Clinical Trials and Skin of Color: The Example of Hidradenitis Suppurativa

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Introduction

Despite the recent momentum of skin of color conversations in dermatology, adequate research on skin of color diseases is still lacking and African Americans/Blacks are often underrepresented in clinical trials. This underrepresentation is especially glaring in hidradenitis suppurativa (HS) clinical trials [1]. HS is a chronic inflammatory skin condition that commonly affects intertriginous areas and is characterized by painful nodules, draining sinus tracts, and hypertrophic scarring [2]. A recent systematic review focusing on racial populations reports the average prevalence rate of HS as highest in African Americans compared to both Whites and Hispanics/Latinos [3]. Additionally, a study evaluating 47,690 HS patients across the USA found that the disease affects 54.1% (25,780/47,690) Whites compared to 32.6% (15,540/47,690) African Americans; however, when standardized to the US population, the adjusted prevalence of HS was shown to disproportionately affect African American patients with a three-fold increase compared to Whites [4]. Taking into account the wide distri-

bution of populations affected, African Americans are minimally included in HS clinical trials [1]. Of 15 phase II and III HS trials published over the last 12 years (2007–2019), 68% of the participants were Caucasian while only 14.0% were of African descent [1]. This disparity hinders our complete understanding of the therapeutic effects and responses in African Americans, which may lead to the development and use of HS treatments that are neither reflective nor fully applicable to diverse patient populations. The lack of racial and ethnic diversity in HS clinical trials has been highlighted in the literature [1], but barriers and possible explanations are still unclear. Herein we explore the lack of African American representation in these studies by examining the clinical trial locations within the USA and by discussing potential barriers to African American inclusion.

We searched the Clinicaltrials.gov website using the search term “hidradenitis suppurativa” and included clinical trials that had started between January 2008 and May 2020. We included studies with trial sites worldwide; however, we excluded those without US locations and those that did not report subjects’ racial demographics.

There were 13 clinical trials taking place at 96 different locations in the USA (Table 1; online suppl. Fig. 1; see www.karger.com/doi/10.1159/000516467 for all online suppl. material). In these trials, 14.9% of participants were classified as Black, African American, or of African descent (Table 1; online suppl. Fig. 1), similar to the previously reported rate in global HS clinical trials [1].

We hypothesized that this disparity could be related to the demographics of the US cities in which the trials were conducted. To explore this possibility, we compared clinical trial locations and the racial distribution of the US population according to the 2010 census data (www.census.gov/quickfacts). Interestingly, almost half (49%) of the US trial sites were located in zip codes with moderate (12.6–49.9%) to high (>50%) African American populations, whereas 43.8% were located in areas with low (0–12.5%) African American populations. This suggests that the demographics of clinical trial sites do not adequately account for the low representation of African Americans in HS clinical trials conducted in the USA. However, there may be other barriers that lead to suboptimal recruitment of African American patients into these trials.

Barriers: Patient Perspective

African American patients may be distrustful of clinical research and avoid participation due to a fear of exploitation. This mistrust of the medical community may prevent African American patients from communicating with their physicians and limit their opportunities to be exposed to research trial information [5]. For some patients, the time commitment, lack of transportation, and financial burden are additional obstacles to enrollment [5]. In addition, African American patients may have multiple comorbidities that potentially make them ineligible for HS trials. For example, African Americans are two times more likely than White individuals to develop diabetes [6]. Although comorbidities were not a common exclusion criterion, the Etanercept study (NCT00107991) excluded patients with severe comorbidities such as diabetes mellitus requiring insulin or uncontrolled hypertension.

Barriers: Physician Perspective

Implicit and explicit forms of bias among physicians may also contribute to low African American enrollment in HS clinical trials [7]. Prior research has shown that

negative stereotypes among referring physicians may make them less likely to offer clinical trials to African American patients [7]. Some clinicians may assume that African American patients are unwilling to participate in research studies [7]. Consequently, they may not offer these clinical trial opportunities to potential candidates [7]. Providers (clinicians/principal investigators) also spend less time explaining the benefits and adverse effects of clinical trials to African American patients [5]. This lack of communication and cultural competency can exacerbate patient concerns, leading to their refusal to participate [5].

Discussion

Our findings demonstrate that although HS trials have been conducted in US regions with diverse populations, African American patients with HS are poorly represented in these studies. This disparity hinders our complete understanding of the disease and its impact on different populations, and decreases African American patients' access to potentially effective new therapies.

Establishing racial and ethnic diversity in dermatology is an important step in addressing this disparity. Despite a 13% African American population in the USA, only 3% of US dermatologists identify as African American [8]. African American and other minority patients feel more comfortable expressing their concerns with physicians of the same race/ethnicity or those who have had similar shared experiences [9, 10]. Minority physicians may have a better understanding of the obstacles that prevent African Americans from participating in HS clinical trials and may therefore help close this gap. In addition, diversifying training materials used during medical school and dermatology residency may improve dermatologists' understanding of how conditions present differently on darker skin tones, which may subsequently lead to earlier diagnoses and potentially more referrals to clinical trials.

It is well known that physician bias contributes to health disparities. The American Academy of Family Physicians has developed the *Implicit Bias Training Guide* (aafp.org), which equips health care professionals with strategies to recognize and address their biases. Physicians who are cognizant of their biases may adjust their behaviors, including offering more clinical trial opportunities to African American patients. We encourage physicians, especially dermatologists, to consult this guide to improve patient's access to HS clinical trials.

Table 1. Depiction of 13 HS clinical trials' US city locations and demographics

Clinical trial Sponsor, year (NCT No.)	Drug	Trial locations	Trial US cities	HS patients in cohort	African descent, %	Caucasian, %	Other or unspecified race, %	Clinical trial sites in US cities with			
								very low Black/AA population ^a	low Black/AA population ^b	moderate Black/AA population ^c	high Black/AA population ^d
Florida Acad. Derm. Center, 2008 (NCT00795574)	Infliximab	USA	Coral Gables, FL	38	26	37	37	0	0	1	0
Univ. of Pennsylvania, 2009 (NCT00107991)	Etanercept	USA	Philadelphia, PA	10	20	80	0	0	0	1	0
Florida Acad. Derm. Center, 2008 (NCT00827996)	Adalimumab	USA	Coral Gables, FL	10	30	50	20	0	1	0	0
Abbott, 2010 (NCT00918255)	Adalimumab	USA, Denmark, Germany, The Netherlands	Birmingham, AL; Bakersfield, CA; Los Angeles, CA; San Diego, CA; Miami, FL; Atlanta, GA; Skokie, IL; Evansville, IL; Boston, MA; St. Louis, MO; Omaha, NE; New York, NY; Winston-Salem, NC; Hershey, PA; Philadelphia, PA; Dallas, TX; San Antonio, TX; Norfolk, VA	154	19	71	10	0	7	12	1
UCSF, 2013 (NCT01516749)	Anakinra	USA	San Francisco, CA	6	33	33	33	0	1	0	0
PIONEER I/Abbvie, 2015 (NCT01468207)	Adalimumab	48 study locations ^e	Birmingham, AL; Bakersfield, CA; Encino, CA; Mather, CA; Colorado Springs, CO; Dunedin, FL; Jacksonville, FL; Miami, FL; Atlanta, GA; Macon, GA; Newnan, GA; Champaign, IL; Boston, MA; Clinton Township, MI; Fort Gratiot, MI; Grand Blanc, MI; Troy, MI; Fridley, MN; Verona, NJ; New York, NY; Winston-Salem, NC; Cleveland Heights, OH; Gahanna, OH; Hershey, PA; San Antonio, TX	307	20	76	4	0	11	11	3
PIONEER II/Abbvie, 2015 (NCT01468233)	Adalimumab	53 study locations ^f	San Diego, CA; Farmington, CT; Dunedin, FL; Orange Park, FL; Tampa, FL; Chicago, IL; Boston, MA; Fort Gratiot, MI; Sterling Heights, MI; Omaha, NE; Henderson, NV; Chapel Hill, NC; Winston-Salem, NC; Pittsburgh, PA; Nashville, TN; Norfolk, VA; Seattle, WA	326	9	84	7	0	9	9	0
University of North Carolina, 2017 (NCT02781818)	Triamcinolone acetoneide	USA	Chapel Hill, NC	48	48	52	0	0	1	0	0
Abbvie, 2019 (NCT02808975)	Adalimumab	55 study locations ^g	Beverly Hills, CA; Encino, CA; Irvine, CA; Boston, MA; Ann Arbor, MI; Chapel Hill, NC; New Orleans, LA; Hershey, PA; Providence, RI	206	4	94	2	0	6	2	1
Tufts Medical Center, 2019 (NCT03099980)	Secukinumab	USA	Boston, MA	20	40	50	10	0	0	1	0

Table 1 (continued)

Clinical trial sponsor, year (NCT No.)	Drug	Trial locations	Trial US cities	HS patients in cohort	African descent, %	Caucasian, %	Other or unspecified race, %	Clinical trial sites in US cities with			
								very low Black/AA population ^a	low Black/AA population ^b	moderate Black/AA population ^c	high Black/AA population ^d
Incyte Corporation, 2020 (NCT03569371)	INCB054707	USA	Los Angeles, CA; Tampa, FL; New York, NY; Hershey, PA	10	30	60	10	0	2	2	0
University of Pittsburgh, 2020 (NCT03275870)	Hydroxy-chloroquine	USA	Pittsburgh, PA	17	18	82	0	0	0	1	0
InflaRx GmbH, 2020 (NCT03487276)	IFX-1	41 study locations ^h	Birmingham, AL; Fort Myers, FL; Miami, FL; Sandy Springs, GA; Dearborn, MI; Columbia, MO; Saint Joseph, MO; St. Louis, MO; Chapel Hill, NC; Cincinnati, OH; Hershey, PA	179	9.5	85	5.5	0	5	7	1

AA, African American; HS, hidradenitis suppurativa; NCT, National Clinical Trial Number; UCSF, University of California San Francisco. ^aCities with 0.0–0.9% AA population. ^bCities with 1–12.5% AA population. ^cCities with 12.6–49.9% AA population. ^dCities with >50% AA population. ^eAustralia, Canada, Czech Republic, Germany, Hungary, USA. ^fAustralia, Canada, Denmark, France, Greece, The Netherlands, Sweden, Switzerland, Turkey, USA. ^gBelgium, Canada, Colombia, Czech Republic, Denmark, France, Germany, Greece, Ireland, Italy, Mexico, The Netherlands, Norway, Poland, Portugal, Romania, Russian Federation, Saudi Arabia, Spain, Sweden, Turkey, UK, USA. ^hBulgaria, Canada, Denmark, Germany, Greece, The Netherlands, Poland, USA.

Researchers should expand their recruitment efforts by collaborating with community-based organizations. Generally, African American communities are more likely to trust information received from their local community organizations [5] such as churches, community centers, and support groups. These organizations may have stronger connections to this population and may be regarded as trusted sources of information. Specifically, in-person and online HS patient support groups may provide a safe space for patients to receive accurate information and support as they decide whether or not to participate in clinical trials.

Limitations and Opportunities in International Clinical Trials

The limitation of our study is that the complete racial demographics and recruitment methods were not provided for each clinical trial site. Specifically, studies conducted globally did not state whether the Black, African American, or African descent participants were selected from the USA or from other countries.

There are international biases that should be mentioned. Due to the nondiverse areas of some geographical regions, the representation of African Americans may be minimal. This highlights the imperative need for clinical trial sites to be carefully selected both internationally and within the USA. Additionally, international institutions could foster collaborations with US institutions to ensure inclusion of African Americans and other diverse patient populations.

As we work to eliminate health disparities in the USA, we encourage physicians, researchers, and patients to promote and advocate racial diversity within clinical trial participants. This will contribute to improving access to care for underserved and underrepresented populations, resulting in an improved understanding of HS and other challenging dermatological diseases.

Key Message

Racial demographics do not adequately explain the disparity in African American enrollment in HS clinical trials.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

C.A.V. Okeke, J.D. Perry, W.D. Shipman, T.A. Cole, G.A. Okoye, and A.S. Byrd identified the gap in the field, conceptualized, and were involved in the overall design, and drafted the man-

uscript. C.A.V. Okeke, J.D. Perry, F.C. Simmonds, A.B. Erskine, W.D. Shipman, J.A. Seltzer, M.R. Andrews, A.D. Saini, and A.S. Byrd acquired and analyzed data. C.A.V. Okeke, J.D. Perry, F.C. Simmonds, A.B. Erskine, W.D. Shipman, J.A. Seltzer, M.R. Andrews, A.D. Saini, T.A. Cole, J.A. Perkins, J. Otado, J. Kwagyan, C.I.F. Collins, G.A. Okoye, and A.S. Byrd provided critical review of the data and data interpretation, manuscript revisions, and final approval for publication.

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