Biomarker-Driven Insights From the Phase 2a AFFINITY Study Evaluating Guselkumab + Golimumab Combination Therapy Versus Guselkumab Monotherapy in Psoriatic Arthritis

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Background

Psoriatic arthritis (PsA) is a complex, multi-pathway inflammatory disease in which combination therapies may enhance efficacy by modulating complementary immune mechanisms[1,2]

Guselkumab (GUS) for Active PsA[3]
- Fully human, dual-acting monoclonal antibody that selectively inhibits interleukin (IL)-23 by targeting its p19 subunit and binding CD64 on IL-23-producing inflammatory monocytes[4]

Golimumab (GOL) for Active PsA[5]
- Fully human monoclonal antibody targeting tumor necrosis factor alpha (TNFα)

AFFINITY (NCT05071664)
- Phase 2a, randomized, double-blind, active-controlled, proof-of-concept study that evaluated GUS+GOL combination vs GUS monotherapy in adults with active PsA and inadequate TNFα inhibitor response (TNFi-IR)
- Primary analyses suggested that GUS+GOL combination may offer clinically meaningful benefits in joint disease activity and physical function, particularly among participants with elevated C-reactive protein (CRP), with no new safety signals; no additional benefits were observed in psoriasis/enthesitis/dactylitis[6]

Objective

Assess pharmacodynamic (PD) effects and relationships with clinical responses among TNFi-IR participants with PsA treated with GUS+GOL combination therapy or GUS monotherapy in AFFINITY

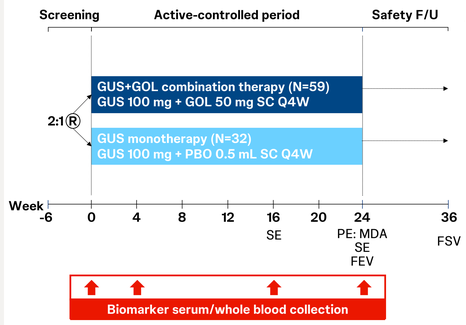
Methods

AFFINITY Study Design

Key Inclusion Criteria
- Adults ≥18 to ≤65 years
- TNFi-IR[a]
- PsA diagnosis for ≥6 months; CASPAR requirement met; ≥1 PsA subset class[b]
- Active PsA (≥3 TJC and ≥3 SJC)
- Active plaque PsO (≥1 plaque ≥2 cm in diameter or psoriatic nail changes)

Protocol Amendment

Changes to inclusion criteria to mitigate significant impact of Ukraine/Russia crisis on study recruitment:
- Removed screening high sensitivity CRP ≥0.3 mg/dL criterion
- Expanded IR to prior TNFi from 1 to 2



Assessments & Analyses

Assessments	Analyses

PD effects and disease markers through W24
• Single Molecule Counting immunoassays:
  • IL-17A, IL-17F (serum Th17 cytokines)
• Whole blood RNA sequencing[7]:
  • TNF activity score
• Meso-Scale Discovery immunoassays:
  • CRP, IL-6 (general inflammation markers)
  • BD-2 (PsO activity marker)
	Wilcoxon rank-sum exact test for changes from baseline in:
	• TNF activity (mean GSVA enrichment score):
	  • Within regimens
	  • For GUS+GOL vs GUS monotherapy
	• Other biomarkers levels (mean $\log_2$):
	  • Within regimens
	  • For GUS+GOL vs GUS monotherapy

Clinical response–biomarker relationships; statistically significant findings presented for: • MDA and ACR50 at W24 (clinical endpoints) • IL-17A, IL-17F, CRP, IL-6, BD-2 (serum biomarkers)	**Wilcoxon rank-sum exact test** for associations of clinical response with biomarker level: • At baseline ($\log_2$; within regimens) • Change from baseline (mean $\log_2$; within regimens)

*[a]IR defined as lack of benefit in response to TNFis after ≥12 weeks of etanercept, adalimumab, certolizumab pegol (or their biosimilars), or ≥14 weeks of infliximab/biosimilars, with last TNFi dose administered >5 half-lives prior to starting study treatment. [b]Subset classification including distal interphalangeal joint involvement, polyarticular arthritis without rheumatoid nodules, asymmetric peripheral arthritis, or spondylitis with peripheral arthritis. **ACR50** =≥50% improvement in American College of Rheumatology response criteria; **BD-2**=Beta-Defensin-2 **CASPAR**=CASsification criteria for Psoriatic ARthritis, **FEV**=final efficacy visit, **FSV**=final safety visit, **F/U**=follow-up, **GSVA**=gene set variation analysis, **MDA**=minimal disease activity, **PBO**=placebo, **PE**=primary endpoint, **PsO**=psoriasis, **Q4W**=every 4 weeks, **R**=randomization, **RNA**=ribonucleic acid, **SC**=subcutaneous, **SE**=secondary endpoint, **SJC**=swollen joint count, **Th17**=T helper 17 cells, **TJC**=tender joint count, **W**=week.*

Key Takeaways

- **In the proof-of-concept, phase 2a AFFINITY study of TNFi-IR participants with active PsA:**
  - ✓ **Consistent with primary clinical findings suggesting benefit in joint disease activity and physical function, particularly in participants with elevated CRP,[6] GUS+GOL combination therapy showed:**
    - ✓ **Significant reductions in serum CRP and IL-6 levels, and TNF activity scores, through W24**
    - ✓ **W24 MDA and ACR50 responders had higher baseline levels and greater reductions in IL-6 and CRP**
  - ✓ **GUS+GOL combination and GUS monotherapy elicited similar reductions in Th17 cytokines and BD-2, consistent with comparable improvements in psoriasis/enthesitis/dactylitis with the addition of TNFi[6]**
- **Participants with TNFi-IR PsA and elevated inflammatory biomarkers may derive additional joint-related benefits with GUS+GOL combination therapy**

Results

Baseline characteristics were generally well balanced across treatment groups

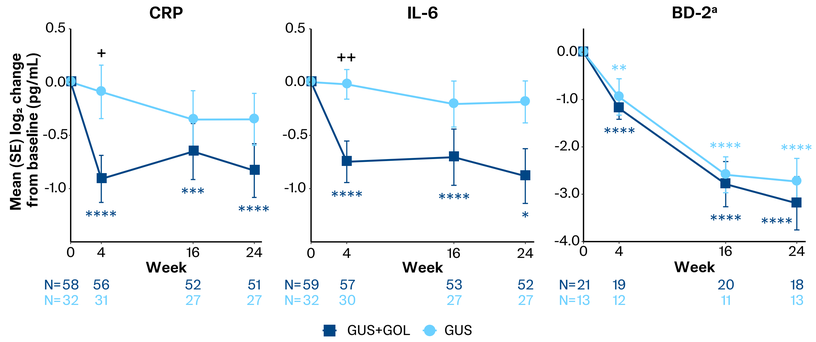
- Approximately 1/3 of participants had baseline CRP <0.3 mg/dL

Baseline Characteristics	GUS+GOL combination (N=59)	GUS monotherapy (N=32)
Demographics		
Age, years	50.2 (10.5)	47.7 (10.3)
Female	61%	62%
Race, White / Not reported or unknown	97% / 3%	100% / 0%
BMI, kg/m^2	31.4 (6.8)	30.5 (6.4)[a]
Clinical Characteristics		
PsA duration, years	8.2 (7.0)	7.2 (7.0)
SJC (0-66), median (range)	7.0 (3; 50)	8.0 (3; 37)
TJC (0-68), median (range)	13.0 (3; 63)	12.0 (3; 66)
Enthesitis per LEI	59%	66%
LEI (1-6)[b]	2.8 (1.7)	2.4 (1.4)
Dactylitis per DSS	22%	25%
DSS (1-60)[c]	9.3 (12.5)	9.6 (14.3)
Screening CRP (Week -6)		
< / ≥0.3 mg/dL	32% / 68%	31% / 69%
Baseline CRP (Week 0)		
< / ≥0.3 mg/dL	29% / 71%	34% / 66%
CRP, mg/dL	0.8 (1.3)	1.4 (3.3)
PsO duration, years	13.4 (11.2)	10.0 (8.7)
≥3% psoriatic BSA and IGA ≥2	37%	41%
PASI[d] (0-72), median (range)	5.1 (0.8; 29.4)[e]	4.0 (0.5; 48.2)[f]

*Data are mean (SD) unless noted otherwise. [a]N=31. [b]Among participants with available assessment and LEI >0. [c]Among participants with available assessment and DSS >0. [d]Among participants with ≥3% psoriatic BSA and IGA ≥2 at baseline. [e]N=22. [f]N=13. **BSA**=body surface area, **BMI**=body mass index, **DSS**=Dactylitis Severity Score, **IGA**=Investigator's Global Assessment, **LEI**=Leeds Enthesitis Index, **PASI**=Psoriasis Area and Severity Index.*

GUS+GOL combination significantly reduced serum CRP and IL-6 levels from baseline as early as W4, with sustained reductions through W24

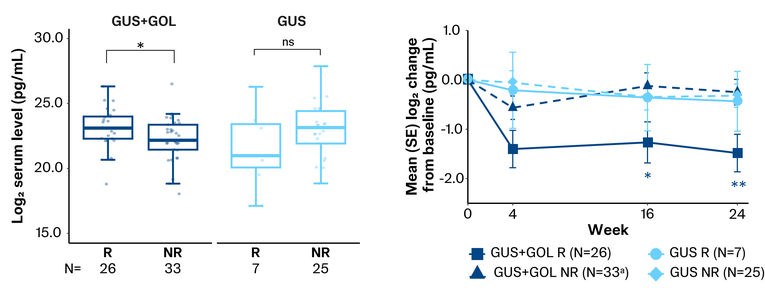
- Among participants with at least mild PsO, both treatment regimens elicited similar reductions in BD-2 levels from baseline through W24



**p≤0.05, **p≤0.01, ***p≤0.001, ****p≤0.0001 vs baseline within regimen. +p≤0.05, ++p≤0.01 for GUS+GOL combination vs GUS monotherapy. [a]Among participants with ≥3% BSA PsO involvement and an IGA score ≥2 at baseline.*

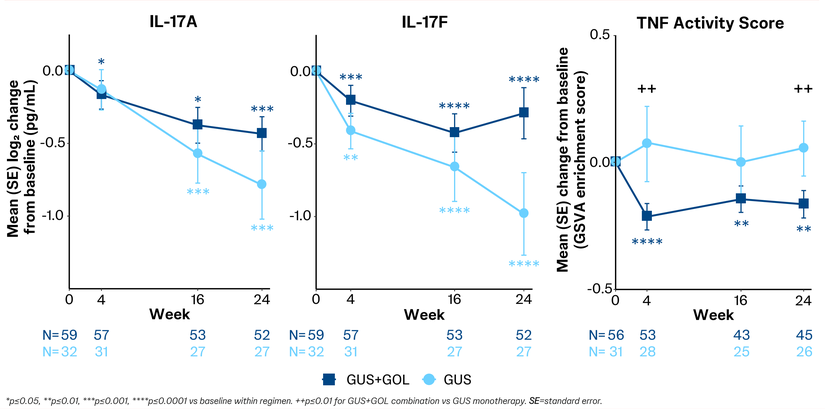
In the GUS+GOL combination group, W24 ACR50 responders had higher baseline levels and greater reductions in serum CRP through W24 vs nonresponders

- In the GUS monotherapy group, no differences in baseline CRP levels or in CRP reductions from baseline through W24 were observed between W24 ACR50 responders vs nonresponders



**p≤0.05, **p≤0.01 for ACR50 R vs NR within regimen. [a]N=32 for W24 GUS+GOL NR.*

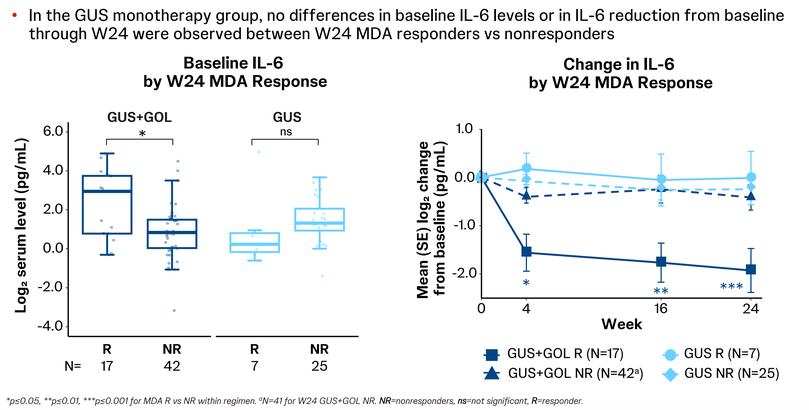
Both regimens significantly reduced serum IL-17A/F levels through W24; only GUS+GOL combination significantly reduced TNF activity score



p≤0.05, **p≤0.01, ***p≤0.001, ****p≤0.0001 vs baseline within regimen. ++p≤0.01 for GUS+GOL combination vs GUS monotherapy. **SE=standard error.*

In the GUS+GOL combination group, W24 MDA responders had higher baseline levels and greater reductions in serum IL-6 through W24 vs nonresponders

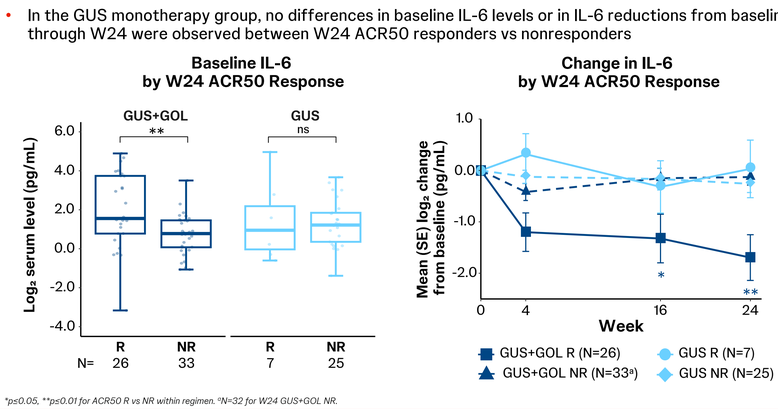
- In the GUS monotherapy group, no differences in baseline IL-6 levels or in IL-6 reduction from baseline through W24 were observed between W24 MDA responders vs nonresponders



p≤0.05, **p≤0.01, ***p≤0.001 for MDA R vs NR within regimen. [a]N=41 for W24 GUS+GOL NR. **NR=nonresponders, **ns**=not significant, **R**=responder.*

In the GUS+GOL combination group, W24 ACR50 responders had higher baseline levels and greater reductions in serum IL-6 through W24 vs nonresponders

- In the GUS monotherapy group, no differences in baseline IL-6 levels or in IL-6 reductions from baseline through W24 were observed between W24 ACR50 responders vs nonresponders



**p≤0.05, **p≤0.01 for ACR50 R vs NR within regimen. [a]N=32 for W24 GUS+GOL NR.*

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