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Taiwanese Dermatological Association (TDA) consensus recommendations for the definition, classification, diagnosis, and management of hidradenitis suppurativa

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ABSTRACT

Hidradenitis suppurativa (HS) is a chronic inflammatory follicular disease characterized by painful, recurrent, inflamed lesions most commonly occurring in the axillary, inguinal, and anogenital regions. HS can inflict immense physical and psychological impact on patients who suffer from this distressing disease. Management of HS generally requires combining various medical and procedural treatment modalities; however, the disease is often recalcitrant to conventional treatments. In light of recent evidence supporting the effectiveness of biologic agents in the treatment of HS, the Taiwanese Dermatological Association established an expert panel of nine dermatologists to develop consensus statements aimed to provide up-to-date evidence-based guidance in optimizing HS patient management in Taiwan. The recommendations described in the statements were summarized in a management algorithm in terms of general care, topical treatment, systemic treatment, and procedural treatment.

Introduction

Hidradenitis suppurativa (HS), also known as acne inversa, is a chronic relapsing inflammatory follicular disease that presents as inflamed lesions in intertriginous parts of the body, including axilla, groin, anogenital region, submammary area, buttocks, nape, post-auricular area, and abdominal folds [1–3]. HS lesions are painful and disfiguring, causing immense physical and psychological burden in patients who suffer from this disease [2]. Lesions appear as deep-seated nodules that can expand and coalesce to form large abscesses which

subsequently progress to draining skin tunnels, and when the tunnels reach the skin surface and rupture, purulent fluid is discharged [2,4]. Fibrosis during the healing process leads to extensive rope-like scarring and can potentially reduce mobility [2,5]. Long-standing untreated disease in the genitoanal area may lead to perinanal or urethral fistulae formation [6].

HS management frequently requires a combination of medical and surgical treatment approaches [7]. HS is often recalcitrant to conventional treatments, and investigations of new therapies in recent years have shown promise in improving patient outcomes; however,

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significant unmet clinical needs remain [8]. A US and European survey study published in 2022 found that despite being actively treated by a dermatologist, nearly half of HS patients still suffered from pain and discomfort from lesions [9]. Therefore, the Taiwanese Dermatological Association (TDA) established an expert panel to develop evidence-based consensus recommendations for the management of patients with HS that take into account recommendations from recent international guidelines and current expert opinion. The aim of these consensus recommendations is to provide guidance in clinical decision-making to optimize HS management in Taiwan.

Methods

TDA established an expert panel of nine dermatologists experienced in the management of patients with HS. After careful consideration of available evidence and existing international guidelines, statements related to the clinical management of HS were drafted. For treatment recommendations, the quality of evidence supporting each statement was classified based on the Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence criteria (Table 1) [10]. A face-to-face meeting was conducted to discuss the evidence and experts' opinions related to each statement and to modify the statements as needed. Once the statements were finalized, the panel members expressed their agreeance to each statement as 'strongly agree', 'agree', or 'disagree'. For each statement, if at least two-thirds of polled members indicated 'strongly agree' or 'agree', consensus was considered achieved.

Epidemiology

Statement 1	
The prevalence rate of HS in Taiwan is lower than prevalence rates reported in	
predominantly Caucasian populations. Whereas female predominance has been	n
reported in Western countries, HS patients in Taiwan are predominantly male.	
Level of agreement:	
Strongly agree: 8/9 (89 %), Agree: 1/9 (11 %), Disagree: 0/9 (0 %)	

Prevalence rates of HS reported across studies vary due to estimations having been performed in different settings and populations, using different methodologies, and at different time points. Reported HS prevalence rates have ranged from 0.03% to 4.1% [11–14]. A recent systematic review and meta-analysis of HS prevalence in countries with predominantly Caucasian populations revealed a 0.4% prevalence rate [15]. A global systematic review and meta-analysis reported an overall pooled prevalence of 0.3% with rates higher in Europe (0.8%) than in the US (0.2%) and the Asia-Pacific region (0.2%) [16]. A multinational registry study found the mean age of HS onset of 23.2 years [17]. In Taiwan, a nationwide population-based study revealed that between 2000 and 2013, the prevalence of HS in persons aged 15 years or older was 185.6/100,000 (0.1856%), and new onset cases were most likely to occur in the age group of 15-24 years [13].

Prevalence in females is higher than in males in the US and Europe, but the sex disparity is reversed in Taiwan, Korea, and Japan [16,18,19]. Male predominance in Asian countries may be associated with the higher male-to-female ratio for smoking, which is a well-known risk factor of HS [18]. In Taiwan, male patients outnumbered female patients (male-to-female ratio: 2.2) in a single-center study including 161

Table 1

Oxford centre for evidence-based medicine 2011 levels of evidence.

Level of Evidence

Level 2: Randomized controlled trial with dramatic effect

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consecutive patients diagnosed with HS, and the smoking rate was 51.5% in males compared to 12.2% in females [19].

Diagnosis and assessment

Statement 2

Statement 2.1
Diagnosis of HS is based on clinical findings of typical lesions (nodules, abscesses,
sinus tracts, and scarring) at typical locations (axillae, groin, perineum, inter- and
inframammary folds, and buttocks) that are chronic and recurrent. Increased
disease awareness may reduce diagnostic delay and improve patient outcomes
through earlier treatment initiation.
Level of agreement:
Strongly agree: 7/9 (78 %), Agree: 2/9 (22 %), Disagree: 0/9 (0 %)

Early diagnosis and treatment initiation may reduce the risk of HS progression to debilitating advanced-stage disease. Unfortunately, the diagnosis of HS is commonly delayed. According to the VOICE Project global survey of 1299 patients diagnosed with HS, the mean time from onset of symptoms to diagnosis was 10.2 years, and 63.7% of patients had visited a physician >5 times for symptoms before being diagnosed with HS [20]. A US and European survey study reported that 73.6% of patients had already progressed to moderate-to-severe HS at the time of diagnosis [9]. Delay in diagnosis may be attributed to patients' reluctance to seek care and/or clinicians not diagnosing correctly, which underscores the need for increased disease awareness [21].

HS is diagnosed clinically in individuals who have a minimum of two typical lesions (inflammatory or non-inflammatory nodules, abscesses, exudative or non-exudative sinus tracts, or scarring) at typical locations (axilla, groin, genital region, inter- and inframammary folds, or buttocks) that are chronic and recurrent (≥ 2 recurrences within 6 months) and that may be painful [6,22,23]. Inflammatory nodules are typically raised, deep-seated, three-dimensional, round, tender, erythematous, infiltrated, and possibly pyogenic granuloma lesions with a diameter >10 mm. Abscesses are often inflammatory, pus-filled, painful, tender, and fluctuating masses with a diameter >10 mm surrounded by an erythematous area. HS should be differentiated from other skin disorders such as furuncles, carbuncles, epidermal cysts, cutaneous Crohn's disease, and acne vulgaris [4].

Statement 2.2
Baseline disease severity should be assessed using the Hurley staging system.
Subsequently, disease severity and treatment response should be monitored using a
dynamic scoring system such as the HS-Physician Global Assessment (HS-PGA) and
the International HS Severity Score System (IHS4).
Level of agreement:
Strongly agree: 7/9 (78 %), Agree: 2/9 (22 %), Disagree: 0/9 (0 %)

At time of diagnosis, physical examination should assess the extent and severity of HS. Disease severity should be classified according to the three-stage Hurley staging system: Hurley stage I (mild disease) is defined as single or multiple lesions without sinus tracts or scarring, Hurley stage II (moderate disease) is defined as recurrent single or multiple separated lesions with sinus tracts and/or scarring, and Hurley stage III (severe disease) is defined as coalescent lesions with sinus tracts and extensive scarring [24]. While the Hurley staging system is useful for evaluating baseline disease severity and guiding initial treatment approach, the tool is non-quantitative and therefore not suitable for monitoring change in disease activity [6]. Scoring tools that take into account the number and severity of lesions, distance between lesions, and severity of inflammation include the HS-PGA, IHS4, modified Sartorius Score (mSS), Hidradenitis Suppurativa Area and Severity Index (HASI), and Hidradenitis Suppurativa Clinical Response (HiSCR) [25-28]. Use of one or more of these dynamic assessment tools is recommended for evaluating treatment effectiveness. Since evaluation using assessment tools is time consuming and may be unfeasible to perform at each follow-up visit, disease activity can be routinely monitored using total abscess and inflammatory nodule count (AN

Level 1: Systematic review of randomized controlled trials

Level 3: Non-randomized controlled study, prospective cohort study Level 4: Case series, retrospective study

Level 5: Mechanism-based reasoning

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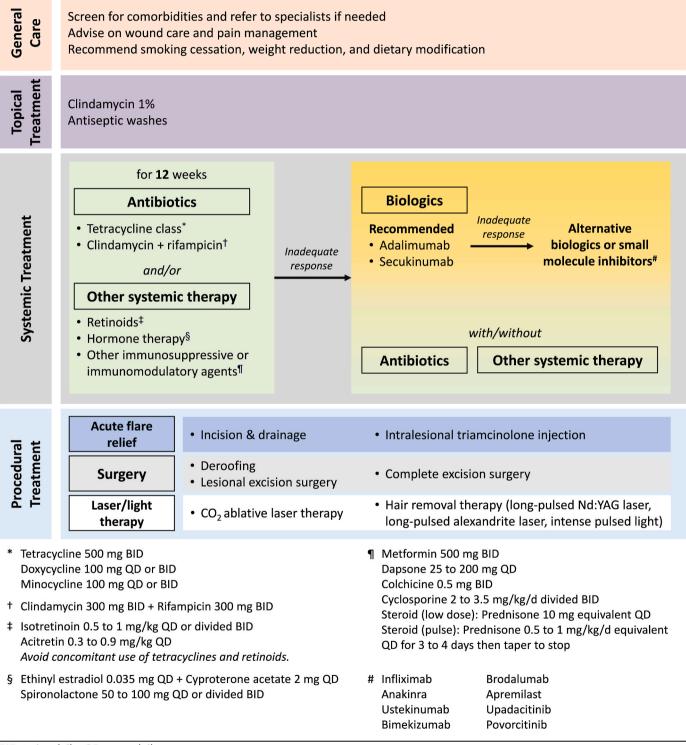
count) plus draining fistula count in each particular anatomic region.

Statement 2.3

Assessment of patient-reported outcomes such as Dermatology Life Quality Index (DLQI) and pain visual analogue scale (VAS) or numerical rating scale (NRS) scoring should be included in patient monitoring and evaluation of treatment response. *Level of agreement:*

Strongly agree: 9/9 (100 %), Agree: 0/9 (0 %), Disagree: 0/9 (0 %)

Patients with HS experience immense physical and psychological burden, and the disease is severely detrimental to quality of life [29]. The presence of disfiguring lesions in intertriginous areas as well as purulent discharge may cause embarrassment and hinder intimate relationships and social interactions [29]. Depression, anxiety, and



BID, twice daily; QD, once daily.

Commonly used dosages as reported in literature are listed. Please use clinical judgement when making treatment decisions.

Fig. 1. Hidradenitis suppurativa management algorithm.

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chronic pain may significantly impair productivity [30]. Studies evaluating health-related quality of life of HS patients have reported mean DLQI scores ranging from 8.9 to 12.7, which is markedly higher than mean DLQI scores reported for patients with other dermatological disorders, including psoriasis, atopic dermatitis, and chronic urticaria [29, 31–33]. HS patients commonly suffer pain resulting from deep-seated inflammatory lesions, and quantitatively assessed pain intensity in HS is significantly higher compared to other dermatological conditions [6]. Assessment of patient-reported outcomes, including DLQI and pain VAS or NRS score, is an important component of HS patient monitoring and treatment response evaluation.

Risk factors and comorbidities

Statement 3.1

HS patients should receive counselling for weight loss, dietary modification, and smoking cessation as needed.

Level of agreement:

Strongly agree: 9/9 (100 %), Agree: 0/9 (0 %), Disagree: 0/9 (0 %)

Obesity has been consistently shown to be associated with increased risk of HS, possibly due to the secretion of pro-inflammatory cytokines by adipocytes that contribute to systemic low-grade inflammation [34]. HS lesions occur in intertriginous areas that are subject to repetitive mechanical stress and can be exacerbated by skin fold friction in obese patients [35]. According to a systematic review, some evidence suggests that improvement in HS severity may be achieved with weight loss and dietary changes (e.g., reducing intake of sugar, dairy, and processed carbohydrates) [36,37]. Patients who are obese or overweight according to the criteria defined by the Ministry of Health and Welfare of Taiwan (obese: body mass index [BMI] \geq 27 kg/m², overweight: BMI \geq 24 kg/m² to <27 kg/m²) should receive multidisciplinary care for weight management. Tobacco smoking is a frequently reported risk factor for HS development as well as HS severity [38-40]. A population-based study conducted in the US reported a nearly two-fold increase in the incidence of HS among smokers compared to non-smokers (adjusted odds ratio [OR], 1.90) [40]. In a Taiwanese single-center study, the association between HS severity and smoking was significant (OR, 2.20) [19]. To improve disease severity and overall health, counselling for weight loss, dietary modification, and smoking cessation is recommended (Fig. 1).

Statement 3.2

HS patients should be screened for comorbidities, including diabetes mellitus, cardiovascular disease, metabolic syndrome, thyroid disorders, spondyloarthritis, inflammatory bowel disease (IBD), and psychiatric disorders, and should be referred to appropriate specialists as needed. *Level of agreement:*

Strongly agree: 9/9 (100 %), Agree: 0/9 (0 %), Disagree: 0/9 (0 %)

HS is associated with multiple comorbidities, including diabetes mellitus, cardiovascular disease, metabolic syndrome, thyroid disorders, spondyloarthritis, IBD, and psychiatric disorders [41-46]. Analysis of data from the Taiwan National Health Insurance Research Database revealed that, compared to controls, HS patients had significantly higher risk of dyslipidemia (adjusted hazard ratio [aHR], 3.86), hypertension (aHR, 1.91), diabetes mellitus (aHR, 1.71), and coronary artery disease (aHR, 2.72) [42]. Results of a meta-analysis of case-control studies found HS to be significantly associated with thyroid disease (OR, 1.36), including both hypothyroidism and hyperthyroidism [46]. Possibly due to shared dysregulated inflammatory pathways, the risk of spondyloarthritis is twice as high in patients with HS compared to the general population (OR, 2.10) [45]. Across multiple studies investigating the association between HS and IBD, HS patients were more than twice as likely to have IBD, particularly Crohn's disease, compared to controls [41]. Psychiatric disorders are common among HS patients, with prevalence of depression up to 33% and prevalence of anxiety up to 18% [44]. A meta-analysis of case-control studies showed that HS patients

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had significantly higher odds of schizophrenia (OR, 1.66), depression (OR, 1.75), anxiety (OR, 1.71), suicide (OR, 2.08), and substance abuse disorder (OR, 2.84) [47]. The evidence supporting the association between HS and comorbidities is robust; therefore, HS patients should be screened for commonly associated comorbidities via signs and symptoms and blood tests at least once a year. More frequent blood testing and additional testing such as colonofibroscopy and thyroid ultrasonography should be performed as warranted, and patients should be referred to appropriate specialists for follow-up as needed.

Medical treatment

Antibiotics

Statement 4.1.1	
Topical clindamycin 1 % treatment applied twice daily to affected areas is	
recommended as first-line treatment for mild-to-moderate HS.	
Level of evidence: 2	
Level of agreement:	
Strongly agree: 9/9 (100 %), Agree: 0/9 (0 %), Disagree: 0/9 (0 %)	

Although HS is not an infectious disease, a dysbiotic microbiome which induces an aberrant immune response is characteristic of the disease [48]. A small randomized study including 27 patients with Hurley stage I or early Hurley stage II HS demonstrated that topical clindamycin 1% was significantly superior to placebo in reducing pustules, but the effect on inflammatory nodules and abscesses was not significant [49]. Clindamycin 1% applied twice daily to affected areas is recommended as first-line treatment for mild-to-moderate HS with predominantly superficial pustules. HS patients using topical clindamycin may be more susceptible to the development of *Staphylococcus aureus* resistance, and prolonged topical clindamycin treatment should be used with caution [50]. Concurrent use of antiseptic washes such as chlorhexidine skin cleansers may help reduce the incidence of bacterial resistance and secondary bacterial infection of lesions [51,52].

Statement 4.1.2
Systemic antibiotic treatment with oral tetracyclines is a recommended first-line
treatment option for mild-to-moderate HS.
Level of evidence: 2
Level of agreement:
Strongly agree: 9/9 (100 %), Agree: 0/9 (0 %), Disagree: 0/9 (0 %)

Results of a randomized study including 46 patients with Hurley stage I or Hurley stage II HS showed that treatment with oral tetracyclines (100 mg doxycycline once or twice daily, 100 mg minocycline once or twice daily, or tetracycline 500 mg twice daily) for at least 3 months was comparable to topical clindamycin in change in nodule count, abscess count, and soreness [53]. A prospective study comparing tetracycline 500 mg, doxycycline 100 mg, and lymecycline 300 mg (all dosed orally twice daily) in 108 HS patients showed that while all treatment groups experienced improvements in pain, number of new lesions, and quality of life after mean treatment duration of 4.3 months, the tetracycline group experienced the greatest clinical improvement [54]. In addition to antibacterial activity, tetracyclines exhibit anti-inflammatory properties that may provide added benefit [55]. Prolonged systemic antibiotic treatment should be avoided out of concern for antimicrobial resistance.

Level of evidence: 3

Level of agreement:

Strongly agree: 7/9 (78 %), Agree: 2/9 (22 %), Disagree: 0/9 (0 %)

Oral clindamycin 300 mg twice daily combined with oral rifampicin

Statement 4.1.3

Systemic antibiotic treatment with combination oral clindamycin plus rifampicin is a first-line treatment option for moderate-to-severe HS and a second-line treatment option for mild-to-moderate HS.

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300 mg twice daily or 600 mg once daily for HS has been investigated in several retrospective and prospective studies, but evidence supporting the efficacy of this regimen is limited [56–60]. In a 12-week prospective cohort study including 283 HS patients treated with oral tetracycline or oral clindamycin plus rifampicin, both treatment groups achieved a significant decrease in IHS4 from baseline with no significant difference between groups [59]. In another prospective cohort study, among 26 HS patients treated with oral clindamycin plus rifampicin for 12 weeks, 19 (73%) patients showed clinical response among whom 10 (59%) patients relapsed after a mean time of 4.2 months [58].

Diarrhea and other gastrointestinal adverse effects frequently occur with combination treatment of clindamycin plus rifampicin, especially during the first weeks of treatment [61]. The potential for adverse effects and how to manage them should be discussed with patients prior to treatment initiation. In addition, rifampicin is a potent inducer of CYP3A4 drug metabolism, and patients should be informed of potential drug-drug interactions with rifampicin and be reminded to notify other healthcare providers of their current treatment [62]. Response to systemic antibiotic treatment may be delayed, and the regimen can be continued for 10–12 weeks as tolerated. Although evidence supporting the superiority of combination therapy with oral clindamycin and rifampicin over oral tetracycline is limited, this regimen can still be considered as a first-line treatment option for moderate-to-severe HS and a second-line treatment option for mild-to-moderate HS.

Statement	1 1	1

Ertapenem can be administered as rescue therapy or as bridging therapy prior to surgery. Other antibiotic regimens, such as rifampicin, moxifloxacin, and metronidazole, can be applied based on clinician's decision and results of bacterial culture and drug sensitivity testing.
Level of evidence: 4
Level of agreement:
Strongly agree: 8/9 (89 %), Agree: 1/9 (11 %), Disagree: 0/9 (0 %)

Evidence supporting the efficacy of intravenously administered ertapenem is scarce and of low quality [63,64]. In a retrospective study of 30 patients with severe HS treated with a 6-week course of intravenous ertapenem 1 g daily, the median Sartorius score was significantly reduced after treatment, but most patients required continuous consolidation treatment with rifampicin, moxifloxacin, and metronidazole to maintain remission [63]. In a telephone interview study including 28 Hurley stage II or III HS patients previously treated with intravenous ertapenem, 24 (85.7%) patients reported improvement in quality of life after treatment [64]. Due to limited evidence and the impracticality of parenteral administration, ertapenem should be reserved as rescue therapy or as preoperative bridging therapy [65].

In a retrospective study including 38 HS patients treated with a combination of oral rifampicin, moxifloxacin, and metronidazole, 6 of 6 Hurley stage I patients, 8 of 10 Hurley stage II patients, and 2 of 12 Hurley stage III patients achieved complete remission [66]. In this study, the duration of treatment ranged from 1 to 12 months; however, metronidazole was stopped after 6 weeks to avoid neurological complications. In patients who exhibit signs of infection, results of bacterial culture and drug sensitivity testing should be considered when selecting an appropriate antibiotic regimen.

Retinoids

Statement 4.2
Retinoid therapy is recommended as an alternative treatment option for moderate-to-
severe HS. Retinoids should be avoided in women of childbearing age.
Level of evidence: 4
Level of agreement:
Strongly agree: 6/9 (67 %), Agree: 3/9 (33 %), Disagree: 0/9 (0 %)

Retinoids are vitamin A analogs that may reduce the initiation of inflammation in the pilosebaceous unit by decreasing follicular keratin Journal of the Formosan Medical Association xxx (xxxx) xxx

plugging. Retinoids have been used to treat HS due to follicular hyperkeratosis in the initial stage of pathogenesis; however, evidence supporting the efficacy of systemic retinoids in improving HS symptoms is limited [67]. Isotretinoin treatment (0.50-0.81 mg/kg/day) in 68 patients with HS resulted in marked improvement in 74% of patients in a retrospective study by Boer et al. [68] However, as reported in a retrospective study by Soria et al., only 16% of 88 HS patients treated with isotretinoin at dosages ranging from 20 to 140 mg/day (mean 44 mg/day) self-reported improvement with treatment [69]. Retrospective and cohort studies assessing the effectiveness of acitretin at dosages ranging from 0.5 to 0.9 mg/kg/day in HS have shown response rates ranging from 47% to 100% [70–72]. However, as reported by Tan et al. acitretin was ineffective as monotherapy, and as reported by Matusiak et al., most patients relapsed after acitretin was discontinued [71,73]. Patients with follicular type HS or a history of severe acne may be more likely to respond to retinoid treatment [69,74,75]. Systemic retinoids and tetracyclines may increase the risk of pseudotumor cerebri, and concomitant use should be avoided [76]. There is some concern that systemic retinoid treatment may impair wound healing; therefore, discontinuation of retinoid therapy should be considered in patients with planned surgery [77]. Due to the risk of teratogenicity, systemic retinoids should be avoided in women of childbearing age [65].

Hormone therapy

Statement 4.3
Hormone therapy is recommended as an alternative or adjunctive treatment for
female patients, especially those who experience perimenstrual HS flares or who
have polycystic ovary syndrome (PCOS).
Level of evidence: 4
Level of agreement:
Strongly agree: 8/9 (89 %), Agree: 1/9 (11 %), Disagree: 0/9 (0 %)

Sex hormones likely play a role in the pathogenesis of HS though the mechanism is not fully understood [78]. Onset of HS usually occurs after puberty, pre-menstrual flare-ups and HS worsening after pregnancy are often observed [78,79]. The likelihood of HS has been observed to be 2-fold higher in patients with PCOS than those without PCOS [80]. Antiandrogen treatment for HS is based on limited evidence from mainly retrospective studies and case series [81-84]. In studies of female HS patients treated with ethinyl estradiol plus cyproterone acetate, the response rate ranged from 55% to 100% [81-83,85,86]. In a randomized double-blind crossover trial including 24 HS patients, similar clinical improvements were observed between treatment with ethinyl estradiol plus cyproterone acetate and ethinyl estradiol plus norgestrel [82]. The anti-mineralocorticoid spironolactone has been shown to have antiandrogen properties, and results of retrospective studies and case series suggest that spironolactone dosed 50-100 mg daily may reduce pain and inflammatory lesions and improve quality of life in HS [85-87].

Other immunosuppressive and immunomodulatory agents

Statement 4.4	
Metformin, dapsone, colchicine, cyclosporine, and systemic corticosteroids are	
alternative adjunct treatment options.	
Level of evidence: 4	
Level of agreement:	
Strongly agree: 6/9 (67 %), Agree: 3/9 (33 %), Disagree: 0/9 (0 %)	

The antihyperglycemic agent metformin has a significant antiinflammatory effect, and clinical response was observed in 68% of 53 HS patients treated with metformin 500 mg twice daily in a retrospective study [84]. Metformin also has beneficial effects on HS comorbidities, including type 2 diabetes, metabolic syndrome, obesity, and PCOS [88]. The sulfone drug dapsone has anti-inflammatory properties, and results of retrospective and uncontrolled studies show

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that the majority of Hurley I and II HS patients experienced clinically significant improvement with dapsone at dosages ranging from 25 to 200 mg/day; however, most studies used dapsone in combination with other agents [89]. Colchicine is an anti-inflammatory drug that is used in the treatment of various dermatological disorders, and a retrospective study including 44 HS patients reported significant improvements in IHS4 and DLQI with colchicine 1 mg/day alone or combined with doxycycline [90]. In a prospective study including 20 moderate-to-severe HS patients, all patients showed signs of improvement in PGA and DLQI with combined colchicine 0.5 mg twice daily and minocycline 100 mg daily treatment for 3 months followed by colchicine maintenance monotherapy [91]. In a retrospective review of 18 patients with recalcitrant HS, treatment with the immunosuppressant drug cyclosporine dosed at 2.0-3.5 mg/kg/day resulted in clinical improvement ranging from slight to significant in 50% of patients [92]. In patients with recalcitrant HS, low-dose systemic corticosteroids (equivalent to prednisone 10 mg per day) added to existing treatment resulted in complete or partial remission in 11 of 13 (84.6%) patients; however, long-term systemic corticosteroid treatment should be avoided [93]. A short course of systemic corticosteroids (e.g., prednisone 0.5-1 mg/kg daily for 3-4 days then taper to stop over weeks) can be considered as rescue therapy for acute flares [2,6,65]. These agents may be considered as alternative adjunct treatment options though evidence supporting the effectiveness of these agents in HS is limited.

Biologic therapy

Upregulation of proinflammatory cytokines, including tumor necrosis factor (TNF)- α , interleukin (IL)-1, IL-17, IL-12/23, and interferon (IFN)- γ , has been implicated in the pathogenesis of HS, and accumulating data support the efficacy of various biologic agents in improving outcomes in HS [94]. Moreover, as clinical studies of adalimumab and secukinumab for the treatment of HS have been conducted with the objective of gaining regulatory approval, the generated evidence is of relatively high quality [2].

Statement 4.5.1 Adalimumab and secukinumab are recommended biologic treatment options for moderate-to-severe HS after failure of systemic antibiotics. Level of evidence: 2 Level of agreement: Strongly agree: 8/9 (89 %), Agree: 1/9 (11 %), Disagree: 0/9 (0 %)

Adalimumab is a fully human monoclonal antibody targeting TNF- α , and its efficacy in moderate-to-severe HS was investigated in the phase 3 multicenter, double-blind, placebo-controlled PIONEER I and PIONEER II trials [95]. In these studies, a total of 633 patients with Hurley stage II or III HS who had inadequate response to systemic antibiotics were randomized to receive subcutaneous adalimumab 40 mg or placebo weekly for 12 weeks followed by rerandomization to receive adalimumab or placebo weekly or bi-weekly for 24 weeks. At the primary endpoint at Week 12, significantly more patients receiving adalimumab weekly achieved HiSCR (at least 50% reduction from baseline in total abscess and inflammatory nodule count, with no increase in abscess or draining fistula count) compared to those receiving placebo in both PIONEER I (41.8% vs. 26.0%; P=0.003) and PIONEER II (58.9% vs. 27.6%; P<0.001). Rates of adverse events, serious adverse events, and infectious events were comparable between treatment and placebo groups. In the open-label extension study of the PIONEER I and II studies, the HiSCR rate among patients treated with adalimumab weekly was 52.3% at Week 168, mean improvement in DLQI score from baseline was clinically meaningful from Week 4 through Week 72, and no additional safety concerns were reported [96]. HiSCR rates reported in retrospective and observational studies of adalimumab for the treatment of HS ranged from 44% to 75% between Weeks 12 and 16 [97-100].

Secukinumab is a fully human monoclonal antibody that selectively neutralizes IL-17A. Its efficacy in moderate-to-severe HS is supported by

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the results of the phase 3 multicenter, double-blind, placebo-controlled SUNSHINE and SUNRISE trials [101]. A total of 1084 patients with Hurley stage II or III HS were randomized to subcutaneous secukinumab 300 mg every 2 weeks (Q2W) or every 4 weeks (Q4W) or to placebo. In both studies, higher HiSCR rates were observed with secukinumab compared to placebo at all time-points starting from Week 2. The primary endpoint was met in both trials-at Week 16, a significantly greater proportion of patients achieved HiSCR with secukinumab dosed Q2W than with placebo in SUNSHINE (45.0% vs. 33.7%; P=0.0070) and in SUNRISE (42.3% vs. 31.2%; P=0.0149). At Week 16, the proportion of patients experiencing flares was significantly lower with secukinumab than placebo, and the proportions of patients experiencing clinically meaningful improvement in Patient's Global Assessment of Skin Pain and DLQI were greater with secukinumab than with placebo. Clinical response rates were sustained through the end of study at Week 52. Rates of adverse events, non-fatal serious adverse events, infectious events, and discontinuation due to adverse events were comparable between treatment and placebo groups. HiSCR rates reported in retrospective and open-label studies of secukinumab for the treatment of HS ranged from 41% to 78% between Weeks 16 and 28 [102-105].

In PIONEER II, SUNSHINE, and SUNRISE, a proportion of patients received concomitant biologic and systemic antibiotic treatment; however, findings did not suggest a clear trend of improved outcomes in patients treated with combined biologic and antibiotic compared to biologic alone [95,101]. In patients treated with a biologic, use of concomitant systemic antibiotic therapy should be decided based on the individual patient's condition and should be considered especially when the patient experiences pus drainage, secondary infection, or flare-up.

Statement 4.5.2	
Alternative treatments related to IL-1, IL-17, TNF-a, phosphodiesterase 4 (PD	E-4), or
Janus kinase (JAK) pathway inhibition can be considered after failure of o	r
intolerance to recommended biologic treatment.	
Level of evidence: 2 (Anakinra, Bimekizumab, Upadacitinib, Povorcitinib)	
Level of evidence: 3 (Apremilast, Brodalumab, Infliximab, Ustekinumab)	
Level of agreement:	
Strongly agree: 6/9 (67 %), Agree: 3/9 (33 %), Disagree: 0/9 (0 %)	

Several other biologic and small molecule agents have been investigated for the treatment of HS, and many have shown some promising results. Infliximab is a chimeric mouse/human monoclonal antibody targeting TNF α . A meta-analysis of 6 prospective and 13 retrospective studies including a total of 314 patients with HS (mostly with moderateto-severe disease) reported a response rate of 83% with infliximab treatment [106]. In a phase 2 randomized controlled trial including 38 patients with moderate-to-severe HS, 27% of patients treated with infliximab and 5% of patients receiving placebo showed a 50% or greater improvement in HS Severity Index (HSSI) from baseline at Week 8, but the difference between groups was not significant [107]. The anti-TNF fusion protein etanercept did not show significant efficacy in a placebo-controlled phase 2 trial [108].

Treatment with the IL-1 receptor antagonist anakinra for HS has been explored, but evidence supporting its efficacy is sparse [109,110]. In an open-label study including 6 patients with moderate-to-severe HS, mean mSS and DLQI decreased significantly from baseline after 8 weeks of anakinra treatment [110]. Results of a randomized controlled trial including 20 patients with Hurley stage II or III HS showed that 78% of patients achieved HiSCR after 12 weeks of anakinra treatment compared to 30% with placebo (P=0.04), but mean changes in Sartorius score, disease severity VAS score, and DLQI were not different between groups [109].

Ustekinumab is a human monoclonal antibody directed against IL-12 and IL-23. In an open-label study of 17 patients with moderate-to-severe HS, 47% of patients achieved HiSCR and 82% of patients experienced moderate-to-marked improvement in mSS with weight-based ustekinumab treatment at Week 40 [111]. Response to ustekinumab treatment reported in a retrospective study and several case series of HS patients

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has been inconsistent [112–115]. Despite initial positive trends observed in phase 2 trials evaluating the efficacy of the anti-IL-23 agent guselkumab in HS, HiSCR rates with guselkumab were not significantly improved compared to placebo at Week 16 in a study including 181 patients with moderate-to-severe HS [116,117]. Phase 2 trial results of risankizumab, another anti-IL-23 agent, also failed to show efficacy in moderate-to-severe HS [118].

Brodalumab is a human monoclonal antibody that binds to IL-17 receptor A (IL-17RA) thereby inhibiting multiple forms of IL-17, including IL-17A, IL-17C, and IL-17F. In two open-label cohort studies (each n=10), Hurley stage II or III HS patients who received brodalumab dosed weekly or bi-weekly all achieved HiSCR at Week 2 or 4, which was sustained to Week 24 [119,120]. By Week 24, all patients achieved 75% reduction in AN count with 40–50% of patients achieving 100 % reduction in AN count.

Recently presented data from the BE HEARD I (n=505) and BE HEARD II (n=509) phase 3 trials of the anti-IL-17A/17F monoclonal antibody bimekizumab support its potential as an efficacious treatment for moderate-to-severe HS [121,122]. In these studies, patients were randomized to bimekizumab Q2W or Q4W or to placebo, and the primary endpoint of HiSCR at Week 16 was achieved in significantly more patients in the bimekizumab Q2W group (BE HEARD I, 47.8% vs. 28.7%, P=0.006; BE HEARD II, 52.0% vs. 32.2%, P=0.003) and in the bimekizumab Q4W group (BE HEARD I, 45.3% vs. 28.7%, P=0.030; BE HEARD II, 53.8% vs. 32.2%, P=0.004) compared to the placebo group. At Week 48 in both studies, over 75% of patients achieved HiSCR with both regimens.

In an open-label single arm phase 2 study of the PDE-4 inhibitor apremilast, 65% of 20 patients with mild-to-moderate HS achieved a 30% or more reduction in abscesses and nodules at Week 16 [123]. Orismilast is a highly potent and selective next-generation PDE-4 inhibitor that showed greater decrease in AN count compared to placebo at Week 16 in a phase 2 study including patients with mild, moderate, or severe HS [124]. A phase 2 trial evaluating the oral selective JAK1 inhibitor upadacitinib in moderate-to-severe HS showed that 38.3% of upadacitinib-treated patients achieved HiSCR compared to 23.8% with placebo at Week 12 [125]. The selective JAK1 inhibitor povorcitinib demonstrated clinical efficacy in a phase 2 trial including 209 HS patients, and phase 3 trials evaluating povorcitinib in moderate-to-severe HS are currently ongoing [126]. Sonelokimab is a novel anti-IL-17A/F nanobody currently being investigated for the treatment of moderate-to-severe HS in the randomized phase 2 MIRA trial using HiSCR reduction of 75% as the primary endpoint [127].

Procedural treatment

Intralesional triamcinolone injection

Statement 5.1
Intralesional triamcinolone may be considered for reducing pain and swelling caused
by acutely inflamed HS lesions in the absence of overt bacterial infection.
Level of evidence: 4
Level of agreement:
Strongly agree: 8/9 (89 %), Agree: 1/9 (11 %), Disagree: 0/9 (0 %)

Intralesional corticosteroid treatment in HS is aimed at rapidly reducing pain, redness, and swelling of acutely inflamed lesions, but supporting evidence is scarce and inconsistent [7]. In a prospective case series, intralesional injection of triamcinolone 10 mg/mL significantly reduced pain VAS scores after 1 day and significantly improved signs of inflammation after 7 days [128]. Retrospective studies have shown promising results of ultrasound-guided intralesional corticosteroid treatment, with response rates of up to 95% [129,130]. However, a double-blinded randomized controlled trial comparing the efficacy of intralesional triamcinolone to normal saline found no significant difference between treatment and placebo in terms of pain reduction,

lesion clearance, or patient satisfaction [131]. Intralesional triamcinolone may be considered for short-term management of painful acutely inflamed lesions. In patients with overt bacterial infection, intralesional corticosteroid treatment is contraindicated [6].

Incision and drainage

Statement 5.2
Incision and drainage is a supplemental treatment option for relief of acute pain from
tense HS lesions with abscess formation.
Level of evidence: 4
Level of agreement:
Strongly agree: 9/9 (100 %), Agree: 0/9 (0 %), Disagree: 0/9 (0 %)

Incision and drainage is a relatively simple procedure that can relieve acute pain from tense HS lesions with abscess formation [132]. Incision and drainage alone is not sufficient treatment as it provides symptomatic relief only and recurrence rate is nearly 100% [23].

Deroofing and excision

Lesional excision and deroofing are recommended treatment options for recurrent nodules, abscesses, and sinus tracts in mild-to-moderate HS. Level of evidence: 4 Level of agreement:	Statement 5.3.1
Level of evidence: 4	Lesional excision and deroofing are recommended treatment options for recurrent
	nodules, abscesses, and sinus tracts in mild-to-moderate HS.
Level of agreement:	Level of evidence: 4
	Level of agreement:
Strongly agree: 8/9 (89 %), Agree: 1/9 (11 %), Disagree: 0/9 (0 %)	Strongly agree: 8/9 (89 %), Agree: 1/9 (11 %), Disagree: 0/9 (0 %)

Statement 5.3.2
In eligible patients, complete local or regional excision is a recommended treatment
option for patients with moderate-to-severe HS.
Level of evidence: 4
Level of agreement:
Strongly agree: 9/9 (100 %), Agree: 0/9 (0 %), Disagree: 0/9 (0 %)

Many HS patients require both medical and surgical treatments, and referral to a dermatologic surgeon or collaboration between dermatologist and surgeon is an integral component of multidisciplinary management of HS. Although evidence supporting surgical treatment of HS is based mainly on findings from low-quality uncontrolled studies, surgical management is potentially curative; therefore, all HS patients should be evaluated for eligibility for surgical treatment [23]. The decision to treat surgically and the surgical approach should be based on the severity and mutilating status of lesions, the presence of sinus tracts/fistulae, accordion-like scars, contracted scars, suspected malignancy, required margins, and the patient's health status and preference [132].

Deroofing involves removing all or the large majority of skin overlying a nodule, abscess, or sinus tract, curettage of gelatinous granulation tissue or contents of the cavity with the base left intact, then leaving the wound open for secondary intention healing [6,23,132,133]. In a study of 44 patients with recurrent mild-to-moderate HS lesions, 83% of lesions treated with deroofing were recurrence-free after a median follow-up of 34 months [134].

Conventional excision involves removing the epidermis, dermis, and subcutaneous fat or deeper affected tissues in the affected region, and the excised area may be left open to heal by secondary intention, closed primarily, or closed using skin grafts or flaps [135]. Lesional excision can be used to treat limited disease with solitary lesions, and recurrence rate and recovery time are comparable to that of deroofing [133,135, 136]. Regional excision involves the excision of the large majority of or an entire affected body region, thus leaving a large wound that may require prolonged recovery [2,133,137]. In retrospective studies of HS patients treated with wide (complete lesional or regional) excision, recurrence-free rates ranged from 59.7% to 97.5% [137–140]. Complete regional excision is considered the mainstay surgical approach for more

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severe HS as the procedure results in a lower recurrence rate compared to other surgical procedures and is potentially curative; however, patients' eligibility must be carefully determined due to increased risk of postoperative complications such as infection, bleeding, and scar contracture [2,137,141].

Acute inflammation should be controlled with antibiotic or biologic treatment prior to surgery. Current evidence suggests that biologic therapy in conjunction with surgery may improve treatment response and reduce the rate of recurrence compared to surgery alone [142,143]. Results of the SHARPS randomized trial showed that in 206 moderate-to-severe HS patients undergoing wide-excision surgery, patients receiving adalimumab treatment initiated 12 weeks prior to and continued for 24 weeks after surgery had significantly greater HiSCR rate compared to placebo (48% vs. 34% at Week 12, P=0.049) with no increased risk of postoperative wound infection, complication, or hemorrhage [143].

Laser and light therapy

Statement 5.4.1	Ī
Carbon dioxide (CO ₂) ablative laser therapy is a treatment option for mild-to-	
moderate HS.	
Level of evidence: 4	
Level of agreement:	
Strongly agree: 6/9 (67 %), Agree: 3/9 (33 %), Disagree: 0/9 (0 %)	

 CO_2 ablative laser therapy is a tissue-sparing approach to excising or vaporizing HS lesions [144]. Focalized tissue destruction using CO_2 laser may lead to less bleeding and faster wound healing compared to conventional surgery [6,132]. Numerous retrospective studies have reported varying but overall satisfactory outcomes of CO_2 laser therapy in the treatment of HS lesions [145–148]. In the largest of these studies, among 185 sites in 61 patients with long-standing HS treated with CO_2 laser excision and marsupialization, only two sites had recurrence during follow-up from 1 to 19 years [145].

Statement 5.4.2
Hair follicle destruction using long-pulsed neodymium-doped yttrium aluminum
garnet (Nd:YAG) laser, long-pulsed alexandrite laser, or intense pulsed light (IPL)
therapy, is a treatment option for mild-to-moderate HS.
Long-pulsed Nd:YAG laser, Level of evidence: 2
Long-pulsed alexandrite laser, Level of evidence: 3
IPL, Level of evidence: 2
Level of agreement:
Strongly agree: 9/9 (100 %), Agree: 0/9 (0 %), Disagree: 0/9 (0 %)

Since follicular occlusion, rupture, and inflammation drive the pathogenesis of HS, destruction of hair follicles using long-pulsed Nd: YAG laser therapy has shown good efficacy in reducing HS severity in randomized controlled studies [149,150]. In a split-body controlled study conducted by Tierney et al., 22 patients with Hurley stage II or III HS received monthly Nd:YAG laser sessions on one half of the body, and after 3 months, HS severity score was reduced by 65.3% on the treated side and by 7.5% on the control side compared to baseline [150]. The same group of investigators conducted a second similarly designed study including 22 Hurley stage II patients, and after 4 monthly Nd:YAG laser sessions, HS severity score improved by 72.7% on the treated side of the body and by 22.9% on the control side, and improvement after treatment was maintained for 2 months after the last treatment [149].

Effectiveness of hair follicle destruction using a long-pulsed alexandrite laser in HS is supported by the results of a case-control study [151]. The study included 40 female patients with Hurley stage I or II HS among whom 20 patients were treated with alexandrite laser (5 treatments at 6-week intervals) and 20 patients served as controls. At Week 30, alexandrite laser-treat patients had significantly lower IHS4, pain VAS score, and DLQI scores compared to controls.

The efficacy of hair removal using IPL therapy in reducing HS

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severity has been supported by results of small randomized controlled trials and retrospective studies [152–154]. Andersen et al. conducted a split-body randomized study in which 17 patients with Hurley stage I or II HS received monthly IPL therapy on one side of the body while the contralateral side served as the untreated control, and results showed significant improvement in mSS from baseline on the treated side while the control side did not improve significantly [152]. In another split-body randomized study including 18 Hurley stage II or III patients, twice weekly IPL therapy for 4 weeks was shown to significantly improve Sartorius score from baseline while the change in disease severity was insignificant on the control side [154].

Since abnormality of the pilosebaceous-apocrine unit is implicated in HS pathophysiology, axillary hyperhidrosis therapy involving ablation of eccrine and apocrine glands using a microwave-based energy device has been explored in HS treatment [155,156]. However, interim analysis of a split-body randomized study including 20 HS patients showed worsening of HS symptoms after microwave ablation in the majority of patients, and this study was discontinued [156]. Though limited, current evidence suggests possible aggravation of HS from microwave-based treatment, and this treatment modality is not recommended in patients with HS.

Conclusion

HS is a chronic disease that inflicts immense physical and psychological burden. Delayed diagnosis, improper diagnosis, or ineffective treatments may negatively affect patient outcomes. Recalcitrant and potentially debilitating, HS presents many challenges in its management, and there is a general paucity of high-quality evidence to support the efficacy of conventional treatments. Fortunately, HS disease pathogenesis is becoming better understood and recent investigations of biologic treatments, particularly adalimumab and secukinumab, have shown promising results. These consensus statements and the recommended treatment algorithm were developed based on current evidence and aim to provide guidance in clinical decision-making. Importantly, an individualized multimodal treatment approach that incorporates both medical and procedural treatments and a multidisciplinary team approach to provide comprehensive care are critical for optimizing the management of patients suffering from this difficult disease.

Contributions

Yi-Hua Liao made significant contribution to the conceptualization of the consensus and chaired the panel discussion; Yi-Hua Liao, Chia-Bao Chu, Chung-yee Rosaline Hui, Cheng-Yuan Li, Sheng-Yao Lin, Han-Chi Tseng, Yen-Jen Wang, Jennifer Wu, and Wei-Wen Yu participated in consensus discussions and voting for each statement; Sheau-Chiou Chao strongly endorsed and supported the development of the consensus; and all authors gave final approval of the submitted and revised versions of the manuscript.

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grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

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