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**Article Type:** Systematic Review

**Article Title:** Demographic Gaps and Hardships Imposed by Participation in Hidradenitis Suppurativa Clinical Trials: A Systematic Review and Call for Change

**Running Title:** Inclusion Criteria for HS Trials: A Systematic Review

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**Key Points (100/100)**

**Question:** What demographic gaps and hardships exist in clinical trials for patients with hidradenitis suppurativa (HS)?

**Findings:** Clinical trials for patients with HS were often lacking in diversity of race and age and systematically excluded patients with skin disease that was categorized as “too severe” or “too mild.” Many hardships were imposed on clinical trial participants, including long wash-out periods, prolonged periods in the study’s placebo arm, and preclusion of analgesic use.

**Meaning:** Investigators should consider broader inclusion criteria to reflect the real-world treatment settings, consider recruitment sites in diverse communities, and strategies for reducing trial burdens on participants.

**Abstract (350/350 words):**

**Importance:** Hidradenitis suppurativa (HS) is a chronic inflammatory disease that disproportionately affects women and persons of color. While adalimumab remains the only FDA-approved therapy for moderate to severe HS, many HS clinical trials for novel therapies are ongoing or upcoming. To optimize treatment equity and facilitate trial participation, it is critical to elucidate aspects of clinical trial protocols that may systematically exclude specific patient groups or impose undue suffering on participants.

**Objective:** To systematically review inclusion and exclusion criteria as well as participant demographics in HS clinical trials.

**Evidence Review:** A literature search of PubMed, Embase, Cochrane Central, and Web of Science databases was conducted. Peer reviewed publications of randomized controlled trials that were written in English and had at least 10 participants were included. Title and abstract screening and data extraction were completed by two independent reviewers, with disagreements resolved by a third.

**Findings:** Twenty-three studies totaling 1,489 adult participants met inclusion criteria. Trial participants were predominantly white (774/886, 78.5%) and female (1057/1457, 72.5%). The median of each study's average age was 35.9 years (IQR 4.6), and 15/23 (65%) trials excluded pediatric patients. Nearly all participants had Hurley Stage II (490/901, 54.4%) or Hurley Stage III (366/901, 40.6%) disease. Many trials excluded patients who were pregnant (19/23, 83%) or breastfeeding (13/23, 57%), had a history of Human Immunodeficiency Virus (HIV) infection (10/20, 50%), or had HS that was "too severe" (6/20, 30%) or "too mild" (15/20, 75%). Hardships imposed on clinical trial participants included prolonged wash-out periods from HS

therapies, long duration in the study's placebo arm, and prohibiting concurrent exclusion from participation due to analgesic use.

**Conclusions and Relevance:** This systematic review identified hardships imposed on participants by HS clinical trial participation, which may contribute to disease progression and patient suffering. Further, this study demonstrates low representation of key patient groups affected by HS, including persons of color, pediatric patients, pregnant and breastfeeding women, individuals living with HIV, and patients with very severe or mild HS disease. Future trials should consider broader inclusion criteria, implementation of pragmatic study designs that reflect real-world treatment settings, and reduction of trial burdens on study participants.

## **Introduction:**

Hidradenitis suppurativa (HS) is a chronic, debilitating, inflammatory skin condition characterized by painful, malodorous nodules, abscesses, and tunnels. Although many medications are used off-label to treat HS, adalimumab remains the only Food and Drug Administration (FDA) approved treatment for moderate to severe HS. Numerous trials for novel HS therapeutics are in the pipeline, signifying an urgent opportunity to develop trial protocols that will facilitate recruitment and inclusion of participants who represent the population of HS patients who will benefit from these medications. Studying prior trial protocols and patterns of recruitment may identify best practices for minimizing hardships of trial participation and improve the generalizability of results to HS patients in real-world treatment settings.<sup>1</sup>

In the United States, the annual incidence and prevalence of HS are estimated to be 11.4 per 100,000 population and 0.10%, respectively.<sup>2</sup> Although persons of color are approximately 2.5-3 times more likely to be affected by HS than white participants, a recent review of 15 phase II and phase III trials found that whites comprised 68.0% of the patient population in HS clinical trials, whereas black participants comprised only 14%.<sup>3</sup> Inadequate trial representation of the population at risk may threaten the ability of clinicians to draw meaningful conclusions and apply these findings to the diverse HS patients. In addition to underrepresentation of key patient groups in HS clinical trials, narrow inclusion criteria have the potential to systematically exclude key patient groups. Likewise, requiring extended wash-out periods for HS medications and analgesics does not reflect routine clinical management of HS and may impose unnecessary suffering on participants. Extended wash-out periods may also create barriers to participation in clinical trials, which ultimately may affect external generalizability of the study.

It remains unknown which patient groups, if any, are systematically excluded from HS trials and which aspects of trial protocols may impose hardships on participants, inadvertently leading to underrepresentation of key patient groups. This systematic review aimed to characterize participant demographics and inclusion/exclusion criteria of published HS clinical trials to inform future HS trial designs, improve equity of treatment, and serve broad and diverse patient populations.

## **Methods:**

This systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO 2020 CRD42020162660) and followed the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA)<sup>4</sup> reporting guideline.

### **Search Strategy**

On February 19, 2020, a systematic search of PubMed (Legacy), Embase (Embase.com), Cochrane Central (cochranelibrary.com) and Web of Science (Clarivate Analytics via webofknowledge.com) databases was conducted. An updated search was completed on April 08, 2021 to search for newly published trials that met inclusion criteria. Controlled vocabulary utilizing MeSH or Emtree terms, when available, in combination with keywords was searched (Appendix 1). When controlled vocabulary was unavailable, proximity term searching was performed. Duplicate articles were removed using EndNote X9© and Covidence©.

### **Eligibility Criteria**

Inclusion and exclusion criteria were specified prior to literature search. Randomized control trials published in English in peer-reviewed journals that included  $\geq 10$  participants diagnosed with HS were included.

Titles and abstracts were independently screened for eligibility by two authors. Disagreements in eligibility were resolved by a third author prior to full data retrieval.

### **Data Extraction**

Data extraction was completed independently by two authors using structured data collection forms that included study design, intervention(s) and primary outcome, location/setting, sponsor/funding, inclusion/exclusion criteria, participant demographics including age, race, ethnicity, sex, Hurley stage, and Body Mass Index (BMI). Discrepancies in data extraction were resolved prior to analysis.

### **Statistical Analysis:**

Medians with interquartile ranges were used to describe continuous variables. Proportions were used to describe categorical variables. Software for calculations was done via Microsoft Excel©.

## **Results:**

### ***Study Characteristics***

The literature search yielded 1,214 records. Duplicates were removed, yielding 600 unique publications. Following title and abstract screening, 86 manuscripts were reviewed as full texts. Twenty-three studies encompassing 1,489 participants met inclusion criteria (**Figure 1**). Study years ranged from 1986-2021, and the majority of studies were conducted in Europe and/or the United States. Study characteristics are detailed in **Table 1**.

### ***Demographics of Study Participants***

Participant demographics for 23 included studies are detailed in **Table 2**. Nearly 95% (22/23) of all studies reported participants' ages. The median of each study's mean age was 35.9



years (IQR 4.6). The youngest participant was 16 years old, and 17/23 (74%) studies excluded pediatric patients. Of the 23 studies, 22 reported sex, with 1074/1457 (73.7%) participants being female. Participant race was reported in 10 studies, totaling 774/986 (78.5%) white participants and 157/986 (13.1%) black participants. Seven of the 10 studies missing race data were performed in Europe. Ethnicity data were available from three studies, with 14/76 (15.6%) participants identified as Hispanic, Latino, or Spanish. Ten studies (50%) reported participants' Hurley stage; 45/901 participants (5.0%) had Hurley stage I disease, 490/901 (54.4%) had Hurley stage II disease, and 366/901 (40.6%) had Hurley stage III disease. Ten studies reported mean BMI; the median of each study's mean BMI was 32.5 (IQR 2.3).

#### ***Inclusion and Exclusion Criteria of HS Trials***

Groups systematically excluded by trial criteria were evaluated (**Table 3**). 19 studies (83%) excluded pregnant women, and 13 excluded women who were breastfeeding (56%). Additionally, 15 studies (65%) excluded patients because their HS was considered “too mild,” and 8 (30%) excluded patients whose disease was “too severe.” Some trials defined HS as “too mild” for inclusion when participants were Hurley stage I disease, had less than 3 active HS lesions, or only had one affected anatomical site. Likewise, the definitions of disease that was “too severe” for inclusion varied across studies. Patients excluded for disease considered “too severe” were those with Hurley stage III HS, those with greater than 20 active lesions, or those with severe disease based on the HS-Patient Global Assessment (HS-PGA)<sup>5,6</sup> scoring system. Common exclusion criteria included history of Human Immunodeficiency Virus (HIV), congestive heart failure (CHF), and malignancy.

Nearly all studies (7/12, 58%) placed limitations on HS therapies deemed permissible during and prior to the study period (**Table 4**). Among studies that precluded concurrent oral

antibiotics, the systemic antibiotic wash-out periods ranged from 7-28 days (median 14 days). For prior biologic therapy use, the wash-out periods ranged from 14-180 days (median 30 days). Of the studies with shorter wash-out periods (14 days) two of the three were conducted several years prior to routine usage of biologic therapies in the care of HS. Furthermore, 5/12 (42%) studies excluded participants taking analgesics at the time of inclusion. Of the studies with a placebo arm, the time without any active HS treatment ranged from 8 weeks to nearly 9 months. Only 13/20 (65%) trials ultimately offered active therapy to all study participants.

## **Discussion**

This systematic review of 23 HS clinical trials totaling 1,489 participants identified substantial hardships imposed by trial participation and low representation of key patient groups, including persons of color. To alleviate the burden of trial participation on individuals living with HS, future trials could consider implementing pragmatic designs with shorter wash-out periods and permissive analgesic use. Many studies prohibited use of concurrent HS therapies and required wash-out periods of up to 6 months, after which participants in placebo arms spent additional time without active medication and sometimes did not receive active therapy, even after completing the placebo period. Prolonged periods without treatment may contribute to HS disease progression and unnecessary patient suffering.<sup>1,7</sup> Ensuring that all participants in HS clinical trials are offered active therapy after conclusion of the placebo-controlled study period is important for upholding ethical principles of beneficence, nonmaleficence, and justice.

This study also demonstrates the exclusion of key patient groups from HS trials, including women who were pregnant or breastfeeding and individuals with medical comorbidities, such as HIV, CHF, and malignancy. While such exclusions may be medically or

ethically warranted depending on the therapy under investigation, few studies may have systematically excluded these key patient groups unnecessarily. Importantly, HS disproportionately affects women with onset often times at childbearing age;<sup>9</sup> thus, therapies that are safe and effective during pregnancy and lactation are needed. Efforts to broaden inclusion criteria when appropriate to reflect the true HS patient population will improve the external validity of trial results and improve clinicians' ability to treat HS patients with complex medical problems.

Other commonly marginalized patient groups in HS clinical trials were pediatric patients and those with mild disease or very severe disease.. Although the prevalence of HS among children in the United States (0.028%)<sup>8</sup> is only 3.6-fold lower than that of adults (0.1%),<sup>9</sup> children comprise a much smaller proportion of trial participants. Similarly, only 5% of clinical trial participants had Hurley stage I disease, while Hurley stage I disease comprise 64.7% of individuals living with HS worldwide.<sup>10-13</sup> Because HS often becomes increasingly recalcitrant to medical therapy over time, it is critical that clinicians have treatment options that are safe and effective for pediatric patients and those with mild disease.<sup>10-13</sup> An important step to establishing such therapies is to ensure the representation of these patient groups in future trials when medically and ethically appropriate.

In agreement with a recent review of HS trials,<sup>3</sup> this systematic review identified low representation of persons of color among trial participants. Although persons of color are approximately 2.5-3 times more likely to be affected by HS than white patients, this current study found that white patients comprised 78.5% of trial participants.<sup>9</sup> The true proportion of white participants included in these trials is likely higher than reported, as 368 of the 430 participants with missing race data were from trials in European countries. Efforts to conduct

trials in racially diverse settings may increase the representation of persons of color.

Additionally, the consistent report of patient baseline characteristics, including race, ethnicity, age, BMI, and sex, is vital to the reproducibility and generalizability of HS trial findings in real-world clinical settings.

This study is limited to reporting information from HS clinical trials published in English. Additionally, numerous ongoing clinical trials for HS therapies may have more inclusive criteria for participation and fewer hardships imposed by participation compared to prior trials. Finally, while attempts were made to contact authors of all studies with missing information, many did not respond.

## **Conclusion**

This systematic review demonstrates hardships imposed by HS trial participation and low representation of key patient groups, such as persons of color, those with mild or very severe HS, children, pregnant and breast feeding women, those requiring analgesia at baseline, and patients with medical comorbidities. To ensure HS therapies benefit and are applicable to all affected patients, efforts should be made to provide opportunities for inclusion of these underrepresented groups when medically appropriate.

Underrepresentation of key patient populations in HS clinical trials threatens the external validity of study findings, hinders the ability to draw meaningful conclusions that may be applied in clinical settings, and compromises patient care. To facilitate translation of study findings into clinical practice, it is important that HS clinical trials recruit participants who represent the true target patient population. Studies should also accurately depict the setting in which these therapies will be applied (for example, in conjunction with analgesics). Hence, more pragmatic HS studies with inclusive criteria for participation and shorter wash-out and placebo treatment

periods are encouraged to reduce the burden of trial participation, capture a more representative patient group, and assess outcomes in a more realistic treatment setting.

**Conflicts of Interest:**

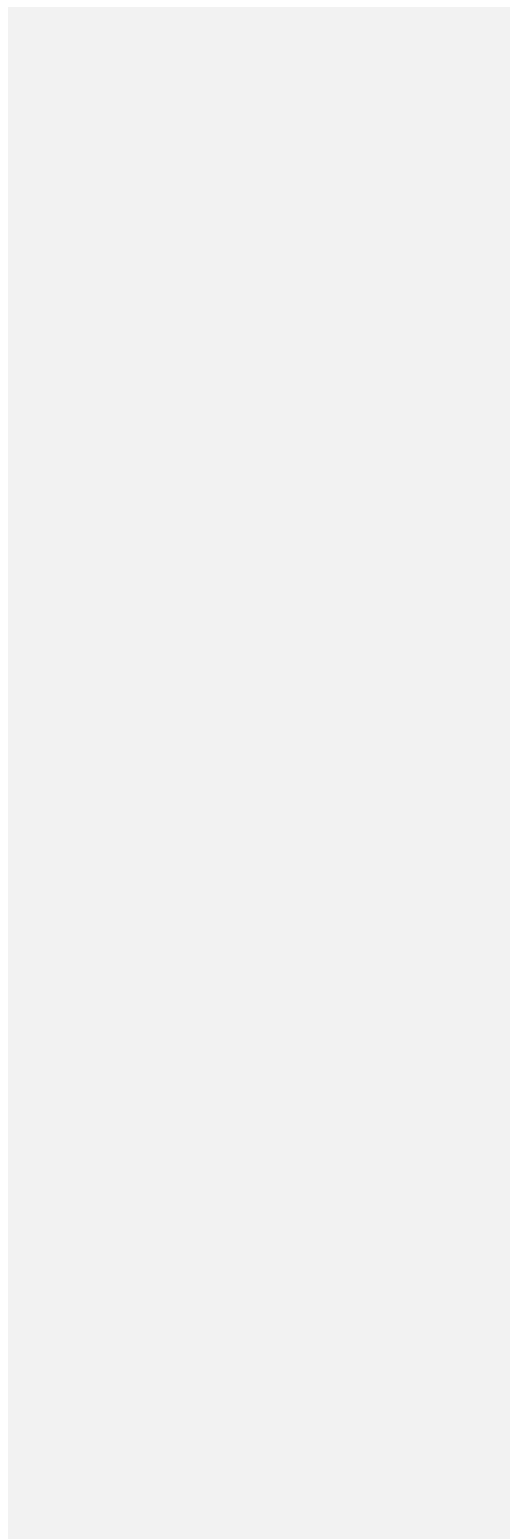
LAVO has served as an investigator Chemocentryx. She has been a consultant to Chemocentryx, Incyte, MedEd Consulting, and Huron Consulting Group and received lecture honoraria from Frontline Medical Communications.

JRI is Editor-in-Chief of the *British Journal of Dermatology* and receives an authorship honorarium from *UpToDate*. He is a consultant for UCB Pharma, Boehringer Ingelheim, ChemoCentryx and Novartis and has served on advisory boards for Viela Bio and Kymera Therapeutics.

JSK has been a speaker for AbbVie, advisory board participant for AbbVie, Incyte and consultant to AbbVie, Bayer, ChemoCentryx, Incyte, InflaRx, Janssen, Novartis, and UCB, and participated in clinical trials with AbbVie, ChemoCentryx, Incyte, InflaRx, Novartis, and UCB.

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**Figure 1:** Summary of literature search and study selection.



**Table 1.** Characteristics of included randomized controlled trials

Study	N	Study years	Location	Intervention	Control	Blinding	1 <sup>o</sup> Outcome	Funding
<b>Pioneer II</b> <sup>14</sup>	326	2011-2014	Europe and USA	Adalimumab	Placebo	Double	HiSCR <sup>6</sup>	Industry
<b>Pioneer I</b> <sup>14</sup>	307	2011-2014	Europe and USA	Adalimumab	Placebo	Double	HiSCR <sup>6</sup>	Industry
<b>Buimer</b> <sup>15</sup>	200	2008 <sup>c</sup>	Netherlands	Excision and closure with gentamicin sponge	Excision and closure without sponge	NR	Postoperative complications	Investigator initiated
<b>Kimball 2012</b> <sup>6,17</sup>	154	2009-2010	Europe and USA	Adalimumab	Placebo	Double	HS-PGA <sup>5,6</sup>	Industry
<b>Jemec</b> <sup>18</sup>	46	1996-1997 <sup>b</sup>	Denmark	Oral tetracycline + topical placebo	Topical clindamycin + oral placebo	Double	VAS	Industry Partnership
<b>Yildiz</b> <sup>19</sup>	43	2012-2014	Turkey	Hyperbaric oxygen, oral clindamycin + rifampin	Oral clindamycin + rifampin	None	NR	NR
<b>Wilden</b> <sup>20</sup>	43	2014-2015	Germany	IPL+RF (LAight®)	RF or IPL	Double <sup>a</sup>	Number of inflammatory nodules, abscesses, and draining fistulae	Industry Partnership
<b>Grant</b> <sup>21</sup>	38	2005-2008	USA	Infliximab	Placebo	Double	HSSI <sup>16,22</sup>	Investigator Initiated
<b>Naouri</b> <sup>23</sup>	36	2021 <sup>c</sup>	France	Nd:YAG laser (1064 nm)	No treatment on contralateral side	Single	Number of inflammatory lesions	Investigator Initiated
<b>Fajgenbaum</b> <sup>24</sup>	32	2016-2017	USA	Intralesional triamcinolone	Saline injection	Double	Days to resolution of lesions, pain reduction	Investigator Initiated
<b>Angel</b> <sup>25</sup>	31	1987 <sup>c</sup>	NR	Staphage lysate	Placebo	Double	Decrease in "point system" used to grade severity	Investigator initiated
<b>Mortimer</b> <sup>26</sup>	24	1986 <sup>c</sup>	United Kingdom	Ethinylloestradiol + cyproterone acetate	Ethinylloestradiol + norgestrel	Double	NR	Industry Partnership
<b>Andersen</b> <sup>27</sup>	24 <sup>d</sup>	2017-2018	Denmark	IPL (Palomar LuxY, Series II, Cynosure Inc)	No treatment on contralateral side	Single	HiSCR <sup>6</sup>	Investigator Initiated
<b>Mahmoud</b> <sup>28,29</sup>	22	2007-2009	USA	Nd:YAG laser (1064 nm) + Topical clindamycin and BPO	Topical clindamycin and BPO	Single	HS-LASI <sup>28</sup>	Investigator initiated
<b>Miller</b> <sup>30</sup>	21	2007-2010	Denmark	Adalimumab	Placebo	Double	Sartorius <sup>22</sup> and Hurley scoring systems	Industry Partnership
<b>Adams</b> <sup>31</sup>	20	2010 <sup>c</sup>	USA	Etanercept	Placebo	Double	4-point PGA	Industry Partnership



<b>Tzanetakou</b> <sup>32</sup>	20	2012-2014	Greece	Anakinra	Placebo	Double	HS disease severity <sup>33</sup>	Investigator Initiated
<b>Kanni</b> <sup>34</sup>	20	2015-2017	Greece	MABp1	Placebo	Double	HiSCR <sup>6</sup>	Industry Partnership
<b>Vossen</b> <sup>35</sup>	20	2017	Netherlands	Apremilast	Placebo	Double	HiSCR <sup>6</sup>	Industry
<b>Grimstad</b> <sup>36</sup>	20	2017-2018	Norway	BTX-B (NeuroBlock®)	Placebo	Double	DLQI <sup>37</sup>	Investigator Initiated
<b>Azim</b> <sup>38</sup>	20	2017	Egypt	Fractional CO <sub>2</sub> (10,600nm) + Nd:YAG (1064 nm)	Nd:YAG (1064 nm)	Single	HS-PGA <sup>5,6</sup>	NR
<b>Highton</b> <sup>39</sup>	18	2011 <sup>c</sup>	United Kingdom	Intense pulsed light (Harmony®)	No treatment on contralateral axilla	Single	Sartorius score <sup>22</sup>	NR
<b>Fadel</b> <sup>40</sup>	11	2013	Egypt	IPL (EPI-C Plus ®) + niosomal MB gel	IPL + free MB gel	Single	HS-LASI <sup>28</sup>	Investigator Initiated

<sup>a</sup>Only patients in the IPL+RF and IPL only groups could be blinded.

<sup>b</sup>From private communication with authors.

<sup>c</sup>Publication date listed, as study dates not reported.

<sup>d</sup>17 of the 24 randomized participants were included in the final analysis

BPO: Benzoyl peroxide

BTX: Botulinum Toxin

CRP: C-reactive Protein

DLQI<sup>37</sup>: Dermatology Life Quality Index

ESR: Erythrocyte Sedimentation Rate

HiSCR<sup>6</sup>: Hidradenitis Suppurativa Clinical Response (50% reduction from baseline in the total abscess and inflammatory nodule count, with no increase in the abscess or draining fistula count)

HS-LASI<sup>28</sup>: Hidradenitis Suppurativa Lesion, Area and Severity Index

HS-PGA<sup>5,6</sup>: Hidradenitis Suppurativa Physician's Global Assessment

HSSI<sup>16,41</sup>: HS Severity Index

IPL: Intense pulsed light

MB: methylene blue

N: number of participants randomized

NR: Not reported

RF: Radiofrequency

US: United States

VAS: Visual Analogue Scale

**Table 2.** Demographics of study participants

Study	Age, mean (SD); range	Female, n (%)	Race, %			Hurley Stage, %			BMI, mean (SD)
			White	Black	Other	I	II	III	
Pioneer II <sup>14</sup>	35.5 (11.2)	221/326 (67.8)	83.7	8.9	7.4	0.0	53.7	46.3	32.1 (7.7)
Pioneer I <sup>14</sup>	37.0 (11.1)	196/307 (63.8)	76.2	20.2	3.6	0.0	52.4	47.6	33.8 (7.8)
Buimer et al <sup>15</sup>	31 (8); 18-52	180/200 (90.0)	--	--	--	--	--	--	--
Kimball 2012 <sup>16</sup>	36.3 (11.8)	110/154 (71.4)	71.4	18.8	9.7	15.6	55.2	29.2	32.8 <sup>a</sup> (--)
Jemec <sup>18</sup>	32.5 (2.4); 27-37	39/46 (84.8)	100.0 <sup>b</sup>	0.0 <sup>b</sup>	0.0 <sup>b</sup>	--	--	--	--
Yildiz <sup>19</sup>	35.7 (--) ; 20-55	25/43 (58.1)	--	--	--	--	--	--	30.0 (--)
Wilden <sup>20</sup>	38 (--) ; 23-57	31/43 (72.1)	--	--	--	16.3	53.5	30.2	37.1 (--)
Grant <sup>21</sup>	33.5 (12.1); 16-61	26/38 (68.4)	73.6	26.3	0.0	--	--	--	--
Naouri <sup>23</sup>	31.1 (8.5); 18-53	27/36 (75.0)	97.2	2.7	0.0	--	--	--	--
Fajgenbaum <sup>24</sup>	36 (--) ; --	30/32 (93.8)	50.0 <sup>d</sup>	50.0	0.0	--	--	--	--
Angel <sup>25</sup>	--	--	--	--	--	--	--	--	--
Mortimer <sup>26</sup>	-- ; 20-44	24/24 (100.0)	--	--	--	--	--	--	--
Andersen <sup>27</sup>	35 <sup>a</sup> (--) ; 27-49 <sup>c</sup>	16/17 <sup>f</sup> (94.1)	100.0 <sup>d</sup>	0.0	0.0	94.1	5.9	0.0	27.5 <sup>a</sup> (22.8-32.5) <sup>c</sup>
Mahmoud <sup>29</sup>	41 (--) ; 19-72	19/22 (86.4)	45.5 <sup>b</sup>	50.0 <sup>b</sup>	4.5 <sup>b</sup>	0.0	100.0	0.0	--
Miller <sup>30</sup>	39.1 (--)	17/21 (81.0)	100.0 <sup>b</sup>	0.0 <sup>b</sup>	0.0 <sup>b</sup>	--	--	--	32.1 (--)
Adams <sup>31</sup>	38.4 (--) ; 18-59	13/20 (65.0)	95.0	0.0	5.0	--	--	--	32.8 (--)
Tzanetakou <sup>32</sup>	39.4 (12.8)	9/19 (47.4)	--	--	--	0.0	52.6	47.4	27.9 (5.9)
Kanni <sup>34</sup>	48 (12.5)	7/20 (35.0)	--	--	--	--	10.0	90.0	28.7 (5.9)
Vossen <sup>35</sup>	35.1 (11.8)	17/20 (85.0)	95.0	0.0	5.0	--	--	--	32.7 (6.2)
Grimstad <sup>36</sup>	37.3(7.1) <sup>b</sup>	17/20 (85.0)	100.0 <sup>b</sup>	0.0 <sup>b</sup>	0.0 <sup>b</sup>	70.0	25.0	5.0	33.1 (6.7) <sup>b</sup>
Azim <sup>38</sup>	29.7 (5); 20-35	11/20 (55.0)	--	--	--	50.0	50.0	0.0	--

<b>Highton</b> <sup>39</sup>	34 (--); 17-50	15/18 (83.3)	--	--	--	--	--	--	--
<b>Fadel</b> <sup>40</sup>	27.1 (5.1); 17-35	7/11 (63.6)	--	--	--	36.4	36.4	18.2	--
<b>Overall</b>	35.9 (4.6) <sup>e</sup>	1074/145 7 (73.7)	774/986 (78.5)	157/986 (13.1)	55/986 (5.3)	45/901 (5.0)	490/901 (54.4)	366/921 (40.6)	32.8 (2.3) <sup>e</sup>

--: Not reported; BMI: Body Mass Index; Q1-Q3: Interquartile range

<sup>a</sup>Median reported because mean was not available

<sup>b</sup>Obtained through personal correspondence with author

<sup>c</sup>Quartile 1 – Quartile 3

<sup>d</sup>Hispanic persons were grouped with those of white race

<sup>e</sup>Median and interquartile range of each study's mean

<sup>f</sup>17 of the 24 randomized participants were included in the final analysis

Study	Age <18 years	HS too mild	HS too Severe	Pregnancy	Breastfeeding	CHF	HIV	History of Malignancy
Pioneer II <sup>14</sup>	•	• <sup>a</sup>	• <sup>k</sup>	•	•	•	•	•
Pioneer I <sup>14</sup>	•	• <sup>a</sup>	• <sup>k</sup>	•	•	•	•	•
Buimer <sup>15</sup>	•	• <sup>b</sup>						
Kimball 2012 <sup>16</sup>	•	• <sup>c</sup>		•	•	•	•	•
Jemec <sup>18</sup>			• <sup>l</sup>	•	•	• <sup>Φ, n</sup>		
Yildiz <sup>19</sup>	•			•		• <sup>Φ</sup>		
Wilden <sup>20</sup>	•	• <sup>d</sup>						
Grant <sup>21</sup>	•	• <sup>e</sup>		•		•	•	•
Naouri <sup>23</sup>	•		• <sup>l</sup>	•	•			
Fajgenbaum <sup>24</sup>		• <sup>f</sup>						
Angel <sup>25</sup>		• <sup>g</sup>						
Mortimer <sup>26</sup>	•	• <sup>h</sup>		•				
Andersen <sup>27</sup>	•		• <sup>l</sup>	•				
Mahmoud <sup>29</sup>	•	• <sup>i</sup>	• <sup>l</sup>	• <sup>n</sup>	•			
Miller <sup>30</sup>	•	• <sup>i</sup>		•	•	• <sup>n</sup>	• <sup>n</sup>	• <sup>n</sup>
Adams <sup>31</sup>	•			•		•	•	•
Tzanetakou <sup>32</sup>	•	• <sup>i</sup>		•	•		•	•
Kanni <sup>34</sup>		• <sup>a</sup>		•	•		•	
Vossen <sup>35</sup>	•	• <sup>j</sup>	• <sup>m</sup>	•		• <sup>Φ</sup>	• <sup>Φ</sup>	• <sup>Φ</sup>
Grimstad <sup>36</sup>	• <sup>p</sup>	• <sup>p</sup>		•	•			
Azim <sup>38</sup>	•		• <sup>l</sup>	•	•	• <sup>Φ</sup>	• <sup>Φ</sup>	• <sup>Φ</sup>
Highton <sup>39</sup>		• <sup>i</sup>		•	•			
Fadel <sup>40</sup>				•	•			
Studies with exclusion, n (%)	17 (74)	15 (65)	8 (35)	19 (86)	13 (57)	10 (43)	10 (43)	9 (39)

**Table 3.** Patients groups excluded in HS trials

HIV: Human Immunodeficiency Virus; CHF: Congestive heart failure

• Specified patient group was excluded;

Φ Exclusion not medically necessary; intervention unlikely to cause harm to this subset of patients based on medical comorbidities

<sup>a</sup>Excluded Hurley Stage 1 and individuals with <3 abscesses and inflammatory nodules

<sup>b</sup>Inclusion required at least 1 “active” lesion

<sup>c</sup>Inclusion required HS-PGA of moderate or worse (HS-PGA score  $\geq 3$ ).

<sup>d</sup>Excluded patients with <3 abscesses or inflammatory nodules

<sup>e</sup>Inclusion required moderate to severe disease according to HSSI (score >8)

<sup>f</sup>Inclusion required at least 1 acutely inflamed nodule

<sup>g</sup>Inclusion required HS involving more than 2 anatomic sites. All participants had previously failed antibiotics and local surgery

<sup>h</sup>Only included individuals with “moderate to severe” disease

<sup>i</sup>Excluded individuals with Hurley stage I disease

<sup>j</sup>Required patients to have  $\geq 4$  inflammatory lesions in  $\geq 2$  anatomic locations. Patients with minimal and mild disease according to HS-PGA were also excluded

<sup>k</sup>Excluded those with >20 draining fistulas

<sup>l</sup>Excluded individuals with Hurley stage III disease

<sup>m</sup>Excluded participants with severe or very severe disease according to the HS-PGA

<sup>n</sup>Obtained through personal correspondence with authors

<sup>o</sup>With the exception of non-metastatic squamous cell skin cancer, basal cell skin cancer, and localized carcinoma in situ of the cervix

<sup>p</sup>Obtained via personal correspondence with the author.

Study	Systemic antibiotic wash-out period (days)	Biologic wash-out period (days)	Placebo duration (weeks)	Analgesics permitted at inclusion?	Were all participants eventually offered active treatment?
<b>Pioneer II</b> <sup>14</sup>	28 <sup>a</sup>	30 days or 5 half lives	12-36	✗	✗
<b>Pioneer I</b> <sup>14</sup>	28	30 days or 5 half lives	12	✗	✓
<b>Buimer</b> <sup>15</sup>	--	--	NA	--	✓
<b>Kimball 2012</b> <sup>16</sup>	28 <sup>a</sup>	NA <sup>e</sup>	16	✓	✓
<b>Jemec</b> <sup>18</sup>	7	--	NA	✓ <sup>d,g</sup>	✓
<b>Yildiz</b> <sup>19</sup>	--	--	NA	✓	✓
<b>Wilden</b> <sup>20</sup>	-- <sup>b</sup>	84	12 <sup>d</sup>	✗	✓
<b>Grant</b> <sup>21</sup>	14	NA <sup>e</sup>	8	✓	✓
<b>Naouri</b> <sup>23</sup>	90	180	NA	--	✓
<b>Fajgenbaum</b> <sup>24</sup>	NA <sup>c</sup>	--	NA	--	✗
<b>Angel</b> <sup>25</sup>	--	--	20	--	✗
<b>Mortimer</b> <sup>26</sup>	--	30	NA	--	✓
<b>Andersen</b> <sup>27</sup>	28	28	NA	✗	✓
<b>Mahmoud</b> <sup>29</sup>	14 <sup>d</sup>	14 <sup>d</sup>	NA	✗	✓
<b>Miller</b> <sup>30</sup>	28	180	12	✓	✗
<b>Adams</b> <sup>31</sup>	--	30	12	--	✓
<b>Tzanetakou</b> <sup>32</sup>		180	12	--	✗
<b>Kanni</b> <sup>34</sup>	--	--	12	--	✗
<b>Vossen</b> <sup>35</sup>	28	28	16	✓	✗
<b>Grimstad</b> <sup>36</sup>	28 <sup>d</sup>	NA <sup>f</sup>	12	✓	✓
<b>Azim</b> <sup>38</sup>	14	14	NA	✗	✓
<b>Highton</b> <sup>39</sup>	14	14	NA	--	✓
<b>Fadel</b> <sup>40</sup>	14	--	NA	✓	✓
<b>Overall</b>	14 (14-28) <sup>h</sup>	30 (21-57) <sup>h</sup>	12 (12-16) <sup>h</sup>	7/12 (58%)	13/20 (65%)

**Table 4. Treatment restrictions during trial participation**

--: Not reported; NA: Not Applicable; ✗: no; ✓: yes;

<sup>a</sup>Allowed oral tetracyclines at stable doses

<sup>b</sup>Although there was no placebo group, all patients underwent 12 week screening period during which the only HS treatments allowed were short courses of oral antibiotics and drainage

<sup>c</sup>Concomitant antibiotics were allowed if given at stable doses for  $\geq 4$  weeks

<sup>d</sup>Obtained through personal communication with the author

<sup>e</sup>Excluded patients with any prior biologic use

<sup>f</sup>Biologics not used clinically at the time of the study

<sup>g</sup>Permitted at stable doses

<sup>h</sup>Median (Interquartile Range)

## References

1. Garg A, Neuren E, Cha D, et al. Evaluating patients' unmet needs in hidradenitis suppurativa: Results from the Global Survey Of Impact and Healthcare Needs (VOICE) Project. *J Am Acad Dermatol*. 2020. doi:10.1016/j.jaad.2019.06.1301
2. Seyed Jafari SM, Hunger RE, Schlapbach C. Hidradenitis Suppurativa: Current Understanding of Pathogenic Mechanisms and Suggestion for Treatment Algorithm. *Front Med*. 2020. doi:10.3389/fmed.2020.00068
3. Price KN, Hsiao JL, Shi VY. Race and Ethnicity Gaps in Global Hidradenitis Suppurativa Clinical Trials. *Dermatology*. 2019. doi:10.1159/000504911
4. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Med*. 2009. doi:10.1371/journal.pmed.1000097
5. Robinson A, Kardos M, Kimball AB. Physician Global Assessment (PGA) and Psoriasis Area and Severity Index (PASI): Why do both? A systematic analysis of randomized controlled trials of biologic agents for moderate to severe plaque psoriasis. *J Am Acad Dermatol*. 2012. doi:10.1016/j.jaad.2011.01.022
6. Kimball AB, Jemec GBE, Yang M, et al. Assessing the validity, responsiveness and meaningfulness of the Hidradenitis Suppurativa Clinical Response (HiSCR) as the clinical endpoint for hidradenitis suppurativa treatment. *Br J Dermatol*. 2014. doi:10.1111/bjd.13270
7. Marzano A V., 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*. 2020. doi:10.1111/bjd.18983
8. Mengesha YM, Holcombe TC, Hansen RC. Prepubertal hidradenitis suppurativa: Two case reports and review of the literature. *Pediatr Dermatol*. 1999. doi:10.1046/j.1525-1470.1999.00077.x
9. Garg A, Lavian J, Lin G, Strunk A, Alloo A. Incidence of hidradenitis suppurativa in the United States: A sex- and age-adjusted population analysis. *J Am Acad Dermatol*. 2017. doi:10.1016/j.jaad.2017.02.005
10. Canoui-Poitaine F, Le Thuaut A, Revuz JE, et al. Identification of three hidradenitis suppurativa



phenotypes: Latent class analysis of a cross-sectional study. *J Invest Dermatol*. 2013.

doi:10.1038/jid.2012.472

11. Yang JH, Moon J, Kye YC, et al. Demographic and clinical features of hidradenitis suppurativa in Korea. *J Dermatol*. 2018. doi:10.1111/1346-8138.14656
12. Vazquez BG, Alikhan A, Weaver AL, Wetter DA, Davis MD. Incidence of hidradenitis suppurativa and associated factors: A population-based study of Olmsted County, Minnesota. *J Invest Dermatol*. 2013. doi:10.1038/jid.2012.255
13. Yüksel M, Basım P. Demographic and Clinical Features of Hidradenitis Suppurativa in Turkey. *J Cutan Med Surg*. 2020. doi:10.1177/1203475419887732
14. Kimball AB, Okun MM, Williams DA, et al. Two Phase 3 Trials of Adalimumab for Hidradenitis Suppurativa. *N Engl J Med*. 2016. doi:10.1056/nejmoa1504370
15. Buimer MG, Ankersmit MFP, Wobbes T, Klinkenbijnl JHG. Surgical treatment of hidradenitis suppurativa with gentamicin sulfate: A prospective randomized study. *Dermatologic Surg*. 2008;34(2):224-227. doi:10.1111/j.1524-4725.2007.34041.x
16. Kimball AB, Kerdel F, Adams D, et al. Adalimumab for the treatment of moderate to severe hidradenitis suppurativa: A parallel randomized trial. *Ann Intern Med*. 2012. doi:10.7326/0003-4819-157-12-201212180-00004
17. Scheinfeld N, Sundaram M, Teixeira H, Gu Y, Okun M. Reduction in pain scores and improvement in depressive symptoms in patients with hidradenitis suppurativa treated with adalimumab in a phase 2, randomized, placebo-controlled trial. *Dermatol Online J*. 2016.
18. Jemec GBE, Wendelboe P. Topical clindamycin versus systemic tetracycline in the treatment of hidradenitis suppurativa. *J Am Acad Dermatol*. 1998. doi:10.1016/S0190-9622(98)70272-5
19. Yildiz H, Senol L, Ercan E, Bilgili ME, Karabudak Abuaf O. A prospective randomized controlled trial assessing the efficacy of adjunctive hyperbaric oxygen therapy in the treatment of hidradenitis suppurativa. *Int J Dermatol*. 2016. doi:10.1111/ijd.12936
20. Wilden S, Friis M, Tuettenberg A, et al. Combined treatment of hidradenitis suppurativa with intense

pulsed light (IPL) and radiofrequency (RF). *J Dermatolog Treat.* 2019.

doi:10.1080/09546634.2019.1677842

21. Grant A, Gonzalez T, Montgomery MO, Cardenas V, Kerdel FA. Infliximab therapy for patients with moderate to severe hidradenitis suppurativa: A randomized, double-blind, placebo-controlled crossover trial. *J Am Acad Dermatol.* 2010. doi:10.1016/j.jaad.2009.06.050
22. Sartorius K, Lapins J, Emtestam L, Jemec GBE. Suggestions for uniform outcome variables when reporting treatment effects in hidradenitis suppurativa [11]. *Br J Dermatol.* 2003. doi:10.1046/j.1365-2133.2003.05390.x
23. Naouri M, Maruani A, Lagrange S, et al. Treatment of hidradenitis suppurativa using a long-pulsed hair removal neodymium:yttrium-aluminium-garnet laser: A multicenter, prospective, randomized, intraindividual, comparative trial. *J Am Acad Dermatol.* 2021;84(1):203-205. doi:10.1016/j.jaad.2020.04.117
24. Fajgenbaum K, Crouse L, Dong L, Zeng D, Sayed C. Intralesional Triamcinolone May Not Be Beneficial for Treating Acute Hidradenitis Suppurativa Lesions: A Double-Blind, Randomized, Placebo-Controlled Trial. *Dermatol Surg.* 2020. doi:10.1097/DSS.0000000000002112
25. Angel MF, Ramasastry SS, Manders EK, Granfield D, Futress JW. Beneficial effects of staphage lysate in the treatment of chronic recurrent hidradenitis suppurativa. *Surg Forum.* 1987.
26. Mortimer ps, dawber rpr, gales ma, moore ra. A double-blind controlled cross-over trial of cyproterone acetate in females with hidradenitis suppurativa. *Br J Dermatol.* 1986. doi:10.1111/j.1365-2133.1986.tb05740.x
27. Lindsø Andersen P, Riis PT, Thorlacius L, et al. Intense pulsed light treatment for hidradenitis suppurativa: a within-person randomized controlled trial. *Eur J Dermatology.* 2020;30(6):723-729. doi:10.1684/ejd.2020.3920
28. Tierney E, Mahmoud BH, Hexsel C, Ozog D, Hamzavi I. Randomized control trial for the treatment of hidradenitis suppurativa with a neodymium-doped yttrium aluminium garnet laser. *Dermatologic Surg.* 2009. doi:10.1111/j.1524-4725.2009.01214.x

29. Mahmoud BH, Tierney E, Hexsel CL, Pui J, Ozog DM, Hamzavi IH. Prospective controlled clinical and histopathologic study of hidradenitis suppurativa treated with the long-pulsed neodymium:yttrium-aluminium-garnet laser. *J Am Acad Dermatol*. 2010. doi:10.1016/j.jaad.2009.07.048
30. Miller I, Lynggaard CD, Lophaven S, Zachariae C, Dufour DN, Jemec GBE. A double-blind placebo-controlled randomized trial of adalimumab in the treatment of hidradenitis suppurativa. *Br J Dermatol*. 2011. doi:10.1111/j.1365-2133.2011.10339.x
31. Adams DR, Yankura JA, Fogelberg AC, Anderson BE. Treatment of hidradenitis suppurativa with etanercept injection. *Arch Dermatol*. 2010. doi:10.1001/archdermatol.2010.72
32. Tzanetakou V, Kanni T, Giatrakou S, et al. Safety and efficacy of anakinra in severe hidradenitis suppurativa a randomized clinical trial. *JAMA Dermatology*. 2016. doi:10.1001/jamadermatol.2015.3903
33. Giamarellos-Bourboulis EJ, Pelekanou E, Antonopoulou A, et al. An open-label phase II study of the safety and efficacy of etanercept for the therapy of hidradenitis suppurativa. *Br J Dermatol*. 2008. doi:10.1111/j.1365-2133.2007.08372.x
34. Kanni T, Argyropoulou M, Spyridopoulos T, et al. MABp1 Targeting IL-1 $\alpha$  for Moderate to Severe Hidradenitis Suppurativa Not Eligible for Adalimumab: A Randomized Study. *J Invest Dermatol*. 2018. doi:10.1016/j.jid.2017.10.030
35. Vossen ARJV, van Doorn MBA, van der Zee HH, Prens EP. Apremilast for moderate hidradenitis suppurativa: Results of a randomized controlled trial. *J Am Acad Dermatol*. 2019. doi:10.1016/j.jaad.2018.06.046
36. Grimstad Ø, Kvammen BØ, Swartling C. Botulinum Toxin Type B for Hidradenitis Suppurativa: A Randomised, Double-Blind, Placebo-Controlled Pilot Study. *Am J Clin Dermatol*. 2020;21(5):741-748. doi:10.1007/s40257-020-00537-9
37. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)-a simple practical measure for routine clinical use. *Clin Exp Dermatol*. 1994;19:210-216.
38. Abdel Azim AA, Salem RT, Abdelghani R. Combined fractional carbon dioxide laser and long-pulsed neodymium : yttrium-aluminium-garnet (1064 nm) laser in treatment of hidradenitis suppurativa; a

prospective randomized intra-individual controlled study. *Int J Dermatol*. 2018;57(9):1135-1144.

doi:10.1111/ijd.14075

39. Highton L, Chan WY, Khwaja N, Laitung JKG. Treatment of hidradenitis suppurativa with intense pulsed light: A prospective study. *Plast Reconstr Surg*. 2011. doi:10.1097/PRS.0b013e31821e6fb5
40. Fadel MA, Tawfik AA. New topical photodynamic therapy for treatment of hidradenitis suppurativa using methylene blue niosomal gel: A single-blind, randomized, comparative study. *Clin Exp Dermatol*. 2015. doi:10.1111/ced.12459
41. Sartorius K, Killasli H, Heilborn J, Jemec GBE, Lapins J, Emtestam L. Interobserver variability of clinical scores in hidradenitis suppurativa is low. *Br J Dermatol*. 2010. doi:10.1111/j.1365-2133.2010.09715.x

## **Appendix 1: Search Strategies:**

### **PubMed (pubmed.gov)**

1. "hidradenitis suppurativa"[MeSH Terms] OR "hidradenitis suppurativa"[TW] OR acne inversa[TW]
2. "Clinical Trial" [Publication Type] OR "Clinical Trials as Topic"[Mesh] OR "clinical trial\*"[TW] OR "controlled clinical trial\*"[TW] OR "randomized clinical trial\*"[TW]
3. #1 AND #2
4. #3 AND English [lang]

### **EMBASE (embase.com)**

1. 'suppurative hidradenitis'/exp OR 'hidradentitis supprativa':ti,ab OR 'acne inversa':ti,ab 'clinical trial'/exp OR 'clinical trial\*':ti,ab OR (clinical NEAR/2 trial\*) OR (controlled NEAR/2 'clinical trial\*') OR (randomized NEAR/2 'clinical trial\*')
2. #1 AND #2
3. #3 AND [english]/lim AND ('article'/it OR 'article in press'/it OR 'review'/it)

### **Central (cochranelibrary.com)**

1. MeSH descriptor: [Hidradenitis Suppurativa] explode all trees
2. "hidradenitis suppurativa":ti,ab
3. "acne inversa":ti,ab
4. #1 OR #2 OR #3
5. MeSH descriptor: [Clinical Trial] explode all trees
6. "clinical trial":ti,ab OR clinical NEAR/2 trial\* OR (controlled NEAR/2 "clinical trial\*") OR (randomized NEAR/2 "clinical trial\*")
7. #5 OR #6
8. #4 AND #7

**Web of Science (webofknowledge.com)**

1. (TS=("hidradenitis suppurativa") OR TS=("acne inversa"))
2. (TS=(clinical NEAR/2 trial\*) OR TS=(controlled NEAR/2 "clinical trial\*") OR TS=(randomized NEAR/2 "clinical trial\*"))
3. #1 AND #2
4. #3 AND LANGUAGE: (English) AND (Article OR Review)

**Commented [MSW1]:** I recently discovered that it's not sufficient to state this as Web of Science. I was informed that every institution has different databases for Web of Science and each database should be listed. I will leave it up to you whether you list the list below...

- Science Citation Index Expanded
- Social Sciences Citation Index
- Arts & Humanities Citation Index
- Conference Proceedings Citation Index – Science
- Conference Proceedings Citation Index – Social Science & Humanities
- Book Citation Index – Science
- Book Citation Index – Social Sciences & Humanities
- Emerging Sources Citation Index
- Current Chemical Reactions