Research Letters

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Cardiovascular adverse event reporting in psoriasis and psoriatic arthritis biological therapy clinical trials

Keywords: biological therapy, cardiovascular health, inflammatory skin diseases, psoriasis

Psoriasis is a systemic inflammatory disease that affects around 125 million people worldwide.[1] Plaque psoriasis, the most common form of psoriasis, accounts for 85 to 90% of cases and is associated with an increased risk of cardiometabolic disease and inflammatory arthritis, such as psoriatic arthritis.[2,3] While mild plaque psoriasis is treated with topical agents such as corticosteroids and vitamin D analogues, the American Academy of Dermatology-National Psoriasis Foundation recommends biological therapy as first-line treatment for moderate-to-severe plaque psoriasis due to their acceptable safety profile and efficacy in treating plaque psoriasis.[3] Because of the increased cardiometabolic risk in psoriasis, data describing the impact of biological therapy on cardiovascular risk factors are important to capture.[4] Demographic and cardiovascular adverse event reporting is integral in understanding the safety profiles of Food and Drug Administration (FDA)-approved psoriasis and psoriatic arthritis biological therapies. This cross-sectional analysis investigates the rate of reporting of adverse demographic, cardiometabolic, and cardiovascular events in the clinical trials that led to FDA approval of biological therapy for moderate-to-severe psoriasis.

The clinical trials that led to FDA approval of the currently available plaque psoriasis and psoriatic arthritis biological therapies were identified based on the referenced drug package inserts and from ClinicalTrials.gov. Study demographics were stratified by sex, race, and ethnicity. The reporting of various factors and the distribution across biologic therapy and year were obtained directly from ClinicalTrials.gov and cross referenced by the perspective published studies. Adverse events were obtained in a similar manner and stratified by event, organ system, and cardiometabolic disorders as appropriate.

In total, 39 clinical trials leading to FDA biologic approval in psoriatic disease with 28,152 participants (average composite age across trials, 47 ± 2.3 years, 60% male, 90% White) were identified (Fig. 1A and Table 1). Within these 39 clinical trials, 19 reported race and 12 reported ethnicity, of which the majority of participants were White (90%) and non-Hispanic (91%) (Fig. 1B and C). Qualitatively, the distribution of reporting race and ethnicity increased slightly over time (Fig. 1D and E) with clinical trials of secukinumab, ixekizumab, brodalumab, abatacept, guselkumab, tildrakizumab, certolizumab pegol, risankizumab reporting race and secukinumab, ixekizumab, guselkumab, tildrakizumab, and risankizumab reporting ethnicity. Reporting of at least one cardiovascular or cardiometabolic event occurred in all clinical trials. However, only 82% recorded myocardial infarction, while 72% reported cerebrovascular complications, 59% heart failure, and less than 20% reported a venous thrombotic event (Fig. 1F).

In addition to highlighting the link between psoriasis biological therapy use and cardiovascular disease, our findings show that the clinical trials that allowed modern-day psoriasis biological therapies to gain FDA approval heavily underrepresented and underreported people of color. There is currently very limited data available describing the relationship between biological therapy and cardiovascular risk and plaque psoriasis has been shown to be more difficult to diagnose in patients with

What is known about this subject in regard to women and their families?

- The prevalence of psoriasis is similar between men and women.
- Women with psoriasis often respond better to systemic treatments and yet may experience more adverse effects after systemic treatments.

What is new from this article as messages for women and their families?

- This cross-sectional analysis investigates the rate of reporting of adverse demographic, cardiometabolic, and cardiovascular events in the 39 clinical trials that led to Food and Drug Administration approval of biological therapy for moderate-to-severe psoriasis.
- Women, especially women of color, are sorely underrepresented in clinical trials of biological therapy in psoriasis. About 90% of participants in the 39 trials were non-Hispanic White, of which only 40% of participants were women.
- In addition to underrepresenting women of color, these 39 trials grossly underreported vital demographic information. Twenty of the 39 trials failed to report race demographics and 27 of the 39 trials failed to report ethnicity demographics.
- Finally, each of the 39 trials reported at least one or more cardiovascular or cardiometabolic adverse event. This highlights a possible link between biological therapy use and cardiovascular disease in individuals with psoriasis.

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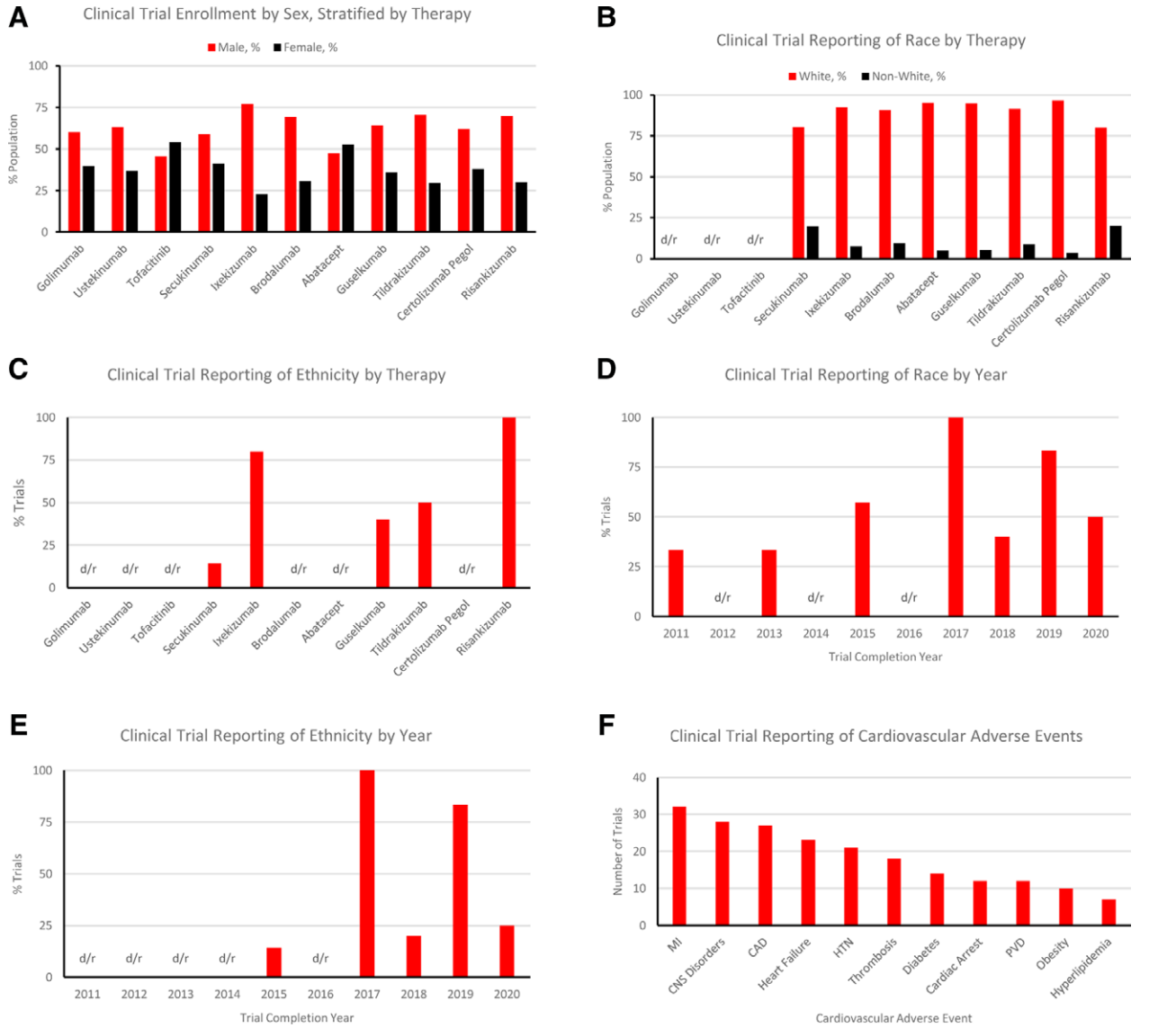

Fig. 1. Sex, race, ethnicity, and cardiovascular adverse event reporting by psoriasis biological therapy clinical trials. (A) Sex (100% reporting), (B) race distribution (49% reporting), and (C) ethnicity (31% reporting) by clinical trial biologic type. (D) Race (49% reporting) and (E) ethnicity (31% reporting) by year of clinical trial publication. (F) Aggregate clinical trial reporting of cardiovascular adverse events. CAD, coronary artery disease; CNS, central nervous system; d/r, did not report; HTN, hypertension; MI, myocardial infarction; PVD, peripheral vascular disease.

darker skin types due to overlapping features with other papulosquamous disorders.[4,5] Future researchers should investigate the association between biological therapy use and cardiovascular disease through clinical trials with more inclusive study populations and adhere to reporting the study sample characteristics, total participants, average age, percent male, percent female, and a thorough breakdown of race and ethnicity demographics including at least percent White, percent Black, percent Asian, and percent Hispanic/Latinx. Incorporating more inclusive study populations and reporting a standard set of demographic variables will allow researchers to better characterize each biological therapy's safety profiles and use in the general psoriasis patient population.

Conflicts of interest

The authors made the following disclosures: M.S.G. is a consultant for Bristol Myers Squibb, Kiniksa, and Horizon Therapeutics. The remaining authors have no conflicts of interest to disclose.

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Study approval

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Author contributions

SS contributed to the data collection, analysis, and drafting of this manuscript. MO contributed to the data collection of this manuscript. BNW and JSB contributed to the review of manuscript. MSG contributed to the project development and review of manuscript.

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Table 1

Composite demographics from all clinical trials of biologics in psoriasis leading to Food and Drug Administration approval

Demographics	
Variables ($N = 28,152$)	
Average age, years	47 ± 2.3
Sex	
Male, *n* (%)	16,972 (60)
Female, *n* (%)	11,180 (40)
Race ($n = 15,025$)	
White, *n* (%)	13,527 (90)
Black, *n* (%)	265 (1.8)
Asian, *n* (%)	1050 (7)
American Indian, *n* (%)	136 (0.9)
Native Hawaiian or Pacific Islander, *n* (%)	47 (0.3)
Ethnicity ($N = 8571$)	
Hispanic or Latinx, *n* (%)	731 (9)
Not Hispanic or Latinx, *n* (%)	7840 (91)

Values in *n* (%) unless otherwise noted. All 39 trials ($N = 28,152$) reported age and gender. About 19 of 39 trials ($n = 15,025$) reported race and 12 of 39 trials ($n = 8571$) reported ethnicity.

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