SPECTREM: Guselkumab Lowers Disease-Related Serum Cytokines in Low BSA, Moderate Psoriasis With High-Impact Sites

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Background

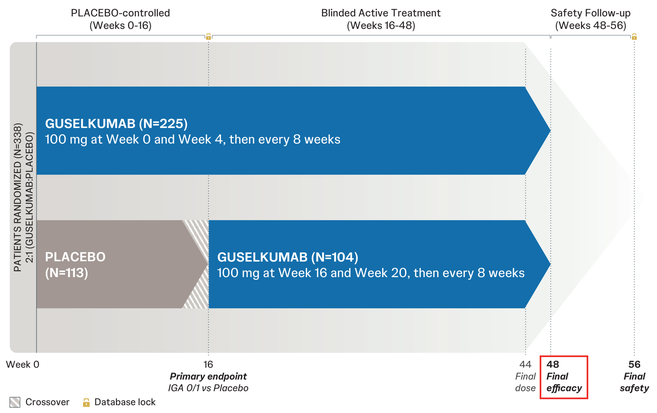
- Historically, psoriasis (PsO) severity was determined by body surface area (BSA)
  - However, 70% of "Low BSA PsO" is not adequately treated with topical agents[1]
  - Patients with PsO covering sensitive areas of the body (e.g., scalp, face, intertriginous areas, or genitals) OR who have failed topicals should be eligible for systemic therapy regardless of BSA[2]
- SPECTREM is a phase 3b, randomized, double-blind, placebo-controlled study that evaluated the efficacy and safety of guselkumab in patients with low BSA (2% to 15%), moderate (Investigator's Global Assessment [IGA]=3) plaque PsO involving ≥1 high-impact site (scalp, face, intertriginous areas, or genitals)

Objective

These analyses evaluated serum biomarkers (interleukin [IL]-17A, IL-17F, IL-22, beta defensin [BD-2]) including

1. Whether baseline levels differed between patients with PsO at different high-impact sites or patients with BSA <10% vs ≥10%, and were associated with clinical response at Weeks 16 and 48
2. Guselkumab pharmacodynamics
3. Correlations between clinical endpoints and biomarker changes

SPECTREM – Study Design



Key Inclusion Criteria

- IGA=3
- BSA=2-15% with ≥1 plaque outside of high-impact sites
- ≥1 high-impact sites (scalp, face, intertriginous areas, genitals) with at least moderate severity (site-specific IGA/PGA ≥3)
- Prior PsO treatment: inadequate topical response or intolerance; advanced oral naïve or experienced; naive to prior biologic (or biosimilars of) for treating PsO, psoriatic arthritis (PsA), or any other conditions affecting PsO assessment

Serum Biomarker Assessments

- Blood for serum biomarker analyses was collected at baseline (Week 0), Weeks 4, 16, and 48
- Analytes were measured by MSD (IL-17A and BD-2) or SMC (IL-17F and IL-22) immuno-assays
- Biomarkers were analyzed with linear mixed effect models accounting for timepoint—variable interactions, baseline biomarker levels, other significant co-variates, and patient random effects

	Baseline (Week 0)	Week 4	Week 16	Week 48
Guselkumab	n=218-224*	n=213-219*	n=210-213*	n=205-207*
Placebo	n=110-112*	n=112-113*	n=103-105*	n=93-95*
Healthy Controls	n=40			

*Sample sizes vary by analyte due to differences in available sample volume.

Correlation Assessments for Pharmacodynamics

- BMI categories: Normal [<25 kg/m^2], Overweight [25 to <30 kg/m^2], and Obese [≥30 kg/m^2]
- Disease duration subgroups: ≤2 years, >2 to ≤5, and >5 years
- Non-responders were defined as those not reaching IGA 0 or 1 at Week 16

MSD=*Meso Scale Discovery,* ***PGA***=*Physician's Global Assessment,* ***SMC***=*Single molecular counting.*

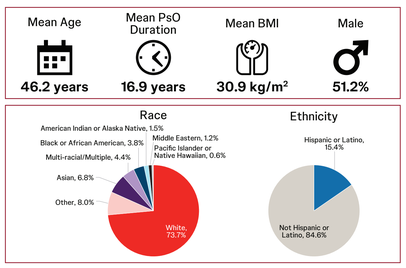
Conclusions and Next Steps

- **Guselkumab showed robust pharmacodynamics for patients with BSA <10% or ≥10% and high-impact site involvement.**
- **Serum proteomic pharmacodynamic data corroborate the clinical efficacy of guselkumab seen in previous studies.**
- **Despite higher baseline cytokine levels in high-BSA patients, guselkumab normalizes cytokine levels of both low-BSA and high-BSA patients to healthy-control ranges by Week 48.**
- **Systemic proteomic changes were similar in patients with PsO affecting different high-impact sites.**
- **Tissue transcriptomic and epigenetic data are being analyzed to further investigate differences at specific sites and will be presented at a future time.**

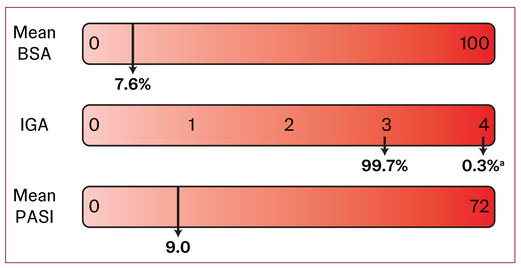
Results

SPECTREM patient population and baseline demographics

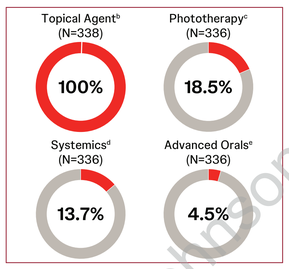
Baseline Demographics (N=338)



Disease Characteristics (N=338)



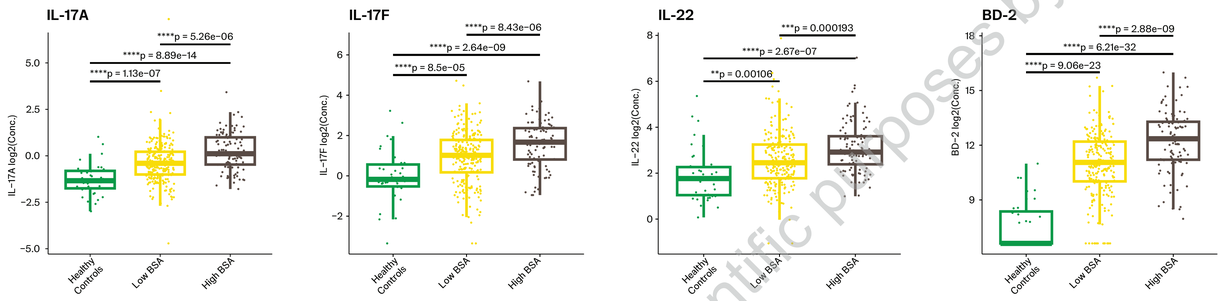
Previous PsO Medications/Therapies



PASI=*Psoriasis Area and Severity Index;* ***PUVA***=*Psoralen plus ultraviolet A;* ***UVB***=*Ultraviolet B.*

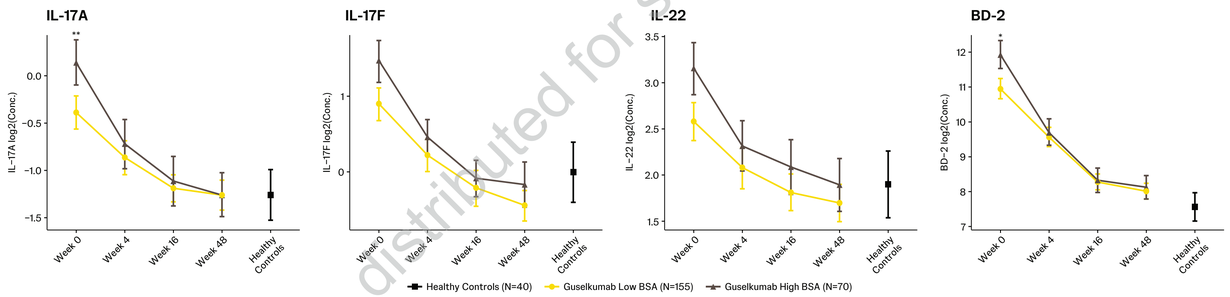
[a]*Inclusion Criterion deviation;* [b]*Topical, anthralin, keratolytics, tar;* [c]*PUVA, UVB;* [d]*PUVA, methotrexate, cyclosporine, acitretin;* [e]*Apremilast, deucravacitinib.*

Patients with BSA <10% had lower baseline cytokine levels vs those with BSA ≥10%



Low BSA = <10%, High BSA = ≥10%

Guselkumab reduced systemic cytokines levels to those of healthy controls regardless of baseline BSA group

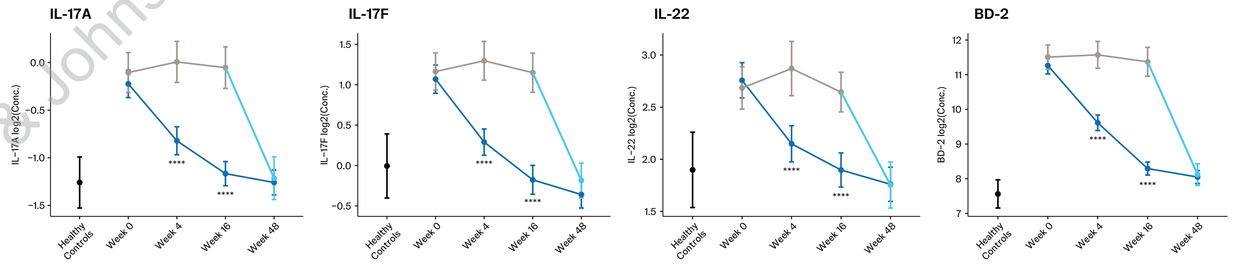


**p<0.05 **p<0.01 for comparisons between low and high BSA groups at each time point, color denotes which treatment; High BSA is >10% and low BSA is <10%; Linear mixed effect model accounts for Timepoint*baseline BSA group, baseline serum protein levels, any other signifcant co-variates, and patient random effect.*

No correlation in baseline serum cytokine levels and responder status, high-impact sites, or co-morbidities was observed (graphical data not shown)

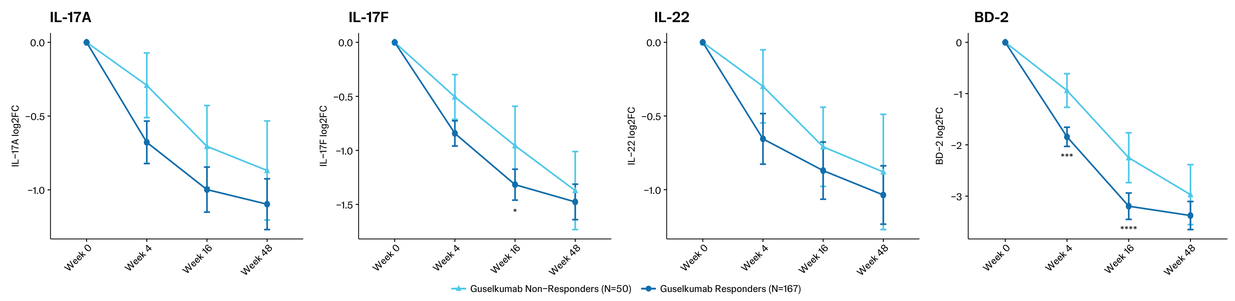
- No significant differences in baseline cytokine levels were seen between responders and non-responders for guselkumab-treated patients at Week 16
- No differences in baseline serum cytokine levels were seen between patients with PsO affecting different high-impact sites
- Baseline biomarker levels were not indicative of baseline BMI group or disease duration

Guselkumab reduced levels of evaluated serum cytokines to those seen in healthy controls, independent of BSA or affected high-impact site group



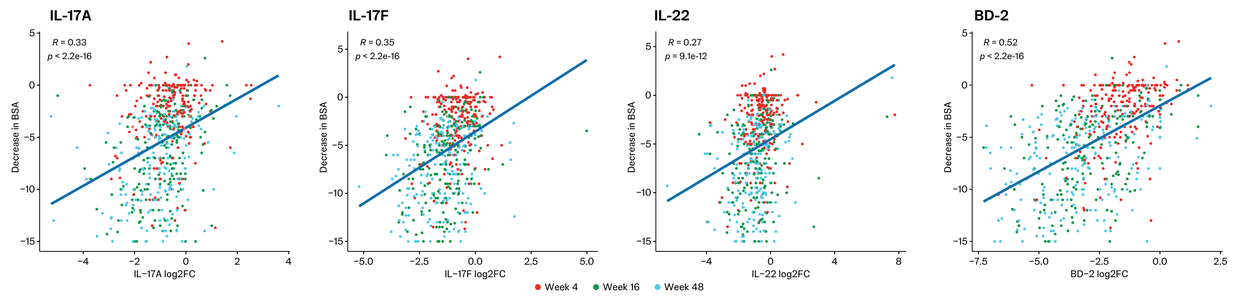
*Mean ± Confidence Intervals ****p<0.0001 for comparison between guselkumab- and placebo-treated patients at each time point; Linear mixed effect model accounts for Timepoint*Responder status, baseline serum protein levels, any other significant co-variates, and patient random effect.*

Guselkumab responders showed greater average reductions in serum BD-2 and IL-17F levels vs non-responders by Week 16



**p<0.05, ***p<0.001 for comparison between guselkumab-treated IGA responders and non-responders; Linear mixed effect model accounts for Timepoint*Responder status, baseline serum protein levels, any other significant co-variates, and patient random effect.*

Decreases in serum cytokines significantly correlated with decreases in patient BSA levels



- Decreases in serum cytokines also significantly correlated with decreases in PASI (graphical data not shown) (IL-17A [*R = 0.35; p<2.2e-16*], IL-17F [*R = 0.32; p <2.2e-16*], IL-22 [*R =0.29; p<1.2e-13*], BD-2 [*R = 0.5; p<2.2e-16*])

No correlation in serum cytokine levels and high-impact sites, PsA status, or co-morbidities was observed (graphical data not shown)

- Reduction of serum cytokine levels did not differ among guselkumab-treated patients with PsO affecting different high-impact sites or when stratified by PsA status
- No difference in pharmacodynamic response was observed across baseline BMI or disease duration subgroups

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