Longitudinal Evaluation of Neutrophil-to-Lymphocyte Ratio in Guselkumab-Treated Patients With Psoriatic Disease and Levels of Systemic Inflammation Associated With Elevated Cardiovascular Risk: Post Hoc Analysis

Joseph F. Merola[1], Alexis Ogdie[2], Arthur Kavanaugh[3], Evan Leibowitz[4], Emmanouil Rampakakis[5,6], Alejandro Lizano Corzo[4], Francois Nantel[7], Frederic Lavie[8], Katelyn Rowland[4], Enrique R. Soriano[9]

[1]UT Southwestern Medical Center, Department of Dermatology, Department of Medicine, Division of Rheumatology, Dallas, TX, USA; [2]University of Pennsylvania School of Medicine, Division of Rheumatology, Philadelphia, PA, USA; [3]Center for Innovative Therapy, Division of Rheumatology, Allergy, and Immunology, University of California San Diego, San Diego, CA, USA; [4]Immunology, Johnson & Johnson, Horsham, PA, USA; [5]Department of Pediatrics, McGill University, Montreal, QC, Canada; [6]JSS Medical Research, Inc, Montreal, QC, Canada; [7]Nantel Medsci Consult, Montreal, QC, Canada; [8]Johnson & Johnson, Issy les Moulineaux, France; [9]Rheumatology Section, Internal Medicine Service, Hospital Italiano de Buenos Aires and University Institute Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

Background

- Psoriatic arthritis (PsA) and psoriasis (PsO) are associated with an increased risk of cardiovascular (CV) disease, likely due to co-occurrence of traditional CV risk factors (eg, elevated systolic/diastolic blood pressure [SBP/DBP] and body mass index [BMI]), and accelerated atherosclerosis owing to chronic inflammation[1]
- Neutrophil-to-lymphocyte ratio (NLR) is a biomarker of systemic inflammation
  - Elevated (≥2.5 to <3.5) or high (≥3.5) NLR have shown an independent association with CV risk vs NLR <2.5[2,3]
- Guselkumab (GUS), a fully human IL-23p19-subunit inhibitor, demonstrated significant multi-domain efficacy in patients (pts) with active PsA (DISCOVER-1[4]&2[5]) and moderate-to-severe plaque PsO (VOYAGE-1[6]&2[7]), with a favorable safety profile and low rates of major adverse CV events through up to 2 years (Y) and 5Y of the PsA and PsO trials, respectively[8]

Objective

In these analyses from DISCOVER-1&2 and VOYAGE-1&2, the effects of GUS were assessed in pts with psoriatic disease (PsD) and NLR levels associated with increased CV risk

Methods

Adults with active PsA		Adults with moderate-to-severe plaque PsO	
DISCOVER-1[4] (N=381)	DISCOVER-2[5] (N=739)	VOYAGE-1[6] (N=837[b])	VOYAGE-2[7] (N=992[b])
Randomized 1:1:1 GUS 100 mg at W0, W4 & Q4W (N=373)[a] GUS 100 mg at W0, W4 & Q8W (N=375) PBO Q4W W0-20; GUS 100 mg at W24 then Q4W (N=372)		**Randomized 2:1[b]** GUS 100 mg at W0, W4 & Q8W (N=825) PBO at W0, W4, W12; GUS 100 mg at W16, W20 & Q8W (N=422)	
Inclusion criteria History of, or current, PsO ≥3 SJC and ≥3 TJC CRP ≥0.3 mg/dL	≥5 SJC and ≥5 TJC CRP ≥0.6 mg/dL	Inclusion criteria IGA score ≥3, PASI score ≥12, BSA ≥10% Candidate for systemic therapy or phototherapy for PsO	
~90% biologic-naïve		~80% biologic-naïve	

[a]Pts randomized to GUS Q4W were excluded from these analyses so as to not skew results, as they comprised exclusively PsA pts. [b]VOYAGE-1&2 also included an active comparator treatment arm; 582 pts were randomized to adalimumab 80 mg at W0, 40 mg at W1, then 40 mg Q2W through W48, after which pts crossed over to GUS. These pts were not included in this analysis. VOYAGE-2 also included a randomized withdrawal period from W28 to W76, after which pts received one dose of GUS to align with the dosing schedule. BSA=Body surface area; CRP=C-reactive protein; GUS=Guselkumab; IGA=Investigator's Global Assessment; PASI=Psoriasis Area and Severity Index; PBO=Placebo; PsA=Psoriatic arthritis; PsO=Psoriasis; Pts=Patients; Q4W=Every 4 weeks; Q8W=Every 8 weeks; SJC=Swollen joint count; TJC=Tender joint count; W=Week.

DISCOVER-1&2/VOYAGE-1&2 cohorts:

- Every 8 weeks (Q8W)- and placebo (PBO)-randomized pts
- Pts with baseline (BL) NLR ≥2.5[2] (N=1,061)
- Cohorts evaluated
  - Total (N=1,061; all pts evaluated through 1Y, the timepoint common to all studies)
  - Biologic-Naïve (N=877; biologic-naïve pts through up to 2Y)

Post hoc analyses among pts with elevated (NLR 2.5 to <3.5) and high (≥3.5) CV risk at BL:

- Least squares mean (LSM) changes in NLR from BL (week [W]0) through W48 (Total Cohort) or W100 (Biologic-Naïve Cohort)
  - GUS vs PBO through W16 (PBO-controlled period common to all trials)
  - Mixed models for repeated measures (MMRM), adjusted for potential confounders listed in the data display footnotes below
- Proportions of pts attaining NLR <2.5 (associated with no increased CV risk) through W48 (Total Cohort) or W100 (Biologic-Naïve Cohort)
  - GUS vs PBO through W16
  - Logistic regression, adjusted for the potential confounders
  - Nonresponder imputation used for missing data through W16; observed data summarized post-W16
- Observed mean values from BL through W100 in traditional CV risk factors (SBP, DBP, BMI)

Key Takeaways

- **In DISCOVER-1&2 and VOYAGE-1&2 PsD pts with elevated or high CV risk:**
  - **GUS led to significantly greater reductions in NLR than PBO as early as W4 that continued through W16 and were sustained through up to 2Y**
  - **Significantly greater proportions of these GUS- vs PBO-treated pts met criteria associated with no increased CV risk (defined by NLR <2.5) by W4/W8**
    - **Substantial proportions of biologic-naïve GUS-treated pts achieved NLR <2.5 through up to 2Y (40%-49%)**
  - **Traditional CV risk factors remained stable with up to 2Y of GUS**
- **Results support previous findings that GUS ameliorated systemic inflammation associated with elevated CV risk through 2Y in biologic-naïve pts with PsA[9]**

Results

53% of 1,992 randomized pts had BL NLR ≥2.5; of these 57% and 43% had elevated and high CV risk, respectively, based on NLR level

- As 83% pts with elevated/high CV risk were biologic-naïve; BL characteristics were generally similar between the Total and Biologic-Naïve cohorts
- A higher proportion of pts were randomized to GUS Q8W:PBO in PsO (2:1) vs PsA (1:1) trials
  - GUS-randomized pts were thus more likely to be male; have PsO, and had higher Psoriasis Area and Severity Index (PASI) scores[b]; and were less likely to have concomitant medication use at BL

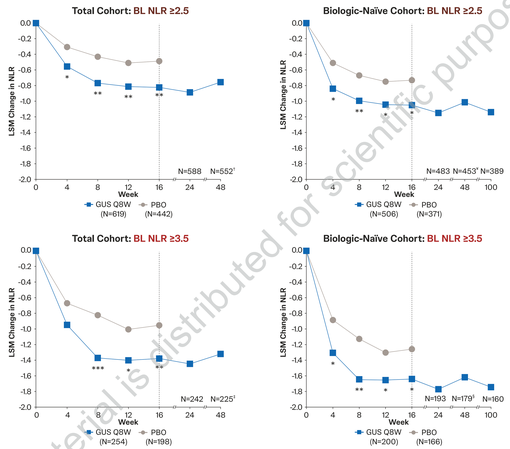
BL Characteristics of Pts With BL NLR >2.5	Total		Biologic-Naïve	
	GUS Q8W (N=619)	PBO (N=442)	GUS Q8W (N=506)	PBO (N=371)
Demographics				
Age, years	44.7 (12.3)	45.3 (12.8)	44.0 (12.4)	44.5 (12.6)
Male sex, %	68	60	67	59
PsD characteristics				
Pts from DISCOVER-1&2, %	35	51	38	54
Pts from VOYAGE-1&2, %	65	49	62	46
Self-reported PsA[a], %	20	19	18	15
PsD duration, years	13.6 (11.9)	12.3 (11.5)	12.3 (11.2)	10.7 (10.4)
PASI score [0-72]	18.5 (12.5)	15.7 (11.6)	18.0 (12.4)	15.2 (11.4)
IGA [0-4]	2.9 (0.8)	2.8 (0.9)	2.9 (0.8)	2.7 (0.9)
CV risk factors				
NLR	3.7 (1.4)	3.9 (1.7)	3.7 (1.5)	3.9 (1.8)
≥3.5 (high), %	41	45	40	45
BMI, kg/m²	29.1 (6.3)	29.1 (6.5)	28.7 (6.1)	29.0 (6.6)
SBP, mmHg	128.7 (13.4)	128.2 (12.3)	128.6 (13.7)	127.9 (11.8)
DBP, mmHg	79.8 (8.8)	80.3 (8.3)	79.8 (8.8)	80.3 (8.1)
Concomitant medication use at BL, %				
csDMARD	23	36	25	37
Corticosteroid	7	12	7	12
NSAID	27	37	28	38

Data are mean (SD) unless noted otherwise. [a]Two pts randomized to GUS Q8W in the VOYAGE-2 trial did not receive study treatment and were not included in the total count. [b]Potentially due to VOYAGE-1/VOYAGE-2 inclusion criteria (ie, IGA score ≥3, PASI score ≥12, and body surface area involvement ≥10% at BL). [c]Proportions based on the number of pts enrolled in VOYAGE-1/VOYAGE-2. BL=Baseline; BMI=Body mass index; csDMARD=Conventional synthetic disease-modifying antirheumatic drug; DBP=Diastolic blood pressure; GUS=Guselkumab; IGA=Investigator's Global Assessment; NLR=Neutrophil-to-lymphocyte ratio; NSAID=Nonsteroidal anti-inflammatory drug; PASI=Psoriasis Area and Severity Index; PBO=Placebo; PsA=Psoriatic arthritis; PsD=Psoriatic disease; Pts=Patients; SBP=Systolic blood pressure; SD=Standard deviation; Q8W=Every 8 weeks.

Reductions in NLR were significantly greater with GUS vs PBO as early as W4 and through W16, regardless of BL NLR-defined CV risk category or prior biologic experience

- Reductions in NLR were sustained through 1Y (Total) and 2Y (Biologic-Naïve) of GUS treatment

Change in NLR From BL Over Time[a]

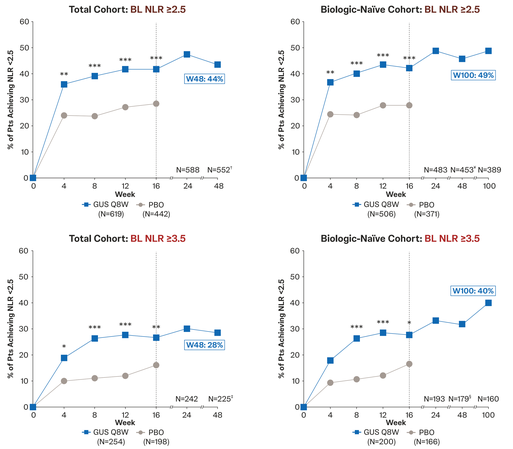


*[a]Using MMRM adjusting for PsD type (PsO vs PsA); sex; prior biologic use; and NLR, presence of MetS, and medication use (csDMARDs, corticosteroids, NSAIDs) at BL. *p<0.05, **p<0.01, ***p<0.001 for GUS Q8W vs PBO. Included 34 (1), 29 (1), 156 (1), and 123 (4) PsO pts from VOYAGE-2 in randomized withdrawal from W28 to W76. BL=Baseline; csDMARD=Conventional synthetic disease-modifying antirheumatic drug; GUS=Guselkumab; LSM=Least squares mean; MetS=Metabolic syndrome; MMRM=Mixed models for repeated measures; NLR=Neutrophil-to-lymphocyte ratio; NSAID=Non-steroidal anti-inflammatory drug; PBO=Placebo; PsA=Psoriatic arthritis; PsD=Psoriatic disease; PsO=Psoriasis; Pts=Patients; Q8W=Every 8 weeks; W=Week.*

Significantly greater proportions of GUS- vs PBO-randomized pts achieved NLR <2.5 by W4/W8, continuing through W16, regardless of prior biologic experience

- In biologic-naïve pts with elevated (NLR ≥2.5)/high (NLR ≥3.5) CV risk at BL, rates of achieving NLR <2.5 increased from W16 (42%/28%) to W100 (49%/40%), respectively, of GUS treatment

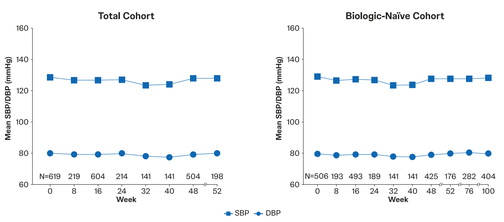
Achievement of NLR <2.5 Over Time



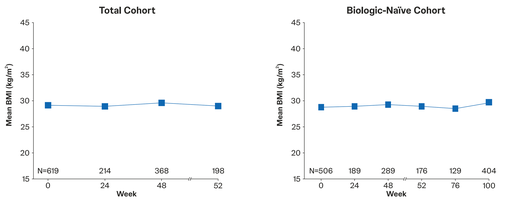
*Nonresponder imputation was used for missing data through W16; observed data are summarized post-W16. P-values based on logistic regression adjusting for PsD type (PsO vs PsA); sex; prior biologic use; and NLR, presence of MetS, and medication use (csDMARDs, corticosteroids, NSAIDs) at BL. *p=0.05, **p<0.01, ***p<0.001 for GUS Q8W vs PBO. Included 34 (1), 29 (1), 156 (1), and 123 (4) PsO pts from VOYAGE-2 in randomized withdrawal from W28 to W76. BL=Baseline; csDMARD=Conventional synthetic disease-modifying antirheumatic drug; GUS=Guselkumab; MetS=Metabolic syndrome; NLR=Neutrophil-to-lymphocyte ratio; NSAID=Non-steroidal anti-inflammatory drug; PBO=Placebo; PsA=Psoriatic arthritis; PsD=Psoriatic disease; PsO=Psoriasis; Pts=Patients; Q8W=Every 8 weeks; W=Week.*

GUS Q8W-treated pts with elevated/high CV risk exhibited stable mean SBP, DBP, and BMI

Mean SBP/DBP Over Time



Mean BMI Over Time



Using observed data. BMI=Body mass index; DBP=Diastolic blood pressure; SBP=Systolic blood pressure.

PRESENTED AT: Congress of Clinical Rheumatology - East (CCR-East); Destin, FL, USA; May 1–4, 2025. **REFERENCES: 1.** Zheng Z. *Front Cardiovasc Med.* 2022;9:doi:10.3389/fcvm.2022.835439. **2.** Adamstein NH. *Eur Heart J.* 2021;42(9):896-903. **3.** Bhat T. *Expert Rev Cardiovasc Ther.* 2013;11:55. **4.** Deodhar A. *Lancet.* 2020;395:1115. **5.** Mease PJ. *Lancet.* 2020;395:1126. **6.** Blauvelt A. *J Am Acad Dermatol.* 2017;76:405-17. **7.** Reich K. *J Am Acad Dermatol.* 2017;76:418-31. **8.** Strober B. *Drug Saf.* 2023;doi:10.1007/s40264-023-01361-w. **9.** Kavanaugh A. P223B. *Arthritis Rheumatol.* 2023;75(suppl 9). **ACKNOWLEDGEMENTS:** Medical writing support was provided by Alexandra Guffey, MSc of Johnson & Johnson under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med* 2022;doi:10.7326/M22-1460). This presentation was supported by Johnson & Johnson. **DISCLOSURES: JFM:** Consultant of AbbVie, Amgen, Astra-Zeneca, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly, Incyte, Janssen, Leo, Moonlake, Novartis, Pfizer, Sanofi-Regeneron, Sun Pharma, and UCB. **AO:** Consultant of AbbVie, Amgen, Bristol Myers Squibb, Celgene, CorEvitas, Eli Lilly, Gilead, Happify Health, Janssen, Novartis, Pfizer, and UCB; grant/research support to the University of Pennsylvania from AbbVie, Janssen, Novartis, and Pfizer, and to Forward from Amgen and Bristol Myers Squibb. Her husband has received royalties from Novartis. **AK:** Consultant of AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Janssen, Merck, Novartis, Pfizer, and UCB. **EL, FL, KR** and **ALC:** Employees of Johnson & Johnson; may own stock or stock options in Johnson & Johnson. **ER:** Employee of JSS Medical Research; consultant of Johnson & Johnson. **FN:** Consultant of Johnson & Johnson; shareholder of Johnson & Johnson. **ERS:** Consultant of AbbVie, Janssen, Novartis, and Roche; grant/research support from AbbVie, Janssen, Novartis, Pfizer, Roche, and UCB; speakers fees from AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB. Previously presented at EULAR 2024; Vienna, Austria; June 12-15, 2024 and CCR-West 2024; San Diego, CA, USA; September 26-28, 2024.