EFFICACY AND SAFETY OF GUSELKUMAB, A MONOCLONAL ANTIBODY SPECIFIC TO THE p19-SUBUNIT OF INTERLEUKIN-23, THROUGH 2 YEARS: RESULTS FROM A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY CONDUCTED IN BIOLOGIC-NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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BACKGROUND/OBJECTIVE

Guselkumab (GUS), a selective IL-23 inhibitor administered as a 100-mg subcutaneous injection every 4 or 8 weeks (Q4W or Q8W), demonstrated improvement in joint and skin symptoms, inhibition of structural damage progression (Q4W), and safety through Week 24 (W24) of the Phase 3, double-blind, placebo (PBO)-controlled trial in biologic-naïve patients (pts) with psoriatic arthritis (PsA; DISCOVER-2)[1]

Favorable benefit-risk profile, including low rates of radiographic progression with both Q4W and Q8W dosing, was also seen through 1 year[2]

Here we report GUS efficacy and safety through completion of the 2-year DISCOVER-2 study

METHODS

- Adults (N=739) with active PsA despite standard non-biologic therapies:
  - ≥5 swollen and ≥5 tender joints and CRP ≥0.6 mg/dL
  - Naïve to biologic agents and Janus kinase inhibitors
  - Randomized (1:1:1) to:
    - GUS 100 mg Q4W
    - GUS 100 mg at W0, W4, and then Q8W
    - PBO with crossover to GUS 100 mg Q4W at W24 (PBO→Q4W)
- Clinical efficacy and health-related quality of life (HRQoL) were assessed in the modified intention to treat (mITT) population through W100 with missing data imputation (nonresponder imputation [NRI] for categorical endpoints; no change/multiple imputation for continuous endpoints)
- Observed PsA-modified van der Heijde Sharp (vdH-S) scores derived from blinded radiographic images collected at W0, W24, W52, W100 (or discontinuation [d/c])
- AEs reported through W112 are summarized per 100 pt-years of follow-up (100 PY)

CONCLUSIONS

In the 739 biologic-naïve pts with active PsA evaluated in the pivotal DISCOVER-2 study:

- **GUS 100 mg administered Q4W or Q8W significantly improved joint and skin symptoms,physical function, and pt-reported HRQoL at W24. Robust joint and skin response rates and mean improvements from baseline in outcome measures were maintained through 2 years**
- **Low rates of radiographic progression were observed through 2 years among GUS-treated pts, regardless of dosing regimen**
- **GUS safety in pts with active PsA through 2 years was comparable to safety at 6 months and 1 year and generally consistent with GUS safety in psoriasis[3,4]**
- **GUS exhibited a favorable benefit-risk profile through 2 years**

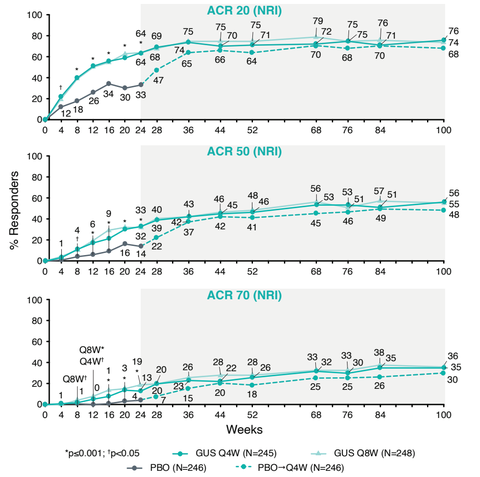
RESULTS

88% of pts completed study agent through W100.

- Among 739 randomized and treated pts in the Q4W, Q8W, and PBO→Q4W groups:
  - 96%, 97%, 97%, respectively, continued study agent at W24
  - 93%, 94%, 93%, respectively, continued study agent at W52
  - 89%, 90%, 85%, respectively, completed study agent through W100

ACR response rates among GUS-treated pts increased after W24 and were maintained through W100.

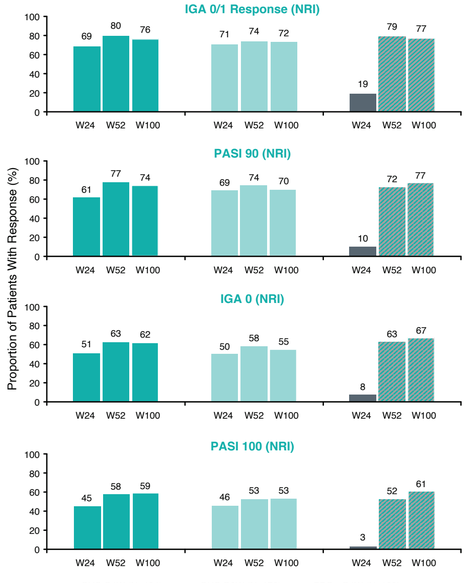
- Among pts receiving GUS Q4W or Q8W: **74-76%** achieved **ACR20**, **55-56%** achieved **ACR50**, **35-36%** achieved **ACR70**



Includes randomized pts who received at least 1 dose of study agent. PBO-controlled period from W0-24. Active-treatment period from W24-100 (shown in gray shading).

Robust skin response rates were seen through W100 across GUS dosing regimens.

- **Minimal-to-clear** (IGA 0/1 Response and PASI 90) skin disease was achieved **by 70-77%** of GUS-treated pts at W100
- **Clear skin** (IGA 0 and PASI 100) was achieved **by 53-67%** of GUS-treated pts at W100



Among patients with BSA ≥3% and IGA ≥2 at baseline. IGA 0/1 response: IGA score of 0 or 1 and ≥2 grade reduction from baseline; IGA=0 cleared skin; IGA=1 minimal skin disease. BSA=Body surface area; IGA=Investigator global assessment; PASI=psoriasis area and severity index.

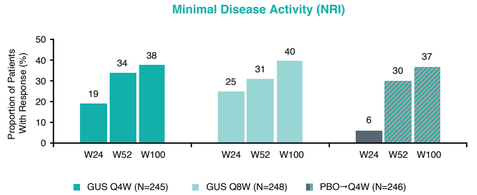
Rates of enthesitis and dactylitis resolution were maintained through W100.

- Response rates conservatively estimated using NRI
- Resolution of **enthesitis** at W100 was achieved by **62%** (Q4W), **70%** (Q8W), and **65%** (PBO→Q4W) of pts with enthesitis at baseline
- Resolution of **dactylitis** at W100 was achieved by **72%** (Q4W), **83%** (Q8W), and **73%** (PBO→Q4W) of pts with dactylitis at baseline

In GUS-treated pts, LS mean changes in physical function and physical aspects of HRQoL at W100 exceeded those generally regarded to represent minimum clinically important differences (MCIDs) to pts.

- HAQ-DI at W100 (MCID 0.35):
  - LS mean changes from baseline in **HAQ-DI** were **-0.55** (Q4W), **-0.53** (Q8W), and **-0.46** (PBO→Q4W)
  - Among GUS-treated pts with a baseline **HAQ-DI score ≥0.35**, 63% (Q4W), 64% (Q8W), and 55% (PBO→Q4W) achieved change ≥0.35
- SF-36 PCS and MCS scores at W100 (MCID 5):
  - LS mean changes from baseline in **PCS** scores were **10.0** (Q4W), **10.4** (Q8W), and **9.3** (PBO→Q4W)
  - LS mean changes from baseline in **MCS** scores were **4.9** (Q4W), **4.2** (Q8W), and **3.9** (PBO→Q4W)

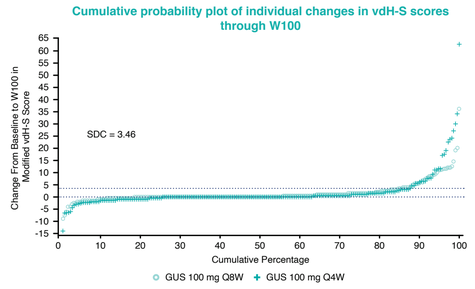
Substantial proportions of GUS-treated pts (37-40%) achieved the treatment target of MDA at W100.



Low rates of radiographic progression were observed through W100 among GUS-treated pts, regardless of dosing regimen.

- Observed mean changes in total PsA-modified vdH-S score from **W0-52 were 1.06 (Q4W) and 0.99 (Q8W)** and from **W52-100** were 0.75 (Q4W) and 0.46 (Q8W)
- In the PBO→Q4W group, the mean changes from **W24-52 (0.34) and W52-100 (0.13)** were smaller than that during during receipt of PBO from **W0-24 (1.12)**

Most pts in the GUS Q4W and Q8W treatment groups exhibited low rates of radiographic progression through W100.



The favorable benefit-risk profile demonstrated by data through W24 and W52 was supported by GUS safety data through W112.

- Through W112, the incidence of AEs, serious AEs (SAEs), AEs leading to d/c, infections, serious infections, and injection site reactions were generally consistent with the PBO-controlled period and through 1 year among pts in the Q4W, Q8W, and PBO→Q4W groups:
  - Opportunistic infections: 2 Q8W pts (fungal esophagitis, disseminated herpes zoster) and 1 PBO→Q4W pt (listeria meningitis)
  - Death: 1 PBO→Q4W pt (road traffic accident)
  - No GUS-treated pt had IBD (1 PBO-randomized pt had suspected IBD prior to W24)
  - No pt had an anaphylactic or serum sickness reaction, or active TB

Table 1. AEs Reported Through W112 (events/100 PY)

	PBO (W0-24)	PBO→Q4W (W24-112)	GUS Q4W (W0-112)	GUS Q8W (W0-112)	All GUS* (W0-112)
Patients, N	246	238	245	248	731
Mean weeks of follow-up	24.4	84.2	106.4	107.1	99.4
Overall PY	115	384	499	509	1392
AEs					
# events/100 PY	188.9	110.7	121.2	158.0	131.7
95% CI	(164.6, 215.8)	(100.5, 121.8)	(111.7, 131.2)	(147.3, 169.3)	(125.8, 137.9)
SAEs					
# events/100 PY	**6.1**	**6.0**	**5.2**	**6.1**	**5.8**
95% CI	**(2.5, 12.6)**	**(3.8, 9.0)**	**(3.4, 7.6)**	**(4.1, 8.7)**	**(4.6, 7.2)**
AEs leading to study agent d/c					
# events/100 PY	3.5	2.9	3.2	1.6	2.5
95% CI	(1.0, 8.9)	(1.4, 5.1)	(1.8, 5.2)	(0.7, 3.1)	(1.8, 3.5)
Infections					
# events/100 PY	50.5	34.9	35.8	40.5	37.3
95% CI	(38.3, 65.3)	(29.3, 41.4)	(30.8, 41.5)	(35.1, 46.4)	(34.1, 40.6)
Serious infections					
# events/100 PY	**0.9**	**2.6**	**1.0**	**2.2**	**1.9**
95% CI	**(0.02, 4.9)**	**(1.3, 4.8)**	**(0.3, 2.3)**	**(1.1, 3.9)**	**(1.2, 2.7)**

**Includes all pts who received ≥1 administration of GUS, including pts who crossed over from PBO at W24.*

Disclosures

Iain B. McInnes - received grant/research support from Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, and UCB and consulting fees from AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, Novartis, Pfizer, and UCB. **Proton Rahman** - received grants from Janssen and Novartis; personal fees from AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB; speakers bureau for AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB. **Alice B. Gottlieb** - received honoraria as an advisory board member and consultant for Anaptyps Bio, Avotres Therapeutics, Beiersdorf, Boehringer Ingelheim, Bristol-Myers-Squibb, Eli Lilly, Janssen, LEO Pharma, Novartis, Sun Pharmaceuticals, UCB, and Xbiotech (stock options only) (less than $10,000 each) and research/educational grants from Boehringer Ingelheim, Janssen, Novartis, Sun Pharmaceuticals, UCB, and Xbiotech (all paid to Mt. Sinai School of Medicine). **Désirée van der Heijde** - received consulting fees from AbbVie, Amgen, Astellas, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, and UCB Pharma; and serves as the director of Imaging and Rheumatology BV. **Philip J. Mease** - grants and personal fees from AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, SUN, and UCB, and personal fees from Boehringer Ingelheim and GlaxoSmithKline. **Yusang Jiang** - employee of Cytel, Inc. providing statistical support (funded by Janssen). **Elizabeth C. Hsia, Alexa P. Kollmeier, Xie L. Xu, Shihong Sheng, May Shawi, and Soumya D. Chakravarty** - employees of Janssen Research and Development and Scientific Affairs, LLC (a subsidiary of Johnson and Johnson) and own Johnson and Johnson stock or stock options

References

1. Mease PJ. *Lancet*. 2020 Apr 4;395(10230):1126-1136.
2. McInnes IB. *Arthritis Rheumatol*. 2020 Oct 11. doi: 10.1002/art.41553.
3. Griffiths CEM. *J Dermatolog Treat*. 2020. doi:10.1080/09546634.2020.1782817.
4. Reich K. *Am J Clin Dermatol*. 2020. doi:10.1007/s40257-020-00555-7.

Presented at the 2021 Dermatology Nurses' Association; Virtual Convention; April 21–23, 2021.

This poster was supported by Janssen Research & Development, LLC and originally presented at Innovations in Dermatology 2021