Efficacy of non-surgical monotherapies for hidradenitis suppurativa: a systematic review and network meta-analyses of randomized trials

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ABSTRACT
Objective: We determined the relative efficacy of non-surgical monotherapies for hidradenitis suppurativa (HS).
Methods: Network meta-analyses were conducted to determine treatments’ surface under the cumulative ranking curve (SUCRA) value (i.e. an estimate that ranks efficacy); pairwise comparisons were conducted.
Results and conclusions: Ten trials were eligible for quantitative analyses; however, all did not have a common endpoint. Outcomes corresponded to pain severity, clinical response, quality of life and abscess count. For pain reduction, infliximab was ranked most efficacious (SUCRA = 94%) compared to bimekizumab, anakinra and placebo; infliximab reduced pain more significantly (\( p < .05 \)) than anakinra and then placebo. For the occurrence of clinical response, bimekizumab had the highest SUCRA (67%) relative to adalimumab, anakinra and placebo; bimekizumab was more efficacious than placebo (\( p < .05 \)). For the quality of life in mild HS, Botox had the highest SUCRA (94%) compared to adalimumab and placebo; Botox was more efficacious than placebo (\( p < .05 \)). For reduction in abscess count, oral tetracycline had the highest SUCRA (48%) compared to topical clindamycin and vehicle. Our work—being the first NMA study on non-surgical HS monotherapies—contributes to the comparative effectiveness literature for this condition.

Introduction
Hidradenitis suppurativa (HS) was first described in 1839 by the French surgeon Alfred Velpeau (1,2). It is a chronic and painful inflammatory skin condition of multifactorial etiology. According to the comprehensive literature review by Ingram (2020) (3), the prevalence of this disorder remains unresolved. Given that this condition occurs at sites that are rich in hair follicles, HS was believed to be linked to bacterial infection in the apocrine glands (4,5). However, the current body of evidence supports that HS is primarily an inflammatory disorder initiated by hair follicle dysfunction (1,6–10).

While surgical intervention is a treatment option, numerous noninvasive modalities exist (1). Topical and systemic antibiotics have been used to treat HS; newer treatment modalities include immunomodulatory therapies such as inhibitors of tumor necrosis factor-alpha (TNF-\( \alpha \)), interleukin-1 (IL-1) and selective phosphodiesterase-4 (PDE-4) (11). Adalimumab and infliximab are well-known TNF-\( \alpha \) inhibitors whose efficacies have been determined in various randomized trials for HS; apremilast, a PDE-4 inhibitor, and the IL-1 inhibitor anakinra are among the HS therapies that have been investigated more recently (1,11,12). Results from single-arm studies have shown that interleukin-17 antagonists, such as brodalumab and secukinumab, are effective in treating HS (13–15).

There is a paucity of head-to-head evidence for the relative efficacy of non-surgical treatments for HS (16). We systematically reviewed the literature to identify randomized trials that evaluated the efficacy of non-surgical monotherapies for HS; data from these trials were used to determine the relative efficacy of such therapies using network meta-analyses (NMAs).

Methods
Our work was conducted under the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Appendix S1 of Supporting Information). This study was registered with the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42018096927) (Appendix S2 of Supporting Information).

Search details are provided in Appendix S3 (see Supporting Information); systematic searches were made in PubMed, Scopus, EMBASE, EU Clinical Trials Register (https://www.clinicaltrialsregister.eu/), and ClinicalTrials.gov (https://clinicaltrials.gov/). Eligible studies were randomized trials on non-surgical monotherapies for HS; trials published in a non-English language were ineligible. As per our eligibility criteria, no specific endpoint was specified \textit{a priori}: given that core outcome sets (COSs) for HS were not established until very recently (17), we did not expect all the eligible studies to have one or more endpoints in common.
Data were extracted from tables, figures and textual content; extracted information included baseline characteristics and outcome data. More information pertaining to the data extraction process is provided in Appendix S3 (see Supporting Information). The quality of evidence was evaluated using the van Tulder scale (18).

Each network was depicted with a network plot, which can be defined as a diagram of nodes and edges. Each node represents a treatment; an edge, the line between two nodes, corresponds to a pairwise comparison of efficacy from direct evidence. Statistical consistency would be assessed if networks had closed loops (19).

Our NMAs were arm-based and were conducted using a Bayesian random-effects model with uniform priors; for each NMA, four Markov Chain Monte Carlo (MCMC) chains were used where each had 20,000 iterations. Pairwise comparisons of interventions within a given network were presented in league tables. For every network, we computed treatments’ surface under the cumulative ranking curve (SUCRA) value; a treatment’s SUCRA corresponds to their overall rank of efficacy. Statistical analyses were conducted with the software RStudio; the gemtc and BUGsnet packages were used (19,20). In all analyses, the alpha was set to 5%.

Results

Ten randomized trials were eligible for quantitative analyses (Figure 1) (21–29); with the available data across these studies, we were able to construct six networks and details thereof—including endpoint definition—are presented in Table 1. None of the 10 trials had a common measure of outcome; however, some studies had some endpoints in common. In addition to controls (i.e. placebo), eight treatment modalities were considered across the six networks (adalimumab, anakinra, bimekizumab, botulinum toxin type B (Botox-B), clindamycin (topical), infliximab, MABp1 (also known as bermekimumab), and tetracycline (oral)). The common endpoints pertained to pain severity, clinical response, quality of life and abscess count (Table 1). Characteristics of the eligible studies are detailed in Table 2; the earliest one was published by

![Figure. 1 Flow chart depicting inclusion of studies.](image)

**Table 1.** Brief description of the six networks.

| Network | Studies | Outcome/endpoint | Interventions compared | N (sample size of network) |
|---------|---------|------------------|------------------------|---------------------------|
| Ia² | Grant et al. (23), Tzanetakou et al. (30), Kanni et al. (27) | Reduction in skin pain as per the VAS at 8 weeks | Infliximab, anakinra, mabp1², placebo | 72 |
| Ib² | Miller et al. (24), Tzanetakou et al. (30) | Reduction in skin pain as per the VAS at 12 weeks | Adalimumab, anakinra, placebo | 40 |
| Iia³ | Tzanetakou et al. (30), Kimball et al. (26), EudraCT Number: 2017-000892-10 (29) | Clinical response as per the HiSCR at 12 weeks | Anakinra, adalimumab, bimekizumab, placebo | 743 |
| Iib³ | Tzanetakou et al. (30), Kanni et al. (27) | Clinical response as per the HiSCR at 12 weeks | Anakinra, mabp1³, placebo | 40 |
| IIb² | Miller et al. (24), Grimstad et al. (28) | Improvement in quality of life as per DLQI at 12 weeks | Adalimumab, botox-b, placebo | 41 |
| IVc | Clemmensen (21), Jemec & Wendelboe (22) | Reduction in mean number of abscesses at 4 weeks | Clindamycin, tetracycline, vehicle | 61 |

Abbreviations: Botox-B: botulinum toxin type B; DLQI: dermatology life quality index; HiSCR: hidradenitis suppurativa clinical response score; VAS: visual analogue scale

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²Across all the trials, patients with moderate to severe hidradenitis suppurativa were included.

³The trial by Miller et al. (24) included patients with Hurley stage II to III—while the one by Grimstad et al. (28) included patients with Hurley stage I to III. Thus, disease severity was adjusted for through network meta-regression.

⁴Given that the Hurley staging system—that was developed in 1989 (60,61)—did not exist when the trial by Clemmensen (21) was published, the disease severity of the patients therein—and their counterparts in the trial by Jemec & Wendelboe (22)—were deemed to be homogenous: patients with Hurley stage I to II hidradenitis suppurativa were included in the trial by Jemec & Wendelboe (22), while Clemmensen (21) included patients with moderate hidradenitis suppurativa.

⁵MABp1 is currently known as bermekimumab (62).
### Table 2. Characteristics of the included studies.

| Author                  | Trial duration and baseline characteristics | Intervention                                                                 | Sample size after randomization |
|-------------------------|---------------------------------------------|-------------------------------------------------------------------------------|---------------------------------|
| Clemmensen (21)         | Trial duration: 12 weeks                    | Arm 1: clindamycin hydrochloride 1% topical solution in a vehicle that is constituted of: 80% isopropanol, 10% propylene glycol, and 9% water | 15                              |
|                         | Number of participants: 30 patients entered the trial; however, 27 of them completed it | Arm 2: vehicle                                                              | 15                              |
|                         | Demographic information (based on the 27 participants): |                                                                                |                                 |
|                         | - 21 women and 6 men                         |                                                                                |                                 |
|                         | - mean age was 31.3 years (range was 18–59 years) |                                                                                |                                 |
| Jemec et al. (22)       | Trial duration: 16 weeks                    | Arm 1: tetracycline (500 mg twice daily)                                      | 24                              |
|                         | Number of participants: 46 participants entered the trial; however, 34 of them completed it | Arm 2: clindamycin phosphate 1% topical solution in a vehicle of propylene glycol, isopropyl alcohol, and water | 22                              |
|                         | Demographic information (based on the 46 participants): |                                                                                |                                 |
|                         | - 39 women and 7 men                         |                                                                                |                                 |
|                         | - mean age of subjects in the oral tetracycline group was 31.8 years (95% CI: 27.3–36.5), while the mean age of subjects in the topical clindamycin group was 33.3 years (95% CI: 28.9–37.8) |                                 |                                 |
| Grant et al. (23)       | Trial duration: 52 weeks. This trial study had 3 phases, and the current study only focused on the 1st one, i.e. the double-blind placebo-controlled phase; this phase was for 8 weeks. | Arm 1: infliximab (5mg/kg) at weeks 0, 2, and 6 | 15                              |
|                         | Number of participants: 38 subjects entered the trial | Arm 2: placebo                                                              | 23                              |
|                         | Demographic information (based on the 38 participants): |                                                                                |                                 |
|                         | - 26 women and 12 men                        |                                                                                |                                 |
|                         | - mean age of subjects in the infliximab group was 34 years (±SD = 13.44), while those of subjects of the placebo group was 33.2 years (±SD = 11.42) |                                                                                |                                 |
| Miller et al. (24)      | Trial duration: 24 weeks; the first 12 weeks was the treatment period, while the last 12 weeks was an observational period (i.e. a period where subjects received no treatment). | Arm 1: adalimumab 80 mg subcutaneous at baseline, followed by 40 mg subcutaneous every other week for 12 weeks. | 15                              |
|                         | Number of participants: 21 patients entered the trial | Arm 2: placebo                                                              | 6                               |
|                         | Demographic information (based on the 21 subjects): |                                                                                |                                 |
|                         | - There were 17 women and 4 men              |                                                                                |                                 |
|                         | - The mean (95% CI) age of subjects in the adalimumab and placebo groups were 38.7 (30.9–46.4), and 40.2 (25.8–54.5), respectively. |                                                                                |                                 |
| Tzanetakou et al. (30)  | Trial duration: The treatment phase of the trial was for 12 weeks. | Arm 1: anakinra 100 mg subcutaneous in a volume of 0.67 mL once daily for 12 weeks | 10                              |
|                         | Number of participants: 20 subjects were randomized to receive anakinra or placebo | Arm 2: placebo (0.67 mL of sterile water)                                    | 10                              |
|                         | Demographic information (based on 19 of the 20 subjects who completed the study): |                                                                                |                                 |
|                         | - There were 9 women and 10 men              |                                                                                |                                 |
|                         | - The mean ages (±SD), in years, of subjects in the anakinra and placebo groups, were 42.8 (±13.8), and 36 (±11.3), respectively. |                                                                                |                                 |
| Kimball et al. (PIONEER I) (26) | Trial duration: This trial had 2 periods, where the 1st and 2nd spanned 12 and 24 weeks, respectively. The current study focused on the 12-week period. | Arm 1: adalimumab 40 mg subcutaneous once weekly for 12 weeks | 153                             |
|                         | Number of participants: There were 307 subjects where 153 were randomized to 40mg | Arm 2: placebo                                                              | 154                             |

(continued)
| Author                  | Trial duration and baseline characteristics                                                                 | Intervention                                                                 | Sample size after randomization |
|------------------------|-------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|---------------------------------|
| Kanni et al. (27)      | Trial duration: The first treatment phase was for 12 weeks (and the current study focused on the first treatment phase). | Arm 1: placebo  
Arm 2: adalimumab  
Arm 3: bimekizumab                                                                  | 22  
22  
46                                                                 |
| Grimstad et al. (28)   | Trial duration: 6 months (the 1st three months was the blinded placebo-controlled phase)                   | Arm 1: Botox-B was injected intradermally into each lesion; the concentration differed by lesion location; a maximum of 150 units (U), 200U and 600U could be administered to the axilla, groin and perianal (or perigenital) regions, respectively. A maximum dose of 1300 U per session  
Arm 2: placebo (saline)                                                      | 10  
10                                                                 |

Abbreviations: CI: confidence interval; SD: standard deviation; BTX-B: botulinum toxin type b.
Clemmensen (21). Quantitative evaluation of evidence quality is presented in Table 3. To make each network homogenous, we used studies across which outcome(s) were measured at a given time point, and in patients with similar disease severity. Trials that met our eligibility criteria, but whose data were not included in our quantitative analyses, are listed in Table 4. Most of these studies were excluded because the endpoints therein were incongruent with those of our networks. For instance, the three endpoints Fajgenbaum et al. (2020) (36) used were ‘patient satisfaction after 14 days’, ‘pain reduction after 5 days’, and ‘mean duration to the resolution of lesions’ (Table 1). Ineligible (i.e. observational) studies that investigated the efficacy of HS monotherapies are listed in Table 5. As per the published literature, a repertoire of modalities were investigated with observational study designs (Table 5); for example, Romani et al. (2019) (40) retrospectively examined the effectiveness of ustekinumab.

Plots of the six networks are presented in Figure 2. Most of our networks did not have a closed loop, so analyses of inconsistency could not be undertaken. However the transitivity assumption was not violated.

**Clinical response**

Network Ila pertained to the simultaneous comparison of adalimumab, anakinra, bimekizumab and placebo in terms of occurrence of a clinical response—as per the Hidradenitis Suppurativa Clinical Response (HiSCR)—at 12 weeks of follow up—for moderate to severe HS (Table 1). A HiSCR is defined as the occurrence of an at least 50% reduction in the count of inflammatory lesions from baseline, in addition to the absence of new fistulas and abscesses (41).

Meta-analyzing data from trials that investigated bermekimab (formerly known as MABp1) and adalimumab in one network would arguably violate the transitivity assumption as subjects’ eligibility for receiving bermekimab was predicated on their non-eligibility for adalimumab (27). Hence, we created ‘network IIb’ which—for the same outcome as network Ila—simultaneously compared anakinra, bermekimab and placebo (Table 1). Bimekizumab has the highest SUCRA in network Ila (67.38%), while bermekimab had the highest SUCRA in network IIb (82.8%) (Figure 3). Pairwise analyses showed that a HiSCR, on average, was significantly more likely to occur with adalimumab than with placebo (odds ratio = 3.3, p < .05) (Figure 4).

**Pain severity**

Network Ia (Figure 2.) pertained to the simultaneous comparison of infliximab, bermekimab, anakinra and placebo in terms of pain reduction at 8 weeks of follow up for moderate to severe HS (Table 1); pain was evaluated using the visual analogue scale.
(VAS). Infliximab had the highest SUCRA (96.4%) (Figure 3). Furthermore, pairwise analyses showed that infliximab, on average, reduced VAS pain scores significantly more than placebo (mean difference = 8.4, \( p < 0.05 \)) (Figure 4).

Network Ib pertained to the simultaneous comparison of adalimumab, anakinra and placebo in terms of reduction in VAS pain scores at 12 weeks of follow up for moderate to severe HS (Table 1). Adalimumab had the highest SUCRA (67.4%) (Figure 3), and pairwise analyses found no significant comparison (Figure 4).

Quality of life

Network III pertained to the simultaneous comparison of Botox-B, adalimumab and placebo in terms of improvement in Dermatology Life Quality Index (DLQI) scores at 12 weeks of follow up (Table 1); the DLQI is a widely used measure for quality of life (42). Data for this network were obtained from Miller et al. (24) and Grimstad et al. (28); the former study included patients with Hurley stage II–III HS, while the latter included their counterparts with Hurley stage I – III HS (24,28). Hence, we conducted network meta-regression to adjust for disease severity; we created a variable for proportion of individuals who had Hurley stage I (where 1.0 corresponded to all individuals having stage I, 0 corresponds to all individuals having stage II–III).

For stage I HS, Botox-B had the highest SUCRA (94.2%) (Figure 3); pairwise analyses showed that Botox-B, on average, improves DLQI scores significantly more than placebo (mean difference = 8.4, \( p < 0.05 \)) for stage II–III HS, Botox-B also had the highest SUCRA (91.9%), however pairwise analyses showed no significant comparisons (Figure 4).

Abscess reduction

Network IV pertained to the simultaneous comparison of oral tetracycline, topical clindamycin and vehicle (topical) in terms of reduction in mean number of abscesses at 4 weeks for moderate HS (Table 1). Oral tetracycline had the highest SUCRA (47.6%) (Figure 3), and pairwise analyses found no significant comparisons (Figure 4).

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Table 4. Studies that met eligibility criteria, but were excluded from quantitative analyses.

| Authors (or ClinicalTrial.gov ID) | Comparators | Reason for exclusion<sup>a,b</sup> |
|----------------------------------|-------------|----------------------------------|
| Tierney et al. (31)              | Neodymium-doped-yttrium–aluminium–garnet (Nd:YAG) laser, clindamycin | Incongruent endpoints |
| Adams et al. (32)                | Etanercept, placebo | Incongruent endpoints |
| Highton et al. (33)              | Intense pulsed light therapy, no treatment | Incongruent endpoints |
| Kimball et al. (34)              | Adalimumab (2 doses), placebo | Incongruent endpoints |
| Vossen et al. (35)               | Apremilast, placebo | Incongruent endpoints |
| Fajgenbaum et al (36)            | Intraleisional triamcinolone (2 doses), placebo | Incongruent endpoints |
| Mahmoud et al. (37)              | Clindamycin and benzoyl peroxide (i.e. combination) with Nd:YAG laser, clindamycin and benzoyl peroxide (i.e. combination) | Incongruent endpoints |
| Fadel & Tawfik (38)              | Intense pulsed laser with the photosentizer ‘niosomal methylene blue’ (NMB) gel, intense pulsed laser with the photosentizer ‘free methylene blue’ (FMB) gel | Incongruent endpoints |
| Wilden et al. (39)               | Intense pulsed light (IPL), radiofrequency (RF), IPL and RF (i.e. combination) | Incongruent endpoints |
| NCT03827798                     | CFZ533, placebo | Results unavailable |
| NCT03054155                     | Alexandrite laser (755 nm) | Results unavailable |
| NCT03926169                     | Risankizumab, placebo | Results unavailable |
| NCT03607487                     | INCB054707, placebo | Results unavailable |
| NCT04242498                     | Bimekizumab, placebo | Results unavailable |
| NCT04242446                     | Bimekizumab, placebo | Results unavailable |
| NCT04430855                     | Upadacitinib, placebo | Results unavailable |
| NCT04218422                     | Battlefield acupuncture, sham acupuncture | Results unavailable |
| NCT03713632                     | Secukinumab, placebo | Results unavailable |
| NCT03713619                     | Secukinumab, placebo | Results unavailable |
| NCT04493502                     | LY3041658, placebo | Results unavailable |
| NCT0421172                      | CJM112, placebo | Results unavailable |
| NCT03103074                     | Botulinum b toxin, placebo | Results unavailable |
| NCT00494351                     | Long-pulsed Nd:YAG laser (1064 nm) (intra-patient) | Results unavailable |
| NCT03628924                     | 3 Doses of guselkumab, and placebo | Results unavailable |
| NCT03049267                     | 3 Doses of intraleisional triamcinolone, and placebo | Incongruent endpoints |
| NCT0349267                      | Apremilast, placebo | Results unavailable |
| NCT04476043                     | INCB054707, placebo | Results unavailable |
| NCT03852472                     | Avacopan, placebo | Results unavailable |
| NCT04019041                     | Bermekimab, placebo | Results unavailable |
| NCT04092452                     | PF 06650833, PF 0670841, PF 06826647, placebo | Results unavailable |
| NCT03487276                     | IFX-1, placebo | Results not finalized |

<sup>a</sup>Results unavailable: results were not available on the ClinicalTrials.gov website.

<sup>b</sup>Incongruent endpoints: The endpoints were not concordant with that of any of our six networks (description of the networks, including endpoint definition, are provided in Table 1).
incorporate quality of evidence into its estimation of rank abilities) (44). Clinical decisions are more informed when based

Secondly, the NMA technique currently does not

ture; most published systematic reviews have this language limi-

include HS treatments investigated in single-arm studies, case

non-randomized studies, our simultaneous comparison did not

point across the 10 trials included in quantitative analyses

therapies for the treatment of HS. We found no common end-

Discussion

We determined the relative efficacies of non-surgical mono-

for pain and QoL (17). We determined the relative efficacies of

Moreover, the recently published COSs for HS include domains

subjective experiences (48). The use of this instrument is wide-

HS treatments on patients’ assessment of their life quality as per the DLQI. Like

Table 5. Ineligible (i.e. non-randomized) studies that investigated the effect of hidradenitis suppurativa monotherapies.

| Authors (or ClinicalTrials.gov ID) | Design | Comparator(s) |
|----------------------------------|--------|---------------|
| Fardet et al. (63) | Retrospective single-arm | Infliximab |
| Lee et al. (64) | Prospective single-arm | Etanercept |
| Yazdanyar et al. (65) | Case series | Dapsone |
| Randhawa et al. (66) | Case series | Finasteride |
| Anderson et al. (67) | Case series | Cyclosporine |
| Delaunay et al. (68) | Retrospective single-arm | Ofloxacin with clindamycin (i.e. Combination) |
| Caro et al. (69) | Retrospective cohort | Clindamycin with rifampicin (i.e. Combination), clindamycin |
| Romani et al. (70) | Retrospective single-arm | Ustekinumab |
| NCT03512275 | Single group assignment | Bemekimab |
| NCT03569371 | Single group assignment | Incb054707 |
| NCT02786576 | Prospective cohort | Adalimumab |
| NCT04756336 | Prospective cohort | Ltx-109 gel |
| NCT01516749 | Single group assignment | Anakinra |
| NCT03894956 | Prospective cohort | Humira |
| NCT00329623 | Single group assignment | Etanercept |
| NCT03001622 | Single group assignment | Ixf-1 |
| NCT03099980 | Single group assignment | Secukinumab |
| NCT02949002 | Single group assignment | Adalimumab |
| NCT01704534 | Single group assignment | Ustekinumab |
| NCT02695212 | Single group assignment | Apremilast |
| NCT01635764 | Single group assignment | Adalimumab |
| NCT02805595 | Single group assignment | 23.4% Hypertonic saline, saline |
| NCT00134134 | Single group assignment | Efalizumab |
| NCT00827996 | Single group assignment | Adalimumab |
| NCT00395187 | Single group assignment | Photodynamic therapy |
| NCT00107991 | Single group assignment | Etanercept |
| NCT03972280 | Sequential assignment | Cis24 |
| NCT02896920 | Prospective cohort | Humira |
| NCT00949546 | Prospective cohort | Etanercept |
| NCT03275870 | Single group assignment | Hydroxychloroquine |
| NCT04099212 | Case study | Topical resorcin |
| NCT04449354 | Single group assignment | Hidrawear Ax |

Given that diminished quality of life (QoL) and skin pain are consequences of HS (46), treatments that address pain and well-

are extremely important to persons with HS (47). Guidelines

recommend antibiotics as a treatment modality (56). Hendricks

et al. (2019) compared nine international HS management
guidelines and found that all nine—including the 2018 British
Association of Dermatologists HS guidelines (55); this guide-
line recommends treating HS with oral tetracyclines such as
lymecycline and doxycycline. North American guidelines also
recommend antibiotics as a treatment modality (56). We found that oral tetracycline ranked more efficacious than
topical clindamycin for HS management insofar as reducing
number of abscesses; this supports clinicians’ belief of systemic
antibiotics being more effective than their topical counterparts
in HS care. This is also congruent with the 2018 British
Association of Dermatologists guidelines for HS (55); this guide-
line recommends treating HS with oral tetracyclines such as
lymecycline and doxycycline. North American guidelines also
recommend antibiotics as a treatment modality (56). Hendricks
et al. (2019) compared nine international HS management
guidelines and found that all nine—including the 2018 British
Association of Dermatologists HS guidelines—recommend oral
tetracycline as a first-line option (57).

Adalimumab is approved by the Food and Drug Administration (FDA) for treatment of HS (58); this TNF-α inhibi-
tor is also approved by the European Medicine Agency (EMA)
(59). Of the 10 trials that were included in our quantitative anal-
yses, the one by Kimball et al. (34)—where adalimumab was
investigated—had the highest quality score as per the van
Tulder scale. Adalimumab has been recommended as a first-line
biologic in at least nine clinical guidelines including the 2015
European Academy of Dermatology and Venerology; across
these guidelines, infliximab has been recommended as a
second-line therapy (57). Guidelines’ recommendation of inflix-
imbab as a second-line therapy—while adalimumab is a first-line
option—can be due to the fact that randomized-controlled trials
for infliximab are fewer, in addition to being of smaller sample
sizes (57).
Various clinical guidelines for HS management—including the 2018 British Association of Dermatologists—suggest that more evidence regarding the efficacy of anakinra is essential for consideration of it as a first-, second-, or third-line treatment option.

We simultaneously compared the efficacy of various non-surgical monotherapies for HS; all the included studies did not have a common outcome; however, various endpoints were common in some trials. Therefore, we were able to determine the relative efficacy of non-surgical HS monotherapies as per endpoints pertaining to pain severity, clinical response, quality of life and reduction in abscess count. For pain reduction, infliximab had the highest SUCRA (94%) compared to bermekimab (47%), anakinra (34%) and placebo (23%); the mean difference in pain reduction for infliximab vs. anakinra, and infliximab vs. placebo were 30 and 33, respectively. For occurrence of clinical response (as per a HiSCR), bimekizumab had the highest SUCRA (67%) when compared to adalimumab (64%), anakinra (49%) and placebo (19%); the odds of having a clinical response was significantly higher with adalimumab than with placebo (odds ratio = 3.3, p < .05). For quality of life in mild HS, Botox-B had the highest SUCRA (94%) compared to adalimumab (43%) and

Figure 2. Plots of the respective networks. The endpoints corresponding to each of these networks are defined in Table 1. The geometry of the network was represented through network plots. Such plots are characterized by nodes and edges (i.e. the lines between two nodes that represent a comparison from direct evidence). Nodes correspond to an intervention. The number of studies contributing to direct evidence is listed in the edges.
Figure 3. Surface under the cumulative ranking curve (SUCRA) values for treatments in the respective networks. Abbreviations: Botox-B: botulinum toxin type b.

| Treatment         | Network Ia (pain) | SUCRA (%) | Network Ib (pain) | SUCRA (%) | Network Ila (clinical response) | SUCRA (%) |
|-------------------|-------------------|-----------|-------------------|-----------|--------------------------------|-----------|
| infliximab        |                   | 96.43     | adalimumab        | 67.42     | bimekizumab                    | 67.38     |
| bermekimab        |                   | 46.93     | anakinra          | 51.01     | adalimumab                     | 64.0      |
| anakinra          |                   | 33.83     | placebo           | 31.59     | anakinra                       | 49.33     |
| placebo           |                   | 23.14     |                   |           | placebo                         | 19.30     |

| Treatment         | Network Ila (pain) | SUCRA (%) | Network IIa (clinical response) | SUCRA (%) |
|-------------------|-------------------|-----------|--------------------------------|-----------|
| treatment         |                   |           | treatment                      |           |
|                   |                   |           | bimekizumab                    | 67.38     |
|                   |                   |           | adalimumab                     | 64.0      |
|                   |                   |           | anakinra                       | 49.33     |
|                   |                   |           | placebo                         | 19.30     |

Figure 4. League tables for the pair-wise comparisons of hidradenitis suppurativa treatments, in terms of endpoints of the six networks (i.e. Networks Ia, Ib, Ila, IIa, III and IV, see Table 1 for more details of the networks). The league tables for Networks Ila and IIb correspond to pairwise comparisons in terms of the log odds ratio (and 95% credible intervals in parentheses). For all the other networks, pairwise comparisons correspond to mean differences (and 95% credible intervals in parentheses). Each cell compares the column against the row. Alpha was set to 5%, and cells with "**" correspond to statistically significant results (i.e. \( p < .05 \)). Abbreviations: Botox-B: botulinum toxin type b.
placebo (12%); Botox-B had significantly better-quality scores than placebo (mean difference = 8.40, p < .05). Our work is the first to determine the relative efficacy of HS monotherapies; our findings contribute to the comparative effectiveness literature for HS treatments. Our results support the conduct of future randomized trials with consistent endpoints, and larger sample sizes. Such trials would eventually allow for more statistically powered meta-analyses which, in turn, could permit clinicians to more confidently make therapeutic decisions in HS care.

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