Neutrophil-to-Lymphocyte Ratio in Guselkumab-Treated Patients With Psoriatic Disease and Systemic Inflammation Associated With CV Risk

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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

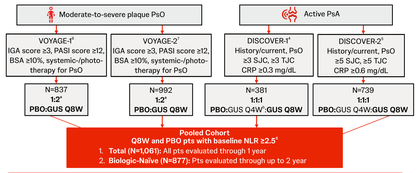
- Elevated (≥2.5 to <3.5) or high (≥3.5) NLR have shown an independent association with CV risk vs NLR <2.5[2,3]

Guselkumab (GUS), a fully human interleukin (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



*VOYAGE-1&2 also included an active comparator treatment arm; 592 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. †Pts randomized to GUS Q4W were excluded from these analyses so as to not skew results, as they comprised exclusively PsA pts. BMI=Body mass index; BSA=Body surface area; CRP=C-reactive protein; DBP=Diastolic blood pressure; GUS=Guselkumab; IGA=Investigator's Global Assessment; NLR=Neutrophil-to-lymphocyte ratio; PASI=Psoriasis Area and Severity Index; PBO=Placebo; PsA=Psoriatic arthritis; PsO=Psoriasis; Pts=Patients; Q4W=Every 4 weeks; Q8W=Every 8 weeks; SBP=Systolic blood pressure; 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 (W0) 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 (NRI) 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

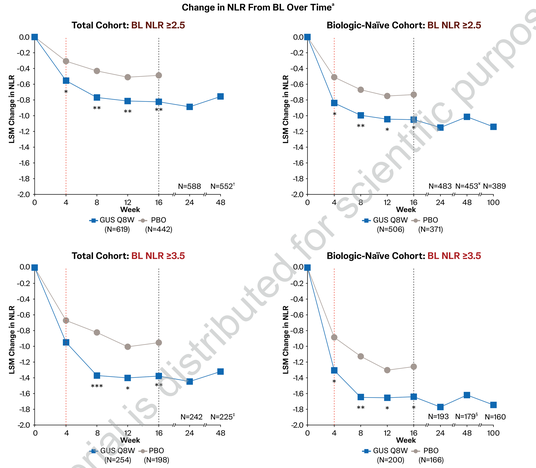
- As 83% pts with elevated/high CV risk were biologic-naïve; BL characteristics were generally similar between the Total and Biologic-Naïve cohorts
- A higher proportion of pts were randomized to GUS Q8W:PBO in PsO (2:1) vs PsA (1:1) trials
  - GUS-randomized pts were thus more likely to be male; have PsO, and had higher 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[c], %	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. aTwo pts randomized to GUS Q8W in the VOYAGE-2 trial did not receive study treatment and were not included in the total count. bPotentially due to VOYAGE-1/VOYAGE-2 inclusion criteria (ie, IGA score ≥3, PASI score ≥12, and body surface area involvement ≥10% at BL). cProportions 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

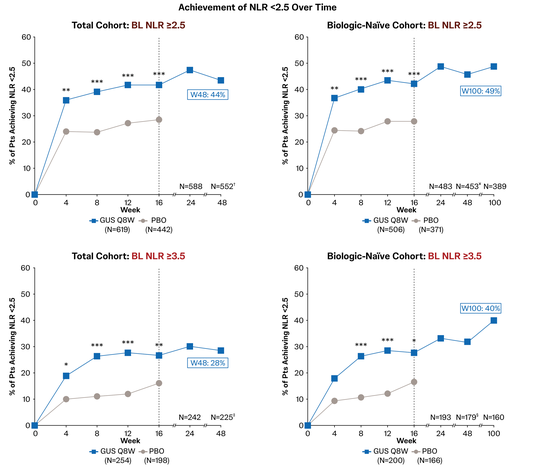
- Reductions in NLR were sustained through 1Y (Total) and 2Y (Biologic-Naïve) of GUS treatment



*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 (Ⓐ), 29 (Ⓑ), 156 (†), and 123 (¥) PsO pts from VOYAGE-2 in randomized withdrawal from W28 to W76. BL=Baseline; GUS=Guselkumab; LSM=Least squares mean; NLR=Neutrophil-to-lymphocyte ratio; PBO=Placebo; Pts=Patients; Q8W=Every 8 weeks.*

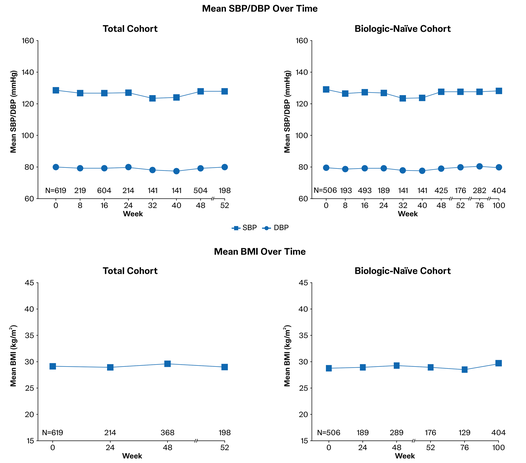
Significantly greater proportions of GUS- vs PBO-randomized pts achieved NLR <2.5 by W4/W8, continuing through W16, regardless of prior biologic experience

- 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



*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 (Ⓐ), 29 (Ⓑ), 156 (†), and 123 (¥) PsO pts from VOYAGE-2 in randomized withdrawal from W28 to W76. BL=Baseline; csDMARD=Conventional synthetic disease-modifying antirheumatic drug; CV=Cardiovascular; GUS=Guselkumab; NLR=Neutrophil-to-lymphocyte ratio; NSAID=Nonsteroidal 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



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

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PRESENTED AT: Congress of Clinical Rheumatology-West (CCR-W); San Diego, CA, USA; September 26-29, 2024. **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. P2.238. *Arthritis Rheumatol.* 2023;75(suppl 9). **ACKNOWLEDGEMENTS:** Medical writing support was provided by Alexandra Guffey, MSc of Janssen Scientific Affairs, LLC under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med* 2022;doi:10.7326/M22-1460). Layout design and reformatting for this encore presentation was provided by Mugdha Rokade of SIRO Clinpharm Pvt Ltd, Thane, Maharashtra, India. This presentation was supported by Janssen Research & Development, LLC. **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, 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:** Employee of Janssen Scientific Affairs, LLC, owns stock or stock options in Johnson & Johnson. **ER:** Employee of JSS Medical Research; consultant of Janssen. **FN:** Consultant of Janssen; shareholder of Johnson & Johnson. **FL:** Employee of Immunology Global Medical Affairs, Janssen Cilag Global Medical Affairs; owns stock or stock options in Johnson & Johnson. **KR:** Employee of Janssen Scientific Affairs, LLC; owns stock or stock options in 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.