GUSELKUMAB IN PSORIASIS PATIENTS WITH A HISTORY OF MALIGNANCY: 5-YEAR SAFETY FROM VOYAGE 1&2

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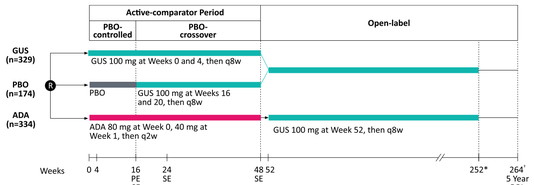
BACKGROUND/OBJECTIVE

- Malignancy is a potential safety concern for all immunomodulatory biologics. Patients with a history of malignancy are often excluded from clinical trials, which limits the availability of safety data for biologics in this population[1,2]
- Guselkumab (GUS), an interleukin-23 p19 subunit inhibitor, is approved for the treatment of moderate to severe psoriasis and active psoriatic arthritis
- VOYAGE 1 and 2 were Phase 3 studies that demonstrated the long-term efficacy and safety of GUS in patients with moderate to severe psoriasis[3,4]
- These studies included a small number of patients with a history of malignancy (excluding non-melanoma skin cancer [NMSC]) at baseline with no evidence of recurrence for greater than 5 years prior to screening
- This analysis examines malignancy and other serious adverse events (SAEs) reported in these patients through 5 years in VOYAGE 1 and 2

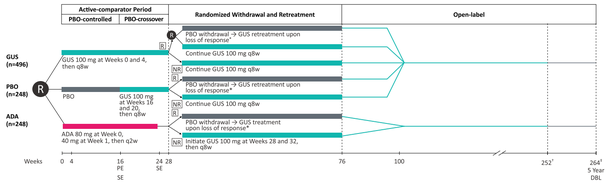
METHODS

Figure 1. VOYAGE 1 Study Design



ADA = Adalimumab; DBL = Database lock; GUS = Guselkumab; PBO = Placebo; PE = Primary endpoint; R = Randomization; SE = Secondary endpoint; q2w = every 2 weeks; q8w = every 8 weeks
*The last dose of GUS was administered at Week 252; efficacy was evaluated through Week 252. †Safety was evaluated through Week 264.

Figure 2. VOYAGE 2 Study Design



ADA = Adalimumab; DBL = Database lock; GUS = Guselkumab; Nonresponders NR = < PASI 90; PBO = Placebo; PASI = Psoriasis Area and Severity Index; PE = Primary endpoint; q2w = every 2 weeks; q8w = every 8 weeks; R = Randomization; Responders R = ≥ PASI 90; SE = Secondary endpoint
*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 GUS; †The last dose of GUS was administered at Week 252; efficacy was evaluated through Week 252; ‡Safety was evaluated through Week 264.

- A descriptive analysis of SAEs of malignancies and other SAEs through Week 264 was performed in GUS-treated patients with a history of malignancy (excluding NMSC) at baseline
  - Exposure to GUS was calculated for these patients with a history of malignancy at baseline
- Patients who were diagnosed with a malignancy during the study (except ≤2 localized basal cell carcinomas) were required to discontinue study treatment

CONCLUSIONS

- **Among 18 patients with a history of malignancy who were exposed to GUS for up to 5 years there were:**
  - **2 new primary malignancies (papillary breast carcinoma and invasive melanoma)**
  - **1 recurrence of bronchial carcinoma confounded by exposure to adalimumab**
- **This analysis did not identify any new safety concerns that would limit the long-term use of GUS in patients with a history of malignancy**
- **More patients and longer duration of follow-up are needed to better characterize the use of GUS in patients with a history of malignancy**

RESULTS

Patients With a History of Malignancy at Baseline

- Of 1721 GUS-treated patients, 18 (1.0%) had a prior history of malignancy at baseline
- Mean (SD) exposure to GUS during the VOYAGE 1 or 2 study=184 (87) weeks; median (range)=225.5 (20-254) weeks

Prior Malignancies[†,‡]

- Cervical, n=4
- Prostate, n=4
- Breast, n=2
- Melanoma, n=2
- Colon, n=1
- Dermatofibrosarcoma, n=1
- Kidney, n=1
- Lung, n=1
- Rectal, n=1
- Testicular, n=1
- Thyroid, n=1

[†]1 patient had a history of both kidney and prostate cancer.
[‡]4 patients (with a history of cervical cancer, kidney and prostate cancer, lung cancer, and thyroid cancer, respectively) received adalimumab during the active-comparator period of the study.

Of these 18 patients, 3 experienced SAEs of malignancy while participating in VOYAGE 1 or 2 for up to 5 years

Patient 1	Patient 2	Patient 3
• History (Hx) of prostate cancer (2007) • SAE of metastatic invasive papillary breast cancer • Investigator: SAE not related to study medication	• Hx of bronchial carcinoma (1997-2007) • SAE of bronchial carcinoma recurrence with metastases • Investigator: SAE not related to study medication	• Hx of prostate cancer (2010) • SAE of invasive melanoma of the right forearm • Investigator: SAE not related to study medication

Patient 1: SAE of Metastatic Breast Cancer

Demographics & Medical Hx	• White; male; USA; age 76 years; body mass index (BMI) 35.4 kg/m^2 • Prostate cancer, early coronary artery disease, hypertension (HTN), psoriatic arthritis, hyperlipidemia, pulmonary mass, alcohol consumption • Prior psoralen with ultraviolet A, topical treatment
VOYAGE 1 Treatment	• Randomized to GUS • Received GUS every 8 weeks (Q8W) from Week (W) 0-28
Malignancy SAE	• **Right breast lump observed ~1 year prior to study entry** • Lump slowly enlarged and became tender • Diagnosis on Day 202: 2.7 cm subareolar right breast mass • Gene mutation identification testing was negative • Grade 3 infiltrating ductal carcinoma with focal micropapillary features • 2 of 6 lymph nodes positive for metastasis • Recovered following right modified radical mastectomy

Patient 2: SAE of Recurrent Bronchial Carcinoma

Demographics & Medical Hx	• White; male; Germany; age 57 years; BMI 36.6 kg/m^2 • **Lung cancer, smoker (0.5 packs/day),** family Hx of cancer, benign prostatic hypertrophy, HTN • Prior methotrexate, ultraviolet B, and topical treatment
VOYAGE 2 Treatment	• **Randomized to adalimumab** • Received GUS from W28-100
Malignancy SAE	• Right lower lobe lung carcinoma diagnosed on Day 753 (Stage IVB; cT4 N3 M1c) • Tumor infiltration into middle lobe; exophytic tumor growth in lower lobe • Poorly differentiated non-cornified squamous cell carcinoma, programmed death-ligand 1 negative • 3 supratentorial brain metastases • Died of bronchial carcinoma ~4 months after study discontinuation

Patient 3: SAE of Invasive Melanoma

Demographics & Medical Hx	• White; male; Canada; age 71 years; BMI 31.9 kg/m^2 • **Type I/II skin; sun exposure from recreational activities (avid golfer)** • Prostate cancer, family Hx of cancer, former smoker, alcohol consumption, hyperlipidemia • Prior topical treatment
VOYAGE 2 Treatment	• Randomized to placebo • Received GUS at W16 and W20; rerandomized to placebo from W28-72 • Open-label GUS Q8W from W72-180 • Total GUS exposure=161 weeks
Malignancy SAE*	• Right forearm invasive melanoma diagnosed on Day 1139 • Ulcerated depth=at least 0.7 mm; mitotic rate=3 cells/mm^2 • Margins involved; no lymphovascular invasion • Had 2 basal cell carcinomas during study (left cheek, Day 211; left ankle, Day 1139) • Recovered after surgical removal of melanoma

*No further information is available about this SAE.

SAEs Other Than Malignancies

- Of 18 patients with a prior history of malignancy at baseline, 5 had SAEs other than malignancies

Age; Race; Sex; Country; Study	Prior Malignancy	Treatment Phase	SAE (Day; Treatment Relatedness; Outcome)
57 y; Asian; F; Korea; VOY 2	Cervical cancer	GUS GUS	• Multiple fractures (Day 141; Not related; Resolved) • Subdural hemorrhage (Day 141; Not related; Resolved)
57 y; White; F; Germany; VOY 2	Breast cancer	Withdrawal Withdrawal	• Noncardiac chest pain (Day 204; Not related; Resolved) • Herniated disc (Day 231; Not related; Resolved)
64 y; White; F; Spain; VOY 2	Breast cancer	GUS Withdrawal	• Cardiac failure (Day 127; Not related; Resolved) • Respiratory failure (Day 238; Not related; Resolved)
68 y; White; M; USA; VOY 2	Dermatofibrosarcoma protuberans	GUS GUS (open-label) GUS (open-label)	• Cellulitis (Day 435; Possible; Resolved) • Presyncope (Day 1201; Not related; Not resolved) • Chest injury (Day 1378; Not related; Resolved)
59 y; White; F; USA; VOY 1	Cervical cancer	GUS (open-label)	• Cellulitis (Day 1456; Doubtful related; Resolved)

F=Female; GUS=Guselkumab; Hx=History; M=Male; SAE=Serious adverse event; VOY=VOYAGE; y=Years.

NMSC Events

- From baseline to Week 264, NMSC was reported in 2 of 18 patients with a prior history of malignancy

Age; Race; Sex; Country; Study	Prior Malignancy	Treatment Phase	NMSC (Location; Study Day; Treatment Relatedness; Outcome)
71 y; White; M; Canada; VOY 2*	Prostate cancer	Withdrawal GUS (open-label)	• BCC (Left cheek; Day 211; Not related; Resolved) • BCC (Left ankle; Day 1139; Not related; Resolved)
72 y; White; M; USA; VOY 2	Rectal cancer	GUS GUS (open-label)	• BCC (Left eyelid; Day 394; Not related; Resolved) • Sebaceous carcinoma (Right eyelid; Day 1168; Possible; Resolving)

*This is the same patient diagnosed with invasive melanoma (right forearm) on Day 1139.
BCC=Basal cell carcinoma; GUS=Guselkumab; M=Male; NMSC=Non-melanoma skin cancer; VOY=VOYAGE; y=Years.

Disclosures

A. Blauvelt: Scientific adviser/investigator for AbbVie, Abcentra, Aligos, Almirall, Amgen, Arcutis, Arena, Aslan, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, EcoR1, Eli Lilly, Evommune, Forte, Galderma, Incyte, Janssen, Landos, Leo, Novartis, Pfizer, Rapt, Regeneron, Sanofi Genzyme, Sun Pharma, UCB, and Vibliome. **D. Thaçi**: Consultant/advisor for AbbVie, Almirall, Beiersdorf, Boehringer Ingelheim, Celgene, Eli Lilly, Hexal AG, Janssen-Cilag, Leo Pharma, Novartis, Pfizer, Sandoz, Sanofi, and UCB; speaker for AbbVie, Almirall, Celgene, Eli Lilly, Hexal AG, Janssen-Cilag, Medac Pharma, Novartis, Pfizer, Regeneron, Sandoz, Sanofi, Schering-Plough, and UCB; investigator for AbbVie, Celgene, Eli Lilly, Glaxo5mithKline, Janssen-Cilag, Leo Pharma, Novartis, Parexel, Pfizer, Regeneron, and UCB. **K. Papp**: Received clinical research grants/honoraria as consultant/speaker/investigator/scientific officer/advisory board member/Steering Committee member for AbbVie, Akros, Amgen, Anacor, Arcutis, Astellas, Avillion, Bausch Health/Valeant, Baxalta, Boehringer Ingelheim, Bristol Myers Squibb, Can-Fite, Celgene, Coherus, Dermavant, Dermira, Dow, Eli Lilly, Evelo, Galapagos, Galderma, Genentech, Gilead, GSK, Incyte, Janssen, Kyowa Hakko Kirin, Leo, Medimmune, Meiji Seika Pharma, Merck (MSD), Merck- Serono, Mitsubishi Pharma, Moberg Pharma, Novartis, Pfizer, PRCI, Research, Regeneron, Roche, Sanofi-Aventis/Genzyme, Sun Pharma, Takeda, and UCB. **V. Ho**: Advisory board participant, investigator, and/or speaker for AbbVie, Lilly, Novartis, Janssen, and Sanofi. **K. Ghoreschi**: Research grants, or honoraria for participation in advisory boards, clinical trials, or as speaker for one or more of the following: AbbVie, Almirall, Boehringer Ingelheim Pharma, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen-Cilag, Leo Pharma, Medac, Novartis Pharma, Pfizer, and UCB Pharma. **B.S. Kim**: Grants from AbbVie, Boehringer Ingelheim, Eli- Lilly, Janssen, LEO, Novartis, Regeneron, Sanofi, and UCB. **J. Crowley**: Consultant/speaker/investigator for AbbVie, Lilly, Novartis, Janssen, Regeneron, Sanofi, Sun Pharma, UCB; consultant/investigator for Dermira, Arcutis; investigator for Merck, Pfizer, Sandoz, MC2 Therapeutics, Verrica Pharmaceuticals; consultant for Boehringer Ingelheim and Bristol Myers Squibb. **M. Miller, Y.-K. Shen, Y. You, J. Yu**: Employees of Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), and own Johnson & Johnson stock/stock options. **Y.-W. Yang**: Employee of Janssen Pharmaceutical Companies of Johnson & Johnson; owns Johnson & Johnson stock/stock options. **P. Foley**: Received grant support, and/or served on advisory boards, and/or served as a consultant, and/or has received travel grants, and/or has served as a speaker for or received honoraria from AbbVie, Akaal, Amgen, Arcutis, Argenx, Aslan, AstraZeneca, BMS, Boehringer Ingelheim, Botanix, Celgene, Celtaxsys, CSL, Cutanea, Dermira, Galderma, GenesisCare, Genentech, GSK, Hexima, Janssen, Leo Pharma, Lilly, Mayne Pharma, MedImmune, Melaseq/Geneseq, Merck, Novartis, Pfizer, Regeneron, Reistone, Roche, Sanofi, Sun Pharma, UCB Pharma, Valeant, Wintermute.

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This poster was supported by Janssen Research and Development, LLC • Originally Presented at EADV's 30th Congress, Virtual, September 29-October 2, 2021.

Presented at The Winter Clinical Dermatology Conference - Hawaii® (WC22), 14th-19th JAN 2022.