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Original Article

Effect of adalimumab treatment on lesions and inflammatory factors in patients with moderate-severe hidradenitis suppurativa

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Abstract: Objectives: To investigate the efficacy and safety of adalimumab (ADA) in the treatment of hidradenitis suppurativa (HS). Methods: A retrospective analysis was conducted on the clinical data of 50 patients with HS. Patients were divided into ADA (n=30) and cyclosporine (CSA, n=20) groups. The Hidradenitis Suppurativa Clinical Response Criterion (HiSCR) and the International Hidradenitis Suppurativa Severity Score System (IHS4) were used to assess clinical efficacy. The Dermatology Life Quality Index (DLQI) was used to evaluate patients' quality of life, and peripheral blood inflammatory factor levels were measured. Safety was also assessed. Results: After treatment, all scores in both groups decreased significantly (all $P<0.05$); the decrease in IHS4 score in the ADA group was significantly greater than that in the cyclosporine (CSA) group ($P<0.05$). From week 2 to week 12 of treatment, there was a significant difference in the clinical response rate between the groups ($P<0.05$). At week 12, the Patient Global Assessment Relief Rate (PtGA RR) for skin pain in the ADA group was significantly higher than that in the CSA group ($P<0.05$). After treatment, the levels of inflammatory cells, NLRP3, and caspase-1 in both groups were significantly lower than those before treatment ($P<0.05$), with the ADA group showing a greater decrease than the CSA group ($P<0.05$). Some patients experienced dry mouth, abdominal pain, and scalp, which improved after symptomatic treatment. No relapse or secondary infection occurred. Conclusion: ADA demonstrates good clinical efficacy and long-term safety in treating this population.

Keywords: Hidradenitis suppurativa, adalimumab, inflammatory factors, adverse reactions, outcome

Introduction

Patients with hidradenitis suppurativa (HS) may develop painful nodules, abscesses, or sinus tracts due to the chronic inflammatory process [1]. Recurrent inflammation following scar formation can lead to contracture scars, which are often difficult to prevent from becoming permanent [2]. HS lesions are mainly distributed in areas rich in apocrine sweat glands, such as the axillae and perianal region, where friction and a moist environment can exacerbate inflammation and scar formation. Common symptoms of HS include pain and an inflammatory response. Studies have shown that the disease typically occurs between the ages of 21 and 30, but can also occur in childhood [3]. Adalimumab is one of the two biologics approved by the National Medical Products Administration for the treatment of HS. Adalimumab works by inhibiting the pro-inflammatory cytokine tumor necrosis factor-alpha (TNF-α) [4]. Biologics and small-molecule drugs have significantly improved the long-term prognosis of patients with mild to moderate HS. TNF-α antagonists and interleukin-targeting inhibitors can reduce inflammation, improve the condition, and enhance the quality of life (QoL) of patients by acting on related cytokines. Small molecule drugs are mostly oral formulations, which improve patient compliance. These drugs can interfere with intracellular signal transduc-

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tion pathways and regulate the body's immune response, providing diversified treatment options for HS [5]. Multiple studies have shown that in patients with HS who do not respond to standard adalimumab treatment, the blood concentration of most drugs is below the treatment threshold, and a few patients develop anti-ADA antibodies [6]. Other studies have confirmed that patients with severe and refractory HS respond well to high-dose ADA treatment [7]. Therefore, this study explores the therapeutic effect and safety of adalimumab in patients with moderate to severe HS and analyzes its impact on the level of peripheral blood inflammatory factors, aiming to provide a theoretical basis for the efficacy research and clinical application of adalimumab in the treatment of HS.

Materials and methods

General information

This retrospective study collected clinical data from patients diagnosed with moderate to severe HS by two or more dermatologists at Xiantao Hospital of Traditional Chinese Medicine between October 2023 and October 2025. Based on the clinicians' treatment protocols at the time of diagnosis, patients were divided into an ADA group (n=30) and a cyclosporine A (CSA) group (n=20).

Inclusion criteria: (1) Patients meeting the clinical diagnostic criteria for HS; (2) Patients with HS in Hurley stage II or III; (3) Patients with stable physical condition and good mental state.

Exclusion criteria: (1) Patients with severe mental illness; (2) Patients with allergic reactions to the active ingredient of the biological agent or other excipients; (3) Patients with infectious diseases such as tuberculosis or Human Immunodeficiency Virus (HIV); (4) Patients with underlying diseases of the heart, liver, lungs, kidneys, etc.; (5) Patients with a history of malignant tumors.

This study has been approved by the Ethics Committee of Xiantao Hospital of Traditional Chinese Medicine.

Treatment protocols

All patients underwent a comprehensive baseline assessment before treatment, including interferon-gamma release assay for tuberculosis infection, tuberculin skin test, chest X-ray, preoperative infection screening (hepatitis B, hepatitis C, syphilis, and HIV), tumor marker detection, routine blood and urine tests, liver and kidney function tests, and erythrocyte sedimentation rate and C-reactive protein level measurements.

Patients in the ADA group initially received oral erythromycin capsules (0.25 g/capsule, F H Faulding & Co. Limited), 0.5 g twice daily; and oral isotretinoin soft capsules (0.1 g/capsule × 10 capsules, Shanghai Xinyi Yan'an Pharmaceutical Co., Ltd.), 0.2 g once daily; simultaneously, they received subcutaneous injections of ADA (40 mg/0.8 mL, Vetter Pharma-Fertigung GmbH & Co. KG), 160 mg in week 0, 80 mg in week 1, and 40 mg weekly thereafter.

Patients in the CSA group received oral cyclosporine capsules (0.25 g/capsule, North China Pharmaceutical Group Co., Ltd.), 5 mg twice daily.

Observation indicators

(1) The clinical efficacy of HS was assessed using the Hidradenitis Suppurativa Clinical Response (HiSCR) [8] and the International HS Severity Score System (IHS4) [9]. Inflammatory lesions were defined as follows: under strict statistical conditions, active inflammatory nodules, abscesses, or draining sinuses were all considered inflammatory lesions. Active inflammatory nodules were defined as erythematous subcutaneous nodules with a diameter greater than 1 cm and accompanied by tenderness. Nodules without inflammatory changes, old scars, fibrous bands, and healed inactive lesions were not included in the statistics.

HiSCR criteria: The total number of inflammatory lesions (nodules + abscesses + fistulas) decreased by at least 50% from baseline, and the absolute number of abscesses did not increase; no new draining fistula were formed. IHS4 score was calculated using a weighted summation formula: IHS4 = 1 × number of nodules + 2 × number of abscesses + 4 × number of fistulas.

The formula for calculating the reduction rate of IHS4 score after treatment was: (pre-treatment score - post-treatment score)/pre-treatment score × 100%.

(2) The Patient Global Assessment (PtGA) was used to quantitatively evaluate patients' subjective symptoms. To minimize subjective bias and ensure clear evaluation dimensions, the PtGA used a 0-10 numerical rating scale (NRS), where 0 represents "no symptoms" and 10 represents "the most severe symptom imaginable". Instead of using a single, unweighted composite score, the PtGA recorded data from four independent dimensions: pain intensity (PtGA pain), functional impairment (PtGA function), perceived disease severity (PtGA severity), and treatment satisfaction (PtGA response). The PtGA response rate (RR) for each dimension (with pain as the primary endpoint) was calculated as follows: PtGA RR = (baseline score - follow-up score)/baseline score × 100%. Significant clinical improvement was defined as a decrease in the NRS score of ≥30% or an absolute decrease of ≥2 points.

(3) Fasting venous blood was collected from patients, and serum was separated after centrifugation. The expression levels of interleukin-17 (IL-17), interleukin-23 (IL-23), tumor necrosis factor-α (TNF-α), soluble interleukin-2 receptor (SIL-2R), NOD-like receptor thermal protein domain-associated protein 3 (NLRP3), and caspase-1 in serum were detected using a double-antibody sandwich enzyme-linked immunosorbent assay (ELISA). The assays were performed strictly according to the kit instructions, and all kits were purchased from Nanjing Jiancheng BioEngineering Institute.

(4) The Dermatology Life Quality Index (DLQI) was adopted to assess the patients' QoL. This scale contains 10 items covering ten aspects: symptoms and physical sensations, psychological sensations, daily activities, clothing choices, social and recreational activities, physical exercise, work and study, family and interpersonal relationships, sexual life, and treatment status. Each item was scored using a 4-point scale: 0 = no impact, 1 = slight impact, 2 = significant impact, and 3 = extreme impact. The total score ranges from 0 to 30 points, with higher scores indicating poorer QoL. The generally accepted scoring criteria were: 0-1 points indicating no significant impact on the patient's life; 2-5 points indicating a slight impact on QoL; 6-10 points indicating a moderate impact on QoL; 11-20 points indicating a severe impact on QoL; and 21-30 points indicating an extremely severe impact on QoL.

(5) A logistic regression analysis was used to screen for factors influencing absolute HiSCR remission in patients with HS. Absolute HiSCR remission was defined as a reduction of at least 50% in the number of painful nodules and abscesses from baseline.

Statistical methods

SPSS 19.0 was employed for data processing. Count data were presented as number of cases/percentage, and measurement data were presented as mean ± standard deviation ($\bar{x}\pm sd$). The t-test was adopted to compare the differences in serum inflammatory factors and other indicators before and after treatment between the two groups. $P<0.05$ was considered statistically significant. Additionally, G*Power was used to conduct a post-hoc power analysis to evaluate the adequacy of the sample size: based on the change in the primary outcome measure HiSCR, with $\alpha=0.05$ and an effect size of $d=0.75$, and an actual sample size of 15 cases per group, the calculated power was 85%, indicating that the sample size in this study was sufficient to detect the expected treatment effect.

Results

Comparison of images before and after treatment

Figure 1 shows skin imaging data of a 29-year-old female patient in the ADA group before and after treatment. Before treatment, the patient's skin showed well-defined red inflammatory lesions with a darker center and diffuse redness around the periphery. These lesions were sites of HS, with mild swelling and exudation on the surface, suggesting infection or inflammation, possibly caused by sweat gland blockage or bacterial infection. After treatment, the patient's inflammatory response decreased, skin condition improved, and swelling and edema subsided; the patient's HS was well controlled, and the skin essentially returned to near-normal.

Baseline data

Analysis of general data of the subjects showed no statistically significant differences between the two groups in age, sex, body mass index, disease duration, serum high-sensitivity

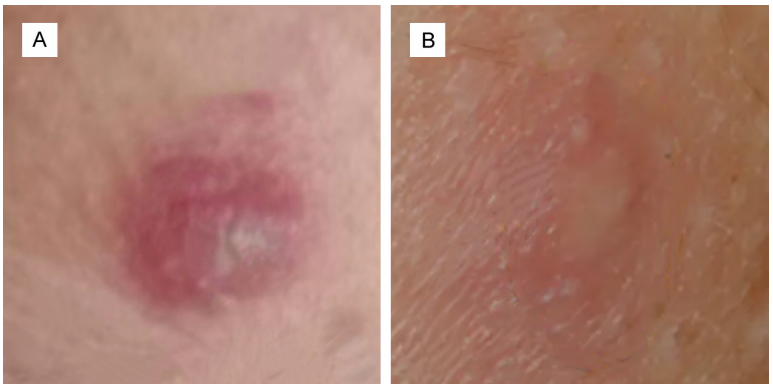

Figure 1. Images of a patient in the adalimumab group before and after treatment (female, 29 years old, with hidradenitis suppurativa; A: Before treatment, B: After treatment).

Table 1. Basic information of the patients

Characteristics	Cyclosporine (CSA) (n=20)	Adalimumab (ADA) (n=30)	t/χ^2	*P*
Age (years)	35.1±6.9	32.7±4.7	1.482	0.145
Gender			0.073	0.792
Male	9	13		
Female	11	17		
BMI (kg/m^2)	25.6±2.0	26.4±1.8	-1.478	0.148
Duration of illness (years)	9.0±3.8	9.5±4.0	-0.442	0.662
hs-CRP (mg/dL)	1.52±0.84	1.63±0.53	-0.583	0.565
IHS4 score	42.1±2.1	43.8±3.8	-1.897	0.065
Hurley's grading			0.032	0.862
II	12	19		
III	8	11		

ADA: adalimumab; CSA: cyclosporine; BMI: body mass index; hs-CRP: high-sensitivity C-reactive protein; IHS4: International hidradenitis suppurativa severity score system.

C-reactive protein, international HS score, and Hurley stage (all *P*>0.05) (**Table 1**).

Outcome evaluation

After treatment, the IHS4 scores of both groups significantly decreased (*P*<0.05). The reduction in IHS4 scores was significantly greater in the ADA group compared to the CSA group (*P*< 0.05) (**Figure 2**).

The changes in HiSCR RR over the 0-12 week treatment period were analyzed. At weeks 0, 2, 4, 6, 8, 10, and 12, the HiSCR RR in the CSA group was 0.0%, 36.0%, 37.2%, 40.6%, 45.8%, 51.3%, and 59.2%, respectively. In the ADA group, the HiSCR RR was 0.0%, 40.0%, 40.0%, 43.3%, 50.0%, 56.7%, and 63.3%, respectively. That was, from week 2 to week 12, the HiSCR RR in the ADA group was significantly higher than that in the CSA group (*P*<0.05) (**Figure 3**).

The differences in PtGA RR for skin pain at week 12 were analyzed. In the CSA group, the RRs for skin pain reduction of ≥30%, ≥1, and ≥30% and ≥1 were 45.0%, 56.0%, and 44.0%, respectively. In the ADA group, the RRs for the same categories were 50.0%, 63.3%, and 50.0%, respectively. Compared to the CSA group, the PtGA RR for skin pain at week 12 was significantly higher in the ADA group (*P*<0.05) (**Figure 4**).

Changes in inflammatory cytokine levels in peripheral blood

Comparison of serum inflammatory cytokines TNF-α, IL-17, IL-23, and SIL2R levels before and after treatment showed a significant decrease in both groups after treatment (all *P*<0.05). Compared to the CSA group, the reduction in these cytokine levels was more pronounced in the ADA group (all *P*<0.05) (**Figure 5**).

The changes in serum levels of NLRP3 and Caspase-1 showed that after treatment, the levels of NLRP3 and Caspase-1 were significantly reduced in both groups (*P*<0.05). Compared to the CSA group, the reduction in these levels was more pronounced in the ADA group (*P*<0.05) (**Figure 6**).

QoL assessment

The changes in DLQI 0-1 scores during the 0-12 week showed that at weeks 0, 2, 4, 6, 8, 10, and 12, the RRs of DLQI 0-1 scores in the CSA group were 0.0%, 2.2%, 5.6%, 7.3%, 22.7%, 18.7%, and 17.2%, respectively. In the ADA group, the RRs of DLQI 0-1 scores were 0.0%, 3.3%, 10.0%, 10.0%, 36.7%, 33.3%, and 33.3%, respectively. Compared to the CSA

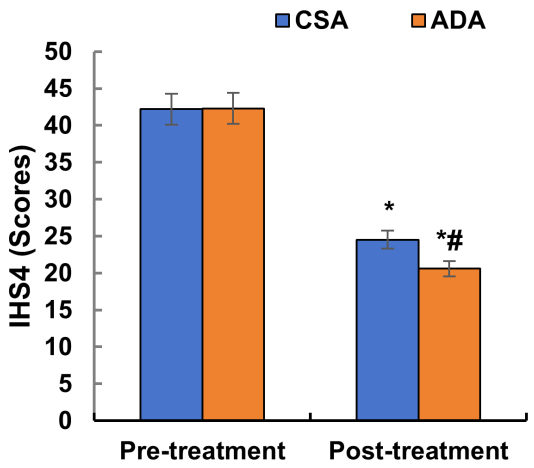

Figure 2. Comparison of international hidradenitis suppurativa severity scores between the groups. ADA: adalimumab; CSA: cyclosporine. # indicates $P<0.05$ compared to the cyclosporine (CSA) group; * indicates $P<0.05$ compared to baseline.

group, the DLQI 0-1 RR in the ADA group was significantly higher ($P<0.05$) (**Figure 7**).

Safety evaluation

No serious infections or malignancies occurred in any patient during treatment and follow-up. Skin lesions significantly improved during treatment, and all other indicators remained within the normal range. A total of 12 patients experienced adverse reactions. In the ADA group, 5 out of 30 patients (16.7%) reported at least one adverse event, including dry mouth (3 cases, 10.0%) and skin desquamation (2 cases, 6.7%). In the CSA group, 7 out of 20 patients (35.0%) reported adverse events, including dry mouth (3 cases, 15.0%), abdominal pain (2 cases, 10.0%), and skin desquamation (2 cases, 10.0%). There was no significant difference in the overall incidence of adverse events between the two groups ($P=0.182$, Fisher's exact test) (**Table 2**). All adverse reactions were tolerable after symptomatic intervention and did not recur.

Logistic regression analysis of factors influencing HiSCR in HS patients

Table 3 presents the logistic regression analysis of predictive factors for the absolute reduction in HiSCR in patients with HS. Multivariate logistic regression analysis used the absolute decrease of HiSCR to evaluate its association with various clinical variables. The higher ORs, the greater the positive difference in IL-23 and SIL2R between the groups, suggesting that the above factors have more significant effects on the risk of disease occurrence.

Discussion

If not intervened in time, HS can lead to sinus tract formation and reduce the patient's QoL. Analgesia and local inflammation suppression can delay or affect the progression of osteoarthritis. There are currently no specific treatment guidelines for this disease in the existing literature, and the general treatment principles for adults are followed in clinical practice [10]. Traditional treatment options include corticosteroids, isotretinoin combined with surgery, all of which have limitations. Although corticosteroids can relieve the pain of patients with HS in the short-term, the long-term efficacy is poor [11]. In recent years, antibiotics have become the first-line treatment for HS, and some antibiotics have significant efficacy, especially suitable for the control of moderate symptoms or acute exacerbations of severe inflammation. Immunomodulatory therapy also has important clinical value, mainly by blocking the TNF-α and IL-17 cytokine pathways [12]. The clinical treatment of HS is challenging, and there is currently no specific treatment plan. Isotretinoin can inhibit the formation of keratin plugs in the hair follicles of patients with HS, but it can cause adverse reactions such as dry mouth, liver damage, and dyslipidemia, which limits its widespread clinical application [13]. Surgical treatment of HS is more invasive, and some patients need to undergo skin grafting. Severe postoperative infection can affect the survival rate of patients [14]. ADA is a recommended drug in the 2018 UK Clinical Practice Guidelines for HS and belongs to the TNF-α inhibitors. TNF-α is a common core proinflammatory cytokine and occupies a core position in the pathogenesis of inflammatory skin diseases such as HS. As a proinflammatory cytokine, TNF-α can activate macrophages, destroy the skin barrier function, and promote angiogenesis, thereby inducing the characteristic chronic inflammation and skin damage of HS [15]. ADA is the first biologic approved by the FDA for the treatment of HS. Its mechanism of action is to specifically inhibit TNF-α. ADA also belongs to the class of TNF-α inhibitors. HS is a refractory chronic inflammatory skin disease that requires treatment with biologics such as anti-TNF-α

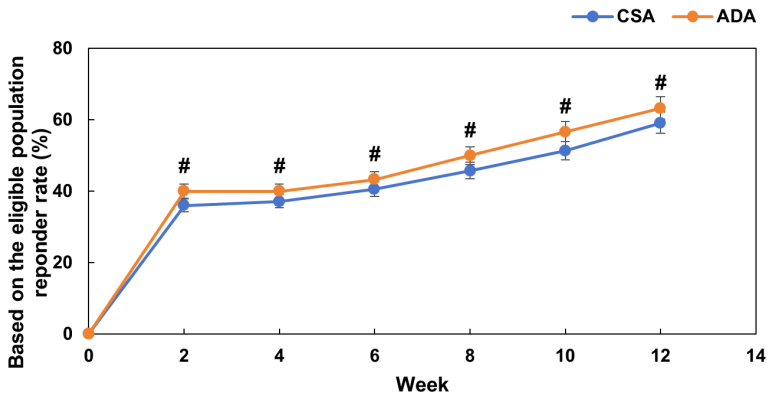

Figure 3. Hidradenitis suppurativa clinical response rate of both groups from week 0 to week 12. ADA: adalimumab; CSA: cyclosporine. # indicates $P<0.05$ compared to the cyclosporine (CSA) group.

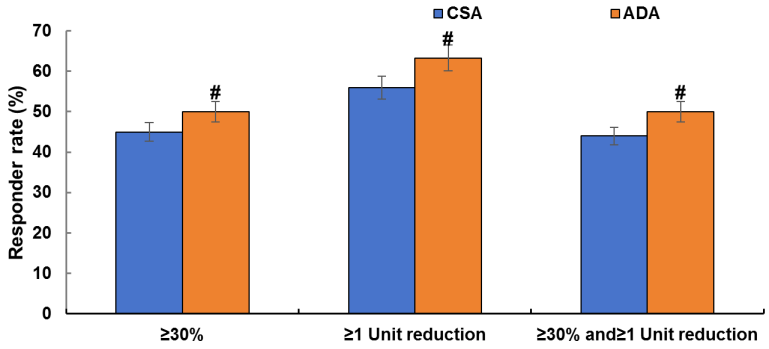

Figure 4. Comparison of patient global assessment relief rate for skin pain at week 12. ADA: adalimumab; CSA: cyclosporine. # indicates $P<0.05$ compared to the cyclosporine (CSA) group.

and anti-IL-17 [16]. ADA has been effectively used in the treatment of plaque psoriasis, ankylosing spondylitis, HS, and other diseases, with definite clinical efficacy. This drug can significantly improve the condition of psoriasis by inhibiting the tumor necrosis factor-α inflammatory pathway. Studies have shown that ADA not only reduces the severity of skin lesions, but also has a positive effect on the sexual function and reproductive health of male patients, such as improving erectile function, increasing sperm motility, and regulating testosterone levels [17]. Other studies have confirmed that ADA is effective for ankylosing spondylitis by regulating the IL-17 pathway, and its mechanism of action overlaps with that of other biological agents such as ixekizumab and bimekizumab [18]. ADA has also been shown to be effective in improving HS [19]. This study further analyzed the outcomes and safety of ADA in HS to provide reference data for clinical practice. First, this study found that the reduction rate of IHS4 score in HS patients receiving ADA intervention was 60.5% (30.0%-90.0%), and the HiSCR RR at 12 weeks was 63.3%. Kimball et al. [20] found that HS patients treated with 40 mg ADA weekly for 12 weeks had a clinical RR of 58.9%. Zouboulis et al. [21] also demonstrated that 73% of patients achieved HiSCR, with sustained improvement in lesion count, skin pain, and life index scores after 12 weeks of treatment with 40 mg weekly ADA. These findings indicate that ADA can significantly improve the clinical symptoms of HS patients.

Studies have confirmed that IL-17 secretion levels in the skin lesions and surrounding tissues of HS patients are higher than those in healthy individuals [22]. Matusiak et al. [23] suggested that compared with healthy people, the serum IL-17 level in HS patients is elevated, and this elevation is positively correlated with disease severity. Both IL-17 and IL-23 belong to T helper cell 17 (Th17) cytokines, and the Th17 cell-mediated IL-17/IL-23 inflammatory axis plays a major role in the pathogenesis of autoimmune and inflammatory diseases. Navrazhina et al. [24] treated moderate to severe HS with a human anti-IL-17 receptor A monoclonal antibody and found that after 12 weeks of treatment, patients' inflammatory responses and signs were significantly improved, and IL-17A levels in the skin and serum around lesions were reduced. Schlapbach et al. [25] confirmed that IL-23 is highly expressed in macrophages infiltrating the dermal papillary and reticular tissues of HS lesions, while IL-17 infiltrates the dermis of lesions. ADA improves psoriasis symptoms by regulating the IL-17/IL-23 axis. TNF-α acts as a key trigger that activates the NLRP3 inflammasome via the nuclear factor κB (NF-κB) pathway, increasing

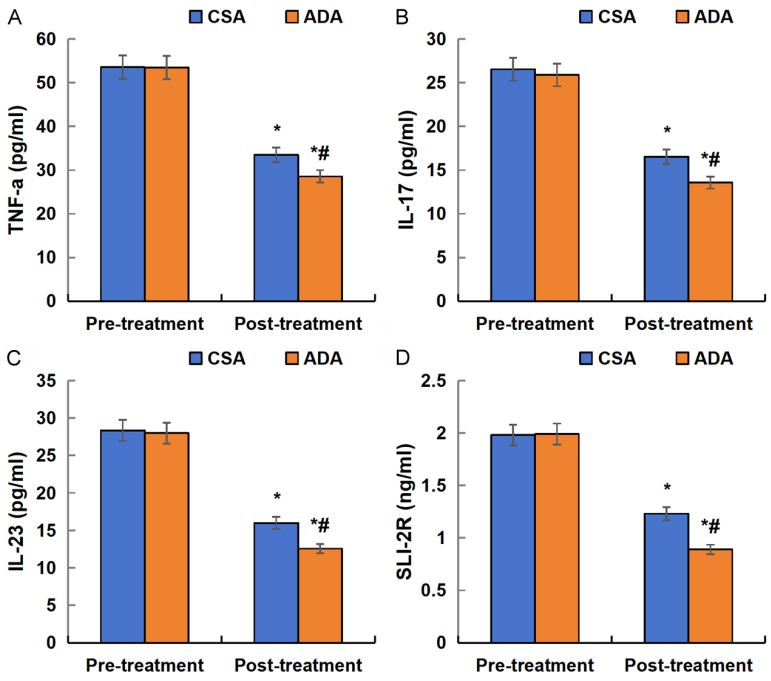

Figure 5. Serum inflammatory cytokine levels before and after treatment. ADA: adalimumab; CSA: cyclosporine. A: Tumor necrosis factor-α (TNF-α); B: Interleukin-17 (IL-17); C: Interleukin-23 (IL-23); D: Soluble interleukin-2 receptor (SIL-2R); # indicates $P<0.05$ compared to the cyclosporine (CSA) group; * indicates $P<0.05$ compared to baseline.

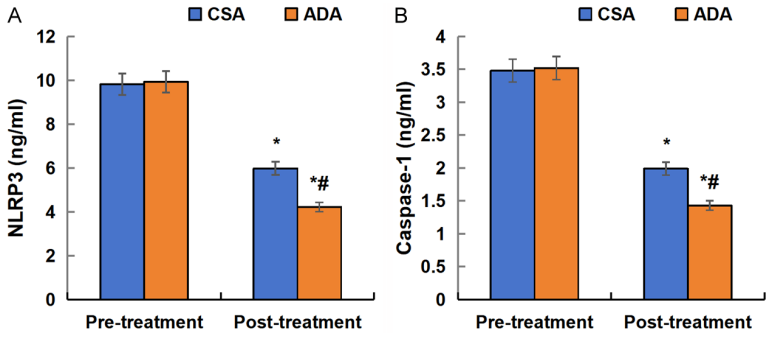

Figure 6. Serum levels of relevant factors before and after treatment. ADA: adalimumab; CSA: cyclosporine; A: NOD-like receptor thermal protein domain associated protein 3 (NLRP3); B: Cysteine aspartate-specific protease-1 (Caspase-1); # indicates $P<0.05$ compared to the cyclosporine (CSA) group; * indicates $P<0.05$ compared to baseline.

NLRP3 expression and amplifying pro-IL-1β [26]. Through neutralization by ADA, TNF-α is inactivated, thereby preventing priming and formation of the NLRP3-Caspase-1 complex. Therefore, caspase-1 is prevented from cleaving pro-interleukin-1 beta (IL-1β) and pro-interleukin-18 (IL-18) into their active forms. Since IL-1β is a potent inducer that stimulates the production of IL-17 and IL-23 in T cells and dendritic cells, inhibition of the NLRP3 pathway by ADA may suppress the IL-17/IL-23 inflammatory loop.

TNF-α blockade may also directly affect the distribution of immune cell subsets. Previous research has shown that TNF-α promotes Th17 cell differentiation and survival by facilitating the expansion of an effector function subpopulation (CD4+ Treg). Thus, the decreased IL-17 expression levels observed in our group may be attributed to changes in the composition of T-helper cell subsets, though other factors may also be involved. TNF-α promotes the transcriptional expression of NLRP3 and pro-IL-1β through the NF-κB signaling pathway. At the molecular level, this process involves the phosphorylation of the IKK complex and subsequent degradation of IκBα. As reviewed by Zhang et al. [27], caspase-8 serves as a critical molecular switch in various inflammatory diseases. Notably, its activity is tightly regulated by post-translational modifications, including phosphorylation at specific tyrosine and serine residues, which determine whether a cell undergoes apoptosis, necroptosis, or pyroptosis. When ADA neutralizes TNF-α, it theoretically blocks this phosphorylation cascade, thereby inhibiting the formation of the NLRP3-Caspase-1 complex. Given that IL-1β is a key factor in inducing Th17 cell differentiation and IL-23 production, its reduced level further interrupts the IL-17/IL-23 inflammatory loop. In addition, TNF-α blockade may exert its effects by altering the distribution of immune cell subsets, such as suppressing Th17 expansion and restoring Treg function. Therefore, although this study did not directly provide evi-

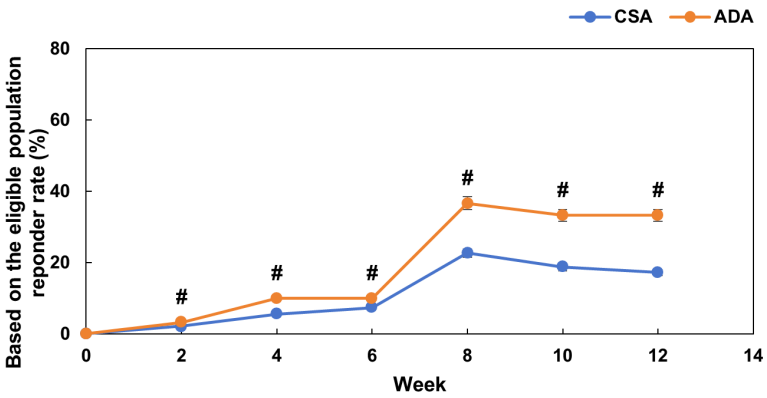

Figure 7. Quality of life assessment from week 0 to week 12. ADA: adalimumab; CSA: cyclosporine. # indicates $P<0.05$ compared to the cyclosporine (CSA) group.

Table 2. Comparison of treatment-related adverse reactions between the two groups

Adverse events	ADA group (n=30)	CSA group (n=20)	*P*	OR (95% CI)
Dry mouth	3 (10.0%)	3 (15.0%)	0.678	0.63 (0.11-3.60)
Abdominal pain	0 (0.0%)	2 (10.0%)	0.160	0.12 (0.01-2.57)
Skin desquamation	2 (6.7%)	2 (10.0%)	0.689	0.64 (0.08-4.98)
Any adverse event	5 (16.7%)	7 (35.0%)	0.182	0.37 (0.10-1.43)

Table 3. Logistic regression analysis of predictive factors for absolute reduction in hidradenitis suppurativa clinical response

Factor	*β*	*SE*	χ^2	*P*	*OR*	*95% CI*
IHS4	0.238	0.412	3.436	0.063	1.444	0.622-1.336
PtGA RR	1.266	0.356	4.074	0.024	1.323	0.435-1.571
TNF-α	0.742	0.477	2.697	0.031	1.224	0.564-1.423
IL-17	0.756	0.375	4.363	0.028	1.953	0.473-1.354
IL-23	1.624	0.475	7.754	0.022	3.622	1.234-7.422
SLI2R	1.924	0.435	7.568	0.026	3.542	1.252-6.323
NLRP3	1.385	0.464	2.543	0.002	1.253	0.323-1.653
Caspase-1	1.317	0.435	2.625	0.003	1.324	0.453-1.652
DLQI 0-1 RR	0.733	0.311	1.875	0.046	0.424	0.522-1.452

β: regression coefficient; SE: standard error; χ^2: Chi-square; OR: odds ratio; 95% CI: 95% confidence interval; IHS4: international hidradenitis suppurativa severity score system; PtGA RR: patient global assessment relief rate; TNF-α: tumor necrosis factor-alpha; IL-17: interleukin-17; IL-23: interleukin-23; SIL2R: soluble interleukin-2 receptor; NLRP3: NOD-like receptor family pyrin domain-containing 3; Caspase-1: cysteinyl aspartate specific proteinase-1; DLQI 0-1 RR: dermatology life quality index 0-1 remission rate.

dence of phosphorylation, the coordinated downregulation of downstream inflammatory factors strongly and indirectly confirmed that ADA exerted its therapeutic effects by inhibiting the TNF-α/NLRP3/IL-17 axis. Consistent with the regulatory functions of caspase-8 outlined in the literature [27], future studies should combine tissue biopsy and molecular biology techniques - such as phospho-specific antibodies or kinase activity assays - to directly verify the phosphorylation status of signaling molecules like NF-κB p65, IKKα/β, or RIPK1, thereby completing the causal chain following ADA treatment.

SIL2R is an important immunosuppressive factor [28]. Matusiak et al. [29] noted that serum SIL2R levels can be used for disease staging in HS. Wieland et al. reported that serum SIL2R levels were significantly lower in HS patients after ADA treatment [30]. The NLRP3 inflammasome mediates inflammatory response activation through the production of pro-inflammatory cytokines, including IL-1β and IL-18 [31]. Increasing evidence supports the involvement of NLRP3 in the pathogenesis of HS. Moran et al. [32] demonstrated via single-cell ribonucleic acid sequencing that IL-17, IL-1β, and NLRP3-related genes and pathways were significantly upregulated in the skin of HS patients. Furthermore, inhibiting the NLRP3 inflammasome in skin explants from these patients can markedly reduce the secretion of other key inflammatory mediators. Using immunohistochemistry, Manfredini et al. [33] proposed that the expression level of NLRP3 protein in skin keratinocytes of HS patients was elevated, and the NLRP3/IL-1β pro-inflammatory axis was overactive in the skin of these patients. This study revealed that serum NLRP3 levels in HS patients were also significantly reduced following ADA intervention. Currently, there is no direct evidence that ADA regulates the expression of SIL2R and

NLRP3 in HS. However, Crommelin et al. [34] found that ADA intervention improved serum SIL2R levels in patients with refractory sarcoidosis. Olivares-González et al. [35] proposed that ADA can reduce retinal cell death by inhibiting Caspase-3 activation and can also downregulate the NLRP3 inflammasome. This indirectly confirms that ADA may act in HS by regulating the expression of SIL2R and NLRP3.

A broader perspective on post-translational regulation further supports these observations. As extensively reviewed by Liao et al. [36], ubiquitination is a fundamental mechanism for maintaining protein homeostasis and regulating immune and inflammatory responses. The ubiquitin-proteasome system controls the degradation of key inflammatory signaling molecules, including TNF-α, NF-κB pathway components, and NLRP3 inflammasome elements. Dysregulation of ubiquitination is closely linked to inflammatory diseases. Therefore, the reduction in NLRP3, Caspase-1, and various cytokines following ADA treatment observed in our study may be partly attributed to enhanced ubiquitin-dependent degradation of these pro-inflammatory proteins, a mechanism that warrants further investigation. Additional evidence is needed to confirm these results.

Moreover, the safety profile of ADA in HS requires further investigation. Bechara et al. [37] reported that 48% of patients showed a clinical response to ADA as an adjunctive treatment for moderate to severe HS 12 weeks following major resection. However, 72% of the patients experienced adverse reactions, although none developed complications such as wound infections or bleeding. Glatt et al. [38] found that the HiSCR RR in 21 patients with moderate to severe HS after 12 weeks of ADA treatment was 57.3%. Among them, 46% achieved HiSCR75, 32% reached HiSCR90, and only one patient experienced a serious adverse event. This is consistent with the findings of this study, where no serious adverse events occurred in patients with moderate to severe HS treated with ADA. These results indicate that ADA is safe for the treatment of HS and is worthy of clinical application.

Recently, biologic agents targeting the IL-17 pathway have been introduced; for instance, secukinumab and bimekizumab target this pathway and have also passed regulatory review for the treatment of HS [39]. Among these, bimekizumab is an IgG1 monoclonal antibody that selectively inhibits both IL-17A and IL-17F. Given that both IL-17A and IL-17F are elevated in HS lesion areas, a dual-inhibition approach may provide more potent anti-inflammatory effects [40]. A Network meta-analysis comparing the short-term effects of approved biologics - adalimumab, secukinumab, and bimekizumab - identified no direct head-to-head trials but showed that these treatment options had similar clinical outcomes [41].

This study also has limitations: the sample size was small, resulting in insufficient statistical power for analysis. To address this limitation, future studies should adopt large-scale sample designs to enhance statistical power. In addition, due to the lack of direct assessment of phosphorylated-NF-κB, activated STAT3, or specific immunocyte changes, as well as the absence of analysis at the subcellular localization level - including NLRP3/Caspase-1 activity or associated protein profile changes in inflammatory areas after necrotic tissue destruction - we were unable to experimentally verify the causal relationship between ADA-induced TNF-α inhibition and NLRP3 downregulation in this patient group. Future research directions should include transcriptomic analysis of skin lesion transcripts or in vitro stimulation of peripheral blood mononuclear cells from patients to map molecular changes and verify the pathophysiological mechanisms through experimental data.

In conclusion, ADA exhibits good therapeutic efficacy and low risk in HS patients. ADA can significantly reduce the concentrations of TNF-α, IL-4, IL-17, IL-23, SIL2R, NLRP3, and Caspase-1 in HS patients, thereby alleviating their symptoms.

Disclosure of conflict of interest

None.

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References

[1] Mateu-Arrom L, Puig L and Vilarrasa E. Surgical approach to hidradenitis suppurativa. Actas Dermosifiliogr 2025; 116: 621-627.

[2] Tzellos T. Conventional treatment of hidradenitis suppurativa: serving the "window of opportunity" concept. Clin Dermatol 2025; 43: 485-489.

[3] Górecka A, Barańska-Rybak W, Lewandowski M, Szymańska E, Świerczewska Z and Walecka I. Pediatric-onset hidradenitis suppurativa: a case series of 42 patients. Postepy Dermatol Alergol 2024; 41: 525-529.

[4] Charrow A, Santiago-Soltero K and Porter M. Biologics in hidradenitis suppurativa: progress and new directions. J Am Acad Dermatol 2024; 91: S27-S30.

[5] Xue S, He Y, Pei L and Xu H. Progress of biologics and small molecule drugs in the treatment of hidradenitis suppurativa. J Dermatol 2025; 52: 1337-1350.

[6] Stirton H and Alhusayen R. Therapeutic drug monitoring in hidradenitis suppurativa patients with suboptimal treatment response to adalimumab. J Cutan Med Surg 2025; 29: 587-592.

[7] Jones L, Sun J and Kennedy H. Efficacy of High dose adalimumab for the management of hidradenitis suppurativa: a systematic review. Australas J Dermatol 2025; 66: e197-e201.

[8] Kimball AB, Jemec GBE, Alavi A, Reguiai Z, Gottlieb AB, Bechara FG, Paul C, Giamarellos Bourboulis EJ, Villani AP, Schwinn A, Ruëff F, Pillay Ramaya L, Reich A, Lobo I, Sinclair R, Passeron T, Martorell A, Mendes-Bastos P, Kokolakis G, Becherel PA, Wozniak MB, Martinez AL, Wei X, Uhlmann L, Passera A, Keefe D, Martin R, Field C, Chen L, Vandemeulebroecke M, Ravichandran S and Muscianisi E. 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: 747-761.

[9] Hernández Montilla I, Medela A, Mac Carthy T, Aguilar A, Gómez Tejerina P, Vilas Sueiro A, González Pérez AM, Vergara de la Campa L, Luna Bastante L, García Castro R and Alfageme Roldán F. Automatic International Hidradenitis Suppurativa Severity Score System (AIHS4): a novel tool to assess the severity of hidradenitis suppurativa using artificial intelligence. Skin Res Technol 2023; 29: e13357.

[10] Pustisek N, Bulic SO, Resic A, Bulic L and Brenner E. Hidradenitis suppurativa in children and adolescents. Clin Dermatol 2025; 43: 455-461.

[11] Nosrati A, Torpey ME, Andriano TM, Benesh G, Babbush KM, Hosgood HD, Campton KL and Cohen SR. Importance of a multi-tiered treatment approach for intellectually and developmentally disabled patients with hidradenitis suppurativa. Arch Dermatol Res 2023; 315: 1827-1829.

[12] Becherel PA. An update on the medical treatments of hidradenitis suppurativa. Eur J Dermatol 2025; 35: 14-21.

[13] Fu ZL, Wu QY, Bu WB and Xiao D. Treatment of severe hidradenitis suppurativa with a combination of 5-aminolevulinic acid photodynamic therapy, surgery, and secukinumab. Photodiagnosis Photodyn Ther 2023; 42: 103637.

[14] Orenstein LAV, Nguyen TV, Damiani G, Sayed C, Jemec GBE and Hamzavi I. Medical and surgical management of hidradenitis suppurativa: a review of international treatment guidelines and implementation in general dermatology practice. Dermatology 2020; 236: 393-412.

[15] Campbell C, Mayatra JM, Neve AJ, Fletcher JM and Johnston DGW. Inflammasomes: emerging therapeutic targets in hidradenitis suppurativa? Br J Dermatol 2024; 191: 670-679.

[16] Al-Wattar-Ceballos O, Martínez-Montalvo L and Carmona-Rodríguez M. Safety and efficacy profile of anti-IL17 treatments in hidradenitis suppurativa: systematic review and meta-analysis of randomized placebo-controlled trials. Actas Dermosifiliogr 2025; 116: 945-958.

[17] Yüksek T, Ataş H, Kartal SP, Aygar GT and Karakoyunlu AN. Impact of adalimumab on erectile dysfunction, sperm parameters and hormonal profile in male psoriasis patients: a six-month observational study. Arch Dermatol Res 2024; 317: 21.

[18] Saran A, Nishizaki D, Lippman SM, Kato S and Kurzrock R. Interleukin-17: a pleiotropic cytokine implicated in inflammatory, infectious, and malignant disorders. Cytokine Growth Factor Rev 2025; 83: 35-44.

[19] Martora F, Megna M, Battista T, Potestio L, Annunziata MC, Marasca C, Villani A and Fabbrocini G. Adalimumab, ustekinumab, and secukinumab in the management of hidradenitis suppurativa: a review of the real-life experience. Clin Cosmet Investig Dermatol 2023; 16: 135-148.

[20] Kimball AB, Okun MM, Williams DA, Gottlieb AB, Papp KA, Zouboulis CC, Armstrong AW, Kerdel F, Gold MH, Forman SB, Korman NJ, Giamarellos-Bourboulis EJ, Crowley JJ, Lynde C, Reguiai Z, Prens EP, Alwawi E, Mostafa NM, Pinsky B, Sundaram M, Gu Y, Carlson DM and Jemec GB. Two phase 3 trials of adalimumab for hidradenitis suppurativa. N Engl J Med 2016; 375: 422-34.

[21] Zouboulis CC, Okun MM, Prens EP, Gniadecki R, Foley PA, Lynde C, Weisman J, Gu Y, Williams DA and Jemec GBE. Long-term adalimumab efficacy in patients with moderate-to-severe hi-

dradenitis suppurativa/acne inversa: 3-year results of a phase 3 open-label extension study. J Am Acad Dermatol 2019; 80: 60-69.
[22] Mastorino L, Susca S, Cariti C, Sliquini N, Verrone A, Stroppiana E, Ortoncelli M, Dapavo P, Ribero S and Quaglino P. Efficacy of anti-IL-23 and anti-IL-17 after adalimumab failure in psoriatic patients. J Eur Acad Dermatol Venereol 2023; 37: 1848-1853.
[23] Matusiak Ł, Szczęch J, Bieniek A, Nowicka-Suszko D and Szepietowski JC. Increased interleukin (IL)-17 serum levels in patients with hidradenitis suppurativa: implications for treatment with anti-IL-17 agents. J Am Acad Dermatol 2017; 76: 670-675.
[24] Navrazhina K, Frew JW, Grand D, Williams SC, Hur H, Gonzalez J, Garcet S and Krueger JG. Interleukin-17RA blockade by brodalumab decreases inflammatory pathways in hidradenitis suppurativa skin and serum. Br J Dermatol 2022; 187: 223-233.
[25] Schlapbach C, Hänni T, Yawalkar N and Hunger RE. Expression of the IL-23/Th17 pathway in lesions of hidradenitis suppurativa. J Am Acad Dermatol 2011; 65: 790-798.
[26] Tsiogka A, Liakou AI, Agiasofitou E, Gregoriou S, Stratigos A, Rigopoulos D and Kontochristopoulos G. Adalimumab-induced paradoxical psoriasis treated with biologics targeting the IL-17/IL-23 axis in patients with hidradenitis suppurativa. Dermatology 2023; 239: 937-941.
[27] Zhang WZQ, Zhu CL, Liao Y, Zhou M, Xu WY and Zou Z. Caspase-8 in inflammatory diseases: a potential therapeutic target. Cell Mol Biol Lett 2024; 29: 130.
[28] Schimmelpennink MC, Quanjel M, Vorselaars A, Wiertz I, Veltkamp M, Van Moorsel C and Grutters JC. Value of serum soluble interleukin-2 receptor as a diagnostic and predictive biomarker in sarcoidosis. Expert Rev Respir Med 2020; 14: 749-756.
[29] Matusiak Ł, Bieniek A and Szepietowski JC. Soluble interleukin-2 receptor serum level is a useful marker of hidradenitis suppurativa clinical staging. Biomarkers 2009; 14: 432-437.
[30] Wieland CW, Vogl T, Ordelman A, Vloedgraven HG, Verwoolde LH, Rensen JM, Roth J, Boer J and Hessels J. Myeloid marker S100A8/A9 and lymphocyte marker, soluble interleukin 2 receptor: biomarkers of hidradenitis suppurativa disease activity? Br J Dermatol 2013; 168: 1252-8.
[31] Zhao ZQ, Ma XL, Dong SH, Yin HB, Yang Y and Xiong GY. Regulatory effect of zinc finger protein A20 on rheumatoid arthritis through NLRP3/Caspase-1 signaling axis mediating pyroptosis of HFLS-RA cells. Cell Mol Biol (Noisy-le-grand) 2023; 69: 179-184.
[32] Moran B, Smith CM, Zaborowski A, Ryan M, Karman J, Dunstan RW, Smith KM, Hambly R, Musilova J, Petrasca A, Fabre A, O'Donnell M, Hokamp K, Mills KHG, Housley WJ, Winter DC, Kirby B and Fletcher JM. Targeting the NLRP3 inflammasome reduces inflammation in hidradenitis suppurativa skin. Br J Dermatol 2023; 189: 447-458.
[33] Manfredini M, Giuliani AL, Ruina G, Gafà R, Bosi C, Zoppas E, Di Virgilio F and Bettoli V. The P2X7 receptor is overexpressed in the lesional skin of subjects affected by hidradenitis suppurativa: a preliminary study. Dermatology 2021; 237: 111-118.
[34] Crommelin HA, van der Burg LM, Vorselaars AD, Drent M, van Moorsel CH, Rijkers GT, Deneer VH and Grutters JC. Efficacy of adalimumab in sarcoidosis patients who developed intolerance to infliximab. Respir Med 2016; 115: 72-7.
[35] Olivares-González L, Velasco S, Millán JM and Rodrigo R. Intravitreal administration of adalimumab delays retinal degeneration in rd10 mice. FASEB J 2020; 34: 13839-13861.
[36] Liao Y, Zhang WZQ, Liu Y, Zhu CL and Zou Z. The role of ubiquitination in health and disease. MedComm 2024; 5: e736.
[37] Bechara FG, Podda M, Prens EP, Horváth B, Giamarellos-Bourboulis EJ, Alavi A, Szepietowski JC, Kirby J, Geng Z, Jean C, Jemec GBE and Zouboulis CC. Efficacy and safety of adalimumab in conjunction with surgery in moderate to severe hidradenitis suppurativa: the SHARPS randomized clinical trial. JAMA Surg 2021; 156: 1001-1009.
[38] Glatt S, Jemec GBE, Forman S, Sayed C, Schmieder G, Weisman J, Rolleri R, Seegobin S, Baeten D, Ionescu L, Zouboulis CC and Shaw S. 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: 1279-1288.
[39] Gao JL, Otto TS, Porter ML and Kimball AB. Hidradenitis suppurativa: new targets and emerging treatments. Am J Clin Dermatol 2024; 25: 765-778.
[40] Rastrick J, Edwards H, Ferecskó AS, Le Friec G, Manghera A, Page M and Shaw S. The roles of interleukin (IL)-17A and IL-17F in hidradenitis suppurativa pathogenesis: evidence from human in vitro preclinical experiments and clinical samples. Br J Dermatol 2025; 192: 660-671.
[41] Naik HB, Mørup MF, Davis L, Taieb V, Kiri S, Munro I, Hemstock M, Tzellos T, Piguet V and Kirby B. Short-term efficacy of biologics in moderate-to-severe hidradenitis suppurativa: a systematic review and NMA. J Eur Acad Dermatol Venereol 2026; 40: 646-657.