P0669

Safety of intravenous and subcutaneous guselkumab induction administration: results from the GALAXI and GRAVITI studies in participants with Crohn's disease

S. Danese,[1] B.E. Sands,[2] A. Afzali,[3] T. Hisamatsu,[4] A. Armuzzi,[5] D. Wolf,[6] G. Duvall,[7] R. Van Rampelbergh,[8] M. Olurinde,[9] N.A. Terry,[9] J. Yee,[9] H. Li,[9] M. Rosas Ballina,[10] G. D'Haens,[11] D.T. Rubin,[12] R. Panaccione[13]

[1]IRCCS Ospedale San Raffaele and University Vita-Salute San Raffaele, Milano Italy; [2]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [3]University of Cincinnati, College of Medicine, OH, USA; [4]Kyorin University School of Medicine, Tokyo, Japan; [5]IBD Center, Humanitas Research Hospital, Humanitas University, Milan, Italy; [6]Atlanta Gastroenterology Associates, Atlanta, GA; [7]Tyler Research Institute, LLC, Tyler, TX, USA; [8]Johnson & Johnson, Antwerp, Belgium; [9]Johnson & Johnson, LLC, Spring House, PA, USA; [10]Actelion Research & Development, Allschwil, Switzerland; [11]Amsterdam University Medical Centers, Amsterdam, The Netherlands; [12]University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago, IL, USA; [13]University of Calgary, Calgary, AB, Canada

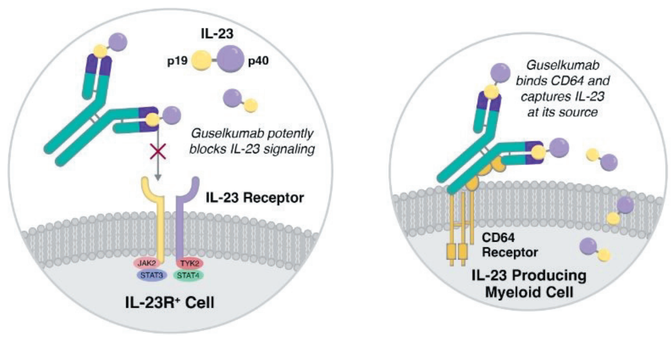
Key Takeaways

- **Both IV and SC induction with guselkumab demonstrated comparable safety results consistent with the well-characterized guselkumab safety profile**
- **SC induction was well tolerated, with few participants reporting injection-site reactions**
- **No new safety concerns were identified when compared to the established safety profile of guselkumab**

Background

Guselkumab is a dual-acting IL-23p19 subunit inhibitor that neutralizes IL-23 and binds to CD64, a receptor on cells that produce IL-23

Induction with both intravenous (IV) and subcutaneous (SC) guselkumab was effective in phase 2/3 clinical trials of participants with moderately to severely active Crohn's disease (CD)



Objective

To characterize the safety of guselkumab IV and SC induction regimens in clinical trials of guselkumab in CD

Methods

- We evaluated data from phase 2 and phase 3 CD studies with IV induction in GALAXI 1, 2, and 3 and SC induction in GRAVITI to assess rates of safety events (proportions of participants with ≥1 event) during the induction period (Week 0-12)
- In GALAXI, participants were assigned to guselkumab 200 mg IV or placebo IV at Week 0, 4, and 8 followed by guselkumab 100 mg SC every 8 weeks or 200 mg SC every 4 weeks or placebo
  - Participants in GALAXI assigned to guselkumab 600 mg IV, 1200 mg IV or a ustekinumab induction dose were not included
- In GRAVITI, participants were assigned to guselkumab 400 mg SC or placebo SC at Week 0, 4, and 8 followed by guselkumab 100 mg SC every 8 weeks or 200 mg SC every 4 weeks or placebo

Results

- *During the induction period, rates were not greater in either the guselkumab IV or the SC groups compared to the respective placebo groups for adverse events, serious adverse events, or adverse events leading to discontinuation*
- *Events of special interest and clinical interest were low overall in the guselkumab treatment groups*

Participants with 1 or more safety events during the induction period (Week 0-12)

	IV Induction		SC Induction	
	Placebo (N=211)	Guselkumab 200 mg IV (N=649)	Placebo (N=117)	Guselkumab 400 mg SC (N=230)
Adverse events, n (%)	109 (51.7)	304 (46.8)	58 (49.6)	107 (46.5)
Serious adverse events, n (%)	13 (6.2)	19 (2.9)	9 (7.7)	5 (2.2)
Adverse events leading to discontinuation, n (%)	9 (4.3)	11 (1.7)	3 (2.6)	1 (0.4)
Serious infections, n (%)	0	1 (0.2)	0	1 (0.4)
Malignancies[a]**,** n (%)	0	0	0	1 (0.4)
Opportunistic infections[b]**,** n (%)	1 (0.5)	2 (0.3)	1 (0.9)	0
Clinically important hepatic disorders[c]**,** n (%)	0	2 (0.3)	0	1 (0.4)
Deaths, n (%)	0	1 (0.2)	0	0

Participants are counted only once for any given event, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 26.0. [a]Malignancies are defined as the narrow terms in the MedDRA SMQ of 'Malignant Tumours'. Nonmelanoma skin cancers are identified by the MedDRA HLT of 'Skin neoplasms malignant and unspecified (excl melanoma). [b]Opportunistic infections are defined as the narrow terms in the MedDRA SMQ of 'Opportunistic Infections'. [c]Clinically important hepatic disorders are defined as hepatic disorder adverse events reported as serious adverse events or adverse events leading to discontinuation of study intervention.

- *Three cases of clinically important hepatic disorders (hepatic disorder adverse events reported as serious adverse events or adverse events leading to discontinuation of study intervention) were identified in the guselkumab treatment groups and resolved by treatment pause or discontinuation*

Clinically important hepatic disorders

Treatment Group	Details
Guselkumab 200 mg IV	Serious adverse event of increased liver function tests (LFT) that met the biochemical criteria for Hy's law. The aspartate aminotransferase (AST) >3x upper level of normal (ULN) threshold was reached. Confounding factors included a diagnosis of Gilbert's disease and macrogol administration at the time of the marked elevation in LFTs. Dosing was paused, the transaminases subsequently normalized, and the participant resumed guselkumab treatment.
Guselkumab 200 mg IV	Adverse event of hepatic enzyme increased. The alanine aminotransferase (ALT) and AST >8xULN and alkaline phosphatase (ALP) >2xULN thresholds were reached. Confounding factors included recent initiation of treatment for latent tuberculosis (isoniazid) and a concurrent adverse event of cytomegalovirus infection (IgM positive and PCR negative). Study intervention was discontinued and the liver test abnormalities resolved.
Guselkumab 400 mg SC	Adverse event of ALT increased at study Week 0, prior to the first and only dose of guselkumab. ALT > 5xULN and ALP >2xULN thresholds were reached at study Week 0, prior to the first dose. ALT and ALP elevations were persistent through study Week 8. Confounding factors included a concomitant medication (fluconazole). Liver test abnormalities resolved at study Week 8 and study intervention was discontinued.

Injection site reactions as assessed by the investigator.

- *No cases of active tuberculosis, anaphylaxis, serum sickness reactions, major adverse cardiovascular events, or venous thromboembolism were reported during the induction period*
- *Serious infections reported were an anal abscess in the GALAXI 200 mg IV induction group and bronchitis in the GRAVITI 400 mg SC group. In both cases the infection resolved, and dose was not changed*
- *One malignancy of basal cell carcinoma was reported in the GRAVITI 400 mg SC group. This case was confounded by use of azathioprine. The malignancy did not lead to discontinuation*
- *Opportunistic infections occurred in two participants in the placebo group with esophageal candidiasis and two participants in the guselkumab 200 mg IV group with cytomegalovirus infection and esophageal candidiasis*
- *One death was reported in GRAVITI during the induction period. The cause of death was attributed to a non-suicidal (not self-inflicted) gunshot wound in a participant treated with guselkumab SC*

Guselkumab infusions and number of participants with ≥1 AEs within 1 hour of infusion

	GALAXI 1, 2, & 3 200 mg IV (N=649)
Total number of guselkumab infusions	1908
Number of participants with ≥1 AEs within 1 hour of infusion	10 (1.5%)
Hyperthermia	1 (0.2%)
Pyrexia	2 (0.3%)
Infusion related reaction (fever related to infusion)	1 (0.2%)
Dizziness	1 (0.2%)
Headache	1 (0.2%)
Erythema	1 (0.2%)
Rash	1 (0.2%)
Hot flush	1 (0.2%)
Hypotension	1 (0.2%)

Participants are counted only once for any given event, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 26.0.

- *The number of participants with one or more adverse events within on 1 hour of administration of guselkumab infusions during the induction period in GALAXI was low (1.5%)*
- *Similar rates were seen with placebo infusions with 1.9% of participants reporting one or more adverse events within on 1 hour of IV administration*
- *No cases of anaphylaxis were reported through Week 12*

Guselkumab injections with injection-site reactions and number of participants with injection-site reactions during the induction period

	GRAVITI 400 mg SC (N=230)
Total number of guselkumab injections	1376
Guselkumab injections with injection-site reactions	6 (0.4%)
Participants with ≥1 injection-site reactions	5 (2.2%)
Application site pruritus	1 (0.4%)
Injection site erythema	1 (0.4%)
Injection site mass	1 (0.4%)
Injection site rash	2 (0.9%)
Injection site swelling	1 (0.4%)
Erythema	1 (0.4%)
Pruritus	1 (0.4%)

Injection site reactions as assessed by the investigator.

- *Of the 1376 guselkumab SC injections during the induction period in GRAVITI, 6 (0.4%) were associated with injection-site reactions and none led to discontinuation. No participants in the placebo group reported injection-site reactions*
- *Injection-site reactions beyond the induction period with guselkumab SC in GALAXI and GRAVITI remained low (≤1%) and were comparable regardless of induction administration route*

PRESENTED BY: S. Danese at the 20th Congress of European Crohn's and Colitis Organization (ECCO), February 19–22, 2025, Berlin, Germany. **ACKNOWLEDGMENTS:** Medical writing support was provided by Kirsten Schuck Gross of Johnson & Johnson under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med.* 2022;175:1298-1304). **DISCLOSURES: SD:** reports consultancy fees from AbbVie, Alimentiv, Allergan, Amgen, AstraZeneca, Athos, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Enthera, Ferring, Gilead, Hospira, Inotrem, Janssen, Johnson & Johnson, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity, Takeda, TiGenix, UCB and Vifor; and reports lecture fees from AbbVie, Amgen, Ferring, Gilead, Janssen, Mylan, Pfizer and Takeda. **BES:** reports consulting fees from AbbVie, Adiso Therapeutics, Agomab, Alimentiv , Amgen, AnaptysBio, Arena Pharmaceuticals, Artugen Therapeutics, Astra Zeneca, Biolojic Design, Biora Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Calibr, Celgene, Celltrion, ClostraBio, Equillium, Enthera, Envied Biosciences, Evommune, Ferring, Fresenius Kabi, Fiat, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Imhotex, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Kaleido, Kallyope, Merck, Microba, Mobius Care, Morphic Therapeutics, MRM Health, Nexus Therapeutics, Nimbus Discovery, Odyssey Therapeutics, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Rasayana Therapeutics, Recludix Therapeutics, Reistone Biopharma, Sanofi, Spyre Therapeutics, Sun Pharma, Surrozen, Target RWE, Teva, TLL Pharmaceutical, Tr1X, Union Therapeutics, and Ventyx Biosciences; consulting and speaking fees from Abivax; consulting and speaking fees and other support from Lilly; research grants, consulting and speaking fees and other support from Bristol Myers Squibb, Janssen, Pfizer, and Takeda; research grants and consulting fees from Theravance Biopharma; and stock/stock options from Ventyx Biopharma. **AA:** reports potential conflicts of interest with AbbVie, Bristol Myers Squibb/Celgene, DiaSorin, Eli Lilly, Gilead, IBD Horizons, Janssen, Pfizer, Takeda, and TLL Pharmaceuticals. **TH:** reports grant support from Mitsubishi Tanabe Pharma Corporation, EA Pharma Co. Ltd., AbbVie GK, JIMRO Co. Ltd., Zeria Pharmaceutical Co. Ltd., Kyorin Pharmaceutical Co. Ltd., Nippon Kayaku Co. Ltd., Takeda Pharmaceutical Co. Ltd., Pfizer Inc., Mochida Pharmaceutical Co. Ltd., Boston Scientific Corporation, and Kissei Pharmaceutical Co. Ltd.; consulting fees from Mitsubishi Tanabe Pharma Corporation, EA Pharma Co. Ltd., AbbVie GK, Janssen Pharmaceutical K.K., Pfizer Inc., Eli Lilly, Gilead Sciences, Bristol Myers Squibb; and lecture fees from Mitsubishi Tanabe Pharma Corporation, AbbVie GK, EA Pharma Co. Ltd., Kyorin Pharmaceutical Co. Ltd., JIMRO Co., Janssen Pharmaceutical K.K., Mochida Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co. Ltd., Pfizer Inc., and Kissei Pharmaceutical Co. Ltd. **AA:** reports consultancy fees from AbbVie, Allergan, Amgen, Arena, Biogen, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring, Galapagos, Gilead, Janssen , MSD, Mylan, Pfizer, Protagonist-Therapeutics, Roche, Samsung Bioepis, Sandoz, and Takeda; reports payment or honoraria for lecture, presentations, speakers bureaus, manuscript writing or education events from AbbVie, Amgen, Biogen, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring, Galapagos, Gilead, Janssen, MSD, Novartis, Pfizer, Roche, Samsung Bioepis, Sandoz, Takeda and Tigenix; research grants from Biogen, MSD, Pfizer and Takeda; and reports support for attending meetings and/or travel from AbbVie, Janssen, Pfizer, Takeda. **DW:** reports relationships with AbbVie, Bristol Myers Squibb, Janssen, Lilly, Pfizer, Takeda. **GD:** reports a financial relationship with Janssen. **RVR, MO, NAT, JY, HL,** and **MRB:** are employees of Johnson & Johnson and may own company stock/stock options. **GDH:** reports consultancy activities for AbbVie, Agomab, Alimentiv, AstraZeneca, AMT, Bristol Myers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly, Exelixm, Galapagos, GlaxoSmithKline, Gossamerbio, Immunic, Index, Johnson & Johnson, Kaleido, Origo, Pfizer, Polpharma, Procise Diagnostics, Prometheus Laboratories, Prometheus Biosciences, Progenity, and Protagonist Therapeutics Inc.; speaker's bureau for AbbVie, Bristol Myers Squibb, Galapagos, Pfizer, and Takeda; and data monitoring board activities for AbbVie, AstraZeneca, Galapagos, and Seres Health. **DTR:** reports potential conflicts of interest with AbbVie, Altrubio, Apex, Avalo Therapeutics, Bristol Myers Squibb, Buhlmann Diagnostics Corp, Celgene, Connect BioPharma, Intouch Group, Iterative Health, Janssen Pharmaceuticals, Lilly, Pfizer, Samsung Neurologica, and Takeda. **RP:** reports serving as a consultant for: Abbott, AbbVie, AbbiVax, Alimentiv (formerly Robarts), Amgen, AnaptysBio, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Elan, Eli Lilly, Ferring, Galapagos, Fresenius Kabi, Genentech, Gilead Sciences, GSK, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pendopharm, Pfizer, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Roche, Sandoz, Satisfai Health, Shire, Sublimity Therapeutics, Spyre Therapeutics, Takeda Pharmaceuticals, Theravance Biopharma, Trellus, Union Biopharma, Viatris, Ventyx, and UCB; a speaker for: AbbVie, Amgen, Arena Pharmaceuticals, Bristol Myers Squibb, Celgene, Eli Lilly, Ferring, Fresenius Kabi, Gilead Sciences, Janssen, Merck, Organon, Pfizer, Roche, Sandoz, Shire, and Takeda Pharmaceuticals; on advisory boards for: AbbVie, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Ferring, Fresenius Kabi, Genentech, Gilead Sciences, GSK, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pfizer, Progenity, Protagonist Therapeutics, Roche, Sandoz, Shire, Sublimity Therapeutics, Takeda Pharmaceuticals, and Ventyx.