Strategies to Increase Patient Diversity in Clinical Trials: Examples From Topical Roflumilast Clinical Development Programs

Amy Paller,[1] Raj Chovatiya,[2] Mercedes E. Gonzalez,[3] David H. Chu,[4] David R. Berk,[4] Robert C. Higham,[4] Saori Kato,[4] Julie Nolte,[4] Jennifer C. Jaworski,[4] Adelaide A. Hebert[5]

[1]Departments of Dermatology and Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL; [2]Rosalind Franklin University of Medicine and Science Chicago Medical School, North Chicago, IL and Center for Medical Dermatology + Immunology Research, Chicago, IL; [3]Pediatric Skin Research, LLC, Miami, FL; [4]Arcutis Biotherapeutics, Inc., Westlake Village, CA; [5]UTHealth McGovern Medical School, Houston, TX

PLAIN LANGUAGE SUMMARY

Individuals participating in clinical trials should represent the diversity of patients with the condition under study, particularly in dermatology trials, because skin diseases may occur at different rates and appear different in various demographic subgroups.

Strategies were implemented to increase diversity in clinical trials of topical roflumilast in atopic dermatitis (AD) and seborrheic dermatitis (SD). These included selecting trial sites in locations with diverse populations and working with diverse sets of investigators.

For both AD and SD, trial sites provided good geographic coverage of the United States. Enrollment among Hispanic and/or non-White patients was higher than prevalence estimates, and/or similar to trials conducted with other drugs.

In the future, engaging additional trial sites and investigators with access to diverse populations may better inform development, further improve diversity in clinical trials, and help sponsors of clinical trials in skin diseases meet diversity enrollment goals.

INTRODUCTION

- Clinical trial participant diversity is important in dermatology, given that the epidemiology and clinical presentation of skin diseases may differ based on race, ethnicity, and other sociodemographic factors[1]
- Roflumilast is a potent phosphodiesterase 4 inhibitor, approved by the US Food and Drug Administration (FDA) as cream 0.15% for AD, foam 0.3% for SD, and cream 0.3% for plaque psoriasis

OBJECTIVE

- Describe efforts to increase ethnic and racial diversity in 2 clinical development programs in inflammatory skin disease and evaluate the impact of these efforts

METHODS

- Strategies were developed to foster diversity in clinical development programs of topical roflumilast in AD and SD

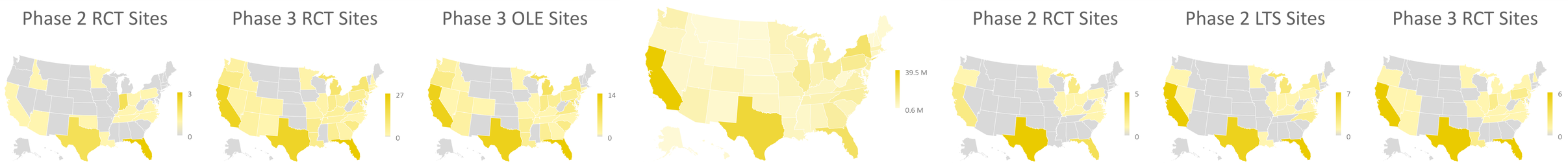
Investigator Involvement/Site Selection	Trial Outcomes	Patient Recruitment
• Inclusion of investigators/ sites with access to diverse populations	• Inclusion of assessments especially relevant to patients with skin of color • Benchmarking to historical internal and external comparator data • Subgroup analyses by race, ethnicity, and Fitzpatrick skin type	• Geographic diversity in site selection • Sites within areas of diverse demographics • Varied advertising methods and outreach specific to different communities

- Effectiveness of these strategies was measured against 2020 US Census data[2]; US disease prevalence estimates from the Centers for Disease Control (CDC)[3] and National Institutes of Health (NIH)[4]; published roflumilast data from Phase (Ph) 2/3 randomized controlled trials (RCTs), open-label extension (OLE) trials, and Ph2 long-term safety (LTS) trials[5–10]; and publicly available comparator data[11–19]
- Site data were calculated for US sites only based on zip codes; in 2 instances where no demographic data were available, an adjacent zip code was chosen from among the 1 or 2 adjacent zip codes listed at https://www.zipdatamaps.com
  - Sites were counted once for each study in which the site participated without regard for enrollment status/number of patients enrolled
- Prevalence estimates are for US populations; population data are for the entire study population (including ex-US sites where applicable)
- Data are descriptive only; no statistical comparisons were made
- Analyses were limited by differences in how data were reported (ie, if race and ethnicity were reported separately or combined and grouping as “other race”)

RESULTS

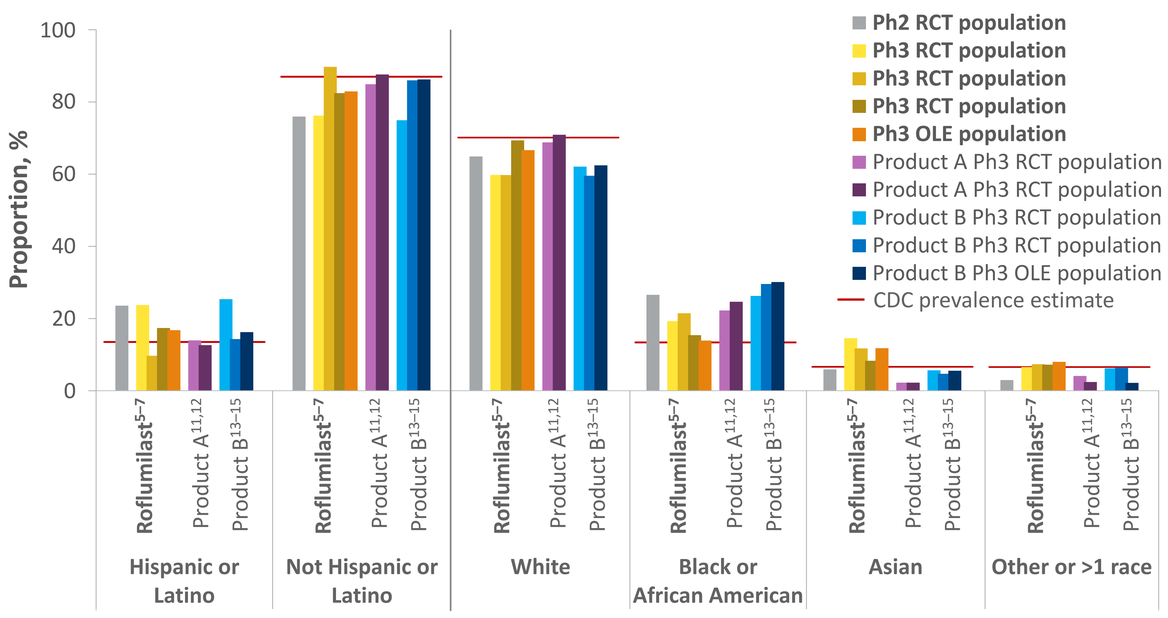
- Trial sites in both programs provided good geographic coverage per US Census data

Number of Sites Versus US Population[2]



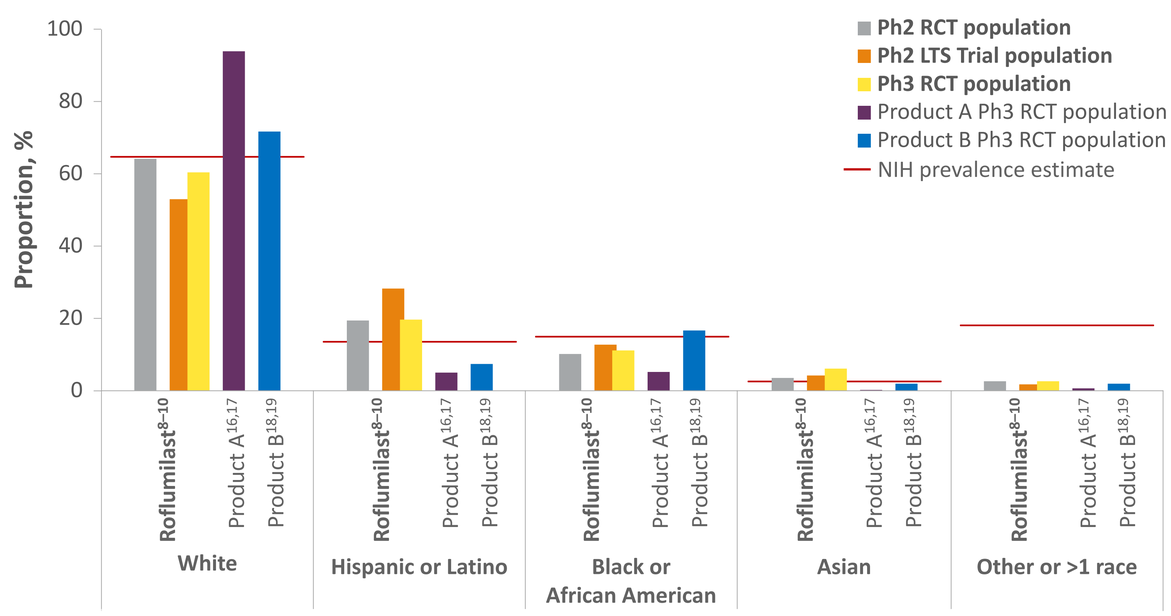
- Across AD trials, overall enrollment among Hispanic and non-White patients was higher than national prevalence estimates and similar to external comparator trials

AD Trial Populations Versus CDC Prevalence Estimate[3]



- In the SD program, enrollment in later trials among non-White patients was higher than national prevalence estimates and external comparator trials

SD Trial Populations Versus NIH Prevalence Estimate[4]



DISCUSSION

- Efforts to increase diversity contributed to trial populations that were reflective of disease prevalence estimates
- Future efforts to develop and engage new sites and investigators may further improve clinical trial diversity
- In June 2024, the FDA issued a draft guidance for industry that would require diversity action plans as part of protocol submissions for Ph3 and other pivotal trials[20]
  - Lessons learned in these clinical development programs may improve diversity outcomes and diversity action plan enrollment goals

ABBREVIATIONS

AD: atopic dermatitis; CDC: Centers for Disease Control; FDA: Food and Drug Administration; LTS: long-term safety; NIH: National Institutes of Health; OLE: open-label extension; Ph: Phase; RCT: randomized controlled trial; SD: seborrheic dermatitis.

REFERENCES

1. Silverberg JI. *Dermatol Clin.* 2017;35:283–289. **2.** US Census Bureau. 2020 Census Demographic and Housing Characteristics File and Demographic Profile. Accessed August 20, 2024. https://data.census.gov. **3.** National Center for Health Statistics. 2021 National Health Interview Survey. Sample Adult Interview and Sample Child Interview. Last reviewed April 9, 2024. Accessed August 20, 2024. http://cdc.gov/nchs/nhis/2021nhis.htm. **4.** Haq Z, et al. *Arch Dermatol Res.* 2024;316:394. **5.** Simpson EL, et al. *JAMA Dermatol.* Published online September 18, 2024. doi:10.1001/jamadermatol.2024.3121. **6.** Eichenfield LF, et al. Presented at: American College of Allergy, Asthma & Immunology (ACAAI) Annual Scientific Meeting; November 9–13, 2023; Anaheim, California. **7.** Simpson EL, et al. Presented at: Revolutionizing Alopecia Areata, Vitiligo, and Eczema (RAVE) Conference; June 8–10, 2024. Chicago, Illinois. **8.** Zirwas MJ, et al. *JAMA Dermatol.* 2023;159:613–620. **9.** Gooderham M, et al. *J Drugs Dermatol.* 2023;22:139–147. **10.** Blauvelt A, et al. *J Am Acad Dermatol.* 2024;90:986–993. **11.** Opzelura (ruxolitinib) cream summary basis for approval. Accessed August 20, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2022/215309Orig1s000TOC.cfm. **12.** Papp K, et al. *J Am Acad Dermatol.* 2021;85:863–872. **13.** Eucrisa (crisaborole) ointment summary basis for approval. Accessed August 20, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2016/207695Orig1s000TOC.cfm. **14.** Paller AS, et al. *J Am Acad Dermatol.* 2016;75:494–503.e6. **15.** Eichenfield LF, et al. *J Am Acad Dermatol.* 2017;77:641–649.e5. **16.** Elewski B, et al. *J Drugs Dermatol.* 2006;5:646–650. **17.** Xolegel (ketoconazole, USP) gel 2% summary basis for approval. Accessed August 20, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2006/021946s000TOC.cfm. **18.** Elewski B, et al. *J Drugs Dermatol.* 2007;6:1001–1008. **19.** Extina (ketoconazole, USP) foam 2% summary basis for approval. Accessed August 20, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2007/021738_extina_toc.cfm. **20.** US FDA. Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies: Guidance for Industry [Draft]. June 2024. Accessed September 22, 2024. https://www.fda.gov/media/179593/download.

ACKNOWLEDGMENTS

This work was supported by Arcutis Biotherapeutics, Inc. Thank you to the investigators and their staff for their participation in the trial. We are grateful to the study participants and their families for their time and commitment. Editorial support was provided by Christina McManus, PhD, CMPP and Lauren Ramsey, PharmD, Alligent Biopharm Consulting LLC, and funded by Arcutis Biotherapeutics, Inc.

DISCLOSURES

AP, RC, MEG, and AAH are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; DHC, DRB, RCH, SK, JN, and JCJ are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.