Study Assesses Diversity in Dermatologic Clinical Trials

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Dermatologic clinical trials within the United States reflect the growing diversity of the US population, but reporting of sex and racial/ethnic diversity of research cohorts is still lacking, especially among studies conducted outside of the US, according to a new report published online by JAMA Dermatology.

Dermatologist Arash Mostaghimi, MD, MPA, MPH, of Brigham & Women’s Hospital and Harvard Medical School, Boston, and coauthors analyzed 626 articles reporting randomized clinical trials for acne, psoriasis, atopic dermatitis and eczema, vitiligo, alopecia areata, seborrheic dermatitis, and lichen planus because the conditions are common and lack specific racial predilection.

Of the 626 articles, 97 studies were exclusively conducted in the United States and 164 were partially conducted in the United States; 58 of the 97 studies conducted exclusively within the United States reported on the racial and ethnic demographics of study participants.

Among those 58 studies conducted exclusively within the United States that recorded race/ethnicity, 74.4 percent of the 13,681 participants were white. Among these studies, 46 noted racial categories other than white and nonwhite for a total of 11,140 participants, of whom 72 percent were white, 13 percent were African American, 14.7 percent were recorded as Hispanic, and 3.3 percent were recorded as Asian.

"While those trials that fully characterized race achieved recruitment of a proportional number of African American participants (compared with the US population at 13 percent), those same trials did not achieve such proportionality with respect to ethnicity," the study authors write. "Although 17 percent of the population identifies as Hispanic by ethnicity, only 14.7 percent of participants in those same studies identified ethnically as Hispanic. Moreover, the dearth of full reporting of ethnicity and race suggests that the actual racial and ethnic makeup of many studies may be decidedly more homogenous."

Articles about eczema and acne were more likely to include more than 20 percent racially/ethnically diverse participants than psoriasis studies, the authors report.

"Journals and funding sources can reinforce our diverse clinical trial population by continuing to prioritize racial, ethnic, and genetic diversity within the articles they fund and publish; requiring reporting of racial and ethnic data in all dermatology RCTs will lead us even further. These combined efforts will enable dermatology to be an example within medicine for how to best achieve diversity within research and, by extension, clinical practice."

Editorials led by Seemal R. Desai, MD, a clinical assistant professor of dermatology at the University of Texas Southwestern Medical Center in Dallas and the founder and medical director of Innovative Dermatology in Dallas, praise the new research. "This work is a welcome specialty-specific addition to the extensive literature documenting the barriers faced when recruiting and maintaining clinical trial patients who are members of minority groups," they write. "We hope this article leads to a reexamination of how we can further increase women and minority participants in trials specific to our specialty."

FDA Approved Eucrisa (Crisaborole) for AD

The FDA approved Eucrisa (crisaborole) ointment to treat mild-to-moderate eczema in patients two years of age and older. Eucrisa, applied topically twice daily, is a phosphodiesterase 4 (PDE-4) inhibitor, although its specific mechanism of action in atopic dermatitis is not known.

The safety and efficacy of Eucrisa were established in two placebo-controlled trials with a total of 1,522 participants ranging in age from two years of age to 79 years of age, with mild to moderate atopic dermatitis. Overall, participants receiving Eucrisa achieved greater response with clear or almost clear skin after 28 days of treatment.

Serious side effects include hypersensitivity reactions. Eucrisa should not be used in patients who have had a hypersensitivity reaction to Eucrisa's active ingredient, crisaborole. The most common side effect of Eucrisa is application site pain, including burning or stinging.

Eucrisa is manufactured by Palo Alto, California-based Anacor Pharmaceuticals, Inc, which was acquired by Pfizer in summer 2016.
Melanoma Incidence, Mortality On The Rise

Melanoma incidence and mortality is on the rise, according to a research letter published online by *JAMA Dermatology*.

An estimated 76,380 Americans will be diagnosed with melanoma in 2016, and the incidence rates per 100,000 population have grown from 22.2 in 2009 to 23.6 in 2016, researchers led by Alex M. Glazer, MD, of the National Society for Cutaneous Medicine in New York, point out. The current lifetime risk of being diagnosed with invasive or in situ melanoma is now 1 in 28, the authors write. The current estimate is that 10,130 Americans will die from melanoma in 2016, up from 8,650 in 2009. Read more about the study in this month’s “Oncology Watch” column on p. 54.

**EZDERM and Healthmonix to Provide Integrated MIPS Reporting**

EZDERM, LLC and Healthmonix have partnered to integrate the MIPSPRO platform into the EZDERM suite of dermatology software solutions, including the integrated EZDERM Electronic Health Record and Practice Management systems.

This partnership gives EZDERM clients access to education, analytics, and improvement resources necessary to stay ahead of the curve for Merit-Based Incentive Payment System (MIPS) reporting. MIPS gives providers and groups the opportunity to assess the quality of care they provide to their patients, helping to ensure that patients get the right care at the right time at the lowest cost providing the best outcomes.

Healthmonix has been a CMS-Qualified PQRS Registry since 2009, enabling streamlined PQRS reporting for tens of thousands of providers with a 99.8 percent success rate in penalty avoidance, and has delivered more than $20 million in total incentive payments to its clients. Integrating Healthmonix’s MIPSPRO qualified registry reporting into EZDERM’s cloud-based and integrated mobile suite of software solutions for dermatologists accelerates EZDERM’s focus on enhancements and automation for patient-centered care, improving quality of care, and productivity with real-time documentation and quality reporting.

“We are excited about our partnership with Healthmonix as it will provide automated MIPS reporting for our clients and give them access to industry-leading tools and expertise necessary to succeed in their quality reporting requirements,” Srdjan Prodanovich, MD, FAAD, EZDERM founder and CEO, said. “These are exciting times for dermatology and all of healthcare. Automation and innovation will be the key to our clients’ ability to grow through positive improvements as they transition to value-based reimbursement models.”

**Sandoz Acquires AmLactin Brand**

Sandoz acquired the AmLactin family of skin care brands from Minnesota-based pharmaceutical company Upsher-Smith Laboratories, Inc. Under terms of the agreement, Upsher-Smith, through existing channels, will continue to distribute AmLactin hand and body lotion products to most US customers for 60 day after the December 15, 2016 announcement until fully transitioned to Sandoz.

Sandoz US President Peter Goldschmidt said, “Adding consumer skin care products to our successful branded and generic pharmaceutical portfolio will enable Sandoz to help even more patients with their skin care needs while continuing to grow a multi-faceted dermatology business.”

Financial terms of the agreement have not been disclosed.

**Restylane Refyne and Restylane Defyne Fillers FDA Approved**

The FDA approved two new products for the treatment of nasolabial folds (NLF) in patients over the age of 21—Galderma’s Restylane Refyne and Restylane Defyne. Restylane Refyne was approved for the treatment of moderate to severe facial wrinkles and folds and Restylane Defyne for the treatment of moderate to severe, deep facial wrinkles and folds. Both products are manufactured with XpresHAn Technology, creating gels that offer a range of flexibility and support for varied patient needs. Restylane Refyne and Restylane Defyne have been shown to maintain effectiveness for the treatment of laugh lines for up to 12 months.

The FDA approval was based on two pivotal, double-blinded, randomized, active-controlled Phase 3 studies investigating Restylane Refyne and Restylane Defyne (involving 171 and 162 subjects, respectively) to evaluate their safety and effectiveness. In both studies, Restylane Refyne and Restylane Defyne met the studies’ endpoints, with both products showing a clinically meaningful improvement in wrinkle severity for up to 12 months in the majority of patients. Study investigators used the Wrinkle Severity Rating Scale (WSRS), a validated 5-point measure of the size and depth of the wrinkles, with grade...
1 defined as absence of wrinkles and grade 5 as extremely deep and long wrinkles. Investigators reported that 79% of Restylane Refyne subjects and 77% of Restylane Defyne subjects had at least a 1-grade improvement on the WSRS after 6 weeks. Subjects also performed self-assessments (SSA) of wrinkle severity, with most subjects reporting at least a 1-grade improvement in SSA scores with Restylane Refyne and with Restylane Defyne after 6 weeks.

"Many of my patients are interested to learn about the latest products that can help them achieve natural-looking results, but are oftentimes unsure about starting dermal fillers," said San Diego-based board-certified dermatologist Mitch Goldman, MD. "The introduction of these next-generation HA dermal fillers with XpresHAn Technology has the potential to change my patients’ views on fillers. Restylane Refyne and Restylane Defyne provide options for patients who want to make sure they can achieve natural-looking results, which is a key need my patients express every day."

Revance Starts Phase III Program for Injectable Toxin in Frown Lines

Revance Therapeutics began two double-blind, placebo-controlled, North American Phase III trials to evaluate single injections of DaxibotulinumtoxinA (RT002) for the treatment glabellar lines in about 600 total patients. These pivotal trials follow on the BELMONT study announced last year that showed RT002 delivered 6-month duration of effect, with no ptosis at the 40-unit level, in treating frown lines.

RT002 is Revance’s proprietary, investigational injectable botulinum toxin. It is a pure, 150kD botulinum toxin, type A molecule without any accessory proteins or animal-derived components. RT002 incorporates the patented TransMTS® peptide technology and is designed to provide a longer duration of effect.

New Compound May Block Spread of Melanoma, Treat Scleroderma

A chemical compound, and potential new drug, may reduce the spread of melanoma cells by up to 90 percent, report researchers from Michigan State University in East Lansing. The findings are published in the January issue of Molecular Cancer Therapeutics.

The man-made, small-molecule drug compound goes after a gene’s ability to produce RNA molecules and certain proteins in melanoma tumors. This transcription process causes the disease to spread, but the compound can shut it down. Up until now, few other compounds of this kind have been able to accomplish this.

"It’s been a challenge developing small-molecule drugs that can block this gene activity that works as a signaling mechanism known to be important in melanoma progression," says Richard Neubig, MD, PhD, a pharmacology professor and co-author of the study, in a news release. "Our chemical compound is actually the same one that we’ve been working on to potentially treat the disease scleroderma, which now we’ve found works effectively on this type of cancer."

The same mechanisms that produce fibrosis in scleroderma also contribute to the spread of cancer. The research team found that the compounds were able to stop proteins, known as Myocardin-related transcription factors (MRTFs), from initiating the gene transcription process in melanoma cells. These triggering proteins are initially turned on by another protein called RhoC, or Ras homology C, which is found in a signaling pathway that can cause the disease to aggressively spread in the body.

The compound reduced the migration of melanoma cells by 85 to 90 percent. The team also discovered that the potential drug greatly reduced tumors specifically in the lungs of mice that had been injected with human melanoma cells. Being able to block along this entire path...
allowed the researchers to find the MRTF signaling protein as a new target.

“The majority of people die from melanoma because of the disease spreading,” says Dr. Neubig. “Our compounds can block cancer migration and potentially increase patient survival.”

Figuring out which patients have this pathway turned on is an important next step in the development of the compound because it would help them determine which patients would benefit the most, the researchers note.

**Scarless Wound Healing**

Scientists can now transform myofibroblasts found in wounds into adipocytes, paving the way toward scarless healing. Researchers began this work at the Perelman School of Medicine at the University of Pennsylvania, which led to a large-scale, multi-year study in connection with the Plikus Laboratory for Developmental and Regenerative Biology at the University of California, Irvine.

Adipocytes, which don’t cause scarring, are normally found in the skin, but they’re lost when wounds heal as scars. The study showed hair and fat develop separately but not independently. Hair follicles form first, and the researchers previously discovered factors necessary for their formation. Now they’ve discovered additional factors actually produced by the regenerating hair follicle to convert the surrounding myofibroblasts to regenerate as fat instead of forming a scar. That fat will not form without the new hairs, but once it does, the new cells are indistinguishable from the pre-existing fat cells, giving the healed wound a natural look instead of leaving a scar.

“Essentially, we can manipulate wound healing so that it leads to skin regeneration rather than scarring,” says George Cotsarelis, MD, the chair of the Department of Dermatology and the Milton Bixler Hartzell Professor of Dermatology at Penn, and the principal investigator of the project, in a news release. “The secret is to regenerate hair follicles first. After that, the fat will regenerate in response to the signals from those follicles.”

As they examined the question of what was sending the signal from the hair to the fat cells, researchers identified a factor called Bone Morphogenetic Protein (BMP). It instructs the myofibroblasts to become fat. This signaling changed what was previously known about myofibroblasts.

“Typically, myofibroblasts were thought to be incapable of becoming a different type of cell,” Dr. Cotsarelis says. “But our work shows we have the ability to influence these cells, and that they can be efficiently and stably converted into adipocytes.” This was shown in both the mouse and in human keloid cells grown in culture.

“The findings show we have a window of opportunity after wounding to influence the tissue to regenerate rather than scar,” adds the study’s lead author Maksim Plikus, PhD, an assistant professor of Developmental and Cell Biology at the University of California, Irvine. Plikus began this research as a postdoctoral fellow in the Cotsarelis Laboratory at Penn, and the two institutions have continued to collaborate.

The first and most obvious use would be to develop a therapy that signals myofibroblasts to convert into adipocytes – helping wounds heal without scarring, but the increase of fat cells in tissue can also be helpful for more than just wounds. Adipocyte loss is a common complication of other conditions, especially treatments for HIV, and right now there is no efficient strategy for treatment. “Our findings can potentially move us toward a new strategy to regenerate adipocytes in wrinkled skin, which could lead us to brand new anti-aging treatments,” Dr. Cotsarelis says.

The Cotsarelis Lab is now focusing on the mechanisms that promote skin regeneration, especially with respect to hair follicle regeneration. The Plikus Laboratory is focusing on other aspects of cell reprogramming in skin wounds. Researchers there are examining the role of other signaling factory beyond BMP as well as conducting further studies using human cells and human scar tissue.

The findings appear online in the journal *Science*. ■