IMMUNOGENICITY OF GUSELKUMAB AMONG PSORIASIS PATIENTS IN VOYAGE 1&2 STUDIES

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BACKGROUND/OBJECTIVE

- VOYAGE 1 & 2 were phase 3, randomized, double-blinded, placebo- and active comparator-controlled studies of guselkumab (GUS) in adult patients with moderate-to-severe plaque psoriasis[1,2]
- The development of anti-drug antibodies (ADA) to biologic agents is a normal immune response but may affect efficacy and/or safety[3]
- Here, we assessed the association between the development of ADA to GUS and either the extent of clinical response or incidence of injection-site reactions (ISRs) through 5 years in the VOYAGE 1 and VOYAGE 2 studies

METHODS

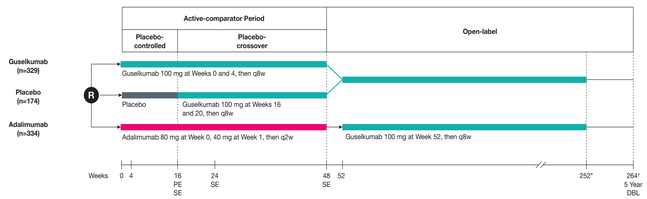
- VOYAGE 1 and VOYAGE 2 were identical through Week 24; patients were randomized at baseline as follows (Figures 1 and 2):
  - GUS 100 mg administered by subcutaneous (SC) injection at Weeks 0, 4, and 12, then every 8 weeks (q8w)
  - Placebo at Weeks 0, 4, and 12, followed by GUS 100 mg SC at Weeks 16 and 20, then q8w
  - Adalimumab 80 mg SC at Week 0, 40 mg at Week 1, then 40 mg every 2 weeks (q2w) through Week 23
- In VOYAGE 1 (Figure 1), patients in the adalimumab group continued on adalimumab 40 mg q2w through Week 47 and crossed over to receive GUS at Week 52. All patients entered the open-label GUS treatment period during Weeks 52-252.
- In VOYAGE 2 (Figure 2), patients entered a randomized withdrawal and retreatment period from Week 28 to 72. Patients entered the open-label GUS treatment period during Weeks 76-252.
- Venous blood samples were collected at regular visits for the detection of antibodies to GUS. The ADA were detected using a validated electrochemiluminescence immunoassay (ECLIA) method.
- The incidence and titres of ADA to GUS were summarized through Week 264 for all patients who were treated with at least one dose of GUS and had evaluable serum samples following treatment
- If a patient had a positive sample at the reference baseline visit, the patient was considered as positive only if the peak titre of the post-GUS treatment samples was ≥2-fold higher than that of the reference sample at baseline
- Serum samples that tested positive for ADA to GUS were further characterized to determine if the antibodies that had developed could neutralize the biologic activity of GUS in vitro (i.e., neutralizing antibodies [NAbs] to GUS)
- The proportions of patients achieving clinical response at Week 252 were evaluated by positive/negative ADA status
- Clinical response was defined as achieving ≥90% improvement in the Psoriasis Area and Severity Index (nearly complete clearance; PASI 90) or 100% improvement (complete clearance; PASI 100) and as an Investigator's Global Assessment (IGA) score of 0/1 (cleared or minimal) or 0 (cleared)
- The proportions of patients experiencing ISRs through Week 264 were evaluated by positive/negative ADA status

CONCLUSIONS

- **Through the end of the 5-year VOYAGE 1 and VOYAGE 2 studies of GUS in psoriasis, 15% of patients had developed ADA to GUS. Of these, 5% had antibodies that were classified as neutralizing, which equates to 0.8% of all GUS-treated patients.**
- **The development of ADA (or NAb) was not associated with either reduced clinical efficacy or increased ISR rates. However, these data should be interpreted with caution due to the limited number of patients developing ADA/NAb and/or experiencing ISRs within 5 years of commencing treatment.**

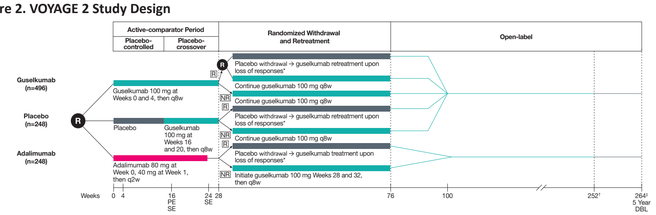
METHODS (CONT'D)

Figure 1. VOYAGE 1 Study Design



DBL, database lock; PE, primary endpoint; R, randomization; SE, secondary endpoint; q2w, every 2 weeks; q8w, every 8 weeks.
*The last dose of guselkumab was administered at Week 252; efficacy was evaluated through Week 252.
†Safety was evaluated through Week 264.

Figure 2. VOYAGE 2 Study Design



DBL, database lock; Nonresponders [NR] <PASI 90; PASI, Psoriasis Area and Severity Index; PE, primary endpoint; R, randomization; SE, secondary endpoint; Responders [R] ≥PASI 90; q2w, every 2 weeks; q8w, every 8 weeks.
*Upon loss of ≥50% of improvement in PASI achieved at Week 28 or at Week 72 if prerequisite loss of PASI improvement was not observed, then reinitiate or initiate guselkumab.
†The last dose of guselkumab was administered at Week 252; efficacy was evaluated through Week 252.
‡Safety was evaluated through Week 264.

RESULTS

- Of all GUS-treated patients with evaluable samples, 14.4% (111/770) in VOYAGE 1 and 15.5% (146/943) in VOYAGE 2 were positive for ADA through Week 264
- In both studies, ADA titres were predominantly low, with 82.0% in VOYAGE 1 and 82.2% in VOYAGE 2 having peak titres ≤1:160
- Only 5 (4.5%) and 8 (5.5%) ADA positive patients in VOYAGE 1 and VOYAGE 2, respectively, were positive for NAbs to GUS

The proportions of patients who achieved PASI 90, PASI 100, IGA 0/1, or IGA 0 were not impacted by the development of ADA to GUS

Table 1. Proportions of Patients With Clinical Response at Week 252 by ADA Status Through 5 Years; GUS-treated Patients[a] With Samples Evaluable for Immunogenicity

	VOYAGE 1		VOYAGE 2	
	Negative[b]	Positive[c]	Negative[b]	Positive[c]
Efficacy				
Patients treated with GUS[d]	536	101	619	117
PASI 90	445 (83.0)	87 (86.1)	505 (81.7)	94 (80.3)
PASI 100	280 (52.2)	57 (56.4)	323 (52.3)	67 (57.3)
IGA 0/1[e]	437 (81.5)	89 (88.1)	527 (85.1)	95 (81.2)
IGA 0[e]	292 (54.5)	58 (57.4)	337 (54.4)	70 (59.8)

Data are presented as n (%).
ADA, anti-drug antibodies; GUS, guselkumab; IGA , Investigator's Global Assessment; IGA 0, cleared psoriasis; IGA 0/1, cleared or minimal psoriasis; PASI, Psoriasis Area and Severity Index; PASI 90, nearly complete clearance (≥90% improvement); PASI 100, complete clearance (100% improvement).
[a]Includes patients who received ≥1 dose of GUS, including those who crossed over from placebo or adalimumab.
[b]Includes all patients whose last sample was negative and excludes patients who were positive for antibodies to GUS through Week 264.
[c]Includes all patients who had ≥1 positive sample (treatment-boosted or treatment-induced) at any time after their first GUS administration through Week 264.
[d]Includes patients who had ≥1 evaluable sample after their first GUS administration and for whom efficacy assessments at Week 252 were performed.
[e]IGA results were not available for 1 patient in VOYAGE 2.

No direct association between the development of ADA and development of ISRs was apparent through Week 264. However, the small number of patients who were ADA positive and/or had ISRs limits drawing a definitive conclusion.

Table 2. Proportions of Patients With ISRs by ADA Status Through 5 Years; GUS-treated Patients[a] With Samples Evaluable for Immunogenicity

	VOYAGE 1		VOYAGE 2	
	Negative[b]	Positive[c]	Negative[b]	Positive[c]
Safety				
Patients treated with GUS[d]	659	111	797	146
Patients with ISRs	33 (5.0)	9 (8.1)	41 (5.1)	15 (10.3)
Number of GUS injections	17578	3158	20760	3832
Injections with ISRs	66 (0.4)	18 (0.6)	37 (0.2)	50 (1.3)

Data are presented as n (%).
ADA, anti-drug antibodies; GUS, guselkumab; ISRs, injection site reactions.
[a]Includes patients who received ≥1 dose of GUS, including those who crossed over from placebo or adalimumab.
[b]Includes all patients whose last sample was negative and excludes patients who were positive for antibodies to GUS through Week 264.
[c]Includes patients who had ≥1 positive sample at any time after their first GUS administration through Week 264.
[d]Includes patients who had ≥1 evaluable sample after their first GUS administration.

Among the 13 patients who were positive for NAbs, all maintained IGA 0/1 and/or PASI 90 responses; 1 patient experienced a mild ISR after developing NAbs

Disclosures

Kristian Reich – served as advisor and/ or paid speaker for and/or participated in clinical trials sponsored by AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Forward Pharma, Galderma, Gilead, Janssen-Cilag, Kyowa Kirin, Leo, Medac, Novartis, Ocean Pharma, Pfizer, Sanofi, UCB, co-founder of MoonLake Immunotherapeutics. **April W. Armstrong** - research investigator and/or scientific advisor to AbbVie, Boehringer Ingelheim, BMS, Dermavant, Dermira, EPI Health, Incyte, Janssen, KHK, Leo, Lilly, Modmed, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, Sun, and UCB. **Peter Foley** - received grant support from AbbVie, Amgen, Celgene, Janssen, Leo Pharma, Lilly, Merck, Novartis, Pfizer, Sanofi, and Sun Pharma. He has served as an investigator for AbbVie, Akaal, Amgen, Arcutis, Argenx, Aslan, AstraZeneca, BMS, Boehringer Ingelheim, Botanix, Celgene, Celtaxsys, CSL, Cutanea, Dermira, Galderma, Genentech, GSK, Heximа, Janssen, Leo Pharma, Lilly, MedImmune, Melaseq/Geneseq, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals Inc, Reistone, Roche, Sanofi, Sun Pharma, Teva, UCB Pharma, and Valeant, He has served on advisory boards for AbbVie, Amgen, BMS, Boehringer Ingelheim, Celgene, Galderma, GSK, Janssen, Leo Pharma, Lilly, Mayne Pharma, Merck, Novartis, Pfizer, Sanofi, Sun Pharma, UCB Pharma, and Valeant. He has served as a consultant for BMS, Galderma, GenesisCare, Janssen, Leo Pharma, Lilly, Mayne Pharma, MedImmune, Novartis, Pfizer, Roche, UCB Pharma, and Wintermute. He has received travel grants from AbbVie, Galderma, Janssen, Leo Pharma, Lilly, Merck, Novartis, Pfizer, Roche, Sun Pharma, and Sanofi, and has served as a speaker for or received honoraria from AbbVie, Amgen, Celgene, Galderma, GSK, Janssen, Leo Pharma, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi, Sun Pharma, and Valeant. **Christopher E. M. Griffiths** - received honoraria as an advisory board member and/or speaker from AbbVie, Almirall, Bristol Myers Squibb, Eli Lilly, Galderma, Janssen, Leo, Novartis, Pfizer, Sun Pharma, and UCB Pharma and research grants from AbbVie, Celgene, Eli Lilly, Janssen, Leo, Novartis, Pfizer, and Sandoz. **Bruce Strober** - received honoraria or research grants as a consultant, speaker, and/or investigator for AbbVie, Almirall, Amgen, Arcutis, Arena, Aristea, Boehringer Ingelheim, Bristol Myers Squibb, Cara, Celgene, Dermavant, Dermira, Equillium, GlaxoSmithKline, Janssen, Leo, Eli Lilly, Meiji Seika Pharma, Mindera, Novartis, Ortho Dermatologics, Pfizer, Sanofi-Genzyme Sun Pharma, Regeneron, and UCB Pharma; as scientific director for the CorEvitas Psoriasis Registry; and as Editor-in-Chief at the *Journal of Psoriasis and Psoriatic Arthritis*. **Yaowei Zhu, Megan Miller, Yin You, and Yaung-Kaung Shen** are all employees of Janssen Research & Development, LLC; and **Ya-Wen Yang** is an employee of Janssen Immunology Global Medical Affairs; employees may own stock in Johnson & Johnson, of which Janssen is a subsidiary..

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