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IL-36 Trials in Dermatology: Cross-Sectional Analysis of ClinicalTrials.gov-Registered Trials

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Dear Editor,

Interleukin 36 (IL-36) inhibitors block the interaction of IL-36 and its receptor, attenuating the downstream inflammatory signaling cascade.[1] Given the therapeutic potential for IL-36 inhibitors in treating dermatological conditions, adequate representation among trial participants is warranted.[2] Clinical trials serve an important role in providing evidence for the safety and efficacy of novel therapies for skin conditions.[3] To gain insights into the current landscape of clinical trials research related to IL-36 inhibitors, a systematic search was conducted to identify relevant studies.

A clinicaltrials.gov search was conducted on May 19th, 2023 using key words (IL-36 antibody, IL-36 inhibitor, IL-36, interleukin 36, spesolimab, BI-655130, imsidolimab, and ANB019), yielding a total of 46 studies. After applying exclusion criteria, 6 studies were included (Figure 1).

Total enrollment across all six trials was 382 patients, with 71% of participants being female. The pooled mean participant age was 49.41 years (standard deviation 11.83). All included trials were industry funded and Phase 2. All but one trial had at least one US-based trial site. The majority of participants were non-Hispanic (92%) and White (64%), with 4.5% (17/382) Black or African American (Table 1). No American Indian or Alaska Native participants were enrolled. Two trials investigated use of imsidolimab, and 4 trials focused on spesolimab.

We report underrepresentation of Hispanic and Black or African American participants in IL-36 inhibitor dermatology trials. Similarly, in a 2021 study of key clinical trials of U.S. FDA approved dermatology drugs 1995-2019, Blacks and Asians were consistently underrepresented, comprising 9.8% and 5.5% of participants respectively.[4] In addition, in a systematic

FIGURE 1. Study Flow Chart

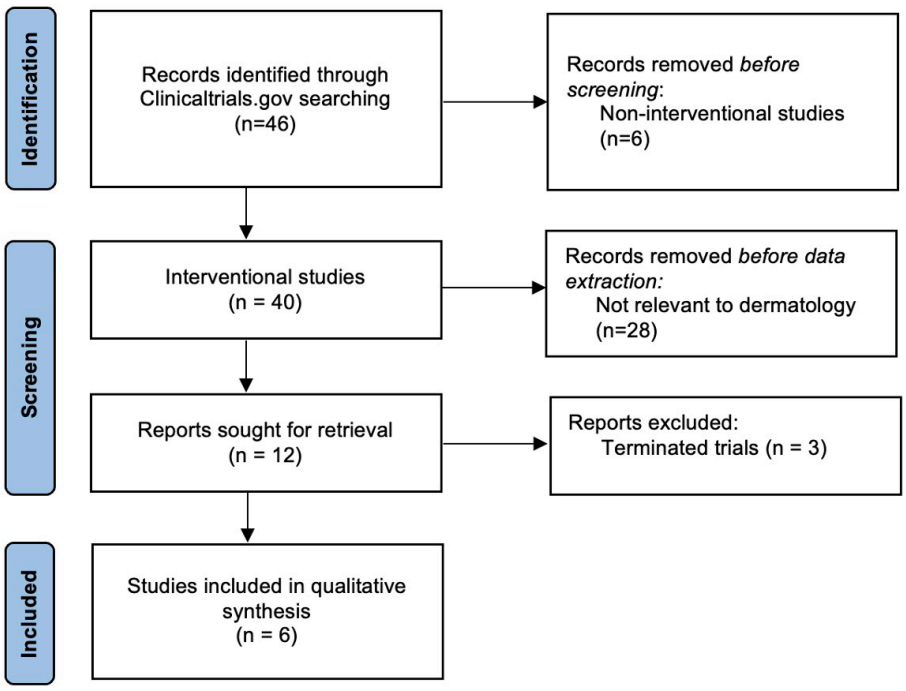

TABLE 1.

Demographic Distribution of IL-36 Trial Participants

Trial identifier	Intervention	Disease	Gender (female), n (%)	Ethnicity (Hispanic or Latino), n (%)	Race (White), n (%)	Age (years), mean (SD)
NCT03782792	Spesolimab (900 mg i.v.) vs. Placebo	Generalized Pustular Psoriasis	36, (67.9%)	0, (0%)	24, (45.3%)	43.0 (10.9)
NCT03619902	Imsidolimab (750 mg i.v. on day 1) with 3 doses of imsidolimab (100 mg s.c.) on days 29, 57, and 85 vs Placebo	Generalized Pustular Psoriasis	4, (50%)	0, (0%)	7, (87.5%)	51.3 (14.91)
NCT03633396	Imsidolimab (200 mg s.c. on day 1) with monthly imsidolimab (100 mg s.c.) on days 29, 57, and 85 vs Placebo	Palmoplantar Pustulosis	46, (78.0%)	3, (5.1%)	53, (89.8%)	50.1 (11.52)
NCT03822832	Spesolimab (600 mg i.v. every 4 weeks) vs Placebo	Atopic Dermatitis	26, (51.0%)	9, (17.6%)	24, (47.1%)	39.4 (15.5)
NCT03135548	Placebo vs Spesolimb 300 mg or 900 mg i.v. every 4 weeks at day 1, 29, 57, and 85 until 12 weeks.	Palmoplantar Pustulosis	49, (83.1%)	6, (10.2%)	56, (94.9%)	50.0 (10.9)
NCT04015518	Total loading dose of spesolimab 1500/3000 mg s.c. vs placebo first 4 weeks, spesolimab 300/600 mg q4w vs placebo. After week 16, patients receiving placebo switched to spesolimab 600 mg q4w; maintenance with spesolimab continued q4w/q8w to week 52.	Palmoplantar Pustulosis	110, (72.4%)	0, (0%)	80, (52.6%)	54.4 (11.0)

review of RCTs on dermatological conditions conducted 2015-2010, among psoriasis trials, only 30% had >20% Non-white representation.[5] Of the six trials included in this study, 5 were related to palmoplantar pustulosis (PPP) or generalized pustular psoriasis (GPP), and only 1 (20%) had >20% Non-white representation.

IL-36 inhibitors, including imsidolimab and spesolimab, show promise for treatment of dermatological conditions such as GPP. Future trials should aim to both enroll more diverse participant populations alongside provide more comprehensive demographic and socioeconomic reporting, to better assess the generalizability of the study findings.

DISCLOSURES

The authors report no conflicts of interest.

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