VISIBLE: SIGNIFICANT SERUM CYTOKINE REDUCTION ACHIEVED WITH GUSELKUMAB IN PARTICIPANTS WITH PSORIASIS AND SKIN OF COLOR

S.G. Kwatra,[1] G. Han,[2] J.E. Hawkes,[3] A. Farberg,[4] B. Ungar,[2] T. Lee,[5] V.R. Moulton,[5] H. Moncrieffe,[5] M. Leung,[6] R. Panchakshari,[6] K. Rowland,[5] T. Alkousakis,[5] O. Choi,[5] J. Talia,[2] J. North[7]

[1]Department of Dermatology, University of Maryland School of Medicine, Baltimore, MD; [2]Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY; [3]Oregon Medical Research Center, Portland, OR; [4]Bare Dermatology, Dallas, TX; [5]Johnson & Johnson, Horsham & Spring House, PA; [6]Johnson & Johnson, San Diego, CA; [7]Departments of Dermatology and Pathology, University of California San Francisco, San Francisco, CA

LB1131

Scan the QR code for the full digital poster

The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.

BACKGROUND

- Levels of disease-driving **cytokines** are typically **elevated** in the skin and blood of patients with **psoriasis** (PsO)[1]
- **VISIBLE**, a Phase 3b randomized, placebo (PBO)-controlled study, is evaluating efficacy & safety of **guselkumab** (GUS) in participants with **moderate-to-severe PsO** across **diverse** objectively measured **skin tones**
- These **post-hoc analyses** evaluated the **effects of GUS** on targeted serum cytokines (interleukin **[IL]-17A, IL-17F, IL-22, β-Defensin [BD]-2**)

METHODS

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

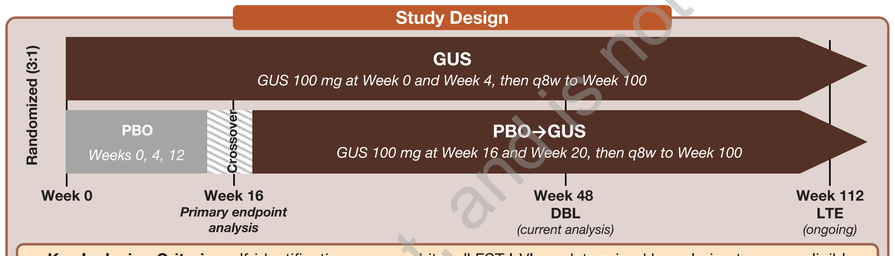
Cohort A: 103 participants with moderate-to-severe plaque PsO

BSA ≥10%, PASI ≥12, IGA ≥3

Cohort B: 108 participants[a] with moderate-to-severe scalp PsO

SSA ≥30%, PSSI ≥12, ss-IGA ≥3, and ≥1 plaque outside of the scalp

Study Design



- **Key Inclusion Criteria:** self-identification as non-white; all FST I-VI, as determined by colorimetry, were eligible
- Serum cytokines were measured by ELISA

Serum Cytokine Levels

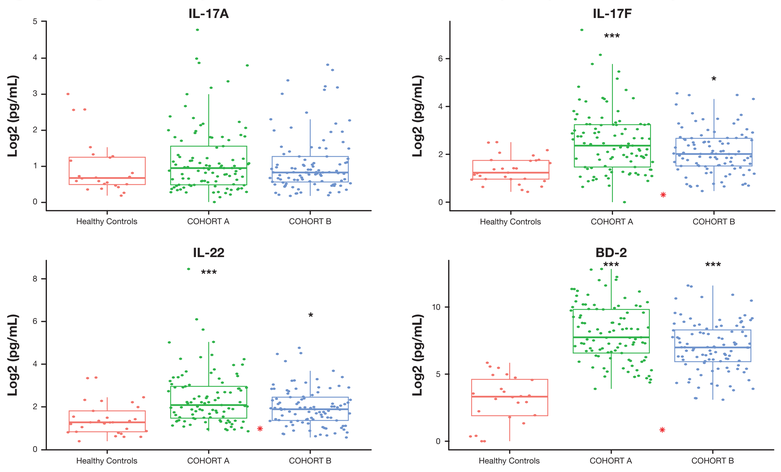
- **IL-17A, IL-17F, IL-22, BD-2**
- Measured at baseline (Week 0), and at Weeks 4, 16, and 48
- 151 GUS and 50 PBO participants across both cohorts and up to 29 age- and race- matched healthy controls

[a]Efficacy analysis population included all participants correctly randomized to Cohort B (n=102).
BSA=Body surface area; DBL=Database lock; ELISA=Enzyme-linked immunosorbent assay; FST=Fitzpatrick skin type; IGA=Investigator's Global Assessment; LTE=Long term extension; PASI=Psoriasis Area and Severity Index; PSSI=Psoriasis Scalp Severity Index; q8w=Every 8 weeks; SSA=Scalp surface area; ss-IGA=Scalp-specific IGA.

RESULTS

- Serum IL-17F, IL-22, and BD-2 levels were significantly higher at baseline in VISIBLE participants vs healthy controls (Figure 1)
- Serum levels of IL-17F, BD-2, and IL-22 at baseline were relatively lower in Cohort B compared to Cohort A – potentially reflective of the scalp predominant nature of the cohort with lower BSA involvement (mean baseline BSA, 16.6% Cohort B and 26.8% Cohort A)

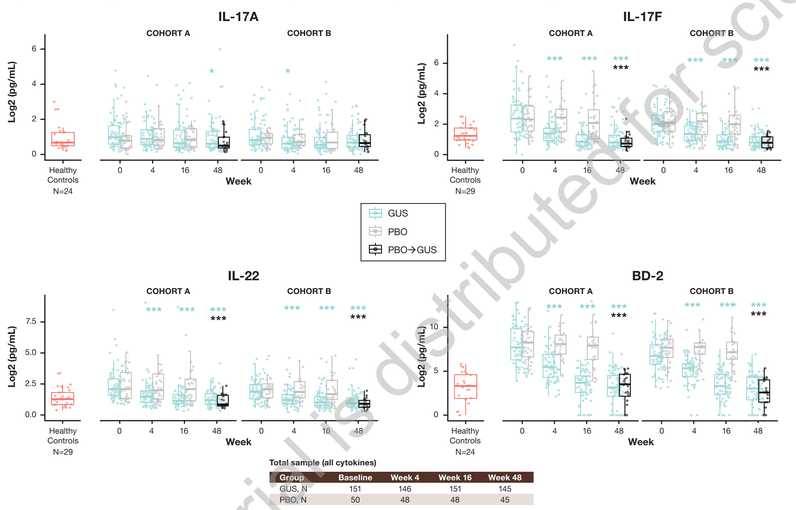
Figure 1. Targeted serum cytokine levels at baseline in all VISIBLE participants and healthy controls



*Linear model was used for pair-wise comparisons between healthy controls, Cohort A and Cohort B with * and *** denoting p<0.05 and p<0.0001, respectively; * denotes p<0.05 for Cohort A vs. Cohort B.*

Significant reductions in serum IL-17F, IL-22, and BD-2 levels were observed through Week 48 in the GUS group and after Week 16 in the PBO→GUS group (Figure 2)

Figure 2. Changes from baseline in targeted serum cytokines levels through Week 48



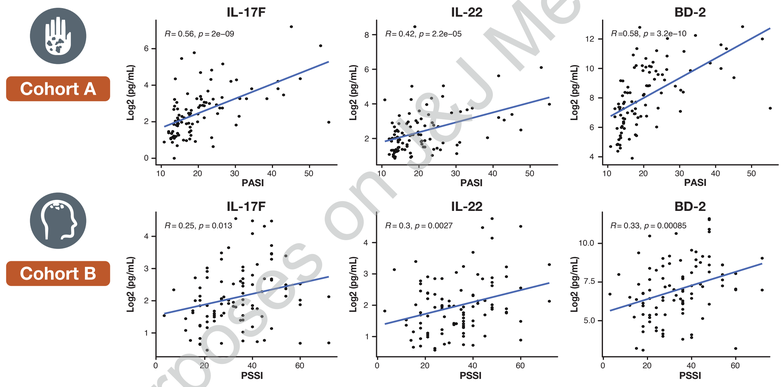
Total sample (all cytokines)

Group	Baseline	Week 4	Week 16	Week 48
GUS, N	151	146	151	145
PBO, N	50	48	48	45

*Linear mixed effect model accounts for treatment x time interaction, baseline serum protein levels, and subject random effect. *p<0.05, **p<0.01; ***p<0.001; denote significant differences from baseline in the mean cytokine value.*

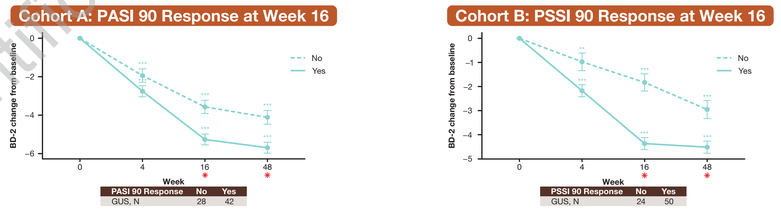
- Baseline IL-17F, IL-22, and BD-2 levels significantly correlated (p<0.05) with PASI and PSSI scores (Figure 3)
- Relatively weaker correlations were observed between IL-17F, IL-22, and BD-2 levels and PSSI in Cohort B at baseline

Figure 3. Correlations between baseline serum cytokine levels and baseline disease severity in all VISIBLE participants



At Weeks 16 and 48, greater reduction in BD-2 levels from baseline were observed in Week 16 PASI 90 and PSSI 90 responders vs non-responders in Cohort A and B participants, respectively (Figure 4)

Figure 4. Change from baseline in BD-2 levels in PASI/PSSI 90 responders vs non-responders through Week 48



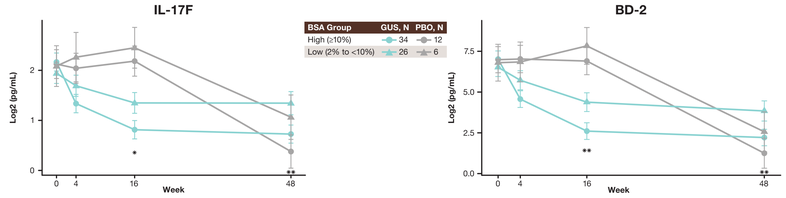
PASI 90 Response	No	Yes
GUS, N	28	42

PSSI 90 Response	No	Yes
GUS, N	24	50

*Linear mixed effect model accounts for treatment x time interaction, baseline serum protein levels, and subject random effect. Values are plotted as mean with error bars representing model-based 95% confidence interval. *p<0.05; **p<0.01; ***p<0.001; denote significance differences from baseline. * denotes significant difference between response vs. no response.*

Low PsO BSA at baseline in Cohort B was associated with significantly less reduction in IL-17F and BD-2 levels at Week 16 and Week 48 (Figure 5)

Figure 5. Serum cytokine levels by low vs high BSA through Week 48 for Cohort B



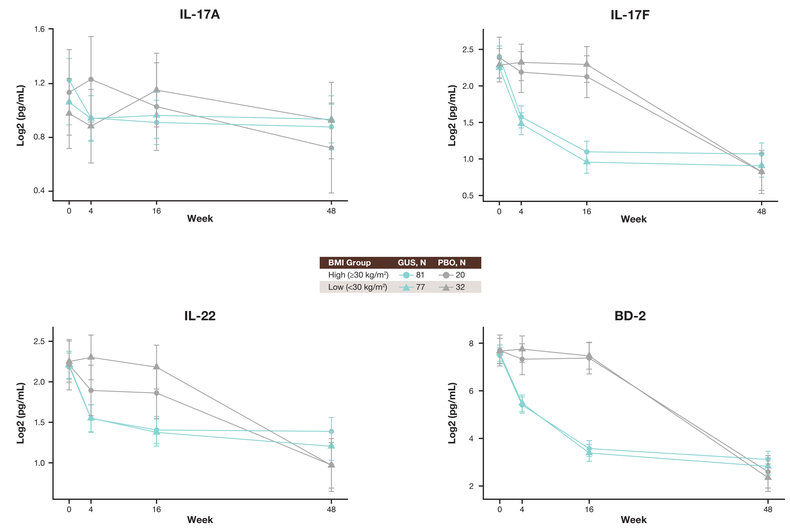
BSA Group	GUS, N	PBO, N
High (≥10%)	34	12
Low (≥% to <10%)	26	6

*Linear mixed effect model accounts for treatment x BSA x time interaction, baseline serum protein levels, and participant random effect. Cytokine values are plotted as mean with error bars representing 95% confidence interval. *p<0.05; **p<0.01; comparison GUS High vs Low BSA.*

These data, in this diverse population, suggest that for PsO involving distinct presentations, such as predominant scalp disease with low BSA, there may be differences in underlying cytokine signaling pathways

- Consistent with subgroup analyses previously reported for clinical efficacy, no significant differences in serum cytokine changes were noted in subgroups by BMI (Figure 6). GUS elicited similar pharmacodynamic effects for participants with low and high BMI with similar efficacy observed across low vs high BMI.
- Similarly, no significant differences in changes in serum cytokine levels were observed for subgroups based on sex or psoriatic arthritis status (data not shown)

Figure 6. Differential serum cytokine changes by low vs high BMI



Cytokine values are plotted as mean with error bars representing 95% confidence interval. Emmeans was used to test for statistical significance between high and low BMI and no differences were observed at any time point. BMI=Body mass index.

CONCLUSIONS

- **VISIBLE is a first-of-its-kind study intentionally designed to evaluate the safety and efficacy of GUS in moderate-to-severe PsO across diverse objectively measured skin tones**
- **VISIBLE participants treated with GUS showed early and sustained reductions in serum cytokine levels through Week 48; GUS-mediated improvement by clinical assessment of disease severity was associated with reductions in serum cytokine levels**
- **GUS treatment induced a robust cytokine pharmacodynamic response in Cohorts A and B, highlighted by significantly reduced serum levels of IL-17F, IL-22, and BD-2**
- **Additional studies may inform our understanding of similarities and differences in PsO pathogenesis or signaling pathways in patients with PsO, across all skin tones**

Reference: 1. Lowes MA, et al. *Annu Rev Immunol.* 2014;32:227-55. **Acknowledgements:** The authors thank the participants who took part in the VISIBLE study. Medical writing support was provided by Teresa Tartaglione, PharmD, an employee of Certara, LLC, under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med.* 2022;175:1298-304). This poster was supported by Johnson & Johnson, Horsham, PA, USA. **Disclosures: T. Lee, H. Moncrieffe, M. Leung, R. Panchakshari, K. Rowland,** and **T. Alkousakis** are employees and stockholders of Johnson & Johnson. **V.R. Moulton** and **O. Choi** are former Johnson & Johnson employees. **S.G. Kwatra** is an advisory board member/consultant for AbbVie, Amgen, Arcutis Biotherapeutics, Aslan Pharmaceuticals, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Dermavant, Galderma, Incyte Corporation, Johnson & Johnson, LEO Pharma, Novartis Pharmaceuticals Corporation, Pfizer, Regeneron Pharmaceuticals, and Sanofi; and has served as an investigator for Galderma, Incyte, Pfizer, and Sanofi. **G. Han** is a consultant, speaker, or received research support from AbbVie, Amgen, Athenex, Beiersdorf, Bristol Myers Squibb, Boehringer Ingelheim, Bond Avillion, Castle Biosciences, Celgene, CeraVe, Dermavant, Dermtech, Johnson & Johnson, LEO Pharma, Lilly, MC2, MedX, Novartis, Ortho Dermatologics, Pfizer, Regeneron/Sanofi, Sun Pharma, Takeda, and UCB. **J.E. Hawkes** is an advisor/consultant for AbbVie, Apogee, Arcutis, Boehringer Ingelheim, Blueprint Medicines, Bristol Myers Squibb, Boxer Capital LLC, Dermavant, Eli Lilly, Galderma, Institute for Systems Biology (ISB), Johnson & Johnson, LEO Pharma, Novartis, Oruka, Regeneron, Sanofi, Sun Pharma, Takeda, and UCB; a speaker for Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly, Galderma, Johnson & Johnson, Novartis, Regeneron, Sanofi, and UCB; and is an investigator for AbbVie, Acelyrin, Allakos, Alumis, Amgen, Apogee Therapeutics, CellDex, Concert Pharmaceuticals, Eli Lilly, Incyte, Johnson & Johnson, LEO Pharma, Novartis, Oruka, Sanofi, Sun Pharma, and Takeda. **A. Farberg** is an advisor and/or investigator for Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Galderma, Incyte, Johnson & Johnson, Novartis, Pfizer, Regeneron, Sanofi, and Sun Pharma. **B. Ungar** received research funds (grants paid to the institution) from: Bristol Myers Squibb, Incyte, Pfizer, Rapt Therapeutics, and Sanofi, and has served as a consultant for AbbVie, Arcutis Biotherapeutics, Bristol Myers Squibb, Botanix Pharmaceuticals, Castle Biosciences, Fresenius Kabi, Galderma, Johnson & Johnson, LEO Pharma, Lilly, Pfizer, Primus Pharmaceuticals, Sanofi, and UCB. **J. Talia** is a consultant for Abbvie, Arcutis Biotherapeutics, Bristol Myers Squibb, Calliditas Therapeutics, Johnson & Johnson, LEO Pharma, Primus Pharmaceuticals, Sanofi Genzyme, Stifel Financial, and UCB; and serves as an investigator for LEO Pharma and Sanofi. **J. North** is currently a consultant for Johnson & Johnson and previously was a consultant for Kiniksa Pharmaceuticals and ADVInow Medical.

Presented at Society for Investigative Dermatology (SID) Annual Meeting: May 7-10, 2025; San Diego, CA, USA.