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Examining Racial Diversity in Hyperpigmentation and Post-Inflammatory Hyperpigmentation Clinical Trials in the United States

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Dear Editor:

Dyspigmentation, specifically hyperpigmentation or post-inflammatory hyperpigmentation (PIH), disproportionately affects those with skin of color. Studies show that dyschromias, including PIH, are one of the most common presenting complaints of darker-skinned racial ethnic groups when visiting a dermatologist.[1] Vashi et al found that Black, Hispanic, and Asian women reported their symptoms of PIH more bothersome than White women, and non-White women were also more likely to be concerned with clearing their hyperpigmentation compared to white women (41.6% vs 8.4%, respectively).[2] Post-inflammatory hyperpigmentation (PIH) is a reactive hypermelanosis and sequela of a variety of inflammatory skin conditions and can have a negative impact on a patient's quality of life, particularly for darker-skinned patients. This is likely due to increased production or deposition of melanin into the epidermis or dermis by labile melanocytes.[1]

Depigmenting agents often include hydroquinone, azelaic acid, kojic acid, arbutin, and certain licorice (glycyrrhiza) extracts. Other agents include retinoids, mequinol, ascorbic acid (vitamin C), and niacinamide, many of which are available as over-the-counter cosmeceuticals and commonly used by patients.[1] Herein, we sought to evaluate published hyperpigmentation clinical trials, both industry-sponsored and investigator-initiated, to determine the racial diversity of patients over the past two decades.

A search was conducted using the Clinicaltrials.gov website and the search terms "Hyperpigmentation" AND "Post-Inflammatory Hyperpigmentation" to determine clinical trials that occurred between January 2002 and January 2022. Studies were only included if they had trial sites in the United States. Two independent authors (JD and CO) reviewed the included studies for data collection, and discrepancies were resolved through consensus discussion. Sixteen (16) total clinical trials met the inclusion criteria.

Of the 16 included studies, only 31.3% (5/16) reported participant race. White participants accounted for 38.8% (91/234) of those studies, Black/African American participants accounted for 30.3% (71/234), Hispanic participants accounted for 28.6% (67/234), and "other" accounted for 2.1% (5/234). Of the five studies that reported race, 20% (1/5) subsequently categorized participants by Fitzpatrick skin types.

Notably, of the studies that did not report participant race, 27.3% (3/11) studies included Fitzpatrick skin types. Of these three studies, 0% (0/79) of the participants had Fitzpatrick Skin Type 1, 22.8% (18/79) had Fitzpatrick Skin Type II, 16.5% (13/79) had Fitzpatrick Skin Type III, 24.1% (19/79) had Fitzpatrick Skin Type IV, 30.4% (24/79) had Fitzpatrick Skin Type V, and 6.3% (5/79) had Fitzpatrick Skin Type VI.

The US Census population projections confirm that by 2045, non-white communities will be the majority, while whites will comprise 49.7% of the population.[3] Therefore, diverse research cohorts are important in all aspects of dermatological clinical trials. In 2017, the NIH updated its policy to include a requirement that recipients conducting applicable NIH-defined Phase III clinical trials ensure the results of valid analyses by sex/gender, race, and or/ethnicity by submitting this information to Clinicaltrials.gov.[4] Despite NIH mandates[4], our study underscores that there is still minimal reporting of ethnic and racial data. Notably, 68.8% of the included studies in this report did not detail race or ethnicity at all.

Moreover, some studies stratified their participants by Fitzpatrick skin typing in lieu of race. The original Fitzpatrick scale was created in 1975 to classify the reactivity of white skin to ultraviolet A phototherapy. The scale was later updated to include nonwhite patients, adding two categories initially based on color alone and later with tanning reactions: 'brown' (type V) and 'black' (type VI). Now, as the standard skin classification system, it is often incorrectly used as a proxy for race/ethnicity.[5] Stratifying patients by the Fitzpatrick scale is problematic because certain racial or ethnic groups may contain individuals who span the entire scale. Therefore, a clinical trial may include a variety of skin types, but still not be racially diverse.

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TABLE 1.

Summary of Hyperpigmentation and Post-Inflammatory Hyperpigmentation Clinical Trials in the United States

Clinical Trial Sponsor, Year, Identifier	Drug/ Intervention	Location	# in Cohort	# White	# African-American	# Hispanic	# Other	FITZPATRICK SKIN TYPES					
								I	II	III	IV	V	VI
Henry Ford Health System, 2016, NCT02905903	Tricholoacetic Acid (TCA)	Department of Dermatology, Henry Ford Medical Center, 3031 West Grand Boulevard, Detroit MI	30	--	--	--	--	--	2	--	5	19	4
Derm Research, PLLC, 2009, NCT01038869	Azelaic Acid	DermResearch, PLLC, Louisville, Kentucky, United States	--	--	--	--	--	--	--	--	--	--	--
Massachusetts General Hospital, 2010, NCT01149876	Other: Nu Skin Product Other: Cosmetic instrument Drug: Tretinoin cream 0.05 Other: CeraVe moisturizer	Massachusetts General Hospital Boston	80	--	--	--	--	--	--	--	--	--	--
Sadick Research Group, 2013, NCT02138539	Herbal depigmenting agent	New York, New York	28	--	--	--	--	--	--	--	--	--	--
Revision Skincare, 2021, NCT05423873	Gentle Cleansing Lotion, Revision Skincare	Nashville, Tennessee,	33	--	--	--	--	-	8	8	13	3	1
Derm Research, PLLC , 2017, NCT03402893	ONEXTON Topical Gel	Louisville, Kentucky	20	--	20	--	--	--	--	--	--	--	--
Integrative Skin Science and Research, 2019, NCT04586816	1% red maple leaf extract in cream base	Sacramento, California,	--	--	--	--	--	--	--	--	--	--	--
Johnson & Johnson Consumer Inc. (J&JCI), 2017, NCT03312543	Active Mask	Broomall, Pennsylvania,	124	90	33	-	1	--	--	--	--	--	--
Alma Lasers Inc., 2013, NCT04519736	Single Band vs. Dual Band Pulsed Light Technology	Hackensack, New Jersey	20	--	--	--	--	*	*	*	--	--	--
SkinCeuticals, 2019, NCT04137263	DOSE formulation	San Diego, California,	24	--	--	--	--	--	--	--	--	--	--
Allergan, 2016, NCT02977507	Lytera 2.0	New York, New York, United States	18	--	6	9	3	--	--	--	--	--	--
Mayo Clinic, 2016, NCT02730819	Illuminate Cream	Jacksonville, Florida,	16	--	--	--	--	0	8	5	1	2	0
University of Utah, 2005, NCT00707174	755nm Alexandrite Laser and Lytera Skin Brightening System (Non-Hydroquinone Topical Therapy)	San Diego, California, United States	--	--	--	--	--	--	--	--	--	--	--
University of Miami, 2008, NCT01162850	Dietary Supplement: Polypodium Leucotomos	Miami, Florida, United States	21	--	--	--	--	--	*	*	*	--	--
University of Texas Southwestern Medical Center, 2008, NCT00616239	20-30% Salicylic Acid peels to the right side of the face	Dallas, Texas, United States	20	--	--	20	--	--	--	--	--	--	--
Galderma R&D, 2006, NCT00472966	Fluocinolone acetonide 0.1%/hydroquinone 4%/tretinoin 0.05% Cream in sequence with glycolic acid peels	Boca Raton, Florida, United States	--	--	--	--	--	--	--	--	--	--	--
Northwestern University, 2007, NCT00467233	Laser treatment; Acid Peel	Chicago, Illinois, United States	15	--	--	--	--	--	--	--	--	--	--
Emory University, 2008, NCT00166192	Jessner's solution chemical peel; Trichloroacetic acid chemical peel	Atlanta, Georgia, United States	19	--	--	--	--	--	--	--	--	--	--
Galderma R&D, 2006, NCT00469183	Fluocinolone acetonide .1%, hydroquinone 4%, tretinoin .05%	Los Angeles, California, United States; Dallas, Texas, United States	52	1	12	38	1	--	--	4	37	9	2
University of Utah, 2005, NCT00707174	Tazarotene Cream 0.1%; Imiquimod Cream	Salt Lake City, Utah, United States	90	--	--	--	--	--	--	--	--	--	--

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Ultimately, lack of diversity in clinical trials leads to an uncertainty of outcomes in these populations, as well as potential overestimation of clinical efficacy. We suggest that trials in hyperpigmentation accurately represent and report the most burdened populations to improve possible patient outcomes. Patients often seek over-the counter-treatment in addition to, or in conjunction with dermatologic care. Not only do patients rely on the validity of these studies, but dermatologists do as well.

DISCLOSURES

The authors have no conflicts of interest to disclose.

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