrative data study in France. Surg Obes Relat Dis 2024;20:947-52.

e-Table 101. GLP-1 Agonists for weight reduction

GLP1 receptor agonists compared to standard care for HS with obesity

Patient or population: HS of any severity with obesity (with or without diabetes)
Intervention: GLP1 receptor agonists (liraglutide 3mg & diet counseling for 3 months or semaglutide mean dose 0.8(0.4) mg weekly for mean of 8.2 (7.2) months) + Standard care or semaglutide mean dose 0.52 ± 0.47 mg/wk, increased to 1.11 ± 0.82 at 6 mo, and 1.36 ± 0.86 at 12 mo; or semaglutide 0.8 mg/wk for 12 weeks or once-weekly tirzepatide, titrated to maximum tolerated dose, for 24 weeks, followed by an 8-week washout). Resulting in a reduction in mean weight, BMI, or waist circumference
Comparison: standard care before GLP1 receptor agonist therapy

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)
Clinical severity assessed with: Mean change in Hurley stage,"HS improvement", or HiSCR50 follow-up: range 3 to 12 months	**Lyons 2024[1] (n=14):** Mean Hurley stage reduced from 2.6(0.5) to 1.1(0.3), p=0.002 **Posada Posada 2025[2]**: HS improved in 27/45 patients at 12 months (>50% reduction in lesions & no new lesions, reduced need for rescue therapy, or clinical documentation of improvement). Improvement was significantly associated with semaglutide dose. **Acosta-Madiedo 2025[3] (n=20):** At week 24 16/20 (80%) achieved HiSCR50. **Gouvrion 2025[4] (n=34):** Mean Hs-PGA decreased from 2.4(1.0) to 1.9(1.2) p<0.001 at 6 months after the addition of a GLP-1 to a stable HS treatment regimen. **Islam 2025[5] (n=40):** Mean HS-PGA decreased from 2.35(1.17) to 1.98(1.00) with a mean of 12 months of adjunctive GLP-1 use (most patients n=31 had changes to dermatologic treatments for HS during follow up).	153 (5 non-randomised studies)	⨁◯◯◯ Very low[a,b]
Recurrence assessed with: Mean frequency of HS flares before and after treatment	**Nicolau 2024 (n=14):** Mean flare frequency decreased from once every 8.5 (12.9) weeks to once every 12.0(13.1) weeks. P=0.38 **Gouvrion 2025[4] (n=34):** Mean number of flares in the previous 3 months decreased from 4.5(2.2) to 3.0(2.3) p<0.001 at 6 months after the addition of a GLP-1 to a stable HS treatment regimen	64 (2 non-randomised study)[6]	⨁◯◯◯ Very low[a,b]
Pain assessed with: Mean VAS10 or NRS pain score follow-up: 3-6 months	**Nicolau 2024[7] (n=14):** Mean VAS 10 pain scores reduced from 5.6(1.5) to 3.2(1.6) p=0.003 **Gouvrion 2025[4] (n=34):** Mean DLQI score decreased from 4.5(2.4) to 3.5(2.5) p<0.001 at 6 months after the addition of a GLP-1 to a stable HS treatment regimen	48 (2 non-randomised study)	⨁◯◯◯ Very low[a,b]

GLP1 receptor agonists compared to standard care for HS with obesity

Patient or population: HS of any severity with obesity (with or without diabetes)
Intervention: GLP1 receptor agonists (liraglutide 3mg & diet counseling for 3 months or semaglutide mean dose 0.8(0.4) mg weekly for mean of 8.2 (7.2) months) + Standard care or semaglutide mean dose 0.52 ± 0.47 mg/wk, increased to 1.11 ± 0.82 at 6 mo, and 1.36 ± 0.86 at 12 mo; or semaglutide 0.8 mg/wk for 12 weeks or once-weekly tirzepatide, titrated to maximum tolerated dose, for 24 weeks, followed by an 8-week washout). Resulting in a reduction in mean weight, BMI, or waist circumference
Comparison: standard care before GLP1 receptor agonist therapy

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)
Quality of life assessed with: Mean change in DLQI scores following treatment; follow-up: range 3 months to 7 months	**Lyons 2024 (n=14):** a reduction in mean DLQI from 13 ± 8.7 to 9 ± 8.2, with 10/30 of the patients experiencing a DLQI reduction greater than 4 points. **Nicolau 2024 (n=14):** reduction in mean DLQI from 12.3(2.8) to 9.7(6.9) p=0.04 **Gouvrion 2025[4] (n=34):** Mean NRS Pain score decreased from 14.2(7.2) to 10.8(7.8) p<0.001 at 6 months after the addition of a GLP-1 to a stable HS treatment regimen	78 (3 non-randomised studies)[4, 6, 8]	⨁◯◯◯ Very low[a,b]
Psychological functioning assessed with: Mean Beck Depression Inventory 21-item; 0-63; Higher scores indicate more severe depressive symptoms follow-up: 3 months	Mean BDI scores improved from 22(7.6) to 16.7 (6.8) p=0.007	14 (1 non-randomised study)[8]	⨁◯◯◯ Very low[a,b]
Discontinuation assessed with: pts discontinuing treatment due to adverse events follow-up: 3 months	0/14 discontinued treatment	14 (1 non-randomised study)[8]	⨁◯◯◯ Very low[a,b]

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations
a. Selection bias is a concern as all included studies did not randomize patients to treatment; co-interventions in al but one study.
b. Small to very small samples are concerning for precision.

1. Lyons D, Louly Nathan A, Pender E, Murray G, Smith C, Kirby B , Hughes R. Semaglutide for weight loss in people with obesity as an adjunctive treatment for hidradenitis suppurativa: its impact on disease control and quality of life. Br J Dermatol 2024;191:631-3.
2. Posada Posada MI, Alora MB , Lima XTV. Impact of semaglutide use in obese and diabetic patients with hidradenitis suppurativa. J Eur Acad Dermatol Venereol 2025;39:e662-e4.
3. Acosta-Madiedo AS, Gutierrez M, Gutierrez M, Villacampa A , Kerdel F. An Open-Label, Single-Center Proof of Concept Study Evaluating the Efficacy and Safety of Tirzepatide for Moderate to Severe Hidradenitis Suppurativa. J Drugs Dermatol 2025;24:1246-51.

4. Gouvrion L, Delage M, Villani AP, Le Naour S, Fite C, Cassius C et al. Glucagon-Like Peptide-1 Receptor Agonists in Hidradenitis Suppurativa. JAMA Dermatol 2025;161:1084-6.
5. Islam Z, Karpoff K, Alicea DS, Wong JH, Wu S, Lu A et al. Glucagon-Like Peptide-1 Receptor Agonists Are Associated With Reduced Disease Severity and Pain in Hidradenitis Suppurativa: A Retrospective Study. Int J Dermatol 2025.
6. Lyons D, Louly Nathan A, Pender E, Murray G, Smith C, Kirby B , Hughes R. Semaglutide for weight loss in people with obesity as an adjunctive treatment for hidradenitis suppurativa: its impact on disease control and quality of life. Br J Dermatol 2024;191:631-3.
7. Nicolau J, Nadal A, Sanchís P, Pujol A, Masmiquel L , Nadal C. Liraglutide for the treatment of obesity among patients with hidradenitis suppurativa. Med Clin (Barc) 2024;162:118-22.
8. Nicolau J, Nadal A, Sanchís P, Pujol A, Masmiquel L , Nadal C. Liraglutide for the treatment of obesity among patients with hidradenitis suppurativa. Med Clin (Barc) 2024;162:118-22.

e-Table 102. Varied weight-reduction methods (case series)

Case series/non-comparative cohorts n=3, 387 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series/non-comparative cohort studies, which are inherently limited due to the lack of control groups and selection bias. Most studies relied on patient reporting of clinical outcomes. The individual studies generally included small sample sizes, increasing concern about random error and imprecision. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Bariatric Surgery-induced weight reduction							
Kromann 2014[1] Retrospective Postal Survey N=45	-Age: Mean 46 (range 21-67) -Pre-surgery BMI ≥30.9km/m2 -HS defined as at least 3 skin eruptions in flexural sites (10/45 reported clinical dx) -Underwent bariatric surgery resulting in >15% weight loss	Bariatric surgery induced weigh loss	NR	NR	Mean (SD) change in # of HS sites	Reduced from 1.93 (1.71) to 1.22 (1.48) **MD 0.71 (1.52) p=0.003** n=45	Murad tool not applicable: -Response rate 69.7% -Representative sample -Total sample size small
					# of pts with HS symptoms	After weight loss, 17 had no symptoms, 7 fewer symptoms, 7 no change and 4 worsening; n=35	
					PGSA (patient's global numeric rating scale 1-10, where 10 is worst	Pre-weight loss mean (SD) 4.8 (2.6) vs post-weight loss 4.6 (2.9) **MD -0.2 p=0.74** n=45	

					possible skin problems)		
Very low-calorie ketogenic diet induced weight reduction							
Verde 2024[2] Case series N=12	-Caucasian women 100% -Age: range 21-54 years -BMI ≥ 25.0 kg/m2 - ≥6-month history of HS - No medical therapy for ≥ 3 months prior	Very low-calorie ketogenic diet resulting in significantly reduced mean BMI & waist circumference	None	28 days	Mean % change in Sartorius score	**-24.37% (SD 16.64), p<0.001**	Murad Tool: Selection N Ascertainment Y Causality N Reporting Y
					Mean % change in DLQI score	**-44.62% (SD 35.74) p=0.001**	
					Adherence (measured by ketone levels)	**12/12 participants**	
Diet-induced weight reduction							
Macklis 2022[3] Social Media Survey N=330	-HS of any severity -Member of an online HS support group -Tried a lifestyle modification	**Popular diet** (Paleo, Keto, Gluten-free, Anti-inflammatory, Low carb) for at least 2 months resulting in weight loss	NR	Cross-sectional	Subjective improvement of HS (using 5-point global assessment scale from no disease to very severe disease)	The average subjective improvement of HS for all weight change categories (2% reported weight gain, 17% reported no change, 19% reported < 10lb loss, 33% reported 10-25lb loss, 16% reported 25-50lb loss, 13% reported >50lb loss) was about **0.6 points, except for patients losing >50lb who demonstrated an average subjective improvement of 1 point.**	Murad tool not applicable: -Response rate 70% -Selected sample -Moderate sample size

1. Kromann CB, Ibler KS, Kristiansen VB , Jemec GB. The influence of body weight on the prevalence and severity of hidradenitis suppurativa. Acta Derm Venereol 2014;94:553-7.
2. Verde L, Cacciapuoti S, Caiazzo G, Megna M, Martora F, Cavaliere A et al. Very low-calorie ketogenic diet (VLCKD) in the management of hidradenitis suppurativa (Acne Inversa): an effective and safe tool for improvement of the clinical severity of disease. Results of a pilot study. J Transl Med 2024;22:149.
3. Macklis PC, Tyler K, Kaffenberger J, Kwatra S , Kaffenberger BH. Lifestyle modifications associated with symptom improvement in hidradenitis suppurativa patients. Arch Dermatol Res 2022;314:293-300.

Diet Modifications Summary of Findings

Contents

e-Table 103. Yeast Exclusion Diets

Yeast exclusion diets for HS

Patient or population: HS of any severity undergoing surgical excision or standard HS treatments
Intervention: yeast restriction/exclusion diet
Comparison: Baseline condition pre-diet intervention

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)
Clinical severity assessed with: Improvement of HS symptoms follow-up: range 3 months to 12 months	**Abound 2020: 26/37 (70%)** participants reported HS symptom improvement with 6 years of brewer's and baker's yeast restriction followed by surgery. 87% of patients demonstrated an immediate recurrence of skin lesions less than a week after consuming food containing the yeast. Immunologic testing showed intolerance to yeast, wheat, and cow's milk in 20%, 29%, and 23% of patients, respectively. 49% reported weight loss following the diet. **Cannistra 2013: 12/12** patients demonstrated immediate stabilization of their clinical symptoms, and the skin lesions regressed over the 12-month treatment period (brewer's yeast-free diet following surgical excision); All of the patients showed an immediate recurrence (24-48 hours) of skin lesions following accidental or voluntary consumption of beer or other foods containing brewer's yeast and wheat. 12/12 patients had igG reaction to yeast prior to diet intervention. **Colboc 2016:** for 20 patients undergoing standard HS treatment & brewer's yeast exclusion diet, at 3 months intensity (0 -10 scale; higher score indicates greater intensity) of **inflammation (4.9 to 2.9p=0.018)** and **discharge (4.7 to 1.9 p=0.005)** were significantly lower. No weight loss was associated with the diet.	69 (3 non-randomised studies)[1-3]	⨁◯◯◯ Very low[a]
Pain assessed with: Pain in the previous month via NRS 0 to 10; Higher score indicates greater pain follow-up: 3 months	Mean pain scores decreased from 4.3 to 1.8; **Difference 2.5**	20 (1 non-randomised study)[3]	⨁◯◯◯ Very low[b]
Adherence assessed with: participants reporting "good adherence"; Scale poor, moderate, good follow-up: 3 months	**10/20** patients reported "good" adherence to the diet at 3 months.	20 (1 non-randomised study)[3]	⨁◯◯◯ Very low[b]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded 2 levels for imprecision: total sample across all studies 69.

b. Downgraded 2 levels for imprecision: total sample 20.

1. Aboud C, Zamaria N , Cannistrà C. Treatment of hidradenitis suppurativa: Surgery and yeast (Saccharomyces cerevisiae)-exclusion diet. Results after 6 years. Surgery 2020;167:1012-5.
2. Cannistrà C, Finocchi V, Trivisonno A , Tambasco D. New perspectives in the treatment of hidradenitis suppurativa: surgery and brewer's yeast-exclusion diet. Surgery 2013;154:1126-30.
3. H C, Fite C , Cannistra C. Interest of Brewer's Yeast-Exclusion Diet in the Management of Hidradenitis Suppurativa. Journal of Clinical & Experimental Dermatology Research 2016;7.

e-Table 104. Mediterranean Diet

Mediterranean diet compared to no Mediterranean diet for HS

Patient or population: Adults with HS of any severity
Intervention: Mediterranean diet
Comparison: no Mediterranean diet

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)
Clinical severity assessed with: Sartorius Score, Hurley Stage, or International Hidradenitis Suppurativa Severity Score System (IHS4) follow-up: Cross-sectional	**Barrea 2018:** Mean HS Sartorius scores were lower (indicating lesser disease severity) with increased adherence^ to the diet**: High adherence (n=9) 39 (SD 8.76) vs Average adherence (n=16) 51.37 (SD 9.81) vs Low adherence (n=16) 59.83 (SD 13.02).** **Bouwman 2024: No significant differences** in dietary adherence^^ scores were found between patients with Hurley Stage I vs Hurley Stages II or III (quantitative data not provided). (n=1004) **Lorite-Fuentes 2022:** On multivariate analysis higher adherence^ to a Mediterranean diet was related to lower **IHS4 score (p=0.03)** and lower self reported **Hurley stage (stages I-II vs III) p=0.01**. (n=221) **Velluzzi 2021: No association** was found between Mediterranean diet adherence^^ and HS severity as assessed by Hurley stage or Sartorius score (quantitative data not reported).(n=35) **Kesik 2024**: In HS patients, MEDAS score was negatively correlated with Hurely staging (r -0.58) and IHS4 score (r-0.687)	1351 (5 non-randomised studies)[1-5]	⊕◯◯◯ Very low[a,b]

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

^Adherence assessed via PREDIMED score
^^Adherence assessed via Mediterranean Diet Score
^^^Adherence assessed via Mediterranean Diet Adherence Scale

Explanations

a. Downgraded one level for RoB: The outcome of interest is minimally reported across all studies, uncontrolled, risk of selection bias
b. Downgraded one level for inconsistency: 3/5 studies suggest decreased severity with increased adherence, while 2 additional studies suggest no association between diet adherence and disease severity.

1. Barrea L, Fabbrocini G, Annunziata G, Muscogiuri G, Donnarumma M, Marasca C et al. Role of Nutrition and Adherence to the Mediterranean Diet in the Multidisciplinary Approach of Hidradenitis Suppurativa: Evaluation of Nutritional Status and Its Association with Severity of Disease. Nutrients 2018;11.
2. Bouwman K, Moazzen S, Kroah-Hartman M, Dijkstra G, Horváth B , Alizadeh BZ. Diet and physical activity as risk-reducing factors for hidradenitis suppurativa. J Eur Acad Dermatol Venereol 2024;38:910-9.
3. Lorite-Fuentes I, Montero-Vilchez T, Arias-Santiago S , Molina-Leyva A. Potential Benefits of the Mediterranean Diet and Physical Activity in Patients with Hidradenitis Suppurativa: A Cross-Sectional Study in a Spanish Population. Nutrients 2022;14.
4. Velluzzi F, Anedda J, Pisanu S, Dell'Antonia M, Deledda A, Boi A et al. Mediterranean diet, lifestyle and quality of life in Sardinian patients affected with Hidradenitis suppurativa. J Public Health Res 2021;11.
5. Kesik F, Dogan-Gunaydin S , Fisunoglu M. The Impact of Diet on Hidradenitis Suppurativa Severity: A Cross-Sectional Case-Control Study. Medicina (Kaunas) 2024;60.

e-Table 105. Intermittent Time-Restricted Circadian Fasting

Intermittent Time-Restricted Circadian Fasting compared to no intermittent Time-Restricted Circadian Fasting for HS

Patient or population: Adults with HS mean Hurley score 2.31 (0.77)on non-surgical standard systemic treatments
Intervention: Intermittent time-restricted circadian fasting
Comparison: Baseline before intermittent time-restricted circadian fasting

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intermittent Time-Restricted Circadian Fasting	**Risk with intermittent Time-Restricted Circadian Fasting**				
Clinical severity assessed with: change in IHS4 score^ follow-up: 1 months	Mean clinical severity before diet 11.00(SD 5.88)	MD **0.85 lower** (1.08 lower to 0.63 lower) P<0.0001	-	55 (1 non-randomised study)[1]	⨁◯◯◯ Very low[a]	
Adverse events assessed with: patients experiencing adverse events follow-up: 1 months	0/12 patients reported diet-related adverse events.			55 (1 non-randomised study)[1]	⨁◯◯◯ Very low[a]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **MD:** mean difference

Intermittent Time-Restricted Circadian Fasting compared to no intermittent Time-Restricted Circadian Fasting for HS

Patient or population: Adults with HS mean Hurley score 2.31 (0.77)on non-surgical standard systemic treatments
Intervention: Intermittent time-restricted circadian fasting
Comparison: Baseline before intermittent time-restricted circadian fasting

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intermittent Time-Restricted Circadian Fasting	**Risk with intermittent Time-Restricted Circadian Fasting**				

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

^ International Hidradenitis Suppurativa Severity Score System (IHS4); based on counting nodules, abscesses, and draing fistulas: mild (≤ 3 points), moderate (4–10 points) and severe (≥11 points)

Explanations

a. Downgraded two levels for imprecision: very small sample total n=55.

1. Damiani G, Mahroum N, Pigatto PDM, Pacifico A, Malagoli P, Tiodorovic D et al. The Safety and Impact of a Model of Intermittent, Time-Restricted Circadian Fasting ("Ramadan Fasting") on Hidradenitis Suppurativa: Insights from a Multicenter, Observational, Cross-Over, Pilot, Exploratory Study. Nutrients 2019;11.

e-Table 106. Diet Modifications (Case series)

Case series n=3, 687 patients

Overall Certainty of the Evidence: Very Low (The evidence comes from case series, which are inherently limited due to the lack of control groups and selection bias. Studies also relied on personal communication and patient surveys for outcome assessment. The individual studies mostly included small sample sizes, increasing concern about random error and imprecision. All studies were judged to have moderate or high risk of bias, further reducing confidence in the findings.)

Study details	Baseline characteristics	Intervention	Concomitant treatment	Time of outcome assessment	Outcome	Results	Risk of bias Murad tool
Dairy-free diet							

Danby 2015[1] Personal communication N=47	NR	Dairy-free diet without glycemic load restriction	NR	NR	Improvement of HS symptoms (undefined)	39/47 (83%) “improved to various degrees”; 0/47 worsened	Murad tool not applicable: -personal communication -minimal reporting
Kurzen 2019[2] Retrospective cohort & interview N=40	-Age: Mean 38.9 -16F, 24M -BMI: Mean 27.3 -Hurley Stage: I n=10, II n=15, III n=14	Low dairy & low carbohydrate diet	NR	NR	Improvement of HS symptoms (undefined)	7 patients reported "considerably improved HS" (total patients on diet not reported)	Murad tool not applicable: -minimal reporting
Various diets							
Macklis 2022[3] Survey N=591	NR	Various diets	NR	At least 2 months of diet intervention	Improvement in clinical severity via 5-point patient global assessment of disease (0=no disease; 4=Very severe disease)	Paleo (n=95), Keto (n=105), Gluten-free (n=115), Anti-inflammatory (n=130) and Low carbohydrate (n=145) diets all demonstrated >50% of respondents endorsing a subjective improvement with at least 7% endorsing a 2+ point subjective improvement; Mediterranean diet 10/25 endorsed improvement, 0 endorsed 2+ point improvement; Detox diet 11/22 reported subjective improvement.	-response rate unclear

1. Danby FW. Diet in the prevention of hidradenitis suppurativa (acne inversa). J Am Acad Dermatol 2015;73:S52-4.
2. Kurzen H , Kurzen M. Secondary prevention of hidradenitis suppurativa. Dermatol Reports 2019;11:8243.
3. Macklis PC, Tyler K, Kaffenberger J, Kwatra S , Kaffenberger BH. Lifestyle modifications associated with symptom improvement in hidradenitis suppurativa patients. Arch Dermatol Res 2022;314:293-300.

Contents

e-Table 107. Oral zinc gluconate

Oral zinc gluconate compared to standard care for HS

Patient or population: HS primarily Hurley stages I and II
Intervention: oral zinc gluconate
Comparison: standard care or no treatment

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)
Clinical severity assessed with: lesion count, mHSS, or IHS4 follow-up: range 4 months to 24 months	**Brocard 2007:** At least 6 months after initiating oral zinc gluconate, 90mg QD monotherapy 8/22 and 14/22 patients had complete (disappearance of all lesions) and partial (50%+ reduction in number of nodules and/or shorter cycle of each inflammatory lesion) remission, respectively. **Hessam 2016:** Following 3 months of oral zinc gluconate, 90 mg QD, combined with topical triclosan, 2% BID, median mHSS significantly decreased from 32.5 to 25(p <0.0001) (n=54). **Molinelli 2020:** Comparing oral zinc gluconate 90 mg +30 mg of nicotinamide once daily for 90 days to no treatment after a 12-week course of systemic antibiotics, at 4 months follow-up there was a significant difference in mean IHS4 scores between the treatment (n=47) and no treatment (n=45) groups: MD -2.20 (-3.25, -1.15) p<0.0001.	168 (3 non-randomised studies)[1-3]	⨁◯◯◯ Very low[a]
Adverse events assessed with: patients with AEs follow-up: range 3 months to 6 months	18/123 (14.6%) patients taking oral zinc for 3 to 6 months experienced adverse events including diarrhea, abdominal distension or pain, esophagitis, nausea/vomiting.	123 (3 non-randomised studies)[1-3]	⨁◯◯◯ Very low[a]
Quality of life assessed with: DLQI; higher score indicates greater negative impact of disease follow-up: 3 months	Following 3 months of oral zinc gluconate, 90 mg QD, combined with topical triclosan, 2% BID, patients experienced a significant improvement in median DLQI scores from baseline: 12.5 vs 8; p = 0.0386	40 (1 non-randomised study)[2]	⨁◯◯◯ Very low[b]
Disease progression assessed with: Disease flares follow-up: range 3 months to 4 months	**Hessam 2016:** Following 3 months of oral zinc gluconate, 90 mg QD, combined with topical triclosan, 2% BID, the median number of new boils or flare-ups during the latest 4 weeks decreased significantly from 3 to 1 (p = 0.0009); (n=54). **Molinelli 2020:** Comparing oral zinc gluconate 90 mg +30 mg of nicotinamide once daily for 90 days (n=47) to no treatment (n=45) after a 12 week course of systemic antibiotics, at 4 months follow-up the mean number of disease flares was significantly lower in the treatment group: **MD -4.30 (-5.41, -3.19) p=0.003** and mean weeks free of disease was significantly longer with treatment: **MD 15.00 weeks (13.90, 16.10), p=0.001.**	146 (2 non-randomised studies)[2, 3]	⨁◯◯◯ Very low[c]
Pain assessed with: VAS 10mm follow-up: 3 months	**Hessam 2016:** Following 3 months of oral zinc gluconate, 90 mg QD, combined with topical triclosan, 2% BID, median VAS score decreased from **3 at baseline to 2 (p = 0.7220)** (n=54). **Molinelli 2020:** Comparing oral zinc gluconate 90 mg +30 mg of nicotinamide once daily for 90 days (n=47) to no treatment (n=45) after a 12-week course of systemic antibiotics, at 4 months follow-up, mean VAS pain scores were significantly lower with treatment: **MD -4.5 (-5.59, -3.41) p=0.003**.	(2 non-randomised studies)[2, 3]	⨁◯◯◯ Very low[c]

Oral zinc gluconate compared to standard care for HS

Patient or population: HS primarily Hurley stages I and II
Intervention: oral zinc gluconate
Comparison: standard care or no treatment

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).**CI:** confidence interval

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded one level for imprecision: total sample 168.
b. Downgraded two levels for imprecision: total sample 40.
c. Downgraded one level for imprecision: total sample 146.

1. Brocard A, Knol AC, Khammari A , Dréno B. Hidradenitis suppurativa and zinc: a new therapeutic approach. A pilot study. Dermatology 2007;214:325-7.
2. Hessam S, Sand M, Meier NM, Gambichler T, Scholl L , Bechara FG. Combination of oral zinc gluconate and topical triclosan: An anti-inflammatory treatment modality for initial hidradenitis suppurativa. J Dermatol Sci 2016;84:197-202.
3. Molinelli E, Brisigotti V, Campanati A, Sapigni C, Giacchetti A, Cota C , Offidani A. Efficacy of oral zinc and nicotinamide as maintenance therapy for mild/moderate hidradenitis suppurativa: A controlled retrospective clinical study. J Am Acad Dermatol 2020;83:665-7.

e-Table 108. Oral vitamin D

Oral vitamin D compared to no vitamin D for HS

Patient or population: HS of any severity with vitamin D deficiency or insufficiency
Intervention: oral vitamin D until sufficiency
Comparison: Baseline standard care pre-vitamin D supplementation

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)
Clinical severity assessed with: Patients achieving ≥20 point reduction in Sartorius score follow-up: 6 months	At 6 months, **27/36 (75%)** of HS patients with vit D deficiency or insufficiency pre-treatment taking oral vitamin D (deficiency= 50.000 IU of Vitamin D/month; insufficiency =25.000 IU/month) until sufficiency achieved a ≥20 point reduction in Sartorius score	36 (1 non-randomised study)[1]	⨁◯◯◯ Very low[a]
Disease progression assessed with: reduction in nodules & flares from baseline follow-up: 6 months	At 6 months, HS patients with vitamin D deficiency pre-treatment taking oral vitamin D until sufficiency had a **51% mean reduction in the number of nodules (p=0.011)** and an **18% mean reduction in the number of flares (p=0.2041)** from baseline.	14 (1 non-randomised study)[2]	⨁◯◯◯ Very low[b]
Adverse events assessed with: patients experiencing adverse events follow-up: range 3 months to 6 months	**0/14** HS patients with vit D deficiency pre-treatment taking oral vit D until sufficiency experienced an adverse event during the 3-6 months treatment period.	14 (1 non-randomised study)[2]	⨁◯◯◯ Very low[b]

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded 2 levels for imprecision: total sample 36.
b. Downgraded 2 levels for imprecision: total sample 14.

1. Fabbrocini G, Marasca C, Luciano MA, Guarino M, Poggi S, Fontanella G , Cacciapuoti S. Vitamin D deficiency and hidradenitis suppurativa: the impact on clinical severity and therapeutic responsivity. J Dermatolog Treat 2021;32:843-4.
2. Guillet A, Brocard A, Bach Ngohou K, Graveline N, Leloup AG, Ali D et al. Verneuil's disease, innate immunity and vitamin D: a pilot study. J Eur Acad Dermatol Venereol 2015;29:1347-53.

e-Table 109. Liposomal magnesium and folic acid added to standard antibiotic care with normocaloric diet

MI 2000 mg, liposomal magnesium and folic acid + antibiotics compared to standard antibiotic care for HS

Patient or population: HS and impaired glucose metabolism with BMI between 25 and 29.9
Intervention: Myo-inositol 2000 mg (liposomal magnesium and folic acid) + topical antibiotic therapy (clindamycin gel 1%), systemic antibiotic therapy (clindamycin 300 mg b.i.d. and rifampicin 600 mg daily for 6 weeks) and a normocaloric diet^ for 6 months
Comparison: topical antibiotic therapy (clindamycin gel 1%), systemic antibiotic therapy (clindamycin 300 mg b.i.d. and rifampicin 600 mg daily for 6 weeks) and a normocaloric diet for 6 months

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with standard antibiotic care + diet	**Risk with MI 2000 mg+ antibiotics + diet**				
Clinical severity-Sartorius score assessed with: mean percentage change in Sartorius score follow-up: 6 months	Patients taking Myo-inositol 2000 mg, liposomal magnesium + folic acid in addition to standard antibiotic interventions, and a normocaloric diet had a significant mean percentage reduction in Sartorius score **-28%, p<0.04** from baseline. While, patients on standard antibiotic therapy and normocaloric diet had a nonsignificant mean reduction of **-19%, p-0.55**.			20 (1 non-randomised study)[1]	⨁◯◯◯ Very low[a,b]	
Clinical severity- HiSCR50 assessed with: 50%+ reduction in total abscess and inflammatory nodule count, with no increase in abscess count, and no increase in draining fistula count relative to baseline follow-up: 6 months	100 per 1,000	**400 per 1,000** (54 to 1,000)	**RR 4.00** (0.54 to 29.81)	20 (1 non-randomised study)[1]	⨁◯◯◯ Very low[c]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

^No information on weight reduction with diet component but noted improvement in glycemic profile acros treatment arms

Explanations

a. Downgraded 1 level for RoB: incomplete outcome reporting.
b. Downgraded 2 levels for imprecision: total sample 20.
c. Downgraded 2 levels for imprecision: The CI crosses both the MID thresholds for harm and benefit (0.75 or 1.25).

1. Donnarumma M, Marasca C, Palma M, Vastarella M, Annunziata MC , Fabbrocini G. An oral supplementation based on myo-inositol, folic acid and liposomal magnesium may act synergistically with antibiotic therapy and can improve metabolic profile in patients affected by Hidradenitis suppurativa: our experience. G Ital Dermatol Venereol 2020;155:749-53.

e-Table 110. Staphage lysate vs placebo

Staphage lysate compared to placebo for hidradenitis suppurativa[1]

Patient or population: chronic recurrent hidradenitis suppurativa
Intervention: Staphage lysate 0.6 ml as an aerosol and 0.3 ml staphage lysate sc, once weekly for 20 weeks
Comparison: Vehicle placebo 0.6 ml as an aerosol and 0.3 ml s/c, once weekly for 20 weeks

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	**Risk with staphage lysate**				
Achieving PGA (judged to be 'improved') follow-up: 24 weeks	133 per 1000	**833 per 1000** (224 to 1000)	**RR 6.25** (1.68 to 23.27)	27 (1 RCT)	⨁⨁◯◯ Low[a]	
Adverse events follow-up: 24 weeks	0 per 1000	**0 per 1000** (0 to 0)	Not estimable	25 (1 RCT)	⨁⨁◯◯ Low[b]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

1. Angel MF RS, Manders EK, Granfield D, & Futress JW. Beneficial effects of staphage lysate in the treatment of chronic recurrent hidradenitis suppurativa. 1987;38.