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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BACKGROUND

- **VISIBLE** is an ongoing, **first-of-its-kind**, large-scale, phase 3b, randomized, double-blind, placebo (PBO)-controlled study to evaluate efficacy and safety of **guselkumab** (GUS) for moderate-to-severe **plaque psoriasis** (PsO) **across all skin tones. VISIBLE** was uniquely prospectively designed to collect data on **post-inflammatory pigment alteration (PIPA)**
- **PIPA** secondary to PsO more frequently impacts individuals with **skin of color**[1,2]
- In one survey of biologic-treated PsO patients, over **80%** considered **PIPA** to be an important but **neglected problem**[3]

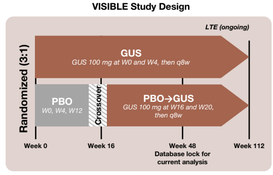
BACKGROUND/METHODS

Objective

Evaluate impact of PIPA on quality-of-life (QoL) using the patient-reported Skin Discoloration Impact Evaluation Questionnaire (SDIEQ)[a] in conjunction with the Dermatology Life Quality Index (DLQI),[b] and PROMIS-29 depression measures

VISIBLE Study Design

VISIBLE included participants who self-identified as non-white, across all skin tones



Cohort A and B Analysis population (N=205)

Outcomes

- Psoriasis Area and Severity Index (PASI) 0-72 scale
- Skin Discoloration Impact Evaluation Questionnaire (SDIEQ) 0-15 scale[a]
- Dermatology Life Quality Index (DLQI) 0-30 scale[b]
- PROMISE-29 Depression

Photos

- Standard & Cross Polarized Photography Over Time

Cohort A: 103 participants with moderate-to-severe PsO	Cohort B: 106 participants with moderate-to-severe scalp PsO
BSA ≥10%, PASI ≥12, IGA ≥3	SSA ≥30%, PSSI ≥12, ss-IGA ≥3, and ≥1 plaque outside of the scalp

[a]SDI=Body surface area, IGA=Investigator Global Assessment, LTE=Long term extension, PROMIS=Patient-Reported Outcomes Measurement Information System, PSS=Psoriasis Scalp Severity Index, SSA=Scalp surface area, ss-IGA=Scalp-specific Investigator's Global Assessment, W=Week. [b]Scores range from 0-30; higher number indicates maximum impact on QoL.

Patient-Reported Outcomes

Pigmentation Effect on Participant QoL[4]

SDIEQ Score

0-6	Mild effect
7-11	Moderate effect
12-15	Severe effect

SDIEQ 5-Question Scale[a]

1. How embarrassed or self-conscious have you been because of your skin?
2. How much have people focused on your skin discoloration rather than on what you are saying or doing?
3. How much has your skin discoloration made you feel unattractive to others?
4. How much effort have you put into hiding your skin discoloration from others?
5. How much has your skin affected any of your social or leisure activities?

PsO Impact on HRQoL[5]

DLQI Score

0-1	No effect
2-5	Small effect
6-10	Moderate effect
11-20	Very large effect
21-30	Extremely large effect

[a]BMI=Body mass index, BP=Blood pressure, BSA=Body surface area, HDL=High density lipoprotein, HRQoL=Healthcare-related quality of life, PsA=Psoriatic arthritis. [b]Defined as meeting ≥3 of the following criteria at Week 0: BMI ≥30 kg/m²; triglycerides ≥150 mg/dL; HDL in men <40 mg/dL or in women <50 mg/dL; BP ≥130/85 mmHg; fasting glucose ≥100 mg/dL. [c]Subcategories shown were reported in ≥5 participants.

Cohort A+B Comorbidities (N=211)

Diabetes	Hypertension	Dyslipidemia	Metabolic Syndrome*	PsA
21.8%	63.0%	71.6%	32.2%	29.9%

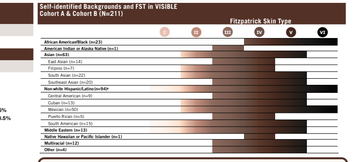
Baseline Disease Characteristics

Cohort A (N=103)	PASI score (0-72)	20.8 (9.1)
	BSA, %	26.8 (19.3)
Cohort B (N=102)	PSSI score (0-72)	34.3 (13.2)
	SSA, %	59.8 (26.0)

Data are mean (standard deviation) unless otherwise specified.

Cohort A & B Race/Ethnicity (N= 211)

Self-identified Backgrounds and FST in VISIBLE
Cohort A & Cohort B (N=211)

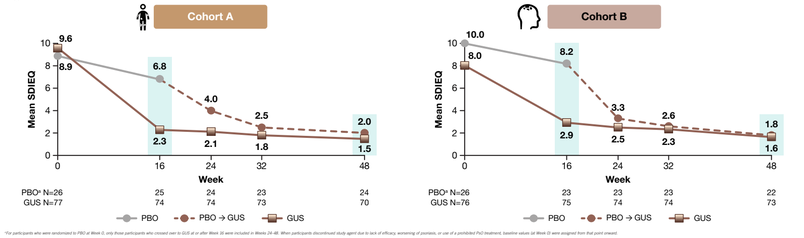


- VISIBLE recruited a diverse population
- Baseline characteristics show that on average, participants had extensive skin/scalp disease and a high comorbidity burden
- 65.9% of participants had a Fitzpatrick Skin Type (FST) in the IV-VI range

RESULTS

- 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

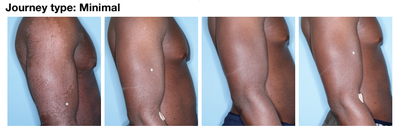
Figure 1. Improvement in mean SDIEQ scores at Weeks 16 and 48



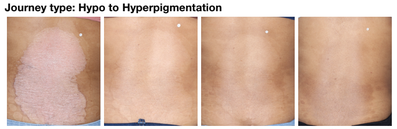
*For participants who were randomized to PBO at Week 0, only those participants who crossed over to GUS at or after Week 16 were included in Weeks 24–48. When participants discontinued study agent due to lack of efficacy, worsening of psoriasis, or use of a prohibited PsO treatment, baseline values (at Week 0) were assigned from that point onward.

Post-inflammatory Pigmentation Journeys Over Time

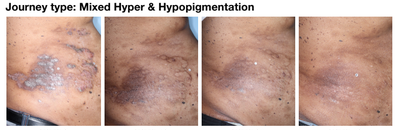
Journey type: Minimal



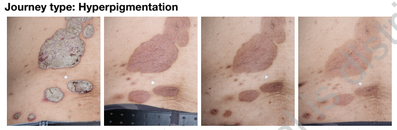
Journey type: Hypo to Hyperpigmentation



Journey type: Mixed Hyper & Hypopigmentation



Journey type: Hyperpigmentation



Photos from ongoing trial NCT05272332 (VISIBLE)

- 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

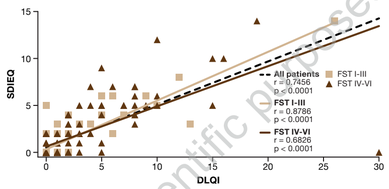
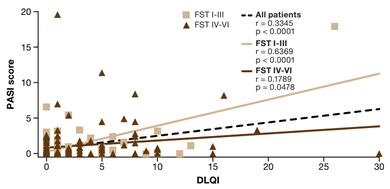


Figure 3. Correlation between PASI and DLQI at Week 48



- 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

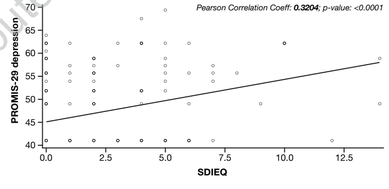
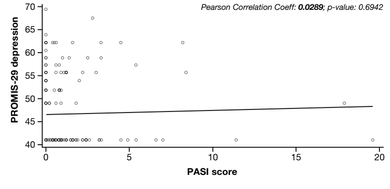
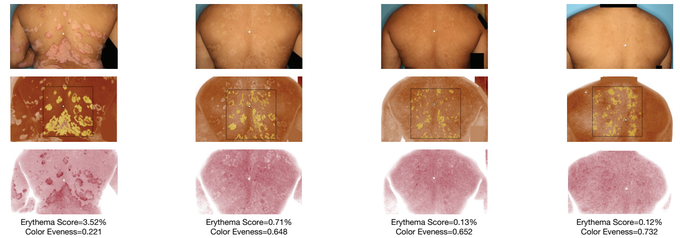


Figure 5. Correlation between PASI and PROMIS-29 depression score at Week 48: all skin tones



Exploratory Analyses: Objective evaluation of cross-polarized photos for erythema, pigmentation, and skin tone evenness over time



CONCLUSIONS

- **VISIBLE is a first-of-its-kind prospective study evaluating GUS in participants across all skin tones with moderate-to-severe PsO intentionally designed to collect information on post-inflammatory pigmentation after treatment for PsO**
- **Substantial, rapid improvements in PIPA, measured by SDIEQ, were reported by participants at Week 16 after 3 doses of GUS, with sustained improvements observed through Week 48 with continued treatment**
- **SDIEQ is more strongly correlated with DLQI than PASI, which indicates that discoloration is more impactful than skin clearance, especially among darker skin tones, and suggests that PASI outcomes do not not adequately measure psoriatic disease burden across all skin tones**
- **The VISIBLE study demonstrates the importance of capturing standard and cross-polarized photography across skin tones. These photos showcase the various journey types a patient may take and allow for objective analyses to provide insights into PIPA following PsO to inform and improve patient counseling**

References: 1. Amico S, et al. *J Am Acad Dermatol.* 2020;83:1188-1191. **2.** Kaufman BP, et al. *Am J Clin Dermatol.* 2018;19:405-423. **3.** Chiu HY, et al. *J Am Acad Dermatol.* 2022;86:642-645. **4.** Maymone MBC, et al. *J Dermatol.* 2018;45:361-2. **5.** Hongbo Y, et al. *J Invest Dermatol.* 2005;125:659-664. **6.** Balkrishnan R, et al. *J Drugs Dermatol.* 2004;3:377-381.

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