SHADES OF PROGRESS: UPDATES IN CLINICAL STUDY OF PATIENTS OF COLOR

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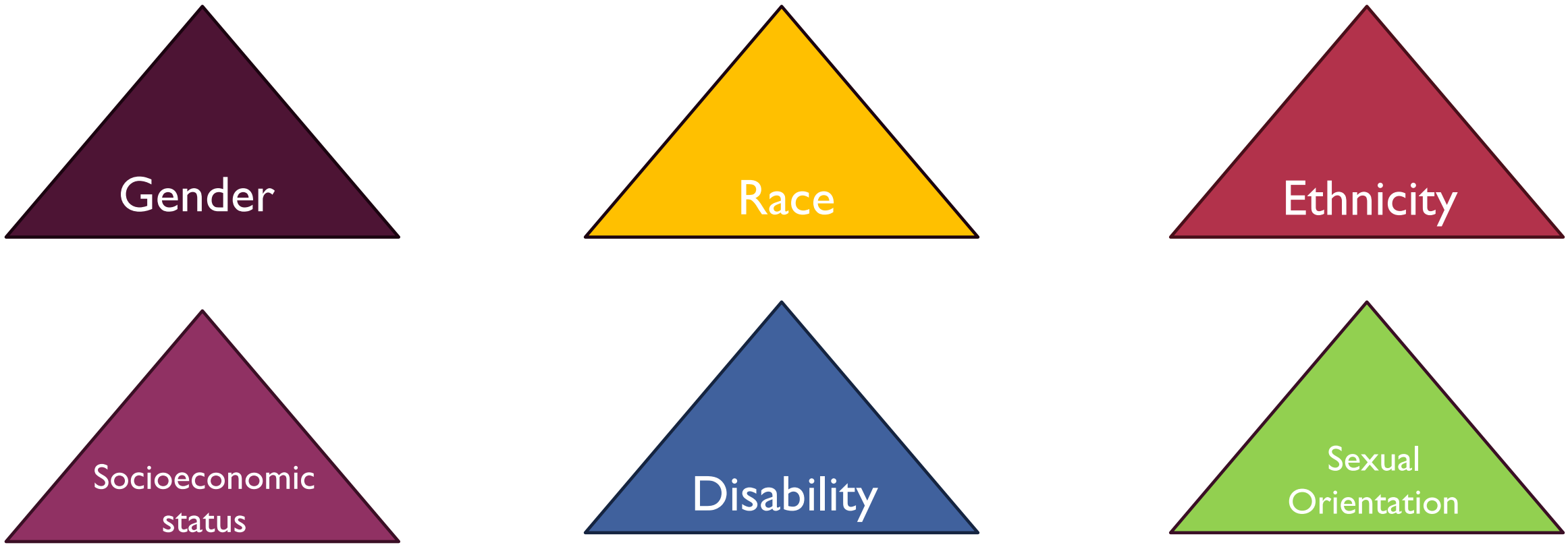
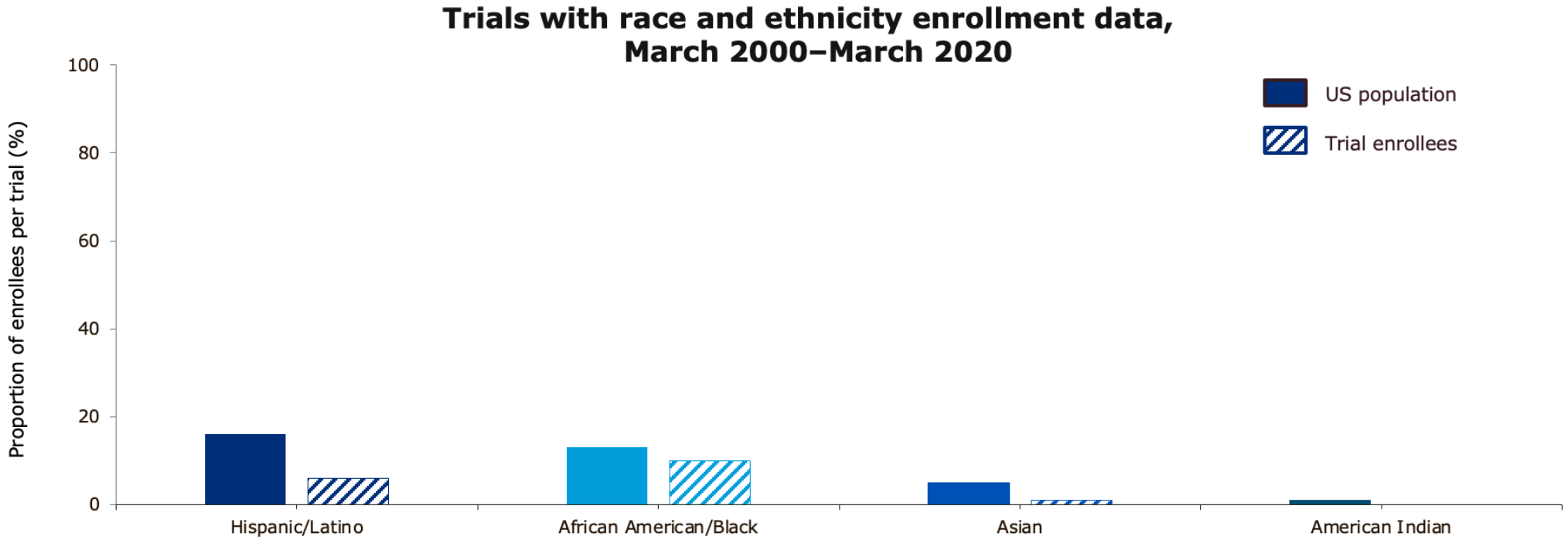
THE US POPULATION IS BECOMING INCREASINGLY DIVERSE



Pandya AG et al. Increasing racial and ethnic diversity in dermatology: A call to action. J Am Acad Dermatol. 2016 Mar;74(3):584-7

UNDERREPRESENTATION OF MINORITY RACIAL AND ETHNIC GROUPS IN U.S. CLINICAL TRIALS



Turner BE, Steinberg JR, Weeks BT, Rodriguez F, Cullen MR. Race/ethnicity reporting and representation in US clinical trials: a cohort study. Lancet Reg Health Am. 2022 Jul;11:100252

Table IV. Racial and ethnic representation as a percent of total participants per dermatologic disease category

Racial data from 215 clinical trials

Demographic	Psoriasis (n = 18,741)	Eczema/atopic dermatitis (n = 9992)	Acne (n = 7076)	Nonmelanoma skin cancer (n = 2232)	Aesthetics (n = 1890)	Melanoma (n = 1855)	Alopecia (n = 1381)	Rosacea (n = 1201)	Tinea (n = 788)	Papillomavirus (warts) (n = 688)
White	84.9% (15,917)	66.5% (6649)	77.5% (5487)	91.5% (2043)	75.1% (1420)	89.1% (1653)	73.0% (1008)	97.0% (1165)	51.9% (409)	89.5% (616)
Black/African American	2.9% (536)	11.6% (1163)	12.6% (893)	2.2% (50)	8.1% (154)	4.4% (82)	7.9% (109)	0.6% (7)	47.5% (374)	6.8% (47)
American Indian/ Alaskan Native	1.6% (292)	0.5% (47)	0.5% (32)	0.2% (4)	0.7% (13)	0.0% (0)	0.4% (6)	0.4% (5)	0.0% (0)	0.1% (1)
Asian	8.0% (1492)	18.6% (1163)	4.1% (293)	0.4% (10)	5.3% (100)	1.7% (32)	15.9% (220)	1.2% (14)	0.0% (0)	1.0% (7)
Native Hawaiian and other Pacific Islander	0.3% (61)	0.4% (35)	0.4% (30)	0.0% (0)	0.5% (10)	0.1% (2)	0.4% (5)	0.0% (0)	0.0% (0)	0.0% (0)
Two or more races	0.8% (141)	1.0% (99)	2.3% (160)	0.0% (0)	0.7% (14)	0.8% (15)	0.6% (8)	0.1% (1)	0.6% (5)	0.3% (2)
Other	0.2% (39)	1.0% (101)	0.0% (0)	3.0% (68)	0.2% (3)	0.0% (0)	1.2% (16)	0.0% (0)	0.0% (0)	1.2% (8)
Unknown or not reported	1.4% (263)	0.4% (43)	1.4% (99)	2.6% (57)	1.1% (20)	3.8% (71)	0.7% (9)	0.7% (9)	0.0% (0)	1.0% (7)

Ethnic data from 152 clinical trials

	Psoriasis (n = 14,315)	Eczema/atopic dermatitis (n = 7716)	Acne (n = 6234)	Nonmelanoma skin cancer (n = 1740)	Aesthetics (n = 1202)	Melanoma (n = 1290)	Alopecia (n = 1381)	Rosacea (n = 765)	Tinea (n = 407)	Papillomavirus (warts) (n = 688)
Hispanic or Latino	10.7% (1530)	10.3% (794)	22.1% (1375)	3.0% (52)	17.3% (208)	7.1% (132)	12.5% (161)	25.0% (191)	0.0% (0)	16.3% (112)

Mineroff J et al., J Am Acad Dermatol, 2023.

CHALLENGES IN ACHIEVING DIVERSITY IN CLINICAL TRIALS

Personal level

- Social, educational, economic difficulties
- Fear & mistrust
- Past experiences
- Knowledge/aware ness
- Fear of being a guinea pig
- Logistic issues: work, time, transportation
- Cultural & language barriers

Provider level

- Lack of minority health care professionals & scientists to recruit minority patients
- Stereotyping that minority patients are difficult to reach and "non-compliant"
- Bias & discrimination
- Less discussion of enrollment in clinical trials with minority patients
- Assumption that minority patients are not interested in clinical trials

Health systems

- Lack of racial concordant providers/staff for clinical trials
- Lack of culturally appropriate methodology & materials
- Lack of access
- Lack of health care for the population
- Lack of cultural sensitivity in health care delivery
- Lack of funding
- Lack of inclusiveness and tailoring to disparity populations
- Time

Protocol level

- Informed consent procedures
- Rigid inclusion/exclusion criteria, e.g. due to comorbidities, multiple cancers, adherence issues
- Information too technical
- Lack of evaluation for improvement of process
- Research design issues
- Poor performance
- Feedback on previous protocols
- Lack of community input
- Cost

Odedina FT, Wieland ML, Barbel-Johnson K, Crook JM. Community Engagement Strategies for Underrepresented Racial and Ethnic Populations. Mayo Clin Proc. 2024 Jan;99(1):159-171

WHY IS DIVERSITY IN CLINICAL TRIALS IMPORTANT?

Contains Nonbinding Recommendations

Draft — Not for Implementation

Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies Guidance for Industry[1]

- Intended to increase enrollment of participants who are members of historically underrepresented populations in clinical studies
  - Age, ethnicity, race, sex
- This will help improve the strength and generalizability of the evidence for the intended use population

FDA GUIDANCE

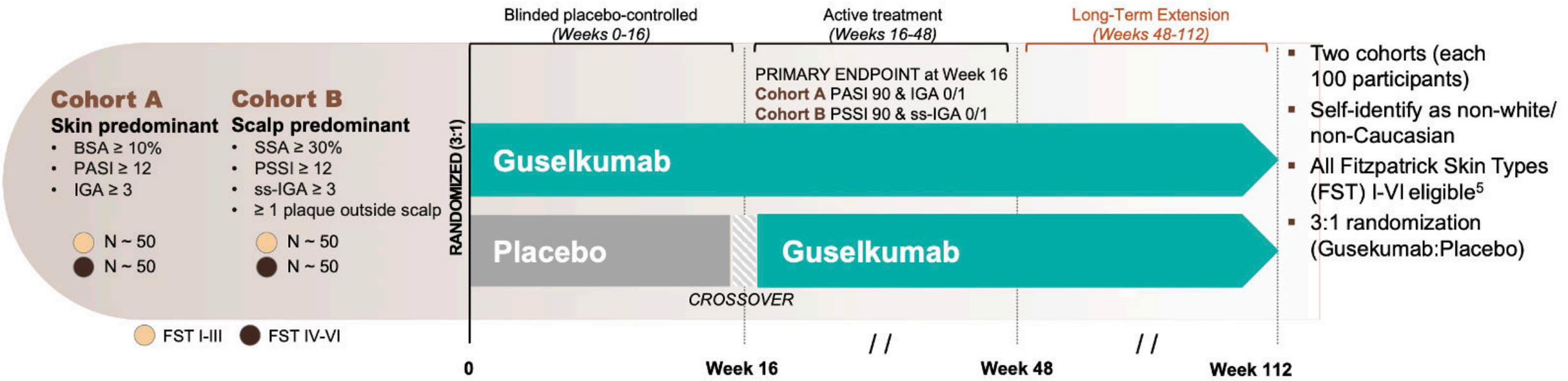
- Broaden eligibility criteria and avoid unnecessary exclusions
- Design trials in ways that achieve participant diversity
  - Initiate studies in sites with diverse populations
  - Consider transportation barriers for those that live in rural or remote locations
    - Flexibility in visit times and frequency of in person visits, consider televisits
  - Consider participation challenges for older adults, children, people with disabilities and those with cognitive impairments
- Improve practices for recruiting participants to clinical trials
  - Consider diverse investigators and study coordinators to assist with trial recruitment
  - Trial related resources in multiple languages
  - Sponsor's can engage with the participants' community and build trust

PROGRESS IN PSORIASIS CLINICAL TRIALS:

VISIBLE STUDY- FIRST LARGE SCALE DEDICATED SKIN OF COLOR IN PSORIASIS STUDY

CLINICAL TRIAL DESIGN

VISIBLE is a phase 3b, multicenter, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of GUS



Alexis A, et al. AAD Annual Meeting; March 2023; New Orleans, LA

THE VISIBLE APPROACH TO ENHANCE DIVERSITY

During trial design

- Consult dermatologists with prior experience of treating underrepresented patients
- Include a minimum enrollment criteria for inclusion of diverse participants
- Allow self reporting of race/ethnicity
- Use objective skin tone/pigmentation measures

Recruitment

- Offer transport and reimbursement for time missed at work
- Produce study materials in multiple languages and provide on-site translation
- Broaden inclusion criteria
- Utilize referral and patient networks and advertising to promote enrolment

Site selection

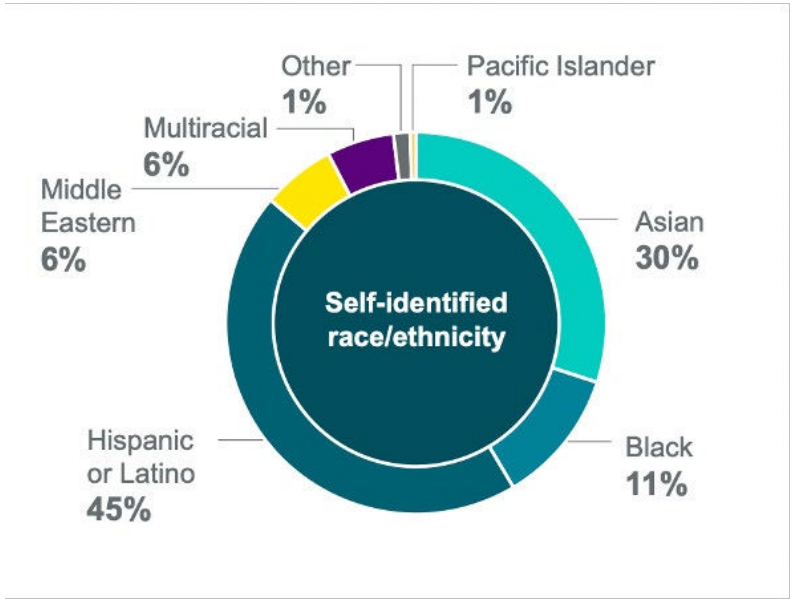
- Assess patient diversity at study sites using questionnaires
- Use claims databases to identify sites with underrepresented populations

Training for investigators

- Provide cultural sensitivity training
- Give training in disease appearance across all skin tones to increase knowledge and understanding

Alexis A, McMichael A, Vashi N, Bhutani T, Rodriguez AO, Yeung J, Choi O, Chan D, Alkousakis T, Bronner DN, Park-Wyllie L, Gao LL, Grimes P, Shahriari M, Yadav G, Kindred C, Taylor SC, Desai SR. JAMA Dermatol. 2024 Dec 11.

AN INCLUSIVE PATIENT POPULATION



Fitzpatrick Skin Type: Race/Ethnicity Distribution in VISIBLE*

	I	II	III	IV	V	VI
Black						
Central American (Guatemalan, etc)						
Cuban						
Hispanic or Latino						
American Indian or Indigenous						
Middle Eastern (Egyptian, Persian, etc)						
Mexican						
Multiracial or Other						
Puerto Rican						
South American (Brazilian, Argentinian, etc)						
South Asian (Pakistani, Sri Lankan, etc)						
Southeast Asian (Filipino, Thai, etc)						

The Challenge

- Fitzpatrick skin type (FST) is subjective and prone to bias
- Limiting SOC to FST IV-VI and or certain races or ethnicities results in exclusion of some groups (e.g., Middle Eastern populations)

The Intervention

- Use of colorimeter to objectively determine skin tone-based FST
- Inclusion of FST I-VI and all who self-identify as non-white
- Increased number of primary race/ethnicity categories with multiple subcategories with the ability to self-report

Alexis A, et al. AAD Annual Meeting; March 2023; New Orleans, LA

ENHANCING DIAGNOSIS AND DISEASE SEVERITY ASSESSMENTS

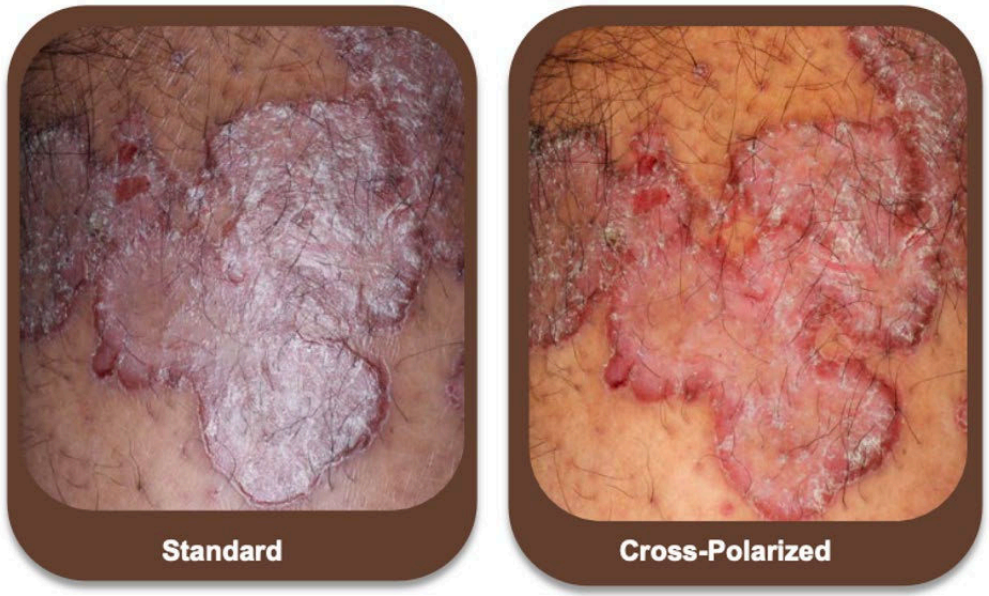
The Challenge

- Historical misdiagnosis and delayed diagnosis of PsO in SOC
- Objective visual evaluation of erythema and pigmentation may be difficult
- Limited SOC images in dermatology textbooks

The Intervention

- Screening photos submitted to an expert panel to confirm the PsO diagnosis and confirm study eligibility
- Measurement of erythema in PsO and melanin in post-inflammatory pigment alteration (PIPA) via colorimetry
- Use of cross-polarized light and photography to objectively evaluate the progression/improvement of psoriasis plaques and PIPA over time
- Creation of a database of about 20,000 clinical images showcasing the presentation of PsO across skin tones

Cross polarized photography can enhance erythema visualization

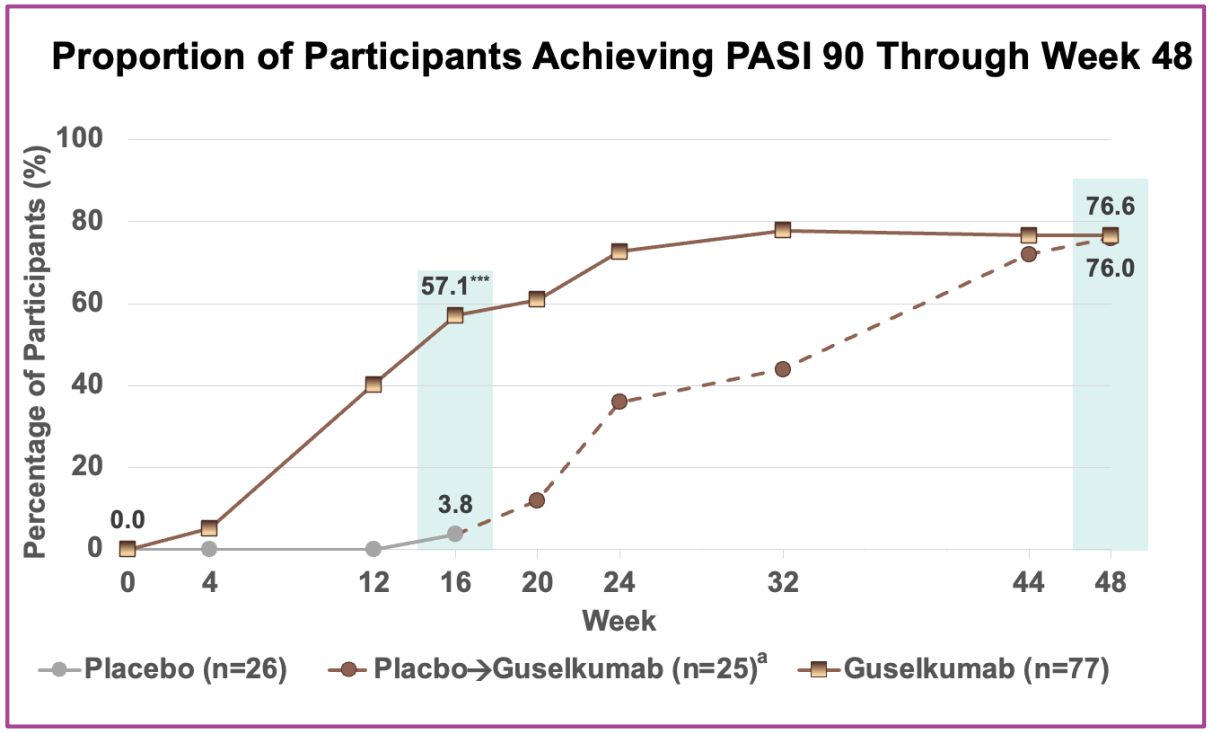


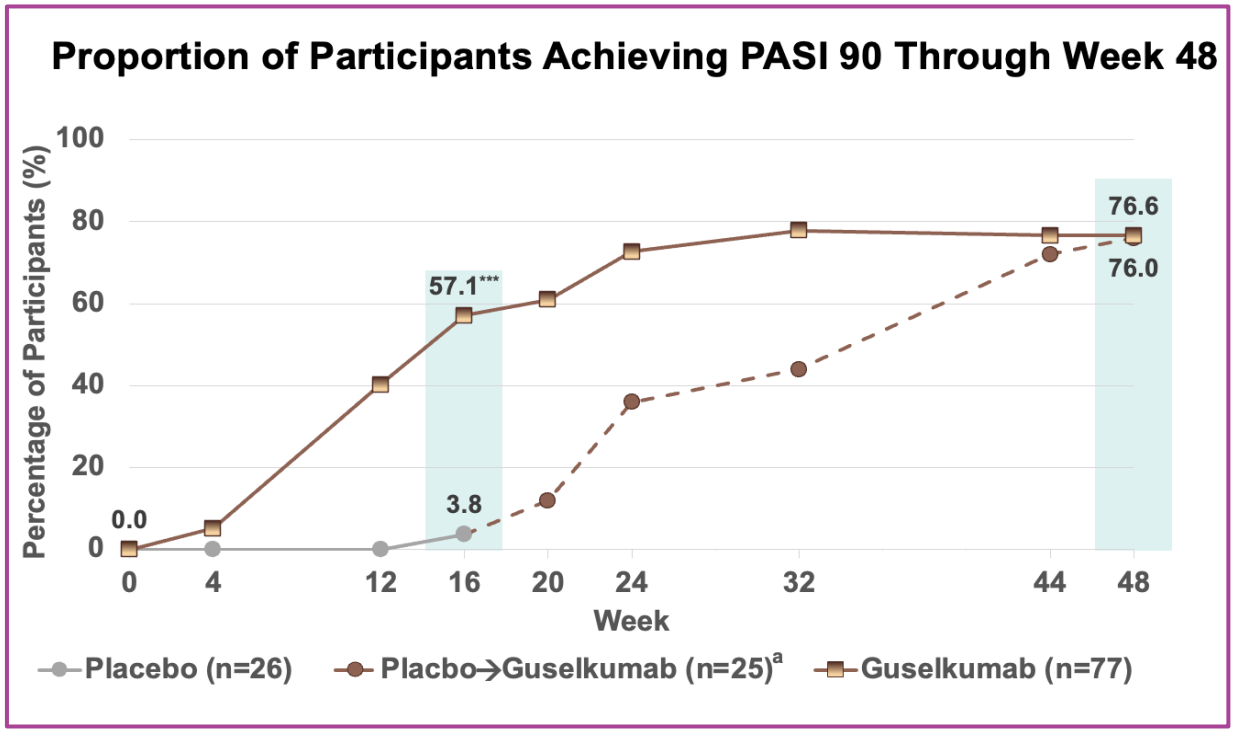
Alexis A, et al. AAD Annual Meeting; March 2023; New Orleans, LA

ADDRESSING THE GAPS

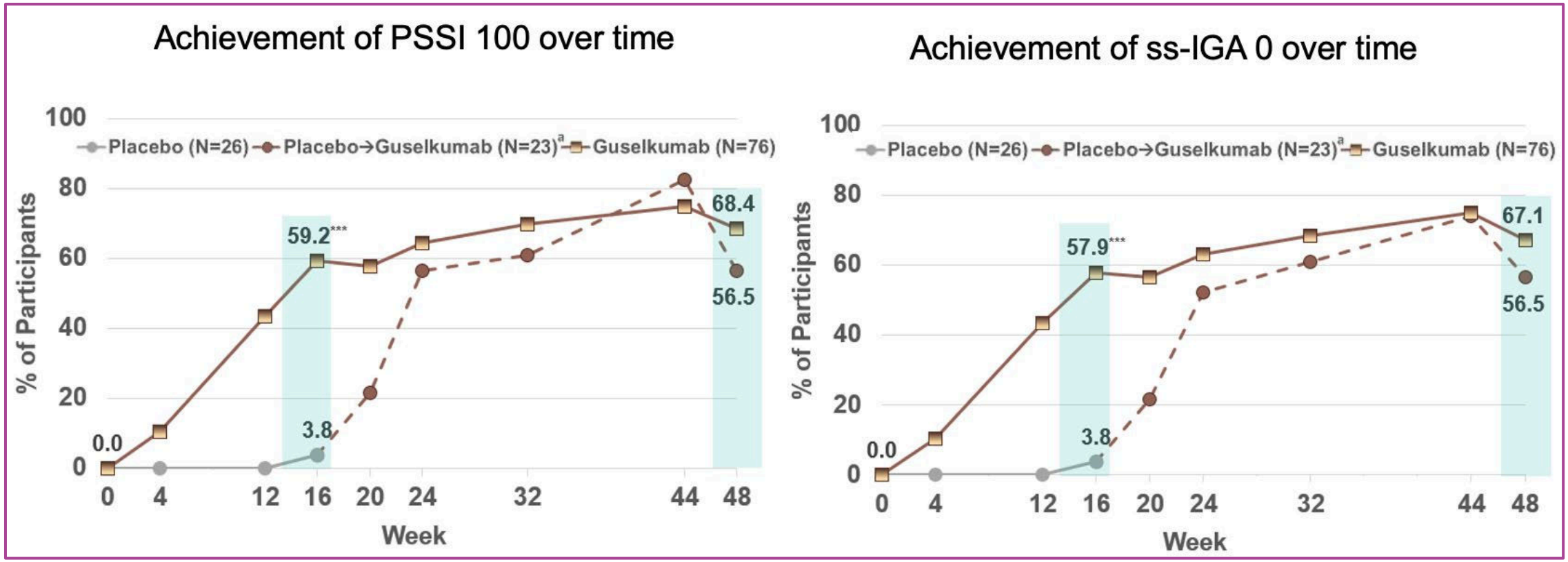
- The natural history of post-inflammatory pigment alteration
- The impact of treating psoriasis on the trajectory of post-inflammatory pigment change
- Assessment of novel biomarker data

PASI 90 AND IGA 0/1: SKIN CLEARANCE ACROSS ALL SKIN TONES THROUGH WEEK 48 WITH GUSELKUMAB





PROPORTION OF PATIENTS WITH COMPLETE SCALP CLEARANCE THROUGH WEEK 48 WITH GUSELKUMAB

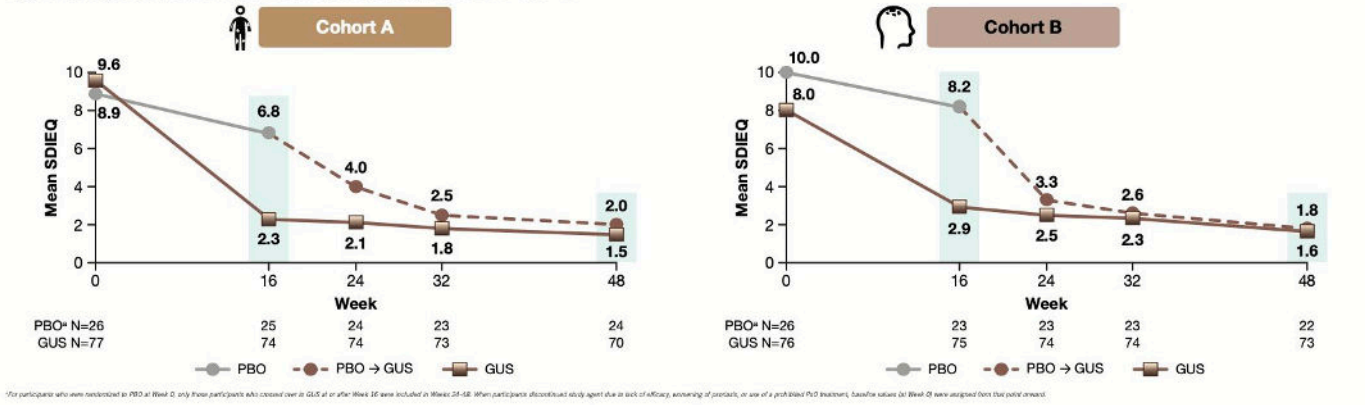


SHADOWS OF INFLAMMATION: EXPLORING POST-INFLAMMATORY PIGMENT CHANGES IN PSORIASIS IN VISIBLE, A PHASE 3b RANDOMIZED CONTROLLED STUDY OF GUSELKUMAB FOR MODERATE-TO-SEVERE PLAQUE PSORIASIS DEDICATED TO PEOPLE OF COLOR

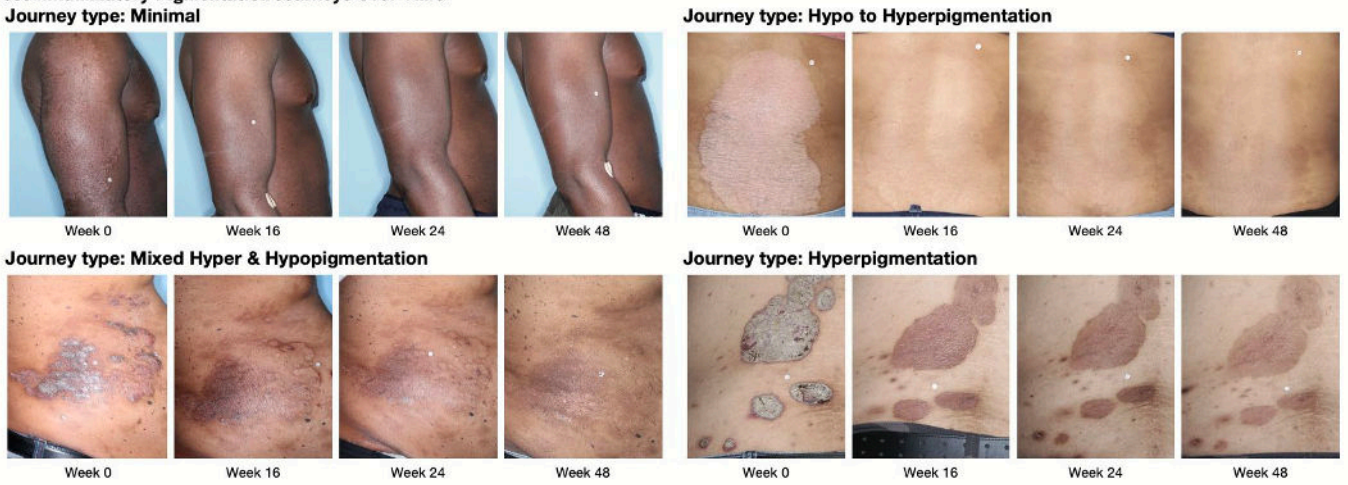
A Alexis,[1] A McMichael,[2] T Bhutani,[3] M Shahriari,[4] O Choi,[5] T Alkousakis,[5] K Rowland,[5] A Rodriguez,[6] G Yadav,[7] J Yeung,[8] T Ma,[9] N Abbarin,[10] D Chan,[5] C Kindred,[11] N Vashi,[12] P Grimes,[13] S Desai,[14] S Taylor[15]

- At Baseline, participants from both VISIBLE Cohorts A and B reported substantial impact of skin discoloration due to PsO on QoL (mean SDIEQ scores 8-10)
- Rapid and substantial reductions in mean SDIEQ scores were achieved at Weeks 16 and 48, and continued to improve through Week 48 consistent with pigment improvement observed in clinical photography

Figure 1. Improvement in mean SDIEQ scores at Weeks 16 and 48



Post-inflammatory Pigmentation Journeys Over Time



Alexis A et al. Presented at Fall Clinical Dermatology October 2024

SHADOWS OF INFLAMMATION: EXPLORING POST-INFLAMMATORY PIGMENT CHANGES IN PSORIASIS IN VISIBLE, A PHASE 3b RANDOMIZED CONTROLLED STUDY OF GUSELKUMAB FOR MODERATE-TO-SEVERE PLAQUE PSORIASIS DEDICATED TO PEOPLE OF COLOR

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- Overall, there was a stronger correlation between SDIEQ and DLQI scores (**Figure 2**) vs PASI and DLQI scores (**Figure 3**) for all skin tones at Week 48
- This effect was more pronounced in the darker skin tone strata (Fitzpatrick IV-VI) for SDIEQ and DLQI scores (r=0.6826) vs PASI and DLQI scores (r=0.1789)

Cohort A & B Combined

Figure 2. Correlation between SDIEQ and DLQI at Week 48

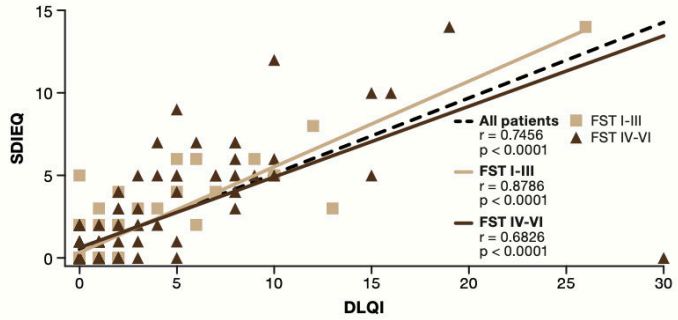
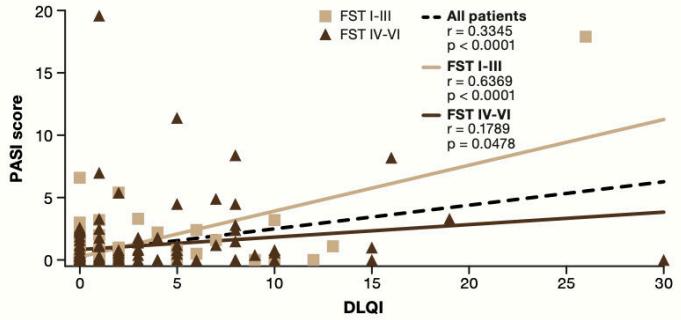


Figure 3. Correlation between PASI and DLQI at Week 48



- This post-hoc anlaysis showed that PROMIS-29 depression scores were more strongly correlated with SDIEQ scores (**Figure 4**) than PASI clearance scores (**Figure 5**) for all skin tones

Cohort A & B Combined

Figure 4. Correlation between SDIEQ and PROMIS-29 depression score at Week 48: all skin tones

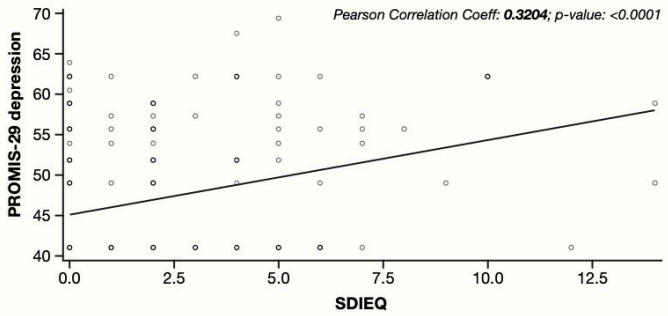
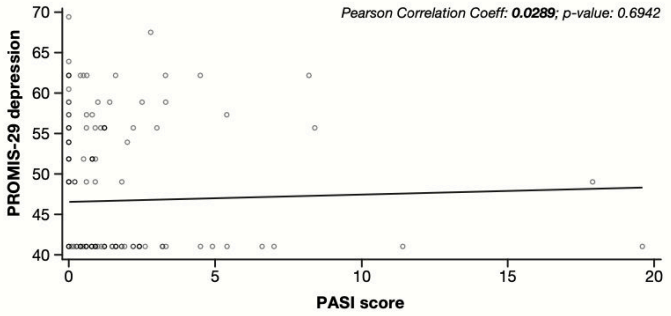


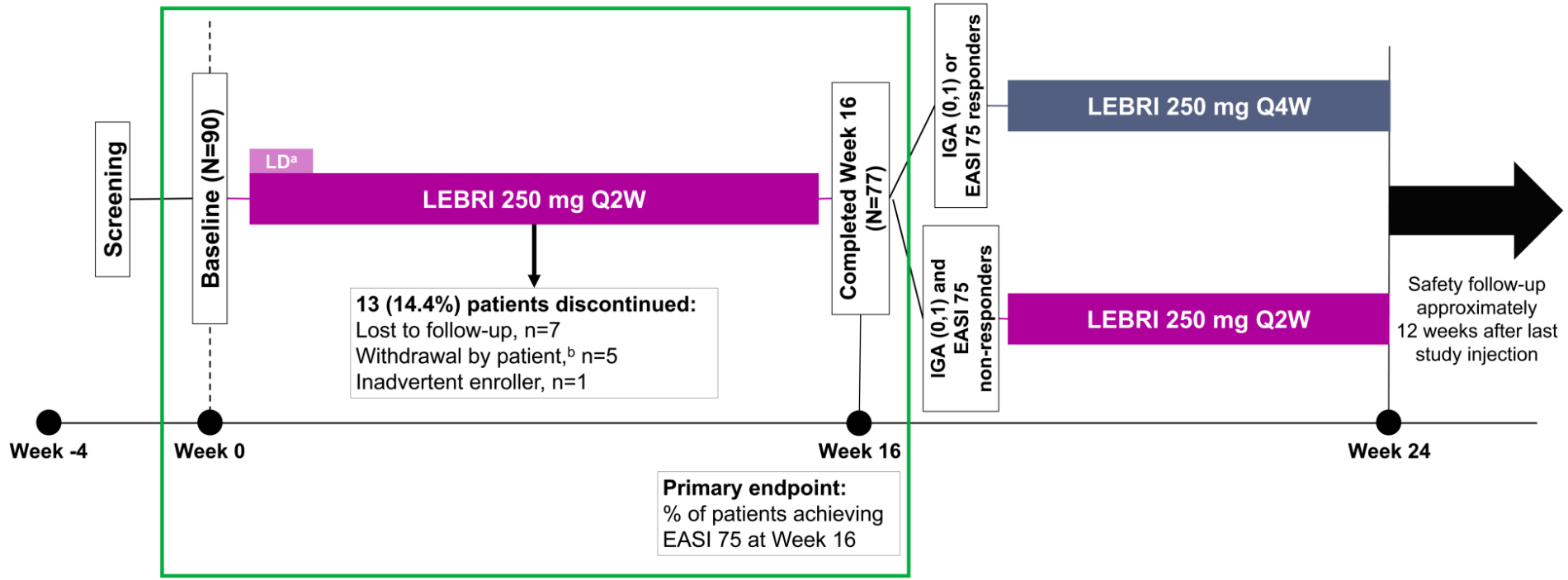
Figure 5. Correlation between PASI and PROMIS-29 depression score at Week 48: all skin tones



PROGRESS IN ATOPIC DERMATITIS CLINICAL TRIALS:

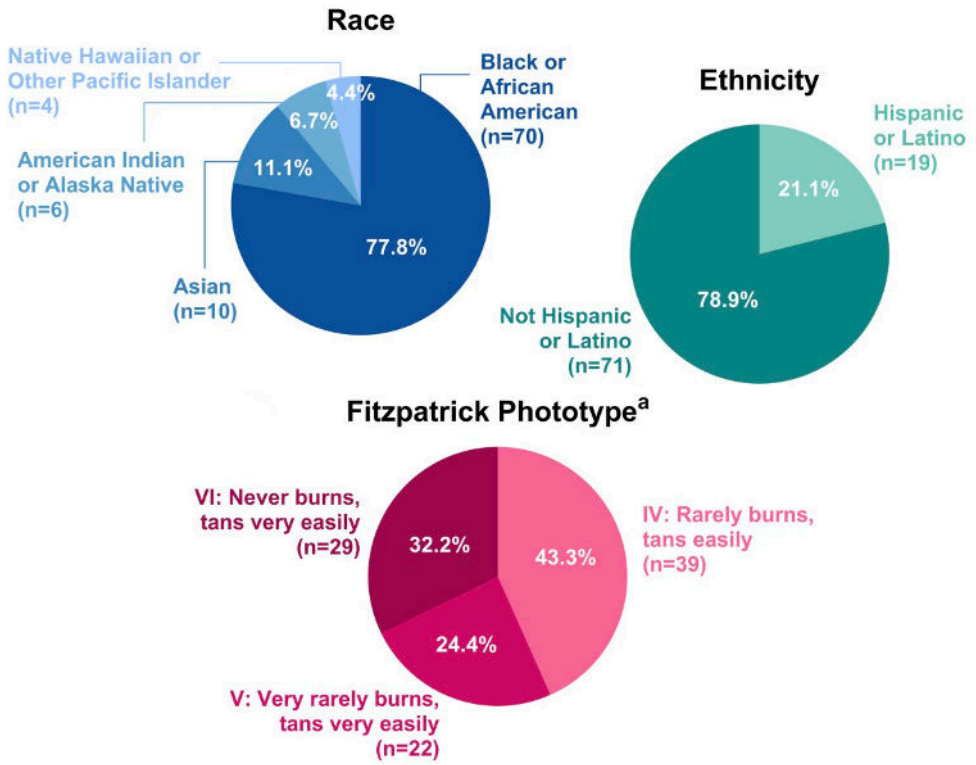
ADMIRABLE STUDY- FIRST DEDICATED SKIN OF COLOR IN ATOPIC DERMATITIS STUDY

CLINICAL TRIAL DESIGN



A DIVERSE PATIENT POPULATION

- Included patients with a self-reported race other than white
- FST IV-VI

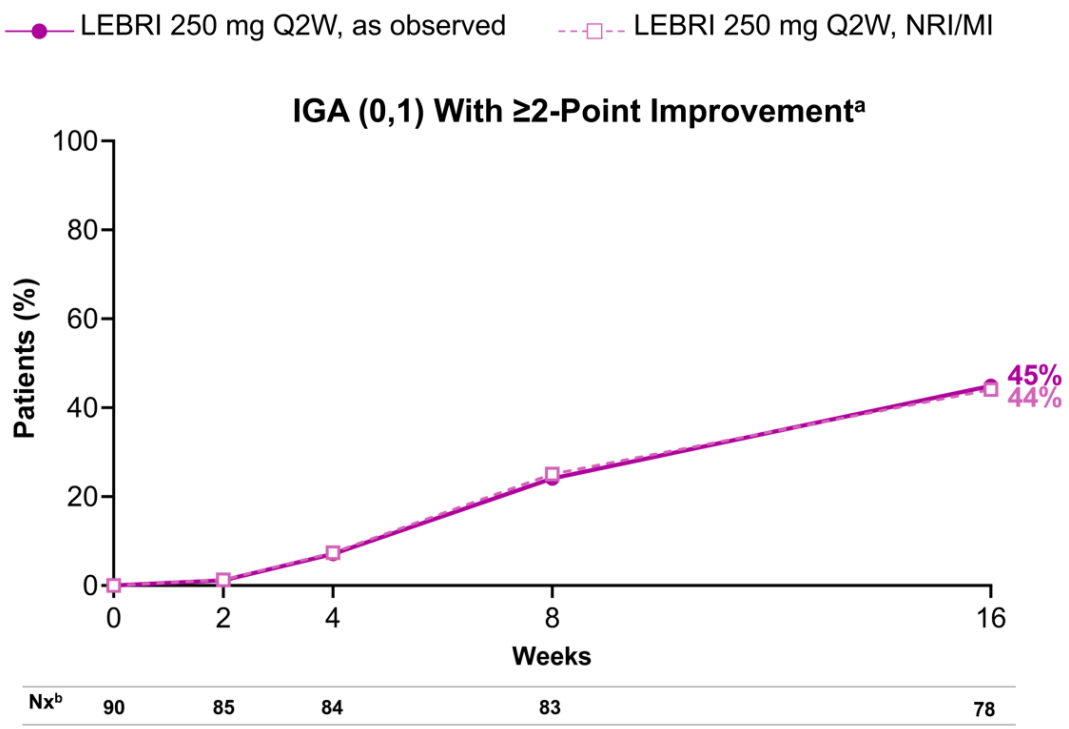


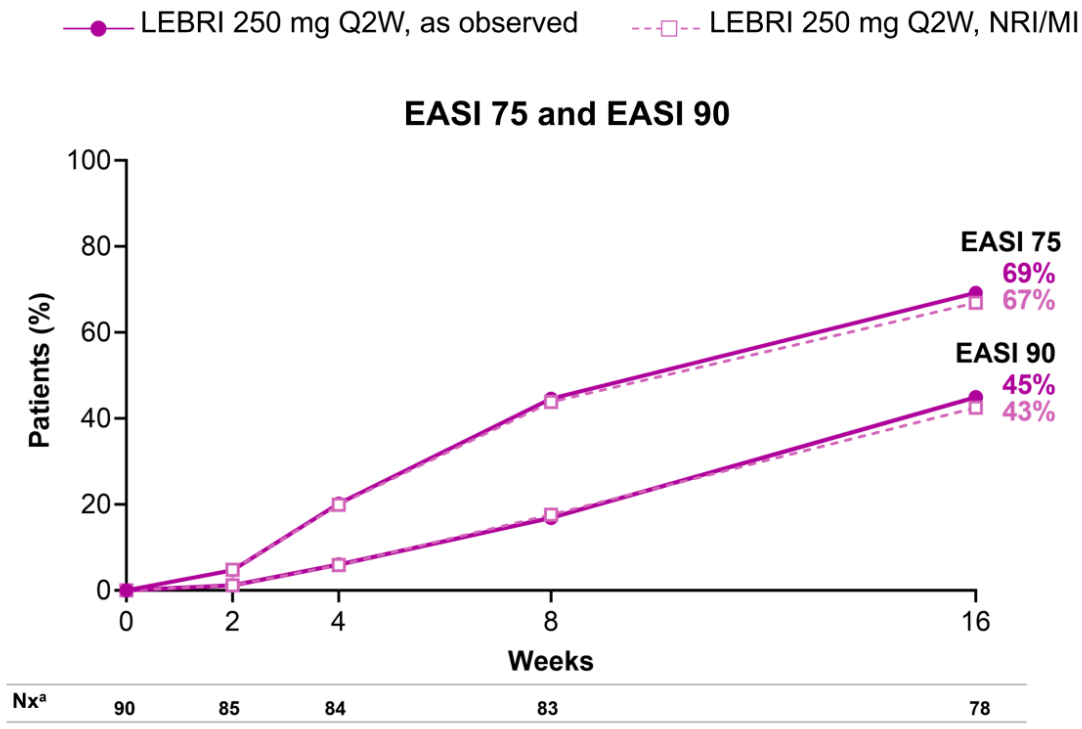
PDCA-DERM: ASSESSING POST-INFLAMMATORY HYPOPIGMENTATION AND HYPERPIGMENTATION IN ATOPIC DERM

Post-inflammatory hypopigmentation				Post-inflammatory hyperpigmentation		
-3	-2	-1	0	+1	+2	+3
Severe hypopigmentation	Moderate hypopigmentation	Mild hypopigmentation	Normal skin tone	Mild hyperpigmentation	Moderate hyperpigmentation	Severe hyperpigmentation
Prominent hypopigmentation	Clearly perceptible hypopigmentation	Barely perceptible hypopigmentation		Barely perceptible hyperpigmentation	Clearly perceptible hyperpigmentation	Prominent hyperpigmentation

Alexis et al, Fall Clinical 2024, Las Vegas, NV

IGA 0/1 AND EASI 75/90 ACHIEVEMENT WITH LEBRIKIZUMAB





Alexis et al, Fall Clinical 2024, Las Vegas, NV

IMPROVEMENTS IN PIGMENTARY CHANGE AS MEASURED BY PDCA-DERM

At Week 16:

33%

Improved hypopigmented lesions[a]

17%

Hypopigmented lesions improved to normal skin tone[a]

20%

Hyperpigmented lesions improved to normal skin tone[b]

63%

Improved hyperpigmented lesions[b]

Alexis et al, Fall Clinical 2024, Las Vegas, NV

ClinicalTrials.gov

Completed

Dupilumab in Adolescent and Adult Skin of Color Participants: Open-label Moderate-to-severe Eczema Trial (DISCOVER)

ClinicalTrials.gov ID NCT05590585

Sponsor Regeneron Pharmaceuticals

Information provided by Regeneron Pharmaceuticals (Responsible Party)

Last Update Posted 2024-12-10

Eligibility Criteria

Description

Key Inclusion Criteria:

1. Skin of color, defined as Fitzpatrick skin type ≥4 at screening visit
2. Diagnosis of moderate-to-severe atopic dermatitis (AD) that cannot be adequately controlled with topical AD medications, as defined in protocol
3. Has applied a stable dose of topical emollient (moisturizer) twice daily as per physician recommendation starting at screening visit

TAKE HOME POINTS

- As the US population continues to diversity, individuals studied in clinical trials should resemble the diversity and heterogeneity of real-world populations
- Dedicated skin of color trials in psoriasis and atopic dermatitis have not only confirmed the safety and efficacy of therapeutics across diverse populations, but also highlighted the unique challenges faced by patients from diverse backgrounds
- Diversity action plans have helped improve the representation of historically underrepresented populations in clinical trials