Clinical, Cosmetic and Investigational Dermatology

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REVIEW

The Efficacy and Safety of Biosimilars in Hidradenitis Suppurativa: A Comprehensive Review

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Abstract: Hidradenitis Suppurativa (HS), also known as Acne Inversa, is a chronic, recurrent inflammatory skin condition primarily affecting apocrine gland-bearing areas, such as the axilla and groin. Characterized by painful nodules, abscesses, and scarring, and has a profound psychological impact on patients. Current treatments aim to manage symptoms and prevent new lesions with a combination of non-pharmacological and pharmacological approaches. Emerging biosimilars, which replicate the efficacy and safety profiles of known biologics at a lower cost, offer new options for treating this debilitating cutaneous disorder. The review summarizes recent studies to explain the role of biosimilars in HS, emphasizing their potential to expand effective treatment options.

Keywords: biologics, biosimilars, hidradenitis suppurativa, review

Introduction

Hidradenitis Suppurativa (HS), also referred to as Acne Inversa, is a persistent and relapsing inflammatory dermatological condition predominantly affecting areas of apocrine gland bearing skin such as the axilla, groin and under the breasts (skin folds). This condition is diagnosed based on characteristic lesions that include nodules, abscesses, comedones, sinus tracts, and scarring. Associated comorbidities frequently include obesity, metabolic syndrome, inflammatory bowel disease (IBD), and spondyloarthropathy.[1] The psychological burden of HS is profound, severely impacting patients' physical, social, and emotional well-being.[2] The pathogenesis of HS remains unclear but is believed to involve multiple factors including genetics, as evidenced by up to 40% of patients reporting a familial predisposition.[1] Originally considered a disease of the sweat glands, recent studies have identified it as a disorder of the follicular epithelium, exacerbated by mechanical stress in genetically susceptible individuals.[3,4] Managing HS is challenging due to the absence of a definitive cure. Treatment strategies aim to prevent the development of new lesions, promptly and effectively treat emerging lesions, and remove existing nodules and cysts. A holistic approach to treatment integrates non-pharmacological measures, topical and systemic medications, and surgical interventions.[1,5] Immunosuppressants, particularly biological agents targeting tumor necrosis factor-alpha (TNF-α), such as Infliximab, are central to the therapeutic regimen. Currently, adalimumab (ADA) is the only biologic agent approved by the FDA specifically for HS management, though other biologics like ustekinumab, secukinumab, and ixekizumab have also demonstrated effectiveness.[6–8] The term "window of opportunity" medically refers to the optimal time frame in which initiating a treatment can achieve the best possible outcomes. In HS, it refers to the early phase treatment with adalimumab. Studies indicate that initiating adalimumab medication shortly after the beginning of HS symptoms results in more effective clinical responses and patient outcomes. Delaying treatment beyond this optimal period can impair the drug's effectiveness since the condition may worsen and become harder and more difficult to treat. Thus, early intervention within this window of opportunity, especially before scarring formation, is critical to getting the best therapeutic outcomes.[9]

Received: 18 May 2024
Accepted: 5 August 2024
Published: 12 August 2024

Biosimilars, novel emerging biopharmaceuticals, replicate the complex structure of existing biologic therapies, offering similar efficacy and safety at reduced costs. These include biosimilars of TNF-α inhibitors such as infliximab and etanercept, which have been approved for various dermatological conditions. Regulatory bodies require a rigorous evaluation of the physicochemical and functional characteristics of these biosimilars, supported by clinical trials demonstrating their comparability to their reference products. This process involves at least one clinical trial conducted within a sensitive and homogeneous patient population.[10] The European Medicines Agency (EMA) has approved nine biosimilar medications for treating plaque psoriasis and HS, including Amgevita, Solymbic, Cyltezo, Imraldi, Benepali, Erelzi, Flixabi, Inflectra, and Remsima, with further approvals anticipated.[11] These developments indicate a promising expansion of treatment options for HS, offering both clinical and economic benefits. This review aims to enhance understanding, provide clarification, and offer in-depth insights into the safety and efficacy of biosimilars in HS management through a thorough analysis of recent research.

Methodology and Materials

The electronic database MEDLINE was searched through PUBMED and Google Scholar in December 2023 using the following search keywords: "Biosimilars" - "Biosimilar agents" - "Hidradenitis suppurativa" - "Biosimilars in Hidradenitis suppurativa" - "Biosimilars in HS".

Results

After applying the inclusion criteria, the search revealed a total of nine (9) studies linking the use of biosimilars in hidradenitis suppurativa have been reported in the literature. Herein, we summarize the findings in the literature in order from the oldest to most recent.[12–20] Summary of the clinical data of each research is seen in (Table 1).

Discussion

Hidradenitis suppurativa (HS) is a chronic inflammatory skin condition marked by painful abscesses and scarring, primarily affecting areas such as the axillary and groin regions.[1] Integrating ultrasound in the characterization of HS lesions has proven to be highly valuable, as evidenced by recent studies. Nazzaro et al effectively employed ultrasound and Color Doppler to evaluate vascularization and fibrosis in HS lesions, both before and after treatment with adalimumab. Their findings revealed significant reductions in vascularization and notable increases in fibrosis, changes that might not be detected through clinical examination alone.[12] Additionally, Wortsman's review emphasizes the crucial role of ultrasound in identifying the true extent and nature of anatomical abnormalities in HS, which are often underestimated during clinical evaluations. Ultrasound features such as widened hair follicles, dermal pseudocystic nodules, and fistulous tracts offer a more detailed assessment of HS severity.[13] Crucially, detecting fibrotic fistulas via ultrasound can inform treatment decisions, suggesting that such fistulas might benefit more from surgical intervention than from anti-inflammatory treatments.[12] Therefore, the integration of ultrasound into HS management enhances lesion characterization, leading to better clinical decisions, disease staging, and tracking response to therapy, thus resulting in improved patient outcomes.

The absence of a definitive cure poses significant challenges in HS management.[1] Non-medical measures for the management of HS include lifestyle modification such as (weight loss, smoking cessation, loose fitted clothing, personal hygiene and analgesia). Topical treatments such as resorcinol, clindamycin 1% solution and topical fusidic acid are commonly employed. Systemic oral therapy like antibiotics are used such as tetracycline and combined oral clindamycin and rifampicin. As well as hormonal therapy (anti-androgens) and oral retinoids are often effective.[1,5] Immunosuppressive agents have emerged as pivotal elements in the therapeutic landscape of hidradenitis suppurativa.[6] Employing intralesional corticosteroid injections of (5 to 10 mg/mL) triamcinolone acetonide have been used as an adjunctive therapy to expedite the clearance of early painful inflammatory nodules.[7] When traditional non-biologic systemic drugs fail, biologics, particularly TNF-α inhibitors, become the next line of therapy due to their ability to effectively reduce inflammation by targeting specific cytokines involved in the inflammatory process. Infliximab, a biological drug that targets tumor necrosis factor-alpha (TNF-α), is a key component of HS treatment regimen. Currently,

Table 1 Summary Review Table of Studies Linking the Use of Biosimilar Agents in Hidradenitis Suppurativa

Reference Number	Study	Year	Type of Study	Age (Years)/ Gender	Comorbidities	Hurley stage	Previous Treatments Used	Type of Biosimilar	Prognosis and Recovery	Side Effects
[16]	Patil S. et al	7/2018	Case report	N=2 30(M), 31(M)	N/A	3,3	Doxycycline rifampicin for 6 weeks, rifampicin and levofloxacin for 6 weeks, and dapsone with retinoids.	ZRC-3197 (adalimumab biosimilar)	HiSCR 50% After 12 weeks in the first case HiSCR 75% In the second case	N/A
[17]	Ricceri F et al	10/2020	Observational study	N=11 7(F) 4(M) 37.9± 14.6	Smoker (63.6%) Overweight (28.1 ± 5.8)	n s II 3 1 III 4 3	Topical and/or systemic steriod	SB5 (Imraldi)	HiSCR, (% achieved) n=100 s= 28.6 IHS4 t0, Mean and SD n: 18.5 ± 11.3 s: 7.7 ± 3.1 IHS4 t36, Mean and SD: n: 11.2 ± 5.4 s: 6.7 ± 3.3	Pain at injection site N=4 36.3%
[18]	Kashlan R et al	12/2020	Case report	F 50	Morbid obesity DM	3	ND yag laser, wide local surgical excision, carbon, IFX dioxide laser excision, various oral and intravenous antibiotics, and IFX infusions.	IFX biosimilar	N/A	Infusion reaction (Anaphylaxis like symptoms) Arthralgia Paresthesia ADA formation

(*Continued*)

https://doi.org/10.2147/CCID.S478840

Table 1 (Continued).

Reference Number	Study	Year	Type of Study	Age (Years)/ Gender	Comorbidities	Hurley stage	Previous Treatments Used	Type of Biosimilar	Prognosis and Recovery	Side Effects
[19]	Westerkam LL et al	4/2021	Cohort	N=34 IFX-A (N=14): M= 1 F=13 IFX (N= 20) M=3 F=17 Age, mean IFX 42.2 IFX-A 35.5	Dark skin 64% Obesity 38.58%	n s II 3 2 III 11.18	N/A	Infliximab-abda	HiSCR IFX 10 (71%) IFX-A 12 (60) VAS before treatment and after: IFX (6.12 vs 4.00; IFX-A (6.82 Vs 6) IHS4 score before treatment and after IFX-A (21.36 Vs 6.86) IFX: (23.70 Vs 10.80)	N/A
[20]	Montero-Vilchez T et al	2/2022	Observational study	N= 17 M 12 F 5 Age, Mean 31	Family history 8 (47.06)	I 1 II 4 III 12	Adalimumab	Adalimumab biosimilar	Adalimumab switch effective and tolerable N=7 (41.18%) Adalimumab switch failure N=10	SE: N:17 severe pain at the injection site(23.5%) showed loss of HiSCR response (23.5%) dizziness and nausea. (5.9%)

[21]	Roccuzzo G et al	9/22	Cohort	N=37 M=20 F=17	- smoker 24 (65%) - Family history 8 (21.6%) - obesity 27.5 (18.5–39.9)	Before switching to adalimumab: Hurley 1: 0 (0%) Hurley 2: 29 (78.4%) Hurley 3: 8 (21.6%) After switching to biosimilar Hurley 1: 4 (10.8%) Hurley 2: 28 (75.7%) Hurley 3: 5 (13.5%)	Tetracycline and others not specified, adalimumab	Adalimumab biosimilar	HiSCR achievement (T1) Achieved N: 18 (48.6%) Not achieved: N:19 (51.4%) HiSCR achievement (T3) Achieved: 17 (45.9%) Not achieved: 20 (54.1%)	At (T12) Total N=16 (100%) inadequate clinical response N=5 (31.5%) severe injection site pain
[22]	Kirsten N et al	9/2022	Observational	N=94 Age: 39.3 Gender: M: 45.08 F: 48.92	N/A	Mean Hurley 2?	Not mentioned	Adalimumab biosimilar ABP 501	No loss of response: N= 64 IHS4 t0 10.94 IHS4 T1 6.62 IHS4 T2 5.14 AE or Loss off response: N:31 IHS4 t0(before starting ADAo): 10.84 IHS4 t1 (at time of switch) 6.62 IHS4 t2 (12–14 weeks) 5.14	Total N = 31 experienced LoR but no AE, (N=19) LoR in combination with AEs (N = 7) AEs without LoR. (N=5) AE reported (N=12): injection site pain (n = 6) fatigue (n = 4) pruritus (n = 2).

(*Continued*)

https://doi.org/10.2147/CCID.S478840

Table 1 (Continued).

Reference Number	Study	Year	Type of Study	Age (Years)/ Gender	Comorbidities	Hurley stage	Previous Treatments Used	Type of Biosimilar	Prognosis and Recovery	Side Effects
[23]	Burlando M et al	10/2022	Cohort	Overall N: 326 Non switchers: N(%):174 (100) Mean age 33.26 F: 84(48.3) M: 90 (51.7) On originator: N(%):116 (100) Mean age: 33.16 F:56(48.3) M: 60(51.7) On biosimilar N(%):58 (100) Mean Age: 33.45 F: 28(48.3) M: 30(51.7)	Non switcher smoker 129 (74.1%) Overweight 27.22 (4.66%)	Switcher: N:28 T1-Challenge (originator) I: 1 (3.6) II: 18 (64.3) III: 9 (32.1) T2-De-challenge (biosimilar) I: 6 (21.4) II: 22(78.6) III: 0 (0.0) T3-Re-challenge (originator) I: 0 (0.0) II: 23 (82.1) III: 5 (17.9)	Switchers: adalimumab	Adalimumab biosimilar	Follow-up 13 months in originator Vs 10 months in biosimilar Treatment was effective T6: originator 87.7% biosimilar: 77.1% Treatment was effective after 10 months: Originator: 82.2% Biosimilar: 60.5%	N/A
				Switchers N: 152 N/A		Non switcher N=174 Mean 2.37 Originator: N:116 Mean 2.37 Biosimilar: N:58 Mean 2.36	Non-switchers: N/A			

https://doi.org/10.2147/CCID.S478840 DovePress

[24]	Grau-Pérez M et al	12/22	cohort	Total N(%): 77(100) Mean Age: 39.1 Gender: F: 43 (55.8) M: 34(44.2)	N/A	Total N(%): 77(100) II: 32 (39.0) III: 45 (58.4)	N/A	imiraldi	Kaplan- meyer survival estimates: T6 survival rate: ADA-O 75% ADA-B Between 55% to 60% At 12 months survival rate: ADA-O 70% ADA-B About 50%	Ineffectiveness ADA-O (6) ADA-B (9) Side effects(not specified): ADA-O (9) ADA-B (5)
				Humera: N: 41 Mean Age:37.8 Gender: F:25 (56.8) M:16(39.02)		Humeira N:41 II: 16 (41.6) III: 25 (61.0)				
				Imaraldi: N:36 Mean Age: 41.2 Gender: F:22(61.1) M: 14(38.9)		Imiraldi: N:36 II: 16 (44.4) III: 20 (55.6)				

Abbreviations: N/A, not applicable; N, number of patients; SD, standard deviation; IHS4, International Hidradenitis Suppurativa Severity Score System; HiSCR, Hidradenitis Suppurativa Clinical Response; VAS, The Visual Analogue Scale; DM, diabetes mellitus; n, Naive; s, switcher; IFX, infliximab; IFX-A, infliximab ab-abda; ADA, Anti-drug antibodies; B, biologic; ADA-O, adalimumab originator; ADA-B, adalimumab biosimilar; AE, adverse effects; LoR, loss of respon**se**; T0, time zero; T1, at time of switch; T2, at 12–14 weeks; T3, at 3 months; T6, at 6 months; T12, at 12 months.

https://doi.org/10.2147/CCID.S478840

adalimumab is the only biologic medication licensed by the FDA particularly for HS treatment, however additional biologics including ustekinumab, secukinumab, and ixekizumab have shown effectiveness.[6–8]

Biologics and biosimilars are both biopharmaceuticals used to treat inflammatory skin diseases, but they differ significantly in their development and regulatory requirements. Biologics like Infliximab and Adalimumab are derived from living organisms and target specific biological processes, such as TNF-α, which is involved in systemic inflammation. Biosimilars, meanwhile, are non-patent versions of biologics that closely resemble their reference products in structure and function but require rigorous comparative pharmacokinetic, pharmacodynamic, and efficacy trials to ensure their similarity. Regulatory bodies such as the EMA, FDA, Health Canada, and WHO require a comprehensive "totality of evidence" to approve biosimilars, often for multiple indications.[11] Biosimilars are associated with several reported adverse effects. Commonly reported side effects include skin and subcutaneous tissue disorders such as pruritus (itchiness) and rash. General disorders and administration site conditions, particularly injection site reactions, are also frequent. Gastrointestinal issues like nausea and diarrhea are noted, especially with monoclonal antibodies. Immunogenicity leading to the development of anti-drug antibodies can cause allergic reactions and reduce the drug's efficacy. Patients may also experience increased susceptibility to infections, including respiratory and urinary tract infections. Neurological symptoms like headaches and dizziness, as well as musculoskeletal pain such as arthralgia and myalgia, are frequently observed. Additionally, some patients report vascular disorders like hypertension and respiratory issues such as dyspnea and cough. Serious adverse effects include severe infusion reactions like anaphylaxis, serious infections, potential malignancies, and cardiovascular events like myocardial infarction and stroke.[14]

In the treatment of HS, biosimilars are gaining prominence as viable therapeutic alternatives to their reference biologics. Adalimumab was the first fully human monoclonal antibody approved by the FDA specifically for HS.[6] Following the expiration of its patent, several biosimilars like Amgevita, Cyltezo, and Imraldi have been approved, expanding the treatment options available for HS and plaque psoriasis. Infliximab, another critical TNF-α inhibitor, was originally developed as a chimeric mAb and has seen the introduction of biosimilars such as Remsima and Inflectra in the European market since 2013. The EMA has approved nine biosimilar medicines for plaque psoriasis and hidradenitis suppurativa: Amgevita, Solymbic, Cyltezo, Imraldi, Benepali, Erelzi, Flixabi, Inflectra, and Remsima, with more potentially on the way.[11,15] These biosimilars offer similar therapeutic benefits at a potentially reduced cost, providing healthcare systems and patients more flexibility in managing chronic conditions like HS. As well ensuring that patients receive effective and potentially more accessible treatments options.

(Table 1) provides a summary review of studies linking the use of biosimilars in HS.[16–24] The studies reviewed encompass a varied demographic profile, highlighting the diverse patient population affected with HS. These studies spanned from 2018 to 2022 and involved a total of 65 participants across different regions and clinical environments. Patient ages ranged from 30 to 50 years. Specifically, one study reported an average age of 37.9 years with a standard deviation of approximately 14.6 years, while another study cited a mean age of 31 years for its participants. The gender distribution was varied, with one study involving 11 patients comprising 7 females and 4 males, and another study involving 17 patients with a male predominance (12 males and 5 females). Comorbidities were notably prevalent and diverse, including smoking (63.6% of one study group), obesity (with specific references such as a body mass index of 28.1 ± 5.8 in some patients), morbid obesity, diabetes mellitus, and a family history of HS (47.06% in one study). The only side effects reported were pain at site of injection, infusion reaction (anaphylaxis like), arthralgia, paresthesia, anti-drug antibodies formation, and loss of response.

Patil et al, in a 2018 case report, studied two male patients aged 30 and 31, both treated with ZRC-3197, an adalimumab biosimilar. They found a 50% HiSCR (Hidradenitis Suppurativa Clinical Response) achievement after 12 weeks for the first patient.[16] The study did not report any comorbidities or side effects. Ricceri et al's 2020 observational study included 11 patients with a mean age of 37.9. Most of these patients were smokers and some were overweight. They were treated with SB5 (Imraldi), and 100% achieved HiSCR, although 36.3% experienced pain at the injection site.[12] Kashlan et al conducted another case report in 2020 on a 50-year-old female patient with morbid obesity and diabetes mellitus, using an infliximab biosimilar. The specific outcomes related to HS were not detailed, but the patient experienced an infusion reaction resembling anaphylaxis.[17]

In 2021, Westerkam et al performed a cohort study on 34 patients, a mix of races and predominantly overweight, treated with infliximab-abda (IFX-A). The HiSCR was achieved by 71% and 60% of the patients on infliximab and infliximab-abda, respectively. VAS scores were used to measure pain reduction, though no side effects were reported.[18] Lastly, a 2022 observational study by Montero-Vilchez et al involved 17 patients, mostly males, with an average age of 31, some having a family history of HS. These patients were treated with an adalimumab biosimilar, resulting in 41.18% finding the switch to the biosimilar both effective and tolerable. Severe pain at the injection site was noted as a side effect in all participants.[19]

Across the studies evaluated, biosimilars show significant promise in treating HS. The success of these treatments is primarily measured by the Hidradenitis Suppurativa Clinical Response (HiSCR metric), which indicates a decrease in inflammatory lesion count without an increase in abscesses or draining fistulas. Patil et al reported a 50% HiSCR, demonstrating the potential of ZRC-3197, an adalimumab biosimilar.[16] Meanwhile, Ricceri et al observed a 100% HiSCR among their individuals who received SB5 (Imraldi), demonstrating the treatment's strong efficacy.[17] This range of responses emphasizes the significance of taking unique patient characteristics and illness severity into account when assessing therapy efficacy. The safety profile of biosimilars in HS treatment is critical, given the chronic nature of the disease and the potential for long-term therapy. Among the studies, side effects varied from mild to severe. The most common were injection site reactions, noted in Ricceri et al's study where 36.3% of patients experienced pain at the injection site.[17] More severe reactions included an infusion reaction resembling anaphylaxis in a patient treated with an infliximab biosimilar, as reported by Kashlan et al.[18] These findings highlight the necessity for careful monitoring and management of side effects, particularly in a clinical setting.

Biosimilars are relatively new in the Middle East, with varying levels of experience and regulatory frameworks across different countries.[25,26] As the European Medicines Agency continues to approve biosimilars for conditions like hidradenitis suppurativa and chronic plaque psoriasis, there is an increasing need to consider biosimilars as viable treatment options beyond European borders, extending into regions like the Gulf and Arab countries, North and South America, as well as Asian countries. The introduction of biosimilars holds promise for these regions as they can greatly benefit from the clinical and economic advantages that biosimilars offer, potentially transforming patient access to high-quality, cost-effective medications. The integration of biosimilars into treatment regimens could help in addressing both the direct medical needs and the broader socioeconomic factors affecting patient health outcomes. Expanding the use of biosimilars in these regions requires not only regulatory and market adaptations but also educational initiatives to enhance the understanding of biosimilars among healthcare providers and patients. Enhanced educational systems, better documentation of experiences, formulated patient selection strategies, and robust pharmacovigilance systems are imperative to ensure the safe and effective use of biosimilar agents.[25]

Limitations

Despite the promising results biosimilars offer patients, several challenges remain in the literature concerning their use for HS. The sample sizes in some studies are relatively small, and the demographic diversity is limited, potentially affecting the generalizability of the findings. Additionally, the long-term effects and sustainability of biosimilar treatments have not been extensively studied, necessitating ongoing research and long-term follow-up studies to better understand their role in HS management. To address the gaps in current research, future studies should focus on larger, more diverse populations to enhance the robustness and applicability of the findings. Long-term studies are also required to determine the sustainability and safety of biosimilars over extended time periods. Furthermore, comparative studies between different biosimilars and between biosimilars and their reference biologics could provide deeper insights into their relative efficacies and safety profiles. These efforts would improve our understanding of biosimilars in HS treatment and allow for more informed therapeutic decisions, ultimately improving patient outcomes in this difficult and distressing skin condition.

Conclusion

As the landscape of treatment options for hidradenitis suppurativa continues to evolve, biosimilars emerge as a vital component, offering clinically equivalent and cost-effective alternatives to established biologics. Ensuring the robustness

of biosimilar data through comprehensive, long-term studies will be crucial for their acceptance and widespread use. Such efforts will not These measures will not only boost confidence in biosimilars among healthcare providers and patients, but also reinforce the healthcare system's capacity to manage HS more effectively on a global scale.

Data Sharing Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines.

Funding

There is no funding to report.

Disclosure

The authors declare that there are no conflicts of interest for this work.

References

1. Lee EY, Alhusayen R, Lansang P, Shear N, Yeung J. What is hidradenitis suppurativa? *Can Fam Physician*. 2017;63(2):114–120. PMID: 28209676; PMCID: PMC5395382.
2. Gooderham M, Papp K. The psychosocial impact of hidradenitis suppurativa. *J Am Acad Dermatol*. 2015;73(5 Suppl 1):S19–22. PMID: 26470609. doi:10.1016/j.jaad.2015.07.054
3. Sellheyer K, Krahl D. "Hidradenitis suppurativa" is acne inversa! An appeal to (finally) abandon a misnomer. *Int J Dermatol*. 2005;44(7):535–540. PMID: 15985019. doi:10.1111/j.1365-4632.2004.02536.x
4. Alikhan A, Lynch PJ, Eisen DB. Hidradenitis suppurativa: a comprehensive review. *J Am Acad Dermatol*. 2009;60(4):539–61; quiz 562–3. PMID: 19293006. doi:10.1016/j.jaad.2008.11.911
5. Goldburg SR, Strober BE, Payette MJ. Hidradenitis suppurativa: current and emerging treatments. *J Am Acad Dermatol*. 2020;82(5):1061–1082. PMID: 31604100. doi:10.1016/j.jaad.2019.08.089
6. Tchero H, Herlin C, Bekara F, Fluieraru S, Teot L. Hidradenitis Suppurativa: a systematic review and meta-analysis of therapeutic interventions. *Indian J Dermatol Venereol Leprol*. 2019;85(3):248–257. PMID: 30924446. doi:10.4103/ijdvl.IJDVL_69_18
7. Zouboulis CC, Desai N, Emtestam L, et al. European S1 guideline for the treatment of hidradenitis suppurativa/acne inversa. *J Eur Acad Dermatol Venereol*. 2015;29(4):619–644. PMID: 25640693. doi:10.1111/jdv.12966
8. Martora F, Megna M, Battista T, et al. Adalimumab, ustekinumab, and secukinumab in the management of hidradenitis suppurativa: a review of the real-life experience. *Clin Cosmet Invest Dermatol*. 2023;16:135–148. PMID: 36698446; PMCID: PMC9869696. doi:10.2147/CCID.S391356
9. Marzano AV, Genovese G, Casazza G, et al. Evidence for a 'window of opportunity' in hidradenitis suppurativa treated with Adalimumab: a retrospective, real-life multicentre cohort study. *Br J Dermatol*. 2021;184(1):133–140. PMID: 32119111. doi:10.1111/bjd.18983
10. Gerdes S, Mrowietz U, Augustin M, et al. Biosimilars in Dermatology - theory becomes reality. *J Dtsch Dermatol Ges*. 2018;16(2):150–160. PMID: 29364594. doi:10.1111/ddg.13410
11. Constantin MM, Cristea CM, Taranu T, et al. Biosimilars in dermatology: the wind of change. *Exp Ther Med*. 2019;18(2):911–915. PMID: 31384323; PMCID: PMC6639911. doi:10.3892/etm.2019.7505
12. Nazzaro G, Calzari P, Passoni E, et al. Vascularization and fibrosis are important ultrasonographic tools for assessing response to Adalimumab in hidradenitis suppurativa: prospective study of 32 patients. *Dermatol Ther*. 2021;34(1):e14706. PMID: 33368976. doi:10.1111/dth.14706
13. Wortsman X. Imaging of hidradenitis suppurativa. *Dermatol Clin*. 2016;34(1):59–68. PMID: 26617359. doi:10.1016/j.det.2015.08.003
14. Mohd Sani N, Aziz Z, Kamarulzaman A. Biosimilars in Malaysia: regulatory framework, approved products, and adverse effects. *Ther Innov Regul Sci*. 2021;55(3):490–502. PMID: 33231863. doi:10.1007/s43441-020-00243-y
15. Farhat F, Torres A, Park W, et al. The concept of biosimilars: from characterization to evolution-a narrative review. *Oncologist*. 2018;23(3):346–352. PMID: 29284760; PMCID: PMC5905681. doi:10.1634/theoncologist.2017-0126
16. Patil S. Low-dose Adalimumab biosimilar (ZRC-3197) in the treatment of hidradenitis suppurativa. *Indian J Dermatol Venereol Leprol*. 2018;84(6):745–747. PMID: 30289113. doi:10.4103/ijdvl.IJDVL_232_18
17. Ricceri F, Rosi E, Di Cesare A, Pescitelli L, Fastame MT, Prignano F. Clinical experience with Adalimumab biosimilar imraldi in hidradenitis suppurativa. *Dermatol Ther*. 2020;33(6):e14387. PMID: 33030281. doi:10.1111/dth.14387
18. Kashlan R, Lyons AB, Narla S, Hamzavi IH. Infusion reaction to infliximab biosimilar after transitioning from infliximab. *JAAD Case Rep*. 2020;8:77–79. PMID: 33532531; PMCID: PMC7829107. doi:10.1016/j.jdcr.2020.12.011
19. Westerkam LL, Tackett KJ, Sayed CJ. Comparing the effectiveness and safety associated with infliximab vs infliximab-abda therapy for patients with hidradenitis suppurativa. *JAMA Dermatol*. 2021;157(6):708–711. PMID: 33825849; PMCID: PMC8027935. doi:10.1001/jamadermatol.2021.0220
20. Montero-Vilchez T, Cuenca-Barrales C, Rodriguez-Tejero A, Martinez-Lopez A, Arias-Santiago S, Molina-Leyva A. Switching from adalimumab originator to biosimilar: clinical experience in patients with hidradenitis suppurativa. *J Clin Med*. 2022;11(4):1007. PMID: 35207280; PMCID: PMC8879480. doi:10.3390/jcm11041007

21. Roccuzzo G, Rozzo G, Burzi L, et al. Switching from Adalimumab originator to biosimilars in hidradenitis suppurativa: what's beyond cost-effectiveness? *Dermatol Ther*. 2022;35(11):e15803. PMID: 36062429; PMCID: PMC9788000. doi:10.1111/dth.15803
22. Kirsten N, Ohm F, Gehrdau K, et al. Switching from adalimumab originator to biosimilar in patients with hidradenitis suppurativa results in losses of response-data from the German HS registry HSBest. *Life*. 2022;12(10):1518. PMID: 36294953; PMCID: PMC9605653. doi:10.3390/life12101518
23. Burlando M, Fabbrocini G, Marasca C, et al. Adalimumab Originator vs. Biosimilar in hidradenitis suppurativa: a multicentric retrospective study. *Biomedicines*. 2022;10(10):2522. PMID: 36289787; PMCID: PMC9599334. doi:10.3390/biomedicines10102522
24. Grau-Pérez M, Rodríguez-Aguilar L, Roustan G, Alfageme F. Drug survival of Adalimumab biosimilar vs Adalimumab originator in hidradenitis suppurativa: can equivalence be assumed? A retrospective cohort study. *J Eur Acad Dermatol Venereol*. 2023;37(5):e678–e680. PMID: 36461770. doi:10.1111/jdv.18801
25. Jassim NA, Humadi YA. The use of biosimilars in the middle east: review article. *Curr Rheumatol Rep*. 2018;20(7):45. PMID: 29900477. doi:10.1007/s11926-018-0740-6
26. Batran RA, Elmoshneb M, Hussein AS, et al. Biosimilars: science, implications, and potential outlooks in the middle east and Africa. *Biologics*. 2022;16:161–171. PMID: 36225324; PMCID: PMC9550021. doi:10.2147/BTT.S376959